SYNTHETIC APPROACHES TO CYCLOPENTA[a]PHENALENE

by
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B.S. Yale University (1991)

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Degree of
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Finally, I would like to thank my mom, dad, and sister for their love and support. I feel very fortunate to have such a great family. They seemed to ask me on an almost weekly basis how my research was going!
To Mom and Dad
SYNTHETIC APPROACHES TO CYCLOPENTA[a]PHENALENE

by
Katherine Lin Lee

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ABSTRACT

Studies directed toward the development of a total synthesis of
cyclopenta[a]phenalene, a new non-alternant aromatic hydrocarbon, are described. A
short route for the preparation of a fulvene precursor to the target molecule has been
developed, and attempts to effect cyclization of the fulvene compound are described.
Also, synthetic efforts towards the preparation of an 8-cyclopentadienyl-1-
naphthaldehyde substrate for the construction of cyclopenta[a]phenalene by
intramolecular fulvene preparation are detailed.

Assembly of the carbon framework of cyclopenta[a]phenalene using the
intramolecular Pauson-Khand reaction has been accomplished. Attempts to complete the
synthesis of the title compound by functional group manipulation of the products of the
intramolecular Pauson-Khand reaction of two different enyne substrates are described.

Thesis Supervisor: Rick L. Danheiser
Title: Professor of Chemistry
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Part I

Introduction and Background
CHAPTER 1
UNUSUAL AROMATIC COMPOUNDS

Intriguing Properties of Aromatic Compounds

From Kekulé's 1865 dream-vision of a snake biting its tail leading to his proposal for the cyclic structure of benzene,¹ to the assignment of the structure of naturally-occurring guaiazulene by Pfau and Plattner in 1936,² to the explosion in the 1990s of research relating to buckminsterfullerene (3), aromatic compounds have long enjoyed a colorful history in organic chemistry.³ The focus of the work described in this dissertation is the synthesis of a new non-alternant aromatic hydrocarbon, cyclopenta[a]phenalene (4). Although the structure of this molecule was first suggested by D. H. Reid in 1955,⁴ no syntheses of 4 have been reported to date.

3 For reviews on aromaticity, see:
Why are aromatic compounds important? The label "aromatic" was applied to this class of compounds long ago to acknowledge the propensity of many of these compounds to have fragrant odors. The odors of almonds and cinnamon are two of the many examples of well-known scents which arise from aromatic molecules. Another reason for the importance of aromatic compounds is their ubiquity in nature; from coal tar to salicylic acid to vanillin, benzene derivatives seemingly are everywhere one looks. The significant roles that aromatic molecules play in industry should not be overlooked. With beginnings in the synthetic dye industry, aromatic molecules are found in a myriad of industrial applications today. Aromatic hydrocarbons play an important role, for example, in the design of organic metals and superconductors. Some important applications which exploit the electronic properties of aromatic compounds include activation of developers in photography, rechargeable batteries, LCDs, and diode laser printers.

Certain special classes of aromatic compounds, such as the azulenes, are especially fascinating. One reason that appeals to many people is that aromatic compounds may be highly colored. Whereas many organic compounds are white or yellow, the azulenes can span the visible spectrum, from brilliant blues to intense greens.

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and bright reds, depending on their substitution pattern. In petroleum ether the color of azulene is perceptible in concentrations as low as one part in 10,000.  

![Images of molecules with captions: red, blue-green, violet.]

**What is Aromaticity?**

Although the concept of aromaticity is extremely important and versatile in explaining the structure, stability, and reactivity of molecules, the definition of aromaticity remains controversial. Should the definition be based on experimental fact or on theory? The controversy in part arises from the wide range of properties associated with aromaticity. Albert suggested that *a ring is aromatic if its carbon-carbon bond lengths are like those of benzene*, the archetypal aromatic compound. However, this subjective definition fails to include polycyclic molecules such as azulene and naphthalene, which are commonly believed to be aromatic. In addition, it is unclear how this definition would be applied to heteroaromatic systems. A classical definition based on thermodynamics is that *an aromatic molecule is more stable than would be expected if it were composed of simple two-electron chemical bonds*. What is lacking in this case, though, is a definition of "simple two-electron chemical bonds". A definition based on the Hückel rule is that *aromatic systems are monocarbocyclic, conjugated molecules containing (4n +2) out-of-plane π electrons*. This definition, although it is unambiguous,

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9 For monographs on color chemistry, see:
may be considered too narrow, as it fails to include many molecules that are generally considered to be aromatic, including pyridine and naphthalene. Older definitions of aromaticity stem from the reactivity of benzene, the prime example of an aromatic molecule. Unfortunately, these older definitions are based on the difference in free energy of the ground and transition states and fail to give a basis for comparing ground-state properties, as a molecule may have resonance stabilization yet be very reactive. Also, it is difficult to connect this definition with theoretical considerations. One definition proposed by Dewar states that aromatic molecules are cyclic systems having a large resonance energy in which all the atoms in the ring take part in a single conjugated system. This definition suffers because the idea of a large resonance energy is subjective. One definition of aromaticity based on the behavior of molecules in an external magnetic field is that a molecule is aromatic if it sustains the diamagnetic ring current induced by an external magnetic field, or in other words, if the molecule is diatropic. Garratt prefers a definition based on calculated resonance energy (RE): aromatic compounds are cyclic diatropic systems with a positive calculated Dewar RE in which all the ring atoms are involved in a single conjugated system. Clearly, the definition of aromaticity remains open to debate.

Previous Studies on Non-benzenoid Aromatic Compounds in the Danheiser Group

As discussed further below, our interest in the synthesis of cyclopenta[a]phenalene arose in part from the expectation that this non-benzenoid aromatic system might exhibit interesting "azulene-like" electronic and spectroscopic properties. The chemistry of azulenes has been a subject of interest in our laboratories over the past ten years, and, as summarized below, this research has led to the development of two general methods for the synthesis of substituted azulenes.
A. Azulene Synthesis via [3+2] Annulation with Tropylium Ions

Work in the Danheiser group focusing on azulenes was first reported in 1989 when Becker and Danheiser introduced a [3+2] annulation method employing the reaction of tropylium tetrafluoroborate (TpBF$_4$) with various allenylsilanes for the facile synthesis of substituted azulenes.$^{11}$ In this method (Scheme 1), a 1,3-dialkyl(t-butyldimethylsilyl)allene (9) reacts with TpBF$_4$ (8), generating the β-silicon stabilized carbocation 10. Following 1,2-silyl group migration and cyclization, proton elimination

affords the dihydroazulene 13. Dehydrogenation by abstraction of hydride from 14 by a second equivalent of TpBF$_4$ followed by deprotonation produces azulene 15. In this

method, poly(4-vinylpyridine) or methyltrimethoxysilane is employed as a non-
nucleophilic acid scavenger to prevent protodesilylation of the product and the
allenylsilane starting material.

B. Rhodium-Catalyzed Ring Expansion-Annulation

Recently, Kane and Danheiser developed a method which employs β-halo diazo
ketones in a ring expansion-annulation strategy for the synthesis of 1-hydroxyazulene
derivatives.\textsuperscript{12} In this method, reaction of the rhodium catalyst with the diazo ketone (16)
produces a rhodium carbenoid which undergoes a regioselective intramolecular
cyclopropanation to afford the norcaradienone intermediate 17. Six-π electrocyclic ring
opening, elimination of hydrogen bromide and tautomerization affords the
hydroxyazulene 20, which is isolated as the more stable acetoxy derivative 21 after
treatment in the same pot with acetic anhydride and base.

\textsuperscript{12} Kane, J. L. Ph. D. Thesis, Massachusetts Institute of Technology, May 1994.
Inspiration from Salvilenone

The cyclopenta[a]phenalene system incorporates in its structure the interesting tricyclic phenalenyl ring system. Our interest in phenalenyl systems began when Helgason and Danheiser exploited the photochemical aromatic annulation method developed in our laboratories in the synthesis of salvilenone (22), a phenalenone diterpene isolated from *Salvia miltorrhizia* Bunge. Phenalenones, the largest group of phenalene derivatives, are stable compounds which are accessed readily by oxidation of phenalenes. The naturally occurring phenalenones are polyhydroxylated plant or fungal pigments. Alternative, earlier names for phenalenone (23) include perinaphthenone, "pyrene ketone", phenalone-9, perinaphthindone, 1,8-naphthidenone, and 9-

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ketoperinaphthindene. Phenalene (24) has earlier been named perinaphthene, perinaphthindene and benzonaphthene.

Phenalenyl systems have extremely interesting electronic properties.\textsuperscript{14} Phenalene (24) is an odd-alternant hydrocarbon whose behavior is similar to that of the allyl (25), benzyl (26), and trityl (27) systems. Remarkably, the cation, radical and anion all display unusual thermodynamic stability. All three species have three-fold rotational symmetry with respect to the axis which passes through the central carbon orthogonal to the plane of the molecule and three identical two-fold axes which lie in the molecular plane. In 1950, Boekelheide and Larrabee\textsuperscript{15} proposed that resonance stabilization of the phenalenyl radical, cation, and anion may result from this high degree of symmetry. A decade later, Hückel molecular orbital calculations predicted that the three phenalenyl species should

\textsuperscript{14}For reviews of the chemistry of the phenalenes, see:
\textsuperscript{15}Boekelheide, V.; Larrabee, C. E. \textit{J. Am. Chem. Soc.} 1950, 72, 1245.
possess the same \( \pi \)-delocalization energy of \( 5.83\beta \).\textsuperscript{16} The phenalenyl system has six bonding molecular orbitals and one nonbonding orbital which has zero energy relative to that of a \( p_z \) orbital on an isolated \( sp^2 \) hybridized carbon atom. In the phenalenium cation, twelve \( \pi \)-electrons fill the bonding molecular orbitals. Each additional electron of the radical and anion occupy the nonbonding orbital.

\[
\begin{array}{cccc}
24 & 25 & 26 & 27 \\
\end{array}
\]

The Hückel Molecular Orbitals of the Phenalenyl System

The electron densities of the phenalenyl species reflect the symmetry of the phenalene system. In the cation, the electron density distribution is +0.167 at positions 1, 3, 4, 6, 7, and 9, and zero at the remaining positions. Analogously, the charge densities for the anion are the same except the sign is negative. Because the nonbonding molecular orbital coefficient at the central atom is zero, the central atom bears no charge, despite the fact that the central carbon atom is starred in the assignment of the phenalene nucleus as an alternant hydrocarbon. Thus, the phenalenyl system is best represented as a "symmetrical peripheral species" (28). Support for this model lies in self-consistent field (modified neglect of diatomic overlap) (SCF [MNDO]) calculations which confirm, based on the findings that the three species have equal bond lengths and bond orders, that

a truly non-bonding orbital does in fact exist.\textsuperscript{17} As a result, the Hückel $4n + 2$ rule does not apply to the phenalenyl system. Based on studies of phenalenyl cations and anions by\textsuperscript{1H, 7Li and 13C NMR, Edlund and coworkers proposed a model of the solution structure in which the counterion lies symmetrically above the central carbon atom.}\textsuperscript{18}

![Diagram](image)

Proposal: A New [3+2] Annulation Route to Substituted Cyclopenta[a]phenalenens

Considering our earlier work in synthesizing substituted azulenes by [3+2] annulations, and sparked by an interest in the phenalenens from our more recent synthesis of the phenalenone salvilenone, we envisioned a new [3+2] annulation (eq 1) in which

![Chemical Structure](image)

phenalenium cation would react with allenylsilanes to produce substituted cyclopenta[a]phenalenens. The next chapter of this dissertation surveys previous theoretical and synthetic work on cyclopenta[a]phenalenens. Chapter Three then describes our preliminary work on the [3+2] annulation method for the preparation of substituted cyclopenta[a]phenalenens.


cyclopenta[a]phenalenes. The remainder of this dissertation describes our efforts to synthesize the parent compound, cyclopenta[a]phenalene (4).
CHAPTER 2
CYCLOPENTA[a]PHENALENE: BACKGROUND

Predictions by D. H. Reid: Beyond Azulene

In 1955, the Scottish chemist D. H. Reid, using azulene as a model, predicted that several new condensed and fully conjugated hydrocarbons, including cyclopenta[a]phenalene (4) and cyclohepta[a]phenalene (30), might exhibit aromatic character.\textsuperscript{19,20} Azulene, a nonbenzenoid hydrocarbon with pronounced aromatic behavior, may be depicted as a hybrid of two equivalent neutral forms 31 and 32. Dipolar structures such as 33 are thought to contribute to the aromatic character of azulene.\textsuperscript{21,22} Similar dipolar structures for the new hydrocarbons 4 and 30 led Reid to theorize that these compounds might exhibit aromatic character and properties much like those of azulene.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{azulene_structures}
\caption{Structures of azulene (4) and cyclohepta[a]phenalene (30).}
\end{figure}

\textsuperscript{19}For a preliminary report, see ref. 4.
Reid states there is a dichotomy about the "implied polarization" of azulene and related compounds. On one hand, the dipole representations such as 33 should have added stability because the π-electrons of the azulenyl system may arrange into one of two stable sextets which obey the Hückel 4n+2 rule. Specifically, the seven-membered ring may exist as a tropylium cation or the five-membered ring may form a cyclopentadienyl anion. On the other hand, polarization is disfavored by electrostatic forces that seek to neutralize opposing charges. Azulene has a relatively low dipole moment of 1.08 D; this implies that dipolar resonance structures such as 33 do contribute, albeit minimally, to the ground state structure of azulene. Azulene's reactivity in electrophilic substitution is associated with the formation of an intermediate (34) which contains a tropylium cation, a stable 6-π electron system (eq 2) upon reaction at C-1 of 32. This tropylium cation intermediate also explains azulene's strong basicity: when R+ is a proton, a stable azulenium cation is obtained.

Reid theorized that new aromatic hydrocarbons containing substructures beyond simple five-, six-, and seven-membered rings might exist and be accessible by chemical synthesis. What carbon structures are capable in their charged states of delocalization to form stable π-electron systems? At this point, the phenalene system returns to the stage.
As discussed in the previous chapter, the phenalenyl cation (28a), radical (28b), and anion (28c) all are stable species, bearing twelve, thirteen and fourteen π-electrons, respectively. Reid used the phenalene nucleus in formulating several new types of polycyclic hydrocarbons which would be potentially aromatic.

Cyclopenta[a]phenalene (4), the focus of our work, results from fusion of a five-membered ring to phenalene. In the completely polarized form 36, the five-membered ring of 4 forms a 6-π electron cyclopentadienyl anion and the phenalene system becomes a stable phenalenium cation. Reid states also that electrophilic attack of 4 would be expected to occur at C-1 or C-10 or both. In a similar fashion, fusion of a seven-membered ring to phenalene produces cyclohepta[a]phenalene (30). Reflecting the sense of the expected polarization, the completely polarized structure 37 features a 6-π
electron system associated with the seven-membered ring as a tropylium cation, and fourteen \( \pi \)-electrons delocalized over the phenalene nucleus as a phenalenyl anion. Reid predicted that electrophilic attack would readily occur on the periphery of the phenalene nucleus at C-1, C-3, C-4, C-6, or C-7.

In addition to compounds 4 and 30, which are commonly called Reid's hydrocarbons, Reid further predicted two new classes of potentially dipolar aromatic hydrocarbons which result from peri fusion of a five- and seven-membered ring to the phenalene nucleus. They are cyclopenta[cd]phenalene (38) and cyclohepta[cd]phenalene (40), respectively. In contrast to the dipole forms (e.g. 33) of azulene, in which a pair of \( \pi \)-electrons is shared by both stable \( \pi \)-electron systems, the polarized forms (39 and 41) of these peri-fused hydrocarbons contain separate, stabilized \( \pi \)-electron systems.

**Theoretical Work: Quantifying Aromaticity**

Many theoretical studies of the electronic structure of non-alternant hydrocarbons have been performed, and according to several of these investigations, cyclopenta[\( \alpha \)]phenalene (4) is predicted to have aromatic stability.\(^2\) Two general

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methods for computing energies of molecules have been used for non-alternant hydrocarbons: the first is the simple Hückel molecular orbital (HMO) technique, and the second is the more elaborate Pariser-Parr-Pople (PPP) method. In addition to providing information about the energy of a given system, certain methods may be used to investigate spectral properties and to predict the reactivity of a system.

A. Zahradník, Michl, and Koutecky

The Czech chemists Zahradník, Michl, and Koutecky used HMO theory to tabulate energy characteristics for models of over one hundred fully conjugated non-alternant hydrocarbons including azulene (31), cyclopenta[a]phenalene (4), indeno[2,1-a]phenalene (42), and cyclohepta[a]phenalene (30). In a second publication, Zahradník and Michl revealed the results of a theoretical study focusing on Reid's hydrocarbons. Some pertinent data, including the total π-electronic energy (W) and the specific delocalization energy ($DE_{sp} = DE/m$, where DE is the delocalization energy and m is the number of C-C σ-bonds in the system) for hydrocarbons 31, 4, 42, and 30 are shown in Table 1. Also cited are $k_1$ and $k_{-1}$, the energies of the highest occupied and lowest unoccupied molecular orbitals, respectively.
Table 1. Energy Characteristics and Reactivity Indices in \( \beta \) Units

<table>
<thead>
<tr>
<th>Compound</th>
<th>( W )</th>
<th>DE/m</th>
<th>( k_1 )</th>
<th>( k_-1 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azulene (31)</td>
<td>13.364</td>
<td>0.306</td>
<td>0.477</td>
<td>-0.400</td>
</tr>
<tr>
<td>Cyclopenta[a]phenalene (4)</td>
<td>22.210</td>
<td>0.327</td>
<td>0.433</td>
<td>-0.115</td>
</tr>
<tr>
<td>Indeno[2,1-a]phenalene (42)</td>
<td>28.035</td>
<td>0.335</td>
<td>0.374</td>
<td>-0.169</td>
</tr>
<tr>
<td>Cyclohepta[a]phenalene (30)</td>
<td>24.745</td>
<td>0.321</td>
<td>0.106</td>
<td>-0.339</td>
</tr>
</tbody>
</table>

Zahradňík and coworkers suggest that an aromatic system should have the following requirements: a high value for specific delocalization energy (DE\(_{sp}\)), and also, favorable values of frontier orbital energies and extreme values of chemical reactivity indices. A high value of DE\(_{sp}\) correlates to increased aromatic character because DE\(_{sp}\) is a measure of the tendency of a system to form a conjugated system from less conjugated precursors, as in dehydrogenation. Compounds 4, 30, and 42 have high DE\(_{sp}\) values, comparing favorably to the DE\(_{sp}\) value of azulene. Indeno[2,1-a]phenalene (42), which was synthesized by Reid,\(^4\)\(^2\)\(^1\),\(^2\)\(^8\) is indeed quite stable. Cyclohepta[a]phenalene (30) was synthesized by Murata and coworkers in 1987, and although 30 is reported to be fairly labile, it can be stored in the refrigerator under an inert atmosphere.\(^2\)\(^9\)

B. Andes Hess and Schaad

In 1971, Andes Hess and Schaad applied HMO theory to perform calculations of empirical \( \pi \)-bond energies and determine the resonance energy per \( \pi \) electron (REPE) for nearly 100 nonalternant hydrocarbons.\(^3\)\(^0\) The REPE was determined as follows: using empirical \( \pi \)-bond energies which had been obtained from a series of acyclic polyolefins,

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these energies were summed to obtain the $\pi$ energy of the hypothetical localized structure of each cyclic polyolefin. The resonance energy (RE) was defined as the difference between the HMO $\pi$ energy and the additive localized energy. The RE, divided by the number of $\pi$ electrons, yielded the resonance energy per $\pi$ electron (REPE) in $\beta$ units. Table 2 shows the data for azulene (31), cyclopenta[a]phenalene (4), and cyclohepta[a]phenalene (30).

Table 2. Hückel $\pi$ Energies and Resonance Energies in $\beta$ Units

<table>
<thead>
<tr>
<th>Compound</th>
<th>Huckel</th>
<th>Additive</th>
<th>RE</th>
<th>REPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azulene (31)</td>
<td>13.364</td>
<td>13.132</td>
<td>0.231</td>
<td>0.023</td>
</tr>
<tr>
<td>Cyclopenta[a]phenalene (4)</td>
<td>22.210</td>
<td>21.700</td>
<td>0.510</td>
<td>0.032</td>
</tr>
<tr>
<td>Cyclohepta[a]phenalene (30)</td>
<td>24.745</td>
<td>24.236</td>
<td>0.509</td>
<td>0.028</td>
</tr>
</tbody>
</table>

Interpreting the resonance energy per $\pi$ electron (REPE) value is straightforward: molecules with a positive REPE value are aromatic, those with REPE of zero are nonaromatic (molecules in this category behave like polyolefins), and molecules bearing a negative REPE are antiaromatic. As shown in Table 2, both cyclopenta[a]phenalene (4) and cyclohepta[a]phenalene (30) were predicted to be aromatic. Hess and Schaad observed a good correlation between REPE and "experimental aromaticity", which was defined as unusual qualitative stability and a tendency to undergo substitution rather than addition reactions.

C. Aihara

The Japanese chemist Aihara, in an effort to improve calculations of the resonance energies of nonalternant hydrocarbons, introduced a new measure of aromatic
stabilization called the percent resonance energy (%RE) in 1980. In this work, %RE was determined for forty nonbenzenoid hydrocarbons by using both the simplest HMO model and the Wheland and Mann \(\omega\)-technique. In the HMO model, it is assumed that the Coulomb integral \(\alpha\) is a constant characteristic of a particular atom, and is independent of the conjugated system in which the atom appears. Aihara argues that this assumption is acceptable for alternant hydrocarbons in which each atom bears uniform charge, but he embraces Wheland and Mann's \(\omega\)-technique for theoretical studies of nonalternant systems. In the \(\omega\)-technique, the value of \(\alpha\) is linearly related to the charge on the atom, and \(\omega\) is a dimensionless parameter which is chosen to give the best agreement with experiment. As shown in Equation 3, \(\alpha_s\) is the Coulomb integral for atom \(s\), \(\alpha_0\) is the

\[
\alpha_s = \alpha_0 + (1 - q_s)\omega\beta_0 \quad (3)
\]

standard value of \(\alpha\) for \(sp^2\) carbon atoms, \(q_s\) is the charge on atom \(s\), and \(\beta_0\) is a standard value of the resonance integral between two bonded \(sp^2\) carbons. Resonance energies for azulene (32), cyclopenta[a]phenalene (4), and cyclohepta[a]phenalene (31) calculated using the HMO method and the \(\omega\)-technique are shown in Table 3. The resonance energy (RE) is given in \(\beta\) units. Reference energy, a concept introduced by Aihara, is an energy term which is not dependent on the \(\omega\) parameter and is calculated graph-theoretically assuming equal charge distribution on each atom. The \(\omega\)-technique resonance energy can be calculated relative to the reference energy based on the simplest HMO model. Aihara's new measure of aromatic stabilization, the percent resonance energy (%RE), is defined as 100 times the resonance energy divided by the reference energy.

Table 3. Resonance Energies

<table>
<thead>
<tr>
<th>Compound</th>
<th>Simplest HMO</th>
<th>ω-technique</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RE</td>
<td>%RE</td>
</tr>
<tr>
<td>Azulene (32)</td>
<td>0.151</td>
<td>1.14</td>
</tr>
<tr>
<td>Cyclopenta[a]phenalene (4)</td>
<td>0.418</td>
<td>1.92</td>
</tr>
<tr>
<td>Cyclohepta[a]phenalene (31)</td>
<td>0.400</td>
<td>1.64</td>
</tr>
</tbody>
</table>

The %RE value is reported to quantify the degree of stabilization with which a given conjugated system behaves aromatically. Unlike the methods cited previously, Aihara's theoretical measure of aromaticity is neither dependent on the number of π electrons nor the number of π bonds in a system. Aihara states that compounds with %RE of less than 0.50 might be regarded as olefinic, rather than aromatic species. According to this standard, cyclopenta[a]phenalene and cyclohepta[a]phenalene both lie well within the boundary of aromaticity. On the other hand, azulene suffers a large decrease in resonance energy as calculated by the ω-technique, and is predicted to be substantially nonaromatic. Aihara challenges the use of electrophilic substitution as a criterion of aromaticity, citing the tendency of many olefinic compounds to undergo electrophilic substitution reactions, and concludes that the ω-technique resonance energies agree much better with experiment than values derived from the simplest HMO model.

D. Das Gupta and coworkers

In 1991, Das Gupta and coworkers used the Dewar-modified Pariser-Parr-Pople method to perform a theoretical study on phenalenium systems. In this study, the zero-differential overlap approximation was employed, and four values for the resonance

---

integral $\beta$ were used in the calculations in the self-consistent field (SCF) methods SCF(a), SCF(b), SCF(c) and SCF(d). In addition to presenting data on $\pi \rightarrow \pi^*$ spectra, ionization potential, electron affinity, half-wave reduction potential and $\pi$-dipole moment, Das Gupta, Das Gupta and coworkers discussed stability and resonance energy. Table 4 presents some results pertaining to aromaticity from three methods, and Table 5 shows the criteria of aromaticity or stability for each method.

Table 4. Resonance Energies

<table>
<thead>
<tr>
<th>Compound</th>
<th>Method</th>
<th>RE</th>
<th>RE/m</th>
<th>REPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclopenta[a]phenalene (4)</td>
<td>SCF(a)</td>
<td>5.244</td>
<td>0.276</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SCF(b)</td>
<td>5.466</td>
<td>0.276</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SCF(c)</td>
<td>1.574</td>
<td>0.083</td>
<td></td>
</tr>
<tr>
<td>Indeno[2,1-a]phenalene (42)</td>
<td>SCF(a)</td>
<td>7.202</td>
<td>0.300</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SCF(b)</td>
<td>7.208</td>
<td>0.300</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SCF(c)</td>
<td>2.406</td>
<td>0.100</td>
<td></td>
</tr>
<tr>
<td>Cyclohepta[a]phenalene (30)</td>
<td>SCF(a)</td>
<td>5.502</td>
<td>0.262</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SCF(b)</td>
<td>5.466</td>
<td>0.260</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SCF(c)</td>
<td>1.534</td>
<td>0.073</td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Range of RE/m or REPE for Aromaticity

<table>
<thead>
<tr>
<th>Method</th>
<th>range of RE/m</th>
<th>range of REPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCF(a)</td>
<td>0.26-0.31</td>
<td></td>
</tr>
<tr>
<td>SCF(b)</td>
<td>0.25-0.30</td>
<td></td>
</tr>
<tr>
<td>SCF(c)</td>
<td></td>
<td>0.075-0.112</td>
</tr>
</tbody>
</table>

In this investigation the resonance energy (RE) and resonance energy per carbon-carbon bond (RE/m) again suggest that 4 should be a stable aromatic compound. Similar results were obtained for indeno[2,1-a]phenalene (42). The data for cyclohepta[a]phenalene
(30), however, fall on the lower side of the range of aromaticity and stability and suggest that 31 might not be aromatic.

Syntheses of Fused Cyclopenta[a]phenalene Derivatives


Soon after Reid proposed the possibility that cyclopenta[a]phenalene structure 4 would have aromatic character, Aitken and Reid synthesized a benzo-fused homolog, indeno[2,1-a]phenalene (42), and confirmed that it possessed azulene-like reactivity. In this short but very low-yield synthesis, reaction of 1-naphthylmagnesium bromide with

\[ \begin{align*}
43 & \rightarrow \text{MgBr} \\
& \text{Et}_2\text{O, } \Delta \text{, 1 h} \\
& \text{CH}_2\text{CO}_2\text{H-HCO}_2\text{H} \\
& \Delta, 2 \text{ h} \\
& \text{KOMe, HCO}_2\text{Et} \\
& \text{Et}_2\text{O, } \Delta, 4 \text{ h} \\
& \text{93% H}_2\text{SO}_4 \\
& \text{H}_2\text{O-PhH} \\
\end{align*} \]

42 (7% from 44)

46 (1% from 44)

\[ \]

indan-2-one (43) followed by dehydration of the resulting tertiary alcohol produced naphthalene 44. Treatment of 44 with ethyl formate and potassium methoxide yielded the unstable hydroxymethylene compound 45, which was immediately cyclized under acidic conditions to give indeno[2,1-a]phenalene (42) in ca. 7% yield from 44 accompanied by the dimer 46 in ca. 1% yield.

Aitken and Reid found that the reactivity of indeno[2,1-a]phenalene (42) was remarkably similar to that of the azulenes. Hydrocarbon 42, a reddish-brown solid (mp 210-211 °C), was found to dissolve in strong aqueous sulfuric acid or anhydrous hydrogen fluoride, forming a green cation. Quantification of the base strength of 42 by partitioning it in cyclohexane and sulfuric acid revealed that 42 has a Hammett acidity function (H0) of -4.80, on par with azulene in basicity. Electrophilic substitution of 42 using tetranitromethane in a mixture of pyridine and ethanol produced a mono-nitro derivative, presumably substituted at C-12, which was predicted to be the most activated position. In addition, 42 was found to act as a diene in a Diels-Alder cycloaddition with maleic anhydride (eq 4). The reaction conditions, stereochemistry, and yield were not reported for this reaction.

Two years later, Mitchell and Sondheimer reported a second low-yield synthesis of 42 involving a novel spontaneous transannular condensation. Treatment of the bis-ylid derived from phosphonium salt 48 with o-phthalaldehyde produced 42 as dark red

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crystals (mp 213-214 °C) in 16% yield and dihydrobenzo[k]fluoranthene (50) in 15% yield. These products result from transannular reactions of the tetracyclic intermediate 49. Phenalene 42 arises from C1-C3 bond formation, hydrogen shift, and dehydrogenation. Bond formation between C1-C4 and hydrogen shift produces 50. This work was confirmed by Houlton and Kemp, who obtained 42 in 25% yield and 50 in 10% yield.37

B. 12-Phenylindeno[2,1-α]phenalene

In a study of 1,8-dialkynylnaphthalenes, Ipaktschi and Staab synthesized 12-phenylindeno[2,1-α]phenalene (54) in 1987.38 As depicted below, reaction of 1,8-diodonaphthalene (51) with copper phenylacetylide in pyridine produced the peri-substituted naphthalene 52 in 62% yield and the fused tetracyclic system 53 in 20% yield.37 38

12-Phenylindeno[2,1-α]phenalene (54), a red crystalline solid (mp 173-174 °C), was obtained in nearly quantitative yield upon treatment of dialkynylnaphthalene 52 with mercuric acetate. Muller and coworkers later effected the transformation of 52 to 54 using platinum (IV) chloride.\textsuperscript{39}

\begin{center}
\includegraphics[width=0.8\textwidth]{image}
\end{center}


In 1980, Kemp, Storie, and Tulloch reported the synthesis of a naphtho-fused derivative of 4, benz[5,6]indeno[2,1-α]phenalene (56), by two routes.\textsuperscript{40} One route applied the method used by Mitchell and Sondheimer: intramolecular Wittig reaction of a bis-ylid with naphthalene-2,3-dicarboxaldehyde, followed by spontaneous transannular condensation to produce phenalene 56. No yield was reported for this reaction.


In a second route to 56, Kemp and coworkers used sulfur extrusion chemistry which had been applied by Mitchell and Boekelheide for the synthesis of similar fused polycyclic systems.\textsuperscript{41} Methylation of bisulfide 57, which was prepared in several steps from 1,8-naphthalic anhydride, followed by Stevens rearrangement, yielded a mixture of sulfides 58 and 59. Methylation of the mixture of bisulfides followed by elimination produced 56 via the same olefinic intermediate (55) as in the Wittig route. This route suffered from an abysmal yield in the key sulfur extrusion step.

\textsuperscript{41}Mitchell, R. H.; Boekelheide, V. \textit{J. Am. Chem. Soc.} 1974, 96, 1574.
Synthesis of 7-Methoxycyclopenta[a]phenalene

Sugihara, Fujita, and Murata devised the only known synthesis to date of a simple cyclopenta[a]phenalene derivative, 7-methoxycyclopenta[a]phenalene (60), and found that in its ground state 60 has interesting dipolar character similar to that of azulene. In this synthesis, Murata employed an annulation-ring expansion sequence developed by Greene to construct the five-membered ring. The carbon skeleton of 60 was obtained in two steps from phenalene, and seven more steps were required to produce 60.

As depicted below, cycloaddition of phenalene (24) with dichloroketene produced cyclobutanone 61, which upon reaction with diazomethane underwent regioselective ring expansion, delivering cyclopentanone 62 in good yield. With the carbon skeleton in hand, elaboration to produce 7-methoxycyclopenta[a]phenalene began with dechlorination of 62 to produce cyclopentanone 63. Reduction of the carbonyl group using sodium borohydride and conversion of the resultant alcohol to the chloride produced compound 65, the stereochemistry of which was not determined. Upon benzylic oxidation of 65 and dehydrogenation of 66 using selenium dioxide, phenalenone 67 was obtained.
In the final step of the synthesis, treatment of phenalenone 67 with potassium tert-butoxide in hexamethylphosphoramide followed by addition of methylsulfonyl fluoride produced 7-methoxycyclopenta[a]phenalene (60). In this one-pot reaction, dehydrochlorination to produce the dienone intermediate 68 is followed by O-methylation of enolate 69. 7-Methoxycyclopenta[a]phenalene (60) was isolated as dark brown needles with mp 140-141 °C.
Analysis of the dipole moment and redox potential of 60 indicates that this alkoxy cyclopenta[a]phenalene derivative has azulene-like characteristics. Murata and coworkers made a number of direct comparisons of the properties of 7-methoxycyclopenta[a]phenalene (60) to those of azulene. We question the validity of comparing the properties of the alkoxy derivative with those of the parent azulene because we feel that the contribution of the methoxy group cannot be ignored! The value of a synthesis of the parent cyclopenta[a]phenalene 4 is unquestionably great.

The aromatic character of 60 is evidenced in its behavior in NMR. The C-8, C-9, and C-10 protons of 60 are approximately 0.5 to 1.0 ppm downfield relative to the chemical shifts of analogous protons of fulvenes, indicating that 60 is a semibenzenoid compound whereas fulvenes are olefinic in character. These observations are in agreement with Aihara’s predictions using the α-technique.32

7-Methoxycyclopenta[a]phenalene (60) was reversibly protonated using deuterated trifluoroacetic acid (eq 5). Murata and coworkers observed by $^1$H NMR that only one cationic species was obtained and tentatively assigned the structure 70 resulting from protonation at C-8. HMO calculations predict that C-8 has a higher charge density ($q_\pi = 1.135$) than C-10 ($q_\pi = 1.123$).
Early Synthetic Efforts towards Cyclopenta[a]phenalene

Reid reported the results of some preliminary studies on the synthesis of the parent cyclopenta[a]phenalene in 1958. In this work, Reid used an approach similar to that employed in his earlier preparation of indeno[2,1-a]phenalene (42). Friedel-Crafts acylation of the known 2,3-cyclopentenonaphthalene (71) with acetyl chloride and aluminum chloride gave a mixture of two monoacetylnaphthalenes. The major product (for which no yield was reported) was thought to be either 4-acetyl-2,3-cyclopentenonaphthalene (72) or the 5-acetyl derivative (73), and the minor product was the 6-acetyl isomer (74). Condensation of the major product (72 or 73) with ethyl...
formate produced the hydroxymethylene adduct (75 or 76), which was cyclized using 87% sulfuric acid to produce either 8,9-cyclopentenophenalenone (77) or 4,5-cyclopentenophenalenone (78).

Next, reduction of the phenalenone (77 or 78) with lithium aluminum hydride proceeded in high yield to produce a cyclopentenophenalene, to which structure 79 was assigned arbitrarily. Reid was unable to dehydrogenate 79 using either catalytic or stoichiometric methods. In an attempt to generate 4 via a bromination-dehydrobromination strategy, Reid observed that reaction of 79 with N-bromosuccinimide produced a transient radical species which then formed a high-melting solid, ostensibly the dimer of 79.

\[
\begin{align*}
\text{LIAlH}_4 & \rightarrow \\
77 \quad 78 & \rightarrow \\
79 & \\
\downarrow & \\
4 & \\
\end{align*}
\]

Reid also noted that reaction of naphthalene with cyclopentene-2-carboxylic acid chloride (81) under Friedel-Crafts conditions produced 2,3-cyclopentenophenalenone (82) in "substantial yield" (eq 6), and that 82 might be transformed into 4 by simple functional group manipulation. However, no further elaboration of 82 was reported.
\[
\text{80} + \text{81} \xrightarrow{3 \text{ equiv } \text{AlCl}_3} \text{82}
\]
CHAPTER 3
PRELIMINARY STUDIES ON A [3+2] ANNULATION APPROACH TOWARDS
SUBSTITUTED CYCLOPENTA[a]PHENALENES

[3+2] Annulations in the Danheiser Group

Danheiser and coworkers have developed a [3+2] annulation method\(^{45}\) using
allenylsilanes as three-carbon synthons for the synthesis of carbocycles and heterocycles.
As illustrated in the following scheme, reaction of allenylsilanes with various electron-
deficient species produce a myriad of five-membered annulation products, including
cyclopentenes (83),\(^{46}\) azulenes (15),\(^{11}\) pyrrolines (85),\(^{48}\) dihydrofurans (84),\(^{47}\)
isoazoles (86)\(^{48}\) and furans (87).\(^{49}\) Allylsilanes have also been found to function as three-carbon
synthons in the Danheiser [3+2] annulation.\(^{50}\)

\(^{45}\) For reviews, see:

\(^{46}\) (a) Danheiser, R. L.; Carini, D. J.; Basak, A. J. Am. Chem. Soc. 1981, 103, 1604. (b) Danheiser, R. L.; Carini, D.


Our strategy for the synthesis of substituted cyclopenta[a]phenalenes utilizes phenalenium cation as the allenophile (eq 7). We envisioned the reaction would proceed by a pathway similar to that described in Chapter One for Becker and Danheiser's synthesis of substituted azulenes. As depicted below, reaction between the terminal carbon of the allenylsilane 9 and C-1 of the phenalenium cation (28a) should produce a
β-silicon stabilized vinyl cation (88). 1,2-Silicon group migration, followed by cyclization of 89 and proton elimination should yield the dihydro adduct 91. Finally, exposure to a second equivalent of phenalenium cation (or other oxidizing agent) should induce hydride abstraction from 91, which after deprotonation should produce the substituted cyclopenta[α]phenalene 29.

\[ \text{Preparation of Phenalene} \]

For our proposed new [3+2] annulation, we planned to generate phenalenium cations from phenalene. Phenalene (24) is a relatively unstable hydrocarbon which readily undergoes air oxidation to phenalenone (23).\(^{51}\) Using reductive protocols,

\(^{51}\text{Lock, G.; Gergely, G. Chem. Ber. 1944, 77B, 461.}\)
phenalene (24) has traditionally been prepared from phenalanone (92), and more recently, has been prepared from commercially available phenalenone (23).

Phenalanone (92) has been prepared as shown in the scheme below. α-Chloromethylnaphthalene (93), which may be prepared either directly by chloromethylation$^{52}$ of naphthalene, or indirectly via Vilsmeier reaction,$^{53}$ was subjected by Fieser and Gates to the malonic ester synthesis to produce β-1-naphthylpropionic acid 95 in good overall yield.$^{51a}$ Fieser and Gates effected cyclization of 95 using anhydrous hydrogen fluoride and obtained phenalanone (92) in 81% yield.$^{51a}$ Hempenius and coworkers recently

\footnotesize{$^{52}$a Fieser, L. F.; Gates, M. D., Jr. J. Am. Chem. Soc. 1940, 62, 2335. (b) Darzens, G.; Levy, A. Compt. Rend. 1935, 201, 902.}
\footnotesize{$^{53}$Boekelheide, V.; Larrabee, C. E. J. Am. Chem. Soc. 1950, 72, 1240.}
reported the transformation of 95 to 92 by cyclization of the acid chloride under Friedel-Crafts conditions. 54

As shown in the following scheme, the conversion of phenalanone (92) to phenalene (24) is straightforward. Reduction of the ketone with lithium aluminum hydride produced the alcohol in excellent yield. 55 This alcohol was reported to be stable and storable for months with refrigeration. Acid-catalyzed dehydration of 7-hydroxyphenalene (96) produces phenalene (24) in nearly quantitative yield. 53 Hempenius and coworkers reported that 24 was obtained as lemon-yellow crystals which can be stored for at most for a few hours, so that 24 is best stored under reduced pressure with protection from light.

A more rapid route to phenalene is by the reduction of phenalenone (23). Phenalenone (23) is commercially available but rather expensive (ca. $15/g) and can be prepared in one step from inexpensive starting materials. Fieser and Hershberg reported the reaction of 2-naphthol with glycerol in the presence of sulfuric acid and sodium nitrobenzene sulfonate to produce phenalenone (23) in 28% yield (eq 8). 56, 57

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Sulfuric acid acts as a dehydrating and condensing agent, and the sodium nitrobenzene sulfonate acts as an oxidizing agent in this transformation. Many reagents, including lithium aluminum hydride,\(^{55}\) a mixture of lithium aluminum hydride and aluminum trichloride,\(^{58}\) and 9-borabicyclononane,\(^{59}\) have been reported to effect the reduction of 23 to 24 with limited success. Reduction of phenalenone (23) with diisobutylaluminum hydride in refluxing benzene was reported by Boudjouk and Johnson to produce phenalene (24) in 44\% yield (eq 9).\(^{59a}\) In this reaction, phenalenone was recovered in 52\% yield. Boudjouk and Johnson postulated that the reaction proceeds via 1,2-addition of the metal hydride across the carbonyl group, and that upon hydrolysis, phenalenol undergoes a facile, irreversible disproportionation\(^{60}\) to produce 24 and 23.

![Chemical reaction diagram](image)

Preparation of Phenalenium Cations

The phenalenium cation (with a perchlorate counterion) was first reported by Pettit.\(^{61,62}\) In Pettit's work, phenalenium perchlorate (100) was obtained in several steps from acenaphthylene (97), as shown in the following scheme. A more general approach

\(^{60}\) Pettit, R. *Chem. Ind. (London)* 1956, 1306.
\(^{61}\) For a review of phenalene chemistry, see ref. 14a. For spectral data of phenalenium cations, see refs. 57 and 18.
to phenalenium cations involves hydride abstraction from phenalene by triphenylmethyl perchlorate\textsuperscript{63} (eq 10) or by reaction with a high potential quinone in the presence of perchloric acid\textsuperscript{64} (eq 11). Phenalenium perchlorate (100) was reported by Reid and coworkers to be extremely sensitive to moisture, blackening rapidly in moist air. Irreversible hydrolysis leads to equimolar mixtures of phenalene and phenalenone via disproportionation of phenalenol or diphenalenyl ether.

Results and Discussion

We opted to prepare phenalenium tetrafluoroborate rather than the perchlorate salt because perchlorate salts have the potential to be explosive. First, phenalenone was prepared according the method of Fieser and Hershberg which is reported to provide 23 in 28% yield. In our hands, a modest 8% yield was obtained. Reduction of 23 with DIBAL following the procedure of Boudjouk and Johnson produced phenalene (24) in 63-70% yield, unexpectedly high compared to the 44% yield reported in the literature. According to Boudjouk’s proposed mechanistic pathway, which involves 1,2-reduction of 23 to the alcohol and disproportionation, phenalene (24) should not be obtained in >50% yield. It is unclear how we were able to produce phenalene in 63-70% yield when Boudjouk and Johnson could not. Perhaps the phenalenol intermediate underwent further reduction to phenalene under the reaction conditions. Hydrogenolysis of benzylic alcohols to alkanes is a facile process.\textsuperscript{59b}

\[
\begin{align*}
\text{Ph} & \quad \text{OH} \quad \text{OH} \\
& \quad 3.9 \text{ equiv} \quad \text{HO} \quad \text{OH} \\
& \quad 0.8 \text{ equiv} \quad \text{H} \text{NO}_2 \text{C}_6\text{H}_4\text{SO}_3\text{Na} \\
& \quad \text{H}_2\text{O} \quad \text{H}_2\text{SO}_4, \Delta, 1 \text{ h} \\
& \quad 8\% \\
\end{align*}
\]

Phenalene was then reacted with commercially available triphenylmethyl tetrafluoroborate in deuterated acetonitrile, and by \textsuperscript{1}H NMR analysis, the formation of phenalenium tetrafluoroborate was observed! In this experiment, a solution of phenalene in CD\textsubscript{3}CN was added via cannula to a CD\textsubscript{3}CN solution of triphenylmethyl tetrafluoroborate in an NMR tube. An immediate color change from yellow to green was observed, and a \textsuperscript{1}H NMR spectrum of the reaction mixture after 15 min indicated that phenalenium tetrafluoroborate and triphenylethane were present. The chemical shifts
of H-1, 3, 4, 6, 7, 9 and H-2, 5, 8 were 9.4 ppm and 8.5 ppm, respectively. These results are very close to the values reported by Prinzbach and coworkers for the $^1$H NMR spectrum of the hexachloroantimonate salt 102 in CD$_3$CN (8.48 and 9.30 ppm).$^{56a}$

Unfortunately, the phenalenium cation was rather unstable, as after 30 min, the mixture had turned dark brown with the formation of a brown precipitate, and the phenalenium cation was no longer observable by $^1$H NMR.

This promising early result indicates that phenalenium tetrafluoroborate is easily prepared but must be handled carefully due to its lability. Greater care in ensuring moisture- and oxygen-free reaction conditions, and perhaps conducting the reaction at a lower temperature may prolong the lifetime of 101. These studies were suspended when we decided to focus our efforts on the synthesis of cyclopenta[a]phenalene (4) itself. This "parent" system has never been prepared, and we felt that synthesis of this compound would be extremely significant from a theoretical standpoint. Unlike the 7-alkoxy derivative 60 prepared by Murata and coworkers, hydrocarbon 4 lends itself to directly comparisons with azulene. Evaluation of the reactivity and properties of 4 such as its dipole moment and redox potentials would provide valuable information about the aromaticity of the cyclopenta[a]phenalene nucleus. Once the synthesis of 4 was achieved and its aromatic properties confirmed, we would then return to the application of our
[3+2] methodology to the construction of substituted derivatives of this aromatic system. With the synthesis of cyclopenta[a]phenalene as our goal, we began to explore retrosynthetic disconnections.

Retrosynthetic Analysis of Cyclopenta[a]phenalene

Our retrosynthetic analysis of this fully conjugated hydrocarbon provided a number of intriguing disconnections. Our initial routes were based on the assumption that cyclopenta[a]phenalene (4) would be comparable to azulene in stability, and therefore extraordinary precautions would not be needed in the final steps of the synthesis. We anticipated that, in analogy to azulene synthesis, dehydrogenation of a dihydrocyclopenta[a]phenalene precursor would be a viable option for the final step of the synthesis of 4. In order to achieve a convergent synthesis we considered disconnections in which the B ring was cleaved, as shown below. This type of disconnection also has the advantage of utilizing readily available peri-substituted naphthalenes 103 as precursors to the CD ring system.

Despite its simple appearance, 4 contains some latent functionality which readily lends itself to fruitful retrosynthetic disconnections. The fulvene moiety, for example, offers a good handle for retrosynthetic simplification of 4. Fulvenes are readily prepared by the condensation of a cyclopentadienyl anion and an aldehyde, as shown below. We
considered two routes which had fulvene formation as a key step. These routes differ in the order of bond formation of the C-7-C-7a and the C-1a-C-10a bonds. As shown in the following scheme, disconnection \textit{a}, in which the C-1a-C-10a bond between the fulvene and naphthalene moieties is formed last, is particularly suggestive of a radical cyclization (where \( M = \text{Sn} \), for example), or an intramolecular Heck reaction (\( M = \text{Pd} \)). A logical precursor to intermediate 107, regardless of the metal, is the iodofulvene 108 which would be prepared from the known aldehyde 109. This strategy is the topic of Part Two. Disconnection \textit{b} offers an alternative approach in which the B ring is constructed last. In this strategy, the C-7-C-7a bond is formed in a key intramolecular condensation reaction involving the intermediate cyclopentadienide anion 110 which we envisioned preparing from the same precursor, aldehyde 109. Our efforts to prepare 4 by this strategy are discussed in Part Three. A noteworthy advantage of these two routes is that they provide direct access to the target molecule in the necessary oxidation state. An alternative route to 4, also based on a naphthalenyl precursor, is a Pauson-Khand approach (route \textit{c}) which efficiently generates the A and B rings simultaneously. On the other hand, this route requires more functional group modification after assembly of the cyclopenta[\( a \)]phenalene carbon skeleton. We anticipated that enyne 113 could be readily prepared from a functionalized naphthalenic starting material of the general type 103. Our Pauson-Khand approach is detailed in Part Four.
Part II

The Fulvene Approach
CHAPTER 1
THE FULVENE ROUTE TO CYCLOPENTA[a]PHENALENE: INTRODUCTION

Strategies Based on Fulvene 108

The following scheme outlines the key features of our fulvene approach to cyclopenta[a]phenalene (4). One of the most attractive features of this route is its versatility; a variety of methods could be envisioned to achieve the final cyclization of 107 to target molecule 4. If successful, this key cyclization reaction would deliver cyclopenta[a]phenalene (4) directly. Another desirable feature of this strategy is the availability of extremely short routes to substrate 108. Aldehyde 109 is a known compound and we anticipated that condensation of 109 with cyclopentadienyl anion would produce the fulvene 108.

![Chemical Diagram]

The cyclization of iodide 108 to produce cyclopenta[a]phenalene (4) could in principle be achieved using either radical or organometallic-based carbon-carbon bond-forming reactions, as depicted in the following scheme. For example, the standard tin-mediated radical cyclization would formally be expected to produce a dihydrocyclopenta[a]phenalene which we anticipated would easily be oxidized to produce 4. A palladium-mediated intramolecular Heck reaction, on the other hand,
would possibly produce 4 directly. We also considered performing the cyclization of organolithium species 15. As in the radical method, this reaction might be anticipated to produce a dihydrocyclopenta[a]phenalene from which 4 could be obtained by dehydrogenation. The versatility of this approach appealed to us immensely!

The Intramolecular Heck Reaction

Perhaps the most attractive fulvene-based approach to 4 is the one based on the intramolecular Heck reaction (106 → 115 → 4), because this reaction should give 4 directly. The Heck reaction (eq 15), in which aryl or vinyl groups are coupled with alkenes, is a powerful carbon-carbon bond forming reaction\textsuperscript{65} and the intramolecular version has proven to be particularly useful in the synthesis of bicyclic and polycyclic

\textsuperscript{65} For reviews of the Heck reaction, see:
compounds. Some advantages of the Heck reaction include its catalytic nature, its use of readily accessible starting materials, and its good stereo- and regioselectivity. In the Heck reaction as shown below, an organopalladium species is formed by oxidative addition of the organic halide to a palladium (0) catalyst. Syn addition of the organopalladium intermediate to the alkene followed by syn elimination of palladium hydride affords the coupled product. The palladium catalyst is regenerated by reaction with a base, often a tertiary amine, which becomes an amine salt. Triarylphosphines are often employed in these reactions as palladium ligands.

\[
\text{RX} + \text{H}^\text{C=C} + \text{Base} \xrightarrow{\text{PdL}_2X_2} \text{R}^\text{C=C} + \text{BaseH}^\text{X'}
\]

\( R = \text{Aryl, heteroaryl, benzyl, or vinylic} \)
\( X = \text{Br, I, or Cl} \)
\( L = \text{Ligand} \)
Heck reaction have been carried out under a variety of conditions: in addition to tertiary amines, silver (I) carbonate, potassium carbonate, and potassium acetate are among the bases which have been employed. Certain additives such as silver (I) and thallium (I) salts have been reported to prevent isomerization of the double bond. Phase-transfer conditions have also been employed. Asymmetric Heck reactions employing chiral ligands have been reported. In an important variant of the Heck reaction, the π-allyl- and alkyl-palladium intermediates do not undergo β-hydride elimination, but rather are intercepted by stabilized carbanions, secondary amines, acetate ions, cyanide ions, and a variety of organometallic reagents.


We planned to employ an intramolecular Heck reaction as the final step in our synthesis of 4. In terms of regioselectivity of the ring closure, 6-exo cyclization was expected to be favored over cyclization in the 7-endo mode, as the product of the latter would be an extremely strained system. After an exhaustive search for literature precedence, we found several examples of intramolecular Heck reactions which are similar to our desired transformation. Equation 16 shows a 6-exo cyclization of an aryl iodide performed by Larock and coworkers.\(^\text{70}\) A second example (eq 17) is a 5-exo cyclization of a system which, like our substrate (104), is subject to extreme geometrical constraints.\(^\text{71}\) To our knowledge, Heck reactions involving fulvene olefins have not been reported in the literature.

\[\text{EtC}_5\text{H}_4\text{CO}_2\text{H} \rightarrow \text{EtC}_5\text{H}_4\text{CO}_2\text{H} \quad \text{EtC}_5\text{H}_4\text{CO}_2\text{H} \quad \text{EtC}_5\text{H}_4\text{CO}_2\text{H}\]

\[\text{Pd(OAc)}_2 \quad \text{PPh}_3 \quad \text{AgCO}_2\text{H} \quad \text{CH}_3\text{CN} \quad 80 \degree \text{C} \quad 7 \text{d} \]

\[61\%\]

\[\text{EtC}_5\text{H}_4\text{CO}_2\text{H} \rightarrow \text{EtC}_5\text{H}_4\text{CO}_2\text{H} \quad \text{EtC}_5\text{H}_4\text{CO}_2\text{H} \quad \text{EtC}_5\text{H}_4\text{CO}_2\text{H}\]

\[\text{PdCl}_2 \quad \text{Bu}_2\text{AlH} \quad \text{hexane} \quad 66 \degree \text{C} \quad 10 \text{h} \]

\[85\%\]

It has been reported that an eclipsed alignment of the aryl-palladium \(\sigma\)-bond and the olefin \(\pi\)-bond is favored over a twisted geometry in the alkene insertion step.\(^\text{72}\) Our


60
system has formidable geometric constraints such that in its ground state, iodide 107 is predicted to prefer a conformation such as 107b in which the fulvene and naphthalene lie in orthogonal planes. In this conformation, steric interactions between the fulvene and the peri substituent of the naphthalene moiety (as in 107a) are minimized. Examination of models predicts that it is unlikely that intermediate 115 can adopt a perfectly eclipsed conformation; however, we hoped that 115 could undergo the olefin insertion via a somewhat twisted conformation, as does substrate 118, shown above as an example of a conformationally restricted substrate for an intramolecular Heck reaction.

Another concern in our proposed Heck reaction is the stereochemical requirements of the β-hydride elimination: this step of the catalytic cycle usually requires a syn disposition of the palladium species and the hydrogen atom undergoing elimination. Examples of Heck products which appear to be the net result of trans-β-hydride elimination processes are known, but is it unlikely that they actually arise from trans-β-hydride eliminations. In these examples, because the intermediates are benzylic palladium compounds, it is suggested that radical or ionic intermediates are involved.\textsuperscript{73}

Discussion of an intriguing example of a Heck reaction performed by Dyker is appropriate at this point. In 1991 Dyker reported that the reaction of 1,8-diiodonaphthalene (120) with 2 equivalents of acenaphthylene (121) afforded acenaphth[1,2-a]acenaphthylene (122) as shown in the following scheme.\textsuperscript{74}

\[
\begin{align*}
\text{120} + \text{121} &\rightarrow \text{124} \\
\text{124} &\rightarrow \text{125} \\
\text{125} &\rightarrow \text{126} \\
\text{126} &\rightarrow \text{127} \\
\text{127} &\rightarrow \text{122}
\end{align*}
\]

Dyker suggested the following pathway for this interesting "double" Heck reaction. Oxidative addition of the palladium catalyst to 120 and olefin insertion into 121 leads to structure 124. \(\beta\)-Hydride elimination from 124 then leads to intermediate 125,

which resembles 107, the substrate for our planned intramolecular Heck reaction. Iodide 125 undergoes an apparent 5-endo cyclization to afford 122. This second Heck reaction is particularly interesting to us because it appears to require an anti-β-hydride elimination. However, Dyker suggests that intermediate 127 suffers from tremendous strain and is therefore an unlikely intermediate. Instead, intermediate 126 is proposed to undergo intramolecular dehydroiodination to afford 128, which can undergo reductive elimination to afford product 122.

Our system appears to have the capability of undergoing either 5-endo or 6-exo addition. The 5-endo intermediate (129), however, has no β-hydrogens and we expect that no products would result from the reversible 5-endo addition. The initial product (130) of the 6-exo process is expected to have the naphthalene and palladium species syn to each other. We reasoned that the allyl palladium moiety of 130 could isomerize to the π-allyl species 131, which might undergo further isomerization or rearrangement before β-hydride elimination. In this process we hoped that the predicted aromatic character of the cyclopenta[a]phenalene system would provide the driving force to facilitate the necessary elimination reaction.

![Chemical diagram](image)
Another interesting example of an intramolecular Heck reaction comes from the work of Kagechika and Shibasaki, who reacted cyclopentadienyl substrates under catalytic, asymmetric, anion-capture conditions to produce 5,5-bicyclic products.\(^{68b}\) Reaction of iodide 132 produced 134 in 61% yield and 20% ee (eq 19), while reaction of

\[
\begin{align*} 
\text{iodide } 132 & \xrightarrow{10 \text{ mol } \% \text{ [Pd} \text{(allyl)} \text{Cl]}_2} \xrightarrow{10 \text{ mol } \% \text{ (R,R)-CHIRAPHOS}} \xrightarrow{2.9 \text{ equiv } \text{Bu}_4\text{NOAc}} \xrightarrow{\text{tol, } 60 \degree \text{C, } 6 \text{ d}} 133 & \xrightarrow{\text{H, OAc}} 134 \\
\text{enol triflate } 135 & \xrightarrow{1.7 \text{ mol } \% \text{ Pd(OAc)}_2} \xrightarrow{(S)-\text{BINAP}} 1.7 \text{ equiv } \text{Bu}_4\text{NOAc} \xrightarrow{\text{DMSO, } 20 \degree \text{C, } 2.5 \text{ h}} 136 & \xrightarrow{\text{H, OAc}} 137 
\end{align*}
\]

the enol triflate 135 produced 137 in improved yield and enantiomeric excess (eq 20). The anion-capture modification of the Heck reaction might allow us to circumvent the problem of \(\text{syn } \beta\)-elimination: approach of the acetate group from the face opposite the palladium moiety would result in the formation of acetate 138. We envisioned that elimination of acetic acid from 127 would be extremely facile to provide the aromatic cyclopenta[a]phenalene system.

\[
\begin{align*} 
\text{iodide } 132 & \xrightarrow{10 \text{ mol } \% \text{ [Pd} \text{(allyl)} \text{Cl]}_2} \xrightarrow{10 \text{ mol } \% \text{ (R,R)-CHIRAPHOS}} \xrightarrow{2.9 \text{ equiv } \text{Bu}_4\text{NOAc}} \xrightarrow{\text{tol, } 60 \degree \text{C, } 6 \text{ d}} 133 & \xrightarrow{\text{H, OAc}} 134 \\
\text{enol triflate } 135 & \xrightarrow{1.7 \text{ mol } \% \text{ Pd(OAc)}_2} \xrightarrow{(S)-\text{BINAP}} 1.7 \text{ equiv } \text{Bu}_4\text{NOAc} \xrightarrow{\text{DMSO, } 20 \degree \text{C, } 2.5 \text{ h}} 136 & \xrightarrow{\text{H, OAc}} 137 
\end{align*}
\]
Cyclizations of free radicals provide another powerful means to construct carbon-carbon bonds. One standard method for radical cyclization which has enjoyed much application in synthesis involves the reaction of tributyltin hydride with an organic halide substrate (eq 21). Tin hydride has several advantages over other methods of radical generation. In the tin hydride method, radicals have a relatively long lifetime because tin hydride is a relatively poor hydrogen atom donor; therefore, the formation of undesired direct reduction products is less of a complication. In a typical tin hydride-catalyzed radical cyclization (see below), the tin radical is generated by reaction with an initiator such as azobisisobutyronitrile (AIBN). Propagation of the chain reaction begins by abstraction of the heteroatom X from the substrate (130) (eq 23). Intermediate radical may then undergo the desired exo cyclization to form radical 144, effectively transferring the chain reaction (eq 24), or it may extract a hydrogen atom from tributyltin hydride in a second-order process (eq 25). Alternatively, 142 can cyclize in an endo

75 For reviews of free radical carbon-carbon bond forming reactions, see:

76 For reviews of radical cyclizations, see:

77 For reviews focusing on the use of trialkyltin hydrides, see:
fashion. Abstraction of a hydrogen atom from tin hydride by 143 produces the cyclized product 145 and generates another tin radical (eq 26).

\[
\text{Initiation} \quad \text{Bu}_3\text{Sn-H} + \text{In}^+ \rightarrow \text{Bu}_3\text{Sn}^+ + \text{In-H} \quad (22)
\]

\[
\text{Propagation} \quad \text{X} + \text{Bu}_3\text{Sn}^+ \rightarrow \text{Bu}_3\text{Sn}^+ + \text{Bu}_3\text{Sn-H} \quad (23)
\]

\[
\text{Bu}_3\text{Sn-H} \rightarrow \text{CH}_3 + \text{Bu}_3\text{Sn}^+ \quad (26)
\]

Generally speaking, cyclization to form 5-membered rings with tin hydride may be considered to be the optimal example of this reaction, while cyclizations to form 6-membered rings suffer from a number of limitations. The cyclization step is slower for the formation of 6-membered rings, making simple reduction more likely. Intramolecular 1,5-hydrogen atom transfer is another possibility for many 6-heptenyl radicals. Also, the regioselectivity of 6-exo versus 7-endo cyclization is not as good as in the 5-exo verus 6-endo case. Nevertheless, the radical cyclization to form 6-membered rings remains a useful synthetic method. Our proposed 6-exo cyclization does not suffer from many of the limitations cited above. Intermediates arising from 6-exo radical cyclization of 108 lack hydrogen atoms which may undergo 1,5-hydrogen atom transfer. The
conformational restraints of 108 make 7-endo cyclization impossible. 5-Endo cyclizations suffer for poor stereoelectronics. We believe that 5-endo cyclization, if it occurred, would be reversible.

Cyclization using tin hydride is formally a reductive process, but in some cases reoxidation occurs, and instead of a net substitution of H for the heteroatom X, the overall result is an elimination of HX. One example of this phenomenon is the 6-exo cyclization of aromatic bromide 146 (eq 27), which was used by Narasimhan in a formal synthesis of steganone. This example provides an encouraging precedent for our planned radical cyclization, as like substrate 108, bromide 146 is quite geometrically constrained.

---

Generation of Radicals from Thiohydroxamate Esters: The Barton Method

One alternative method for the generation of carbon radicals has been developed by Barton and involves the decarboxylative cleavage of thiohydroxamate esters. Unlike the tin hydride method, this is not a reductive process, and when used to generate radicals for radical-π cyclization, the resulting cyclic radical intermediate is trapped by addition to the thiohydroxamate. In this fashion, irradiation or heating of thiohydroxamate ester 150 leads to thiopyridyl-substituted adduct 151 (eq 28). The thiopyridine moiety can be oxidized to the sulfoxide and eliminated (eq 29) to produce the exo olefin 152.

Because carbon dioxide is lost in this Barton cyclization, an extra carbon must be incorporated into the substrate as compared to the tin strategy. For our desired cyclization reaction, the required thiohydroxamate ester substrate (154) would be prepared from carboxylic acid 153, either by direct esterification of the acid or via conversion to the acid chloride. We envisioned that carboxylic acid 153 could be easily
prepared from iodide 108 which could also serve as the substrate for the intramolecular Heck and tin hydride reactions.

Cyclizations of Organolithium Compounds

A third possible method for effecting the cyclization of iodide 108 to form cyclopenta[a]phenalene 4 involves cyclization of an organolithium intermediate. Such cyclizations of organolithium compounds have been studied extensively by Bailey and coworkers. In 1987, Bailey and coworkers reported that primary alkyl lithiums such as

\[ \text{E} = \text{H, CO}_2\text{H, OH, etc.} \]

157 can be prepared from the corresponding iodides and undergo clean, 5-exo cyclizations at room temperature to afford cyclopentane derivatives. The cyclized alkyl lithium intermediates (e.g., 158) could be trapped with various electrophiles to

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81 For a monograph describing recent developments in cyclization chemistry, including cyclizations of organolithium substrates at sp² carbon, see: Thebtaranonth, C.; Thebtaranonth, Y. Cyclization Reactions; CRC Press: Boca Raton, 1994.
produce functionalized products. In a similar fashion, the 6-exo cyclization of 6-heptenyllithium afforded methylcyclohexane (3) in 68% yield.

\[
\text{2.0 equiv t-BuLi} \\ 
\text{2.0 equiv TMEDA} \\ 
\text{3:2 pentane-Et}_{2}O \\ 
-78 \degree C \rightarrow rt, 2 \text{ h}
\]

For our desired cyclization, then, we anticipated that lithium-halogen exchange would produce the naphthyllithium intermediate 116. Cyclization of 116 in a 6-exo mode would produce intermediate 162, which upon protonation should produce dihydrocyclopenta[a]phenalene 149. Because the lithiated intermediate 162 might actually have a delocalized anion, other isomers of 149 might be obtained from the reaction. We believed that dihydrocyclopenta[a]phenalenes such as 149 and its isomers would readily undergo dehydrogenation to afford cyclopenta[a]phenalene (4).

Armed with these strategies for performing the cyclization reaction to form the B ring of cyclopenta[a]phenalene (4), we set out to prepare the substrates for these reactions. The syntheses of our substrates and cyclization attempts using various methods are described in Chapter Two of this section.
CHAPTER 2
THE FULVENE ROUTE TO CYCLOPENTA[a]PHENALENE: RESULTS

Preparation of Key Fulvene Cyclization Substrate 108

Our plan for the synthesis of fulvene 108, the substrate for the intramolecular Heck, tin hydride, and organolithium cyclization strategies, involved a rapid, three-step route beginning from commercially available 1,8-diaminonaphthalene (163) as outlined above. Formation of the fulvene would be effected under the standard conditions by condensation of cyclopentadienide anion with the aldehyde 109. This aldehyde has been prepared by Shechter and coworkers from 1,8-naphthalic anhydride in a five-step route in 48% overall yield as shown below, but we felt that this route was too long and sought a shorter route to 109. We opted to prepare aldehyde 109 by monolithiation of diiodide 120 and reaction with a formylating agent. The monolithiation of 120 and trapping with various reactive electrophiles, including trimethylsilyl trifluoromethanesulfonate, dichlorodimethylsilane, and triethylborate, has been reported by H. E. Katz and proceeds in good (50-58%) yield.

The preparation of 1,8-diiodonaphthalene (120) from 1,8-diaminonaphthalene (163) by diazotization and iodination has been reported by House.\textsuperscript{86} Reaction of commercially available 163 (which was purified by distillation from zinc) with sodium nitrite in a mixture of sulfuric acid and water produced a bisdiazonium salt intermediate (145) which was then treated with excess potassium iodide according to House's procedure to afford 1,8-diiodonaphthalene (120) in 53-56% yield. We found that recrystallization as described by House failed to remove colored impurities from 120, and we therefore opted to purify 120 by column chromatography on silica gel, or a mixture of charcoal and silica gel. Although chromatography with the charcoal-silica gel mixture was slow despite the use of air pressure, this system was more efficient in terms of the ratio of charcoal-silica gel to crude material required.

\textsuperscript{86}House, H. O.; Koepsell, D. G.; Campbell, W. J. \textit{J. Org. Chem.} 1972, 37, 1003 and references therein.
Using Katz's procedure\textsuperscript{35} for monolithiation of 120, we treated an ethereal solution of this diiodide at \(-30^\circ C\) with exactly one equivalent of \(n\)-butyllithium for 20 min, and then trapped the resulting monolithio adduct 170 with \(N,N\)-dimethylformamide (DMF) or \(N\)-methylformanilide. These reactions inevitably produced a mixture of the desired aldehyde 109, recovered diiodide 120, and 1-iodonaphthalene (171). 1-Iodonaphthalene presumably results from protonation of the organolithium intermediate 170, and despite exhaustive efforts to exclude moisture from the reaction mixture, some of this byproduct was always obtained. DMF, notoriously difficult to dry, was sequentially dried using three portions of activated 3A molecular sieves following the procedure of Burfield and Smithers.\textsuperscript{87} \(N\)-Methylformanilide, which can be effectively dried using calcium hydride, is considered a suitable alternative to DMF, and gave similar results in our formylation reactions. The number of equivalents of \(n\)-BuLi, the temperature of the reaction, and the concentration of the reaction were systematically varied and it was found that the best yields of aldehyde 109 were obtained by treating a 0.04 M solution of diiodide 144 in ether at \(-30^\circ C\) with 1.0 equivalent of \(n\)-BuLi for 30

minutes, and then cooling the reaction mixture to -78 °C before addition of 1.5 equivalents of DMF as a solution in ether. The reaction mixture was then allowed to warm slowly to 25 °C. Under these optimized reaction conditions aldehyde 109 was obtained in 46-55% yield and only ca. 10% each of 120 and 171 were formed.

Fulvene 108 was easily prepared from aldehyde 109 using a general procedure for fulvene synthesis reported by Stone and Little. In this method (eq 32), reaction of the aldehyde with pyrrolidine generates an pyrrolidinium ion (172) which serves as an activated acceptor towards cyclopentadienide. Little found that this method provides access even to sterically hindered and 6,6-disubstituted fulvenes in good to excellent yields. The formation of 6-phenylfulvene (173, R = Ph), for example, proceeded in 70% yield. Using his procedure we found that reaction of aldehyde 109 under the same conditions proceeded smoothly to produce fulvene 108 in ca. 82-88% yield (eq 33); the product was an extremely viscous orange oil which was unstable upon storage at 25 °C for prolonged periods and was contaminated with ca. 5-10% of dichloromethane.

--

Fulvene 108 underwent decomposition to several unidentified products even when stored frozen as a dilute solution in degassed benzene. It is possible that polymerization is a pathway for the decomposition of 108. Fulvenes are also known to undergo Diels-Alder dimerizations, and are particularly susceptible to nucleophilic attack at the 6-position, as cyclopentadienyl anion intermediates are produced. The decomposition products from 108 were easily removed by column chromatography using 10% methylene chloride-hexane, and for most reactions 108 was best purified immediately before use.

**Attempted Cyclization of Fulvene 108 by Intramolecular Heck Reaction**

There are many, many variations in the reaction conditions for Heck reactions. In general, these reactions require catalytic amounts of a Pd(II) or Pd(0) reagent with an added phosphine ligand and a stoichiometric amount of base (to regenerate the active Pd(0) catalyst). Heck reactions are typically run in coordinating solvents such as
acetonitrile or DMF at elevated temperatures. We sampled a number of reaction conditions in an attempt to effect the transformation of iodofulvene 108 to cyclopenta[a]phenalene (4). Our observations are detailed in Table 6. These reactions were performed using fairly dilute solutions (ca. 0.03 M maximum concentration) of 40-300 mg of fulvene 108. The reactions were monitored by TLC and the reaction mixtures were filtered through Celite and concentrated before analysis using $^1$H NMR spectroscopy.

Table 6. Attempted Heck Cyclizations of Iodofulvene 108

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1$^{89}$</td>
<td>10 mol % Pd(OAc)$_2$ 20 mol % PPh$_3$ 2 equiv K$_2$CO$_3$ CH$_3$CN, Δ, 5 min</td>
<td>SM was consumed after 5 min two spots by TLC poor mass recovery after workup</td>
</tr>
<tr>
<td>2$^{90}$</td>
<td>10 mol % Pd(OAc)$_2$ 30 mol % PPh$_3$ 2 equiv Et$_3$N CH$_3$CN, rt, 6.5 h</td>
<td>clean reaction by TLC poor mass recovery after workup</td>
</tr>
<tr>
<td>3$^{86}$</td>
<td>6 mol % Pd(OAc)$_2$ 20 mol % PPh$_3$ 2 equiv Et$_3$N CH$_3$CN, rt, 6.5 h, then 80 °C, 4 h</td>
<td>several products by TLC poor mass recovery after workup</td>
</tr>
<tr>
<td>4$^{91}$</td>
<td>12 mol % Pd(OAc)$_2$ 3 equiv K$_2$CO$_3$ 1 equiv Bu$_4$N$^+$Br$^-$ DMF, 45 °C, 2 d</td>
<td>no reaction</td>
</tr>
<tr>
<td>5$^{92}$</td>
<td>5 mol % Pd(PPh$_3$)$_4$ 2 equiv Et$_3$N CH$_3$CN, Δ, 1 h</td>
<td>no reaction</td>
</tr>
<tr>
<td>6$^{93}$</td>
<td>10 mol % Pd$_2$(dba)$_3$ 20 mol % P(o-tol)$_3$ 2 equiv K$_2$CO$_3$ CH$_3$CN, 80 °C, 2 d</td>
<td>several products by TLC</td>
</tr>
</tbody>
</table>

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$^{91}$Jeffery, T. Synthesis 1987, 70.
Table 6. Attempted Heck Cyclizations of Iodofulvene 108 (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>789</td>
<td>10 mol % Pd₂(dba)₃</td>
<td>clean TLC</td>
</tr>
<tr>
<td></td>
<td>20 mol % P(o-tol)₃</td>
<td>poor mass recovery upon workup</td>
</tr>
<tr>
<td></td>
<td>2 equiv K₂CO₃</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CH₃CN-H₂O, 70 °C, 2 h</td>
<td></td>
</tr>
<tr>
<td>889</td>
<td>10 mol % Pd₂(dba)₃</td>
<td>several products by TLC</td>
</tr>
<tr>
<td></td>
<td>20 mol % P(o-tol)₃</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 equiv Et₃N</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CH₃CN, 80 °C, 0.5 h</td>
<td></td>
</tr>
<tr>
<td>994</td>
<td>10 mol % Pd₂(dba)₃</td>
<td>several products by TLC</td>
</tr>
<tr>
<td></td>
<td>30 mol % PPh₃</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 equiv Et₃N</td>
<td></td>
</tr>
<tr>
<td></td>
<td>tol, 110 °C, 0.5 h</td>
<td></td>
</tr>
<tr>
<td>1069b</td>
<td>10 mol % [Pd(allyl)Cl]₂</td>
<td>no reaction at 25 °C</td>
</tr>
<tr>
<td></td>
<td>10 mol % DIPHOS</td>
<td>baseline material by TLC after heating</td>
</tr>
<tr>
<td></td>
<td>2 equiv Bu₄N⁺OAc⁻</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CH₃CN, 25 °C, 12 h, then 50 °C, 16 h</td>
<td></td>
</tr>
</tbody>
</table>

Exposure of iodofulvene 108 to the conditions for the Heck reaction appears to have failed to produce cyclopenta[α]phenalene. In the trials which appeared promising by TLC analysis, little useful material was obtained after filtration and concentration. A likely explanation for the poor mass recovery is polymerization, perhaps via intermolecular Heck-type processes. It is possible that the products of these reactions decomposed upon concentration. Anion-capture conditions (entry 10) were also unsuccessful.

We wondered to what degree the iodofulvene 108 was simply undergoing decomposition under the various reaction conditions. As mentioned above, the fulvene decomposed when stored neat at 25 °C under vacuum and showed some decomposition even when frozen in degassed benzene, and intermolecular reactions were postulated to be responsible for the decomposition products. Stability testing of iodofulvene 108 was

---

performed and it was observed by TLC analysis that the fulvene withstood overnight heating in refluxing acetonitrile, both in the presence of triphenylphosphine and triethylamine. However, when air was bubbled through an acetonitrile solution of 108 for several hours, decomposition was noted.

**Attempts at Radical Cyclization of 108 Using Tin Hydride**

We next began to explore tin hydride-mediated radical cyclizations of fulvene 108 to produce cyclopenta[α]phenalene (4) or a dihydro adduct such as 149. In radical cyclizations using tributyltin hydride, slow addition of the tin reagent is often required in order to promote cyclization rather than direct reduction of the substrate. This is particularly important for slower cyclizations. In our attempts to cyclize substrate 108, an excess of tributyltin hydride in benzene solution was added via syringe pump to a solution of iodide 108 containing a catalytic amount of the radical initiator azoisobisbutyronitrile (AIBN) in benzene at reflux. In most reactions we attempted, starting material 108 was still visible by TLC even after prolonged reaction times. Even after addition of more AIBN and tributyltin hydride, 108 was usually not completely consumed.
Procedures for the workup of tin hydride reactions deserve mention at this point. Separation of tin byproducts can be taxing, especially from other nonpolar compounds. We first employed the standard procedure which involves treatment of the reaction mixture with iodine to convert unreacted tributyltin hydride to the corresponding iodide. This was followed by either the traditional potassium fluoride or the more recently reported diazabicycloundecene (DBU) procedure.

The desired cyclization occurs slowly if at all: one of the products which we observed from these cyclization attempts was indeed fulvene 174, the result of direct reduction. We also recovered small amounts of unreacted iodide 108. Some byproducts appeared to have incorporated a tributylstannyl moiety, possibly resulting from a secondary reaction between a radical derived from 108 and a tributylstannyl radical. Another pathway for the formation of tributylstannyl-substituted fulvene byproducts is the addition of tributylstannyl radical to the fulvene at C-6. In light of the low mass recovery which was characteristic of all of the runs of this reaction, it is likely that substrate 108 suffered polymerization.

---

Efforts to Prepare Thiohydroxamate Ester 154

We next sought to explore the Barton decarboxylative method for generating radical intermediate 114, and therefore set about synthesizing the thiohydroxamate ester 154. Unfortunately, these efforts met with little success. Thiohydroxamate ester derivatives are generally prepared from activated carboxylic acids as shown in the scheme below. The most common method (eq 34) is to convert the carboxylic acid to the acid chloride and immediately react it with either the sodium salt of 2-mercaptopyridine-N-oxide or a mixture of 2-mercaptopyridine-N-oxide in pyridine. Alternatively, direct esterification of the carboxylic acid with 178 using dicyclohexylcarbodiimide (DCC) and catalytic dimethylaminopyridine (DMAP) may be employed (eq 35), but this method is mainly limited to unsubstituted carboxylic acids, as branched carboxylic acids yield N-acylureas rather than thiohydroxamate esters. Another method for the preparation of thiohydroxamate esters involves the reaction of the carboxylic acid with isobutyl chloroformate and N-methylmorpholine to form a mixed anhydride which is then treated with thiohydroxamic acid 176.

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98 Ref. 80a and references therein.
For the conversion of iodide 108 to a carboxylic acid derivative, we envisioned two strategies: (a) transition metal-catalyzed carboxylation of 108, and (b) reaction of the lithium anion of 108 with a carboxylating agent. Heck has reported formation of esters from aryl, benzyl, and vinyl halides under palladium catalysis (eq 37).\textsuperscript{101} Formation of carboxylic acids from aryl and benzyl halides with cobalt catalysis under phase-transfer conditions has been reported by Caubere (eq 38).\textsuperscript{102}

We opted to pursue the latter strategy and, as shown below, found that treatment of iodide 108 with 1.2 equiv of n-butyllithium and an excess of methylchloroformate in ether at -78 °C provided ester 182 in 49-66% yield. We also tried to form the desired carboxylic acid 153 directly by trapping lithium derivative 116 with gaseous and solid carbon dioxide, but failed to isolate 140, obtaining instead uncharacterizable decomposition products.

Our attempts to convert methyl ester 182 to carboxylic acid 153 were also unsuccessful. The conditions we explored for this transformation are described in Table 7.103 We sought mild reaction conditions which would minimize side reactions involving the fulvene moiety. In general, we either observed no reaction or decomposition of the

103 For general articles about the conversion of esters to carboxylic acids, see:
(c) Salomon, C. J.; Mata, E. G.; Mascarelli, O. A. Tetrahedron 1980, 36, 2409.
starting material, leading us to theorize that the desired product, carboxylic acid 153, is not a stable compound.

Table 7. Attempted Hydrolysis of Methyl Ester 182

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1104</td>
<td>1M LiOH/H₂O, acetone, 40 °C, 16 h</td>
<td>no reaction</td>
</tr>
<tr>
<td>2105</td>
<td>4 equiv NaOH, H₂O-diethylene glycol, Δ</td>
<td>complex mixture</td>
</tr>
<tr>
<td>3106</td>
<td>2 equiv (Bu₃Sn)₂O, Et₂O, rt, 16 h</td>
<td>no reaction</td>
</tr>
<tr>
<td>4107</td>
<td>2 equiv LiOH, H₂O-DME, Δ</td>
<td>mixture of products complex ¹H NMR</td>
</tr>
<tr>
<td>5108</td>
<td>1 equiv K⁺Me₃SiO⁻, THF, rt, 16 h</td>
<td>no reaction</td>
</tr>
<tr>
<td>6109</td>
<td>1 equiv TMSI, CCl₄, 50 °C, 15 min</td>
<td>decomposition</td>
</tr>
<tr>
<td>7110</td>
<td>3 equiv AlBr₃, EtSH, rt, 30 min</td>
<td>complex mixture</td>
</tr>
<tr>
<td>8111</td>
<td>excess Al₂O₃-KOH, Et₂O, rt, 18 h</td>
<td>no reaction</td>
</tr>
<tr>
<td>9112</td>
<td>8 equiv KOt-Bu, 2 equiv H₂O, Et₂O, rt, 18 h</td>
<td>no reaction</td>
</tr>
</tbody>
</table>

Cyclization Attempts Using Organolithium Intermediates

Another method which we sought to employ for the cyclization of iodide 108 involved halogen-metal exchange to generate an organolithium species such as 116 which we hoped would undergo cyclization to form the B ring of cyclopenta[a]phenalene. We anticipated that this cyclization would produce a dihydrocyclopenta[a]phenalene such as 149, as shown in the above scheme. To this end, we treated iodide 108 with \( t \)-butyllithium and \( n \)-butyllithium under a number of reaction conditions (Table 8), including conditions for alkylcuprate formation (entries 6 and 7). The main product we observed from these reactions was the protonated, uncyclized fulvene 174.

Table 8. Reactions of Iodide 108 with Alkyllithium Reagents

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Product(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 equiv ( t )-BuLi&lt;br&gt;THF, -78 °C → rt</td>
<td>174 (poor mass recovery)</td>
</tr>
<tr>
<td>2</td>
<td>2 equiv ( t )-BuLi&lt;br&gt;3:2 pentane-Et₂O, -78 °C, 40 min</td>
<td>174</td>
</tr>
</tbody>
</table>
Table 8. Reactions of Iodide 108 with Alkyllithium Reagents (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Product(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>2 equiv t-BuLi</td>
<td>174</td>
</tr>
<tr>
<td></td>
<td>3:2 pentane-Et$_2$O, -94 °C, 40 min</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2 equiv t-BuLi</td>
<td>174 + 104</td>
</tr>
<tr>
<td></td>
<td>3:2 pentane-Et$_2$O, -116 °C → rt, 18 h</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1 equiv n-BuLi</td>
<td>174 + 104 (1:1)</td>
</tr>
<tr>
<td></td>
<td>2 equiv TMEDA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Et$_2$O, -78 °C → rt, 18 h</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1.2 equiv n-BuLi</td>
<td>174 (28%)</td>
</tr>
<tr>
<td></td>
<td>1.1 equiv CuCN</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Et$_2$O, -78 °C → rt, 18 h</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.2 equiv n-BuLi</td>
<td>174 (28%)</td>
</tr>
<tr>
<td></td>
<td>1.1 equiv CuBrMe$_2$S</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Et$_2$O, -78 °C → rt, 18 h</td>
<td></td>
</tr>
</tbody>
</table>

In work on the preparation of carboxylic ester 182 from iodide 108 performed after these cyclization studies, we found that exposure of 108 to 1.0-1.2 equiv of n-BuLi in diethyl ether at -78 °C for 5 min produced the organolithium intermediate 116. It is not surprising, however, that in none of these reactions did addition of the aryllithium reagent to C-6 of the fulvene occur, because the temperature of the reaction mixture in these cases was maintained at -78 °C.

We attributed many of the discouraging results of in cyclization studies on fulvene 108 to the special reactivity of the fulvene moiety and the conformation of the substrate. This route was abandoned. We then began to pursue the alternative strategy in which the fulvene is assembled in the last step of the synthesis. Our work on this "condensation approach" is described in Part Three.
Part III

The Condensation Approach
CHAPTER 1
OVERVIEW OF THE CONDENSATION STRATEGY

In this approach for the synthesis of cyclopenta[α]phenalene (4), our line of attack was to construct the B ring of 4 in a key condensation reaction between a cyclopentadienyl anion and an aldehyde, or in other words, to effect intramolecular fulvene formation.\(^{113}\) In the fulvene-based cyclization strategy discussed in Part Two, attempts to cyclize fulvene 108 were impeded in part by the sensitivity of the fulvene moiety.\(^{114}\) In contrast, the strategy of the condensation approach is to install the fulvene last.

The reaction conditions for fulvene formation can be quite mild: recall that fulvene 108 was prepared simply by mixing an aldehyde with cyclopentadiene and

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\(^{113}\) For reviews on fulvenes, see:

\(^{114}\) See Ref. 3a, pp 91-93.
pyrrolidine in methanol at room temperature (eq 39). We believed that these reaction conditions could be applied to the preparation of 4 from the peri-substituted naphthalene 111.

For the preparation of precursor 111 we envisioned two basic approaches as shown below. In disconnection a, the aldehyde is installed on the cyclopentadienyl compound 183. We envisioned that cyclopentadiene 183 could be prepared from 1,8-diiodonaphthalene (120) by a transition metal-mediated cross coupling reaction. In disconnection b, the order of the steps is reversed, and the cyclopentadienyl moiety is introduced to a molecule which contains either an aldehyde or an aldehyde equivalent. Strategy b was explored in depth and our efforts are detailed in Chapter Two of this section. Despite some encouraging related chemistry in the literature, our schemes for achieving strategy a were quickly exhausted, and a detailed discussion of our work on this route immediately follows.
Cyclopentadienyl Reagents

For the preparation of cyclopentadiene 183 from 1,8-diiodonaphthalene, we envisioned performing a transition metal-mediated coupling reaction using a cyclopentadienyl reagent such as cyclopentadienylcopper dimethyl sulfide (186a, X = Cu·Me₂S) or a trialkylstannylcyclopentadiene (186b, X = SnR₃). Rosenblum and coworkers effected the reaction of 1,8-diiodonaphthalene (120) with cyclopentadienylcopper dimethyl sulfide and obtained a 39% yield of a mixture of our target molecules 183a and 183b contaminated with "small amounts" of unreacted 120 and the bis-coupled product 187.¹¹⁵ In our hands, however, this reaction produced 183a and 183b contaminated with traces of 187 and significant amounts of unreacted 1,8-

diiodonaphthalene (Table 9, entries 1 through 3). Unreacted 120 was nearly inseparable from the desired products by column chromatography; careful chromatography improved the ratios of desired products to unreacted starting material, but at best ca. 15% of diiodonaphthalene was still present. Adding a larger excess of the cyclopentadienylcopper dimethyl sulfide (entries 4 and 5) produced a mixture of 183a and 183b contaminated with 1-iodonaphthalene (171), which was easier to separate by chromatography. We resubjected the mixture of products to the reaction conditions and found that the ratio of 183a and 183b to 120 was somewhat improved.

We tested three procedures for the preparation of copper (I) bromide dimethyl sulfide complex (188).116 The complex is commercially available but often contains traces of copper (II) salts. A telltale sign of the presence of copper (II) impurities is green discoloration; in its pure form, 188 is white.117 In the procedure reported by House and coworkers, 188 is prepared from copper (I) bromide and dimethyl sulfide and is purified by recrystallization using dimethyl sulfide and hexanes.117 In a modification of House's procedure, Wuts used methanol to purify the copper (I) bromide before preparation of the dimethyl sulfide complex.118 The method which we favored was reported by Theis and Townsend and involves reduction of copper (II) bromide with sodium sulfite and subsequent dimethyl sulfide complex formation.119

Table 9. Reactions of 120 with CpCu·Me₂S (186a)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Products 183a/183b</th>
<th>120</th>
<th>187</th>
<th>171</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.4 equiv CpCu·Me₂S THF, -23 °C, 2 h</td>
<td>27%</td>
<td>5%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>same</td>
<td>28%</td>
<td>13%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>same</td>
<td>38%</td>
<td>16%</td>
<td>5%</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>2.8 equiv CpCu·Me₂S THF, -23 °C, 2 h</td>
<td>31%</td>
<td>trace</td>
<td>-</td>
<td>31%</td>
</tr>
<tr>
<td>5</td>
<td>2.1 equiv CpCu·Me₂S THF, -23 °C, 2 h</td>
<td>30%</td>
<td>6%</td>
<td>3%</td>
<td>30%</td>
</tr>
</tbody>
</table>

A related reagent, cyclopentadienylcopper tributylphosphine (190), has been shown to undergo coupling with aryl iodides. The reaction of 190 with 4-iodotoluene (189), for example, produced a mixture of 191a and 191b in 50% yield with 22% of recovered iodo-toluene (eq 40). However, Rosenblum found that reaction of 1,8-diiodonaphthalene with 190 gave a mixture of 183a and 183b in poor yield.  

---

In reactions of 1,8-diiodonaphthalene with the cyanocuprate reagent CpCu(CN)Li (192),\textsuperscript{121} we observed that 192 reacts more sluggishly than cyclopentadienylcopper dimethyl sulfide (186a). The reaction time was varied in two runs of this reaction (Table 10), and the desired products were either contaminated with homocoupled starting material (193) or starting material. The higher order cyanocuprate Cp\(_2\)Cu(CN)Li\(_2\) was prepared and upon reaction with 1,8-diiodonaphthalene (120), the only products were recovered starting material (120) and homocoupled material (193). This may indicate that the reagent had not been formed and rather that an extra equivalent of cyclopentadienyllithium had been in the reaction mixture.

Table 10. Reactions of 120 with CpCu(CN)Li and Cp\(_2\)Cu(CN)Li\(_2\)

Table 10. Reactions of 120 with CpCu(CN)Li and Cp$_2$Cu(CN)Li$_2$ (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.0 equiv CpCu(CN)Li</td>
<td>183a/183b</td>
</tr>
<tr>
<td></td>
<td>THF, -78 °C → rt, 16 h</td>
<td>120</td>
</tr>
<tr>
<td>2</td>
<td>1.0 equiv CpCu(CN)Li</td>
<td>24%</td>
</tr>
<tr>
<td></td>
<td>THF, -78 °C → rt, 2 h</td>
<td>184</td>
</tr>
<tr>
<td>3</td>
<td>1.0 equiv Cp$_2$Cu(CN)Li$_2$</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>THF, -78 °C → rt, 16 h</td>
<td>-</td>
</tr>
</tbody>
</table>

Carbonylation Reactions: Aldehydes from Aryl Iodides

The second step in this route for the preparation of aldehyde 111 is carbonylation of iodide 183. Using transition metal catalysis, aryl and benzyl halides can be formylated in one step.$^{122}$ Early work in carbonylation chemistry by Heck using hydrogen gas as the hydrogen donor required harsh reaction conditions (eq 41).$^{123}$ The Israeli chemists Pri-Bar and Buchman used poly(methylhydrosiloxane) (196) as a hydrogen donor in a milder formylation procedure (eq 42).$^{124}$ Yet milder reaction conditions were described in work by Stille in which tributyltin hydride is the hydrogen donor (eq 43).$^{125}$

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The results of our carbonylation studies are depicted below. Reaction of a 4:1 mixture of cyclopentadienes 183 and 1,8-diiodonaphthalene (120) following Stille's procedure yielded a mixture of recovered cyclopentadienes 183 (37%) and 1-naphthaldehyde (197) (eq 44). Intrigued, we then subjected pure 120 to the reaction conditions and confirmed that 197 is obtained in ca. 70% yield (eq 45). We also attempted to carboxylate 183 using the method of Caubere discussed in Part Two.\textsuperscript{102a} Our plan was to prepare aldehyde 111 by partial reduction of the carboxylic acid. However, no carboxylation was observed (eq 46), and instead a 2:1 mixture of 183 and 120 was obtained. Is iodide 183 perhaps too sterically hindered to undergo the carboxylation reaction?
This route clearly was not acceptable for the preparation of aldehyde 111. Having encountered difficulties both in installing the cyclopentadiene and in the subsequent carbonylation step, we next turned our attention to the preparation of the fulvene precursor 111 using an alternate strategy. This work, in which a cyclopentenyl group is installed onto a substrate bearing an aldehyde equivalent, is discussed in Chapter Two of this section.
CHAPTER 2
STILLE COUPLING APPROACH FOR THE PREPARATION OF A CONDENSATION SUBSTRATE

Introduction

In this approach for the preparation of 111, we sought to use a transition metal-catalyzed cross coupling reaction to install the cyclopentadienyl group. If it was not possible to directly couple a cyclopentadienierivative to 185, then our plan was to employ a cyclopentenyl derivative and then to introduce the second double bond at a later stage in the synthesis. Initially we envisioned that iodide 185 would contain an unprotected aldehyde, but we ultimately used a methyl ester, for reasons that will be discussed later. We believed that functional group manipulation would readily provide fulvene precursor 111 from 203. Intramolecular fulvene formation then was anticipated to produce cyclopenta[α]phenalene (4).

The Stille Coupling Reaction

One carbon-carbon bond forming method which we hoped to employ for installation of the cyclopentadiene or cyclopentene functionality was the Stille reaction. The Stille reaction (eq 50) employs palladium catalysis to couple organohalogen and
-sulfonate compounds $\text{R}^1\text{-X}$ with organostannane reagents.\textsuperscript{126} A wide variety of organic $\text{R}^1\text{-X}$ species, including aryl and vinyl halides and triflates, participate in this reaction. Likewise, for the organostannane, the group ($\text{R}^2$) which undergoes transmetallation may be alkynyl, alkenyl, aryl, benzyl, or allyl. Alkyl groups do undergo transmetallation, but simple alkyl groups have relatively slow transfer rates. For this reason, when tributyl- or trimethylstannyll derivatives bearing an activated fourth alkyl group are employed, it is the fourth group ($\text{R}^2$) bonded to the tin which selectively undergoes transmetallation. Some of the particularly attractive features of organostannanes are that they are usually neither sensitive to oxygen nor moisture, they can be prepared by a variety of methods, and lastly they can bear a variety of functional groups.

Much effort has been focused on optimizing the reaction conditions for the Stille coupling reaction.\textsuperscript{126c} The catalyst may be either a palladium (II) or palladium (0) species; palladium (II) catalysts are reduced in the reaction mixture to the active palladium (0) species. Stille originally employed palladium tetrakis(triphenylphosphine), but Farina has observed that using less-donating ligands such as tri(2-furyl)phosphine and triphenylarsine increases the rate of the reaction.\textsuperscript{127} Farina has suggested that the rate-determining step is transmetallation and that ligand dissociation must proceed the formation of a palladium-stannane $\pi$-complex. Highly coordinating solvents such as 1-methyl-2-pyrrolidinone (NMP) and $N,N$-dimethylformamide (DMF) increase the rate of transmetallation.

\textsuperscript{126}For reviews of the Stille reaction, see:
(c) Farina, V.; Roth, G. P. In Advances in Metal-Organic Chemistry; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1995; Vol. 5; pp 162-240.
Preparation of Cyclopentadienyl- and Cyclopentenylstannanes

Trialkylstannycyclopentadienes have been prepared by two methods. Alkylation of sodium cyclopentadienide with trialkylstannyl chlorides was described by Fritz and Kreiter (eq 48). Alternatively, treatment of cyclopentadiene with aminostannane derivatives also produces trialkylstannycyclopentadienes (eq 49). Compounds 199 and 200 are reported to be σ-bonded such that the stannyl substituent lies primarily at C-5 of the 1,3-cyclopentadienes. Thus, 199 and 200 behave for the most part as allyl-

\[
\begin{align*}
1.1 \text{ equiv } \text{Na}^+ & \quad 1.0 \text{ equiv } \text{Bu}_3\text{SnCl} \\
\text{CpH, rt, 2 d} & \\
\rightarrow & \\
199
\end{align*}
\]

\[
\begin{align*}
3.0 \text{ equiv } \text{Me}_3\text{SnNEt}_2 & \quad 1.0 \text{ equiv } \text{Me}_3\text{SnNEt}_2 \\
\text{rt, 0.5 h} & \\
92\% & \\
\rightarrow & \\
200
\end{align*}
\]

rather than the more reactive vinylstannanes. What reactivity has been observed for 199 or 200 in coupling reactions? Beletskaya reported the coupling of allyl acetate with 200 under palladium catalysis (eq 50). To our knowledge, transition metal-catalyzed cross couplings of aryl halides or related compounds with trialkylstannycyclopentadienes have not been successful. Rosenblum attempted to use palladium-mediated coupling of 195 with 1,8-diiodonaphthalene and obtained homocoupled products.

\[\text{References}\]

We prepared both tributylstannylcyclopentadiene (199) and tributyl(cyclopent-1-enyl)stannane (204) for use as the organostannane partners in Stille couplings for the synthesis of substrate 111. Tributylstannylcyclopentadiene (199) was prepared following the method of Fritz and Kreiter\textsuperscript{128} (eq 51) from sodium cyclopentadienide and tributyltin chloride and was obtained in ca. 95% yield after purification by distillation at reduced pressure. The product was contaminated with ca. 5% of tributyltin chloride as estimated by \textsuperscript{1}H NMR analysis.

At the time when we began this work, the preparation of tributyl(cyclopent-1-enyl)stannane (204) had been reported by Moloney and Pinhey.\textsuperscript{133} Their method employed a Shapiro reaction\textsuperscript{134} on tosylhydrazone 203, and was reported to provide 204 in a disappointingly low yield (eq 52). We opted to prepare 204 using Shapiro chemistry

\begin{equation}
\text{O} \quad 1.0 \text{ equiv } \text{H}_2\text{NNHSO}_{2}C_6H_4\text{Me} \\
\text{cat } \rho\text{-TsOH} \\
\text{EtOH, } \Delta \\
81\%
\end{equation}

\begin{equation}
\text{NHTe} \quad 4.0 \text{ equiv } n\text{-BuLi} \\
\text{TMEDA, } -45^\circ \text{C } \rightarrow \text{ rt} \\
20\%
\end{equation}


\textsuperscript{134}For reviews of the Shapiro reaction, see:
(c) Shapiro, R. H. \textit{Org. React.} 1976, 23, 405.
on 2,4,6-triisopropylbenesulfonylhydrazone (trisylhydrazone) 207 as shown below. The trisylhydrazone offers many advantages to the tosylhydrazone in Shapiro reactions: the most important advantage is that exactly two equivalents of base effects the Shapiro reaction of a trisylhydrazone, whereas at least three equivalents are required for tosylhydrazones due to competing ortho-metalation of the aromatic ring. Also, the decomposition of the dianion of trisylhydrazones to the vinyllithium species occurs more rapidly than the analogous process does in tosylhydrazones. Trisylhydrazine (206) was prepared following the procedure of Reese and coworkers from triisopropylbenzenesulfonyl chloride 205 and hydrazine hydrate in 93-95% yield. Reaction of 206 with one equivalent of cyclopentanone with catalytic hydrochloric acid in methanol produced trisylhydrazone 207 in excellent yield. A Shapiro reaction was performed on 207 using 2.5 equivalents of n-butyllithium in the mixed solvent system of 1:1 N,N,N',N'-tetramethylethylene diamine (TMEDA) and hexane to generate tributyl(cyclopent-1-enyl)stannane (204) in ca. 80-97% yield, 90-95% pure as determined.

by analysis of $^1$H NMR. The major contaminant which was present, after fractional distillation at reduced pressure, was tributyltin chloride. A method very similar to the one we employed was reported in 1993 by Adam and Klug.\(^\text{138}\) In their procedure, trisylhydrazone 207 was treated with 2.1 equivalents of $s$-butyllithium and 1.0 equivalent of tributyltin chloride in a 1:1 mixture of TMEDA-petroleum ether to afford 204 in 79% yield.

As shown below, we also briefly investigated the preparation of 1-trimethylstannane 208 by the Shapiro method. An extremely poor yield was observed in the Shapiro reaction when trapping with trimethyltin chloride. In an attempts to find an alternate method for the preparation of 208, enol triflate 210\(^\text{139}\) was prepared from cyclopentanone using the triflating reagent $N$-(5-chloro-2-pyridyl)triflimide (209) introduced by Comins.\(^\text{140}\) Stille couplings of 210 with hexamethylditin using the method of Wulff\(^\text{141}\) were unsuccessful. Although trimethylstannane reagents have the advantage

![Chemical equation]

of being more reactive than their tributyltin counterparts, they also are more toxic. We found the preparation of the tributylstannane 204 to be more facile and observed that 204

was sufficiently reactive in our Stille coupling reactions, and consequently we did not further pursue studies on the trimethyltin reagents.

Preparation of Iodide Substrates for the Stille Reaction

We prepared two organohalogen compounds for use in the Stille reaction. The preparation of aldehyde 109 from 1,8-diiodonaphthalene (eq 53) was described in Part Two. We envisioned that this aldehyde would be an ideal substrate for a Stille coupling with a cyclopentadienylstannane to form the fulvene precursor 111. However, the surprising behavior of 109 in a Stille coupling reactions (described below) forced us to consider using alternative substrates, and therefore we also prepared the known compound methyl 8-iodo-1-napthoate (167). We recognized that esters readily undergo partial reduction to form aldehydes\(^\text{142}\) and noted that 167 was easily prepared on a large scale from inexpensive starting materials.

Following the method of Shechter,\(^\text{84}\) we prepared methyl ester 167 by the route depicted below. Commercially available 1,8-naphthalic anhydride (164) was converted to the stable, isolable anhydro-8-(hydroxymercuri)-1-naphthoic acid (165) in good yield. Conversion to the carboxylic acid 166 by nucleophilic demercuration and subsequent esterification of 166 with diazomethane proceeded smoothly. Literature yields for these

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reactions are described on p 64 of this dissertation. Ester 167 has also been prepared from 166 by alkylation of the silver salt with methyl iodide.\textsuperscript{143}

![Chemical reactions and structures](image)

**Stille Couplings: Results andDiscussion**

With two organostannanes and two iodonaphthalenes in hand, we set out to perform Stille couplings. Unfortunately, cyclopentadienylstannane 199 failed to give coupling products in reaction with ester substrate 167 under a variety of reaction conditions. The products of these reactions were recovered iodide 167 and the reduction product 211 (eq 54). The pathway by which 211 is produced is uncertain. We also observed that in the reaction of 167 with lithium cyclopentadienylcyanocuprate, a similar

mixture of 167 and 211 was obtained. Reaction of 167 with cyclopentadienylcopper dimethyl sulfide (186a) yielded a complex mixture of products. Discouraged by these results, we decided to abandon the cyclopentadienyl reagents and instead investigate coupling reactions using cyclopentenylstannane 204.

Treatment of aldehyde 109 with cyclopentenylstannane 204 under Stille coupling conditions (eq 55) produced a surprising product: ketone 212! How did this ketone, and not the expected aldehyde 213, form? Several mechanistic pathways which may account for the formation of ketone 212 are outlined below. As shown in the top section of the scheme, oxidative addition of palladium (0) could occur at the naphthalene-iodine bond to generate the naphthylpalladium species 214. At this point, we envision two

\[ \text{MeO}_2\text{C} \quad \text{I} \quad \text{Pd(0) or Pd(II) catalyst} \quad \text{THF, DMF, or dioxane} \quad \Delta, 18-36 \, \text{h} \quad 167 \quad + \quad 199 \quad \rightarrow \quad 167 + 211 \quad (54) \]

\[ \text{CHO} \quad \text{I} \quad \text{SnBu}_3 \quad \text{1.4 equiv} \quad \text{2.5 mol % Pd}_2(\text{dba})_3 \quad \text{10 mol% PdAs} \quad \text{NMP, 65 °C, 3 h} \quad 212 \quad \text{50%} \quad \star \quad 213 \quad (55) \]

\[ \text{MeO}_2\text{C} \quad \text{I} \quad \text{Pd(0) or Pd(II) catalyst} \quad \text{THF, DMF, or dioxane} \quad \Delta, 18-36 \, \text{h} \quad 167 + 211 \quad (54) \]

\[ \text{CHO} \quad \text{I} \quad \text{SnBu}_3 \quad \text{1.4 equiv} \quad \text{2.5 mol % Pd}_2(\text{dba})_3 \quad \text{10 mol% PdAs} \quad \text{NMP, 65 °C, 3 h} \quad 212 \quad \text{50%} \quad \star \quad 213 \quad (55) \]

\[ \text{MeO}_2\text{C} \quad \text{I} \quad \text{Pd(0) or Pd(II) catalyst} \quad \text{THF, DMF, or dioxane} \quad \Delta, 18-36 \, \text{h} \quad 167 + 211 \quad (54) \]

\[ \text{CHO} \quad \text{I} \quad \text{SnBu}_3 \quad \text{1.4 equiv} \quad \text{2.5 mol % Pd}_2(\text{dba})_3 \quad \text{10 mol% PdAs} \quad \text{NMP, 65 °C, 3 h} \quad 212 \quad \text{50%} \quad \star \quad 213 \quad (55) \]

\[ \text{MeO}_2\text{C} \quad \text{I} \quad \text{Pd(0) or Pd(II) catalyst} \quad \text{THF, DMF, or dioxane} \quad \Delta, 18-36 \, \text{h} \quad 167 + 211 \quad (54) \]

\[ \text{CHO} \quad \text{I} \quad \text{SnBu}_3 \quad \text{1.4 equiv} \quad \text{2.5 mol % Pd}_2(\text{dba})_3 \quad \text{10 mol% PdAs} \quad \text{NMP, 65 °C, 3 h} \quad 212 \quad \text{50%} \quad \star \quad 213 \quad (55) \]

\[ \text{MeO}_2\text{C} \quad \text{I} \quad \text{Pd(0) or Pd(II) catalyst} \quad \text{THF, DMF, or dioxane} \quad \Delta, 18-36 \, \text{h} \quad 167 + 211 \quad (54) \]

\[ \text{CHO} \quad \text{I} \quad \text{SnBu}_3 \quad \text{1.4 equiv} \quad \text{2.5 mol % Pd}_2(\text{dba})_3 \quad \text{10 mol% PdAs} \quad \text{NMP, 65 °C, 3 h} \quad 212 \quad \text{50%} \quad \star \quad 213 \quad (55) \]

---

\[ ^{144} \text{The structure was assigned by comparison of its } ^1\text{H, } ^{13}\text{C, and IR spectra to that of phenyl-1-cyclopentenylketone, prepared by Smith and coworkers: Smith, A. B.; Agosta, W. C. J. Am. Chem. Soc. 1973, 95, 1961.} \]
possibilities: the carbonyl oxygen may coordinate to the palladium, displacing one the ligands as depicted in structure 215, or instead, 214 may undergo transmetallation with stannane 204 to produce 218. Migratory insertion would then produce the bridged species 216. This intermediate could also arise from 215 by 1,2-addition of the cyclopentenylstannane to the activated carbonyl group. β-Hydride elimination would then produce palladium hydride 217, which would undergo reductive elimination to afford the ketone product 212.

The bottom section of the scheme presents an alternate and less likely mechanism which begins with oxidative addition of palladium (0) at the aldehyde C-H bond rather than at iodine to produce 219. Reaction of 219 with 204 would produce tributyltin hydride and the diorganopalladium species 220, from which palladium can reductively eliminate. Oxidative addition at the naphthyl-iodine bond and reaction with tributyltin
hydride then leads to intermediate 217, which as described above can undergo reductive elimination to produce ketone 212.

Stille couplings with substrates containing aldehydes are not uncommon and generally proceed without complications. In substrate 109 the iodine and aldehyde groups are peri to each other, and their close proximity is probably related to the surprising reactivity in our Stille coupling. The late, great, oft-quoted R. B. Woodward once said that "enforced propinquity often leads to greater intimacy." How right he was!

In contrast to reaction of iodo aldehyde 109, Stille coupling of ester 167 with stannane 204 proceeded as anticipated to produce cyclopentene 222 in good yield. We employed the reaction conditions recommended by Farina\textsuperscript{126c} and found that a 2:1 ratio of ligand to palladium was preferable to a 4:1 ratio. Excess stannane was employed; recall that stannane 204 was available in only ca. 90-95% purity. The reaction mixture was submitted to an aqueous potassium fluoride workup to remove tin byproducts. Although this reaction also gave several byproducts, ester 222 was easily isolated in good yield using column chromatography on silica gel.

Oxidation of the cyclopentene moiety to a cyclopentadiene and reduction of the ester to an aldehyde were the remaining tasks in our route to substrate 111. These functional group manipulations proved to be more taxing than we had planned. Our efforts to prepare 111 from 222 are described in the next chapter.

\textsuperscript{145} Woodward, R. B. Pure Appl. Chem. 1968, 17, 519.
The preparation of fulvene precursor 111 from 222 presented an interesting synthetic challenge. The functional group manipulations were simple in theory: we needed to reduce the methyl ester to an aldehyde and to oxidize the cyclopentenyl moiety to a cyclopentadiene. In the laboratory, however, these transformations were complicated by the close proximity of the ester and cyclopentene. The peri relationship of these substituents is in some ways a double-edged sword. While we believed that the close alignment of the aldehyde and cyclopentadiene moieties in 111 would facilitate the key fulvene-forming condensation, in the end reactions between these peri substituents contributed to our difficulty in successfully achieving the synthesis of cyclopenta[a]phenalene (4) by way of the "condensation strategy".
Strategies for the Conversion of Cyclopentene 222 to Cyclopentadiene 223

We decided to oxidize the cyclopentene moiety before reducing the ester, and a survey of the literature revealed two main strategies for the preparation of dienes from alkenes. One popular method employs standard electrophilic addition\textsuperscript{146} of bromine across the olefin followed by double dehydrohalogenation (eq 56), while a second approach is based on allylic oxidation\textsuperscript{147} of the alkene followed by elimination (eq 57).

\begin{equation}
\begin{array}{c}
\text{R} \\
\text{224} \\
\text{H} \\
\text{Br} \\
\text{225} \\
\text{Br} \\
\text{R} \\
\text{226} \\
\end{array}
\end{equation}

\begin{equation}
\begin{array}{c}
\text{R} \\
\text{224} \\
\text{X} \\
\text{227} \\
\text{and/or} \\
\text{X} \\
\text{228} \\
\text{-HX} \\
\text{226} \\
\end{array}
\end{equation}

For the classic alkene bromination reaction required in the first strategy, many reagent systems in addition to elemental bromine have been reported. Barili and coworkers surveyed the reaction of many brominating agents such as bromine and pyridine perbromide with 1-phenylcyclohexene and observed the formation of a variety of

\textsuperscript{146}\textsuperscript{For a review of electrophilic additions to alkenes, see:
products, including allylic bromides and tribromides. Olah reported a reagent system using hydrogen bromide and hydrogen peroxide with phase transfer catalysis and claimed that this system is more environmentally sound than elemental bromine. Methods using bromination reagents bound to solid-supports have also been reported.

Close literature precedent for allylic oxidation of systems similar to 222 was encouraging with regard to the second approach we envisioned. Hart and Ghosh reported the preparation of cyclopentadienylbenzene (231) by oxidation of 1-phenylcyclopentene with selenium dioxide followed by dehydration with copper sulfate (eq 58). Cyclopentadiene 231 was trapped as the Diels-Alder adduct with maleic anhydride. Compound 231 is reported to be moderately susceptible to polymerization at room temperature but is stable to storage at 0 °C for long periods. 1-Cyclopentadienylnapththalene has been prepared as a mixture of isomers by allylic bromination of 1-naphthylcyclopentene followed by dehydrohalogenation with triethylamine (eq 59).

\[
\text{Cyclopentadienylbenzene (231) preparation:}
\]

Before attempting to oxidize our ester substrate 222, we tested a variety of bromination conditions using 1-cyclopentenynaphthalene (223) as a model system. Model substrate 223 was prepared by addition of naphthylmagnesium bromide to cyclopentanone and subsequent dehydration. Treatment of 223 with excess bromine in chloroform gave the expected allylic bromide 236 in nearly quantitative yield (eq 60).

\[
\begin{align*}
\text{223} &\xrightarrow{1.5 \text{ equiv } \text{Br}_2} \text{236} \\
\text{CHCl}_3, 0 \degree \text{C} \rightarrow \text{rt, 15 min} &\xrightarrow{100\%}
\end{align*}
\]

As shown below, we then exposed the ester substrate 222 to the same reaction conditions and obtained not the allylic bromide 238 but lactone 237. This lactone arises from reaction of the carbonyl oxygen with the intermediate bromonium ion (239) in a textbook halolactonization reaction. This is an example of the interesting reactions that can occur when two substituents are in close proximity to each other, as they are in peri-substituted 208.

The structure of lactone 237 was determined by analysis of $^1$H, $^{13}$C, and IR spectra. No evidence for a methyl ester was found. The carbonyl peak in the IR spectrum of 239 was at 1725 cm$^{-1}$, as expected for lactone 237. Because there is a single clean triplet signal for the hydrogen adjacent to the bromine, we believe that only one diastereomer of 107 was obtained, and we assign the stereochemistry of 237 as shown based on the assumption that the lactone forms via cyclization of the bromonium ion 239.

Undaunted by this unexpected cyclization, we decided to forge onward with lactone 237 rather than to wage a battle against the peri interactions. Reevaluation of our synthetic plan was necessary because the lactone linkage would need to be fragmented at some point. Our revised plan, as shown below, involved dehydrohalogenation of 237 followed by reduction of the lactone moiety to produce lactol 241, which could be converted to the corresponding acetal (242) if necessary. We anticipated that ionization of 241 (or 242) would generate an oxonium ion that would undergo fragmentation and then elimination to produce our target fulvene condensation substrate 111. We hoped this transformation might even be possible under conditions that would bring about the desired fulvene-forming condensation in the same operation! An alternative plan called for reductive elimination of the bromo acetal 244. In this plan, the allylic substituent X (e.g. Br), would have to be introduced (240 → 243) before reduction of the lactone.
Preparation of Lactone 240 by Dehydrohalogenation of Bromide 237

After studying the literature on the formation of alkenes by dehydrohalogenation, we chose to use 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to perform the elimination of hydrogen bromide from 220. DBU is a bicyclic amidine which acts as a non-nucleophilic, efficient dehydrohalogenating agent. Treatment of 237 with 2 equivalents of DBU in refluxing toluene produced lactone 240 in good yield (eq 61). This reaction was slow, and was not complete by TLC analysis even after 7 days, but was extremely clean. Lactone 240 is a stable, white crystalline solid and proved to be a reliable synthetic intermediate.

For reviews of alkene formation by elimination, see:
(c) Bachiocchi, E. Acc. Chem. Res. 1979, 198.
Seeking a faster elimination reaction, we explored the chemistry of the iodine derivative. We were optimistic that the rate of the elimination process would be improved, as we had noted Jager's report that the elimination of HI from spiro-fused dilactone system 245 with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) required a reaction time of only 20 min at 60 °C (eq 62). As shown below, we prepared iodide 247 in poor yield by iodolactonization of ester 222. Despite the fact that iodide is a better leaving group than bromide, dehydroiodination of 247 was still a slow process. Thus iodine intermediate 247, which we had found to be more difficult to prepare than bromide 237, offered little advantage for the preparation of 240.
We planned to reduce lactone 240 to the lactol 241 and then to effect elimination of water to produce the desired substrate 111, as depicted above. Partial reduction of the lactone proved to be very facile. Many reducing agents, including metal alkoxyaluminum hydrides,\textsuperscript{158} alkoxyaluminohydrides,\textsuperscript{159} and diisobutylaluminum hydride (DIBAL)\textsuperscript{160} have been employed for the partial reduction of lactones. Reduction of lactone 223 with 2.0 equiv of DIBAL in methylene chloride at low temperature produced a ca. 2:1 mixture of the diastereomeric lactols 241a and 241b in 80\% yield (eq 63).

We now wished to perform a fragmentative dehydration reaction of the mixture of lactols 241a and 241b to produce the condensation substrate 111. Examination of the


The literature on reactions of lactols\textsuperscript{161,162} revealed little precedent for this type of transformation; however, an interesting related result was reported by Frankin in 1981. As depicted below, base-catalyzed condensation of $\beta$-cyclocitral (248) and benzaldehyde (249) yielded a mixture of products which included hemiacetal 250 and benzopyran 251 (eq 64).\textsuperscript{163} Benzopyran 251 is thought to arise from base-catalyzed dehydration of 250.

A second transformation of interest from the literature was reported in 1995 by Kohmoto and coworkers. As shown below, acid-catalyzed dehydration of norcaradienyl hemiacetal 253 followed by aromatization on alumina led to the formation of benzopyran 254 in good yield.\textsuperscript{164} The dehydration-fragmentation reaction is thought to proceed by formation of an oxonium ion (255) and regioselective cleavage of the cyclopropane to give compound 256.


\textsuperscript{162}See also, for the preparation of tetrahydropyrans, dihydropyrans, and pyrans: Baumeier, G.; Dittus, G.; Muller, E. In \textit{Methoden der Organischen Chemie (Houben-Weyl)}; Kropf, H., Ed.; Georg Thieme Verlag: Stuttgart, 1966, Vol. IV/4, pp 331-442.

\textsuperscript{163}Frank, A. W. \textit{J. Heterocycl. Chem.} 1981, 549.

Keeping the aforementioned examples of lactol dehydrations in mind, we looked into general methods for dehydration of alcohols to prepare alkenes\textsuperscript{165} and for dehydration of allylic alcohols to form dienes. We recognized that the cyclopentadienyl moiety of the desired product 111 could undergo Diels-Alder dimerization or related reactions, and sought mild reaction conditions which would curtail such side reactions. Some of our attempts to dehydrate 241 are listed in Table 11. In addition to treatment of 241 with acid under the conditions for an E\textsubscript{1} elimination, we attempted to functionalize the lactol hydroxyl group as a tosylate, mesylate, triflate, and acetate derivative. A complicating factor in these reactions is the equilibrium between cyclic hemiacetal 241 and the aldehyde (257) (eq 65).\textsuperscript{166}


Our desired reaction could be a stepwise process in which the first step is an ionization reaction which affords an oxygen-stabilized carbocation, as shown below:

![Chemical structure](image)

Table 11. Attempted Dehydration of Lactol 241

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^{167})</td>
<td>0.1 equiv PPTS</td>
<td>brown solid; polymeric material</td>
</tr>
<tr>
<td></td>
<td>dichloroethane, Δ, 1 h</td>
<td></td>
</tr>
<tr>
<td>2(^{168})</td>
<td>2.4 equiv TsCl</td>
<td>25% yield of lactone 223</td>
</tr>
<tr>
<td></td>
<td>pyridine</td>
<td></td>
</tr>
<tr>
<td>3(^{169})</td>
<td>5.0 equiv Et3N</td>
<td>complex mixture of products</td>
</tr>
<tr>
<td></td>
<td>2.0 equiv MsCl, THF, 0 °C</td>
<td></td>
</tr>
<tr>
<td></td>
<td>then 2.0 equiv DBU, PhMe, Δ</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.0 equiv MeLi</td>
<td>complex mixture of products</td>
</tr>
<tr>
<td></td>
<td>1.0 equiv MsCl, THF, -40 °C</td>
<td></td>
</tr>
<tr>
<td></td>
<td>then 2.0 equiv LDA, -30 °C, 1 h</td>
<td></td>
</tr>
</tbody>
</table>


Table 11. Attempted Dehydration of Lactol 241 (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>5170</td>
<td>2.0 equiv Et$_3$N</td>
<td>50% recovered starting material</td>
</tr>
<tr>
<td></td>
<td>1.5 equiv MsCl, CH$_2$Cl$_2$, 0 °C, 3 h</td>
<td>20% mass recovery of decomposition products</td>
</tr>
<tr>
<td></td>
<td>then 1.5 equiv i-Pr$_2$NEt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HMPA, 180 °C, 20 min</td>
<td></td>
</tr>
<tr>
<td>6171</td>
<td>4.5 equiv lutidine</td>
<td>complex mixture of products</td>
</tr>
<tr>
<td></td>
<td>1.0 equiv Tf$_2$O</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CH$_2$Cl$_2$, 0 °C</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>6.0 equiv pyrrolidone</td>
<td>complex mixture of products</td>
</tr>
<tr>
<td></td>
<td>1.2 equiv N-(5-chloro-2-pyridyl)triflimide</td>
<td></td>
</tr>
<tr>
<td>8172</td>
<td>1.2 equiv Ac$_2$O</td>
<td>complex mixture of products</td>
</tr>
<tr>
<td></td>
<td>pyridine, rt, 18 h</td>
<td></td>
</tr>
<tr>
<td>9173</td>
<td>2.0 equiv t-BuOK</td>
<td>50% yield of lactone 223</td>
</tr>
<tr>
<td></td>
<td>DMSO, 40 °C, 18 h</td>
<td></td>
</tr>
<tr>
<td>10174</td>
<td>excess DMSO</td>
<td>decomposition to black tar</td>
</tr>
<tr>
<td></td>
<td>170 °C, 10 min</td>
<td></td>
</tr>
<tr>
<td>11175</td>
<td>3 equiv MTPI</td>
<td>decomposition to black-colored complex mixture</td>
</tr>
<tr>
<td></td>
<td>HMPA, rt, 30 min</td>
<td></td>
</tr>
<tr>
<td>12176</td>
<td>1.2 equiv Burgess reagent</td>
<td>poor mass recovery of a high Rf material; complex $^1$H NMR</td>
</tr>
<tr>
<td></td>
<td>PhH, Δ, 3 h</td>
<td></td>
</tr>
</tbody>
</table>

As indicated in Table 11, all of these dehydration attempts were unsuccessful. Under acidic conditions (entry 1), decomposition occurred. Attempts to convert the lactol hydroxyl group to a leaving group either led to decomposition (entries 3 through 8) or oxidation to the lactone (entries 2, 3, and 9). Methyltriphenoxy-phosphonium iodide (MTPI) (entry 11) is reported to effect E$_2$ eliminations of primary and secondary alcohols.

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172 Zhdanov, R. I.; Zhenodarova, S. M. *Synthesis* 1975, 222.
in HMPA,\textsuperscript{177} but it caused lactol 241 to decompose. The Burgess reagent (entry 12), (methoxycarbonylsulfamoyl)triethylammonium hydroxide (259), is a versatile dehydrating reagent for secondary and tertiary alcohols.\textsuperscript{178} As depicted below, in a prototypical dehydration with this reagent the hydroxyl group of a substrate displaces triethylamine to form the activated sulfamoyl derivative 260, which undergoes elimination to form an olefin. Burgess established that the reaction proceeds with cis-stereospecificity after studying eliminations to form stilbene derivatives,\textsuperscript{176b} but Caspi has observed a trans elimination product from the reaction of 259 with a steroid derivative.\textsuperscript{179} The Burgess reagent is commercially available, but we prepared it from chlorosulfonyl isocyanate following a facile, two-step literature procedure.\textsuperscript{180} However, reaction of 259 with the lactol mixture failed to produce 111.

\begin{equation}
\text{C}=\text{C}+\text{OSO}_2\text{NHCO}_2\text{Me} + \text{HNEt}_2
\end{equation}

An Alternative Strategy for Olefin Synthesis: Reductive Elimination of XOMe

The next strategy we examined for the preparation of 111 as depicted in the above scheme is derived from the well-known reductive elimination of β-haloethers to form olefins (eq 66). This process, which is known as the Boord reaction, tolerates a wide variety of substrates and can be effected with a variety of metals, including zinc, magnesium, and sodium. The Boord reaction has been used to synthesize dienes, including 1,4-pentadiene from bromoether 264 (eq 67). We hoped to perform a reaction in which XOMe is eliminated across the ether bridge of 244 to produce cyclopentadiene 111, as shown above. An interesting example of a similar fragmentation reaction was reported by Kochetkov and coworkers (eq 68).

Preparation of our desired substrate was easily accomplished, as shown below. Allylic bromination of lactone 240 using N-bromosuccinimide with benzoyl peroxide as initiator produced a ca 3:1 mixture of diastereomers 243a and 243b in excellent yield.

---


(eq 69). The major isomer could be separated from the minor isomer by careful column chromatography on silica gel, but 243a and 243b interconverted upon prolonged storage.

The major isomer 243a and minor isomer 243b were assigned based on analysis of $^1$H NMR chemical shift data. In the major isomer 243a, the chemical shifts of $H_b$ and $H_c$ differ by ca. 0.5 ppm. This makes sense because $H_b$ and $H_c$ are in quite different environments. $H_b$ is nearly eclipsed with both the bromine atom and the lactone oxygen atom, while $H_c$ has a dihedral angle of ca 60° with respect to both heteroatoms. In the minor isomer 243b, $H_b$ and $H_c$ have virtually the same chemical shift because both protons have similar interactions with the neighboring heteroatoms.

<table>
<thead>
<tr>
<th>Proton</th>
<th>$\delta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_a$</td>
<td>5.24-5.28</td>
</tr>
<tr>
<td>$H_b$</td>
<td>3.33</td>
</tr>
<tr>
<td>$H_c$</td>
<td>2.81</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Proton</th>
<th>$\delta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_a$</td>
<td>5.09-5.11</td>
</tr>
<tr>
<td>$H_b$</td>
<td>3.08</td>
</tr>
<tr>
<td>$H_c$</td>
<td>3.08</td>
</tr>
</tbody>
</table>
As shown below, reduction of lactone 243a with DIBAL produced mixtures of lactols 244a and 244b. These lactols were unstable compounds, but we found that conversion to the corresponding methyl acetals 245a and 245b immediately after workup of the DIBAL reaction proceeded smoothly using methanol and catalytic BF$_3$·OEt$_2$.\textsuperscript{185} Analogous reactions were carried out on the minor isomer 226b.

We then made several attempts to perform a reductive elimination of MeOBr from 245a and 245b, and 245c and 245d. A summary of these experiments is shown in Table 12. The desired product, cyclopentadiene 111, was not detected in any of these small-scale reactions. A mixture of 245a and 245b, derived from the major isomer of the allylic bromide, was used in most of the experiments. Eliminations of β-haloethers with zinc and lithium have been shown to be non-stereospecific,\textsuperscript{186a, 191} and thus any of the four isomers should have had the potential to undergo the desired elimination reaction.

Table 12. Attempted Reductive Eliminations of Acetals 245a/245b and 245c/245d

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactants</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
</table>
| 1<sup>186</sup> | major | excess Zn dust<sup>187</sup>  
EtOH-H<sub>2</sub>O, Δ, 1 h | low yield of two unidentified diastereomeric products |
| 2 | minor | same | similar products to 1 |
| 3<sup>188</sup> | major | Na, i-Pr<sub>2</sub>O, Δ, 1 h | no reaction |
| 4<sup>189</sup> | major | 3 equiv n-BuLi  
THF, -78 °C, 2 h | protonated product 251 |
| 5<sup>190</sup> | major | 2 equiv LiDBB  
THF, -78 °C, 10 min | decomposition |
| 6<sup>191</sup> | major | 2 equiv Li/NH<sub>3</sub> | decomposition |

We found that these reactions gave either complex mixtures of products, decomposition, or acetal 268, which is thought to arise from protonation of the alkyllithium intermediate before fragmentation. Lithium <i>di-tert</i>-butylbiphenyl (LiDBB) (entry 5) is a lithium radical anion reagent introduced by Freeman<sup>190</sup>. This reagent has the advantage of being soluble in THF and has been used to generate alkyllithium reagents from the corresponding halides. <i>Di-tert</i>-butylbiphenyl (DBB) was prepared by


<sup>187</sup>The zinc dust was activated by treatment with aqueous HCl. See: Fieser, L. F.; Johnson, W. S. <i>J. Am. Chem. Soc.</i> 1940, 62, 575.


Friedel-Crafts reaction of biphenyl according to a literature procedure.\textsuperscript{192} Sadly, we observed decomposition of the starting materials upon treatment with LiDBB.

![Chemical Structure](image)

In light of the poor results obtained in attempted reductive elimination reactions of acetals 245, coupled with the relatively long route (seven steps) for the preparation of acetals 245, we abandoned this route to the preparation of 111. In the remainder of this chapter we will discuss another strategy employed to prepare the elusive substrate 111.

**Carboxylate as a Leaving Group**

In contrast to the elimination strategies discussed above, in this route our aim was to have carboxylate as the leaving group. Thus treatment of 240 with a strong base or reaction of 243 under the conditions for lithium-halogen exchange or metal insertion reaction was envisioned to produce intermediate 269 after elimination of carboxylate. Protonation of 269 would yield the carboxylic acid 270, and reduction of the acid was expected to provide the desired aldehyde 111.

We attempted to use "super" bases for deprotonation of the spirocyclopentenyl system. Reaction of 240 with the ternary complex n-BuLi-t-BuOK-TMEDA\textsuperscript{193} in hexane produced vinyl ether 271, which arises from addition of \( n \)-butyllithium to the lactone carbonyl and subsequent dehydration. Similarly, 271 was obtained from treatment of 240 with \( n \)-BuLi-t-BuOK complex.\textsuperscript{194}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{reaction_diagram}
\caption{Deprotonation reaction of spirocyclopentenyl system with super bases.}
\end{figure}


\textsuperscript{194} Ref. 191, pp 52-53.
Reaction of allylic bromide 244 with n-butyllithium, sodium metal, and Zn dust produced various poor results which are summarized in Table 13.

Table 13. Attempted Elimination Reactions of Allylic Bromide 244

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 equiv n-BuLi</td>
<td>incorporation of butyl group</td>
</tr>
<tr>
<td></td>
<td>Et₂O, -78 °C, 1.5 h</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3 equiv Na</td>
<td>no reaction</td>
</tr>
<tr>
<td></td>
<td>i-Pr₂O, Δ, 18 h</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>50 equiv Zn dust</td>
<td>incorporation of ethoxy group</td>
</tr>
<tr>
<td></td>
<td>EtOH-H₂O, Δ, 2 d</td>
<td></td>
</tr>
</tbody>
</table>

With some regret we abandoned the general approach using a fulvene formation reaction for the synthesis of cyclopenta[a]phenalene 4. Despite the investment of much effort towards the preparation of the aldehyde-cyclopentadiene substrate 111, this compound was never isolated, and we were never able to attempt the intramolecular condensation reaction. We next began work on an exciting, entirely different strategy for the synthesis of 4 using Pauson-Khand chemistry to assemble the skeleton of 4. This work is described in Part Four.
Part IV

The Pauson-Khand Approach
In our third approach for the synthesis of cyclopenta[a]phenalene (4), we planned to construct the A and B rings of the system simultaneously in an intramolecular Pauson-Khand reaction (113 → 112). In contrast to the approaches described earlier, this strategy creates the carbon framework of target molecule 4 early in the synthetic route. We envisioned that the Pauson-Khand substrate, enyne 113, could be rapidly assembled from 1,8-diiodonaphthalene (120). Functional group modification of the Pauson-Khand product 112 was anticipated to furnish cyclopenta[a]phenalene (4). We recognized that a dihydrocyclopenta[a]phenalene molecule such as 272 might be an intermediate in the preparation of 4 from 112 and hoped that dehydrogenation of 272 would be a facile process.
The Pauson-Khand Reaction

The Pauson-Khand reaction\textsuperscript{195} is formally a [2+2+1] cycloaddition reaction in which an alkyne, an alkene, and carbon monoxide undergo a co-cycloaddition process to produce a cyclopentenone (eq 70). The reaction was discovered in 1973 by P. L. Pauson and I. U. Khand as a result of work involving the preparation of cobalt complexes of alkenes and alkynes.\textsuperscript{196} A wide variety of substrates participates in the Pauson-Khand reaction, and the cycloaddition products are typically obtained in 40-60% yield. Many examples of intramolecular Pauson-Khand reactions for the generation of bicyclic systems have been reported.

\begin{equation}
R^1\equiv R^2 + R^3 = R^6 \xrightarrow{\text{Co}_2(\text{CO})_{12}} \text{R}^1\text{R}^2\text{R}^3\text{R}^4\text{R}^5\text{R}^6 \tag{70}
\end{equation}

The mechanism of the Pauson-Khand reaction, as depicted in the scheme below, first involves formation of a complex between the alkyne and the commercially available cobalt reagent, dicobalt octacarbonyl. It is believed that next, a carbon monoxide (CO) molecule dissociates from one of the cobalt atoms and the alkene coordinates to cobalt at this open coordination site, reversibly forming a complex such as 277. Insertion of the olefin into a cobalt-carbon bond, with addition of CO to the coordinately unsaturated cobalt atom, then forms 278 in what is believed to be the rate-determining step.

\textsuperscript{195} For reviews of the Pauson-Khand reaction, see:

Migratory insertion of CO and reductive elimination of Co(CO)₃ produces ketone 280, and loss of Co₂(CO)₆ from 280 produces the cyclopentenone product 281.

The standard procedure for an intermolecular Pauson-Khand reaction first involves formation of the Co₂(CO)₆ complex of the alkyne by stirring the alkyne with one equivalent of Co₂(CO)₈ at room temperature for 2-4 hours in a hydrocarbon or ethereal solvent. The alkene is then added and the resulting reaction mixture is heated under inert or CO atmosphere. Use of a sealed tube is convenient for this procedure.

Some modifications to the standard procedure include the addition of phosphine oxide to the reaction mixture and sonication of the mixture, but mixed results have been obtained.¹⁹⁷ "Dry state" adsorption conditions, in which the reactants are applied to an adsorbent such as silica gel have been reported to improve the yield of the Pauson-Khand

reaction, particularly for substrates which bear a free or protected hydroxyl group. Tertiary amine oxides such as N-methylmorpholine-N-oxide (NMO) and trimethylamine N-oxide (TMANO) have been reported to accelerate the Pauson-Khand reaction. Pauson-Khand reactions which are run using tertiary amine oxide promotion have the advantage of lower reaction temperatures (these reactions typically are run at room temperature), and the reported yields of the reaction using this method are good to excellent. The tertiary amine oxides are believed to promote decarbonylation of cobalt by oxidation of CO to CO₂, thus creating a site for alkene coordination to cobalt.

Reaction conditions requiring catalytic rather than a stoichiometric amount of dicobalt octacarbonyl (274) for intramolecular Pauson-Khand reactions were reported by Jeong and coworkers in 1994, but the reaction conditions were rather harsh (4-5 atm pressure of CO, 3-5 mol % of Co₂(CO)₈, and 10-20 mol % of (PhO)₃P at 120 °C). Very recently, Pagenkopf and Livingstone reported that photochemically promoted Pauson-Khand reactions employing 5 mol % of Co₂(CO)₈ required only mild heating (50-55 °C) and 1 atm pressure of CO. The source of high-intensity visible light in these reactions was a Q-Beam spotlight. The authors of this report also found that reactions employing recrystallized cobalt reagent 274 show improved yields.

For construction of the carbon skeleton of 4, we considered investigating both intermolecular and intramolecular Pauson-Khand reactions as shown in the following scheme. The intramolecular reaction of enyne 113 was expected to give cyclopentenone 112, which we planned to convert to cyclopenta[a]phenalene by functional group manipulation. As discussed above, many examples of intramolecular Pauson-Khand reactions, particularly for the synthesis of 5,5-bicyclic systems, have been reported.

Equation 71 depicts an example of an intramolecular Pauson-Khand reaction reported by Magnus and coworkers.\textsuperscript{203} Note that the reaction of enyne 283 was performed under standard thermal conditions and that a mixture of diastereomers 284 and 285 were formed in an approximately 3:1 ratio.

Literature precedent for the planned intermolecular Pauson-Khand reaction of phenalene (24) with acetylene was less encouraging. Although cyclic alkenes tend to undergo the Pauson-Khand reaction in good yield, the best substrates are polycyclic

\textsuperscript{203}For example, see Magnus, P.; Exon, C.; Albaugh-Robertson, P. Tetrahedron 1985, 41, 5861.
molecules bearing strained alkenes. Modest yields were observed in Pauson-Khand reactions of dihydronaphthalene (286)\textsuperscript{204} and acenaphthene (121)\textsuperscript{205} with cobalt complexes of propyne and phenylacetylene under thermal conditions (eqs 72 and 73). Note that the reactions are regioselective with respect to both the alkene and alkyne counterparts.

\begin{equation}
\text{Me}_{\text{CO}}\text{C}_{\text{C}}\text{H}_{\text{C}}\text{O}
\end{equation}

\begin{equation}
\text{Ph}_{\text{C}}\text{C}_{\text{H}}\text{O}
\end{equation}

\begin{equation}
\text{Me}
\end{equation}

\begin{equation}
\text{35%}
\end{equation}

\begin{equation}
\text{121}
\end{equation}

\begin{equation}
\text{287}
\end{equation}

\begin{equation}
\text{288}
\end{equation}

\begin{equation}
\text{289}
\end{equation}

\begin{equation}
\text{38%}
\end{equation}

\begin{equation}
\text{290}
\end{equation}

\begin{equation}
\text{72}
\end{equation}

\begin{equation}
\text{73}
\end{equation}

\begin{equation}
\text{120}
\end{equation}

\begin{equation}
\text{113}
\end{equation}

\textbf{Preparation of Enyne 113, A Substrate for a Pauson-Khand Reaction}

Enyne 113 was prepared in three steps from 1,8-diiodonaphthalene (120) according to the above scheme. Monolithiation of 120 following the procedure described

\textsuperscript{204}\text{Khand, I. U.; Murphy, E.; Pauson, P. L. J. Chem. Res. (S) 1978, 350.}


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by Katz\textsuperscript{35} and alkylation of the monolithio intermediate with allyl iodide which was generated \textit{in situ} by reaction of allyl bromide with sodium iodide afforded iodide 291 in moderate yield (eq 74). The major byproduct of this reaction was 1-iodonaphthalene, which is believed to result from protonation of the monolithium intermediate. Iodide 291 could be separated from 1-iodonaphthalene by column chromatography on silica gel.

The alkynynaphthalene 292 was prepared from iodide 291 using the Sonogashira modification\textsuperscript{206,207} of the Castro-Stephens reaction. After systematic variation of the palladium catalyst, the ratio of palladium reagent to copper iodide, and the solvent, we found that the following conditions were optimal. Treatment of a mixture of iodide 291 and catalytic amounts of bis(triphenylphosphine)palladium (II) chloride and copper iodide (in a 1:2 ratio) with three one-equivalent portions of trimethylsilylacetylene\textsuperscript{209} produced alkyne 292 in 44-59\% yield (eq 75). We found that the sequential addition of trimethylsilylacetylene, a somewhat volatile liquid, improved the yields of this reaction from the ca. 30\% yield which was observed when a single portion of 1.5 equiv of the reagent was used. This reaction was run at room temperature; we found that heating the reaction mixture caused 291 to undergo a 5-exo intramolecular Heck reaction (eq 76).

\begin{center}
\includegraphics[width=\textwidth]{fig}
\end{center}

\begin{equation}
\text{1.05 equiv } n-\text{BuLi} \quad \text{Et}_2\text{O}, 0 \degree \text{C}, 30 \text{ min} \quad \text{then 1.5 equiv allyl bromide} \quad 0.5 \text{ equiv } \text{NaI} \quad 0 \degree \text{C} \to \text{rt}, 1 \text{ h} \quad 47-65\% \quad 120 \xrightarrow{\text{eq 74}} 291
\end{equation}

\begin{equation}
\end{equation}
We explored several different methods for the desilylation of 292. Upon treatment with two equivalents of potassium fluoride dihydrate in methanol at room temperature, no reaction of 292 was observed.\textsuperscript{210} Similarly, desilylation did not occur when 292 was treated with an aqueous solution of sodium borate in methanol at room temperature.\textsuperscript{211} Desilylation of the acetylene was finally accomplished by treatment of 292 with aqueous potassium hydroxide in methanol following the protocol described by Hagihara and coworkers.\textsuperscript{206b} Enyne 113 was obtained in excellent yield (eq 77), completing the preparation of intramolecular Pauson-Khand substrate in three steps from 1,8-diiodonaphthalene (120).

We also briefly investigated a Stille coupling of (tributylstannyl)acetylene with iodide 291 as an alternate route for the preparation of 113. This route at first glance would be one step shorter than the Sonogashira route because deprotection of the alkyne is unnecessary, but one must also consider that the alkynylstannane is not commercially available. (Tributylstannyl)acetylene was prepared in one step by alkylation of lithium acetylide with tributyltin chloride following a procedure reported by Seitz and coworkers.\textsuperscript{212} Reaction of the stannane with iodide 291 under the conditions of the Stille coupling reaction produced only a trace amount of the desired coupling product 113 (eq 78). The major product was the acenaphthene derivative 293, which resulted again from an intramolecular Heck reaction.

\begin{center}
\begin{tikzpicture}
\node at (0,0) {291};
\node at (2.5,0) {113 (trace)};
\node at (5,0) {293 (ca. 40\%)};
\node at (1,2) {0.025 equiv Pd\textsubscript{2}(dba)\textsubscript{3}};
\node at (1,1) {0.01 equiv (\textit{o}-tol)\textsubscript{3}P};
\node at (1,0) {1.0 equiv \text{SNBu\textsubscript{3}}};
\node at (1,-1) {NMP, 65 °C, 2 h};
\end{tikzpicture}
\end{center}

**Pauson-Khand Cycloadditions for the Synthesis of Cyclopenta[a]phenalene**

We next attempted to perform intramolecular Pauson-Khand reactions of both the enyne 113 and the corresponding silyl derivative 112, as well as the intermolecular Pauson-Khand reaction between phenalene (24) and acetylene. The intermolecular reaction (24 \rightarrow 295) was unsuccessful but both intramolecular reactions gave the desired Pauson-Khand products. The experimental details are discussed below.

We opted to test the intermolecular Pauson-Khand reaction of phenalene (24) with trimethylsilylacetylene (296) rather than acetylene simply because of the relative ease of working with the former alkyne, a liquid, compared to gaseous acetylene. Cobalt complex 297 was prepared simply by stirring trimethylsilylacetylene (296) with commercially available dicobalt octacarbonyl (274) in petroleum ether (eq 79). The complex was a stable, isolable dark maroon solid.
Reaction of cobalt complex 297 with phenalene (24) under a CO atmosphere in a resealable tube produced a complex mixture of products (eq 80), none of which was the desired enone 295. Column chromatography of the reaction mixture on silica gel produced small amounts of brightly colored, unidentifiable compounds.

Intramolecular Pauson-Khand reactions of the free alkyne 113 and its trimethylsilyl derivative 112 were investigated, in both cases with success! Magnus has reported two advantages associated with using terminal acetylenes protected as their trimethylsilyl derivatives for Pauson-Khand reactions. First, the bulk of the silyl group is reported to reduce the probability of oligomerization of the enyne substrate. Second, trimethylsilylacetylene substrates have been shown to undergo intramolecular Pauson-Khand reactions with greater stereoselectivities than substrates bearing less bulky acetylenes. For example, whereas the methyl-substituted acetylene 283 produced a ca. 3:1 mixture of diastereomers (eq 71, above), intramolecular Pauson-Khand reaction of the trimethylsilyl analog produced a 26:1 mixture of the corresponding cyclopentenone products. In our first-generation Pauson-Khand route, however, stereoselectivity is not an issue, as cyclopentenone 112 has only one chiral center.

Cyclization of the free alkyne 113 under thermal conditions proceeded in 48% yield (eq 81). In this reaction, enyne 113 was stirred with dicobalt octacarbonyl (274) in heptane under CO atmosphere at room temperature for 15 minutes to generate the cobalt-acetylene complex. The resulting dark brown solution was then immediately heated in a sealed tube for several hours at 120 °C. Cyclopentenone 112, an orange-brown solid, was easily isolated by chromatography on silica gel. Enone 112 has a carbonyl stretch in the infrared spectrum at 1720 cm⁻¹, and the chemical shift of the vinyl proton in the ¹H NMR spectrum is at 6.54 ppm. We were very excited to have prepared 112, because this was the first time we had assembled the carbon framework of 4!

We also prepared cyclopentenone 112 from enyne 113 following the N-methy morpholine-N-oxide (NMO) promotion conditions reported by Schreiber. In this procedure, treatment of substrate 113 with the Co$_2$(CO)$_8$ in methylene chloride produces the cobalt-alkyne complex. The resulting mixture was cooled to 0 °C, 1-2 equiv of NMO was added, and the heterogeneous mixture was stirred for approximately one hour at room temperature. The cycle of cooling to 0 °C, addition of NMO, and return to room temperature was repeated until four portions of NMO had been added. The promoter is added in portions because the rate of decarbonylation of cobalt may be faster than the rate of olefin insertion, and if decarbonylation occurs too rapidly, starting material, rather than cyclopentenone, may be obtained. Cyclopentenone 112 was obtained in very good yield (77%) under these NMO-promoted reaction conditions (eq 82).

Reaction of the trimethylsilyl-substituted substrate 292 under standard thermal conditions produced cyclopentenone 294 in 64% yield (eq 83). The yield of silylcyclopentenone 294 was significantly better than the yield of cyclopentenone 112.
under thermal conditions. In the infrared spectrum, cyclopentenone 294 showed a carbonyl stretch at 1685 cm\(^{-1}\).

Desilylation of vinylsilane 294 to produce 112 proved to be a surprisingly difficult reaction, despite good precedent for this transformation. Magnus has reported the desilylation of cyclopentenone 298 using aqueous methanesulfonic acid with heating (eq 84).\(^{203}\) Loebach and Danheiser have employed a methanolic solution of methanesulfonic acid for the desilylation of triisopropylsilyl-substituted cyclopentenone 300 (eq 85).\(^{214}\)

When silylcyclopentenone 294 was treated with excess, freshly distilled methanesulfonic acid in methanol at room temperature, no reaction was observed. Heating the reaction mixture to 70 °C for 19 h produced a trace of the desired product.

\(^{214}\)Loebach, J. L.; Danheiser, R. L. unpublished results.
112, but the majority of the starting material appeared to have undergone decomposition to form an intractable, dark purple solid! We therefore concluded that the best route for the preparation of 112 was via Pauson-Khand reaction of enyne 113 under the conditions of NMO promotion.

![Chemical structure](image)

**Strategies for the Preparation of Cyclopenta[a]phenalene from Cyclopentenone 112**

We devised a number of synthetic routes to cyclopenta[a]phenalene (4) from cyclopentenone 112, and some of these strategies are depicted in the following scheme.
In route a, 1,2-reduction of α,β-unsaturated ketone 112 followed by dehydration of the resultant allylic alcohol 302 is envisioned to produce a dihydrocyclopenta[a]phenalene such as 272. Other cyclopentadienyl isomers of 272 might also be obtained. Dehydrogenation of the dihydrocyclopenta[a]phenalene(s) would then produce our target molecule. Route b is an alternative strategy for the preparation of a dihydroaromatic precursor. In this route, enol triflate 303 is prepared from 112 and reductive cleavage of 303 would generate 272 or isomers thereof. This strategy would also provide access to C-9 substituted cyclopenta[a]phenalenes by transition metal-mediated cross-coupling reactions of enol triflate 303.

In contrast to routes a and b, route c circumvents dihydroaromatic precursors such as 272 and begins by benzylic oxidation of 112. This produces an intermediate of the type 304, in which X is a heterosubstituent such as bromine or hydroxyl. 1,2-Reduction of 304 followed by elimination of HX and water would produce cyclopenta[a]phenalene. Route c has potential complications in that intermediate 305 has three chiral centers, and several isomers of intermediate 305 are likely to be generated. We chose to explore route a first, and our work on this route is detailed in the following section.

Attempts to Prepare Cyclopenta[a]phenalene from 112 by a Reduction-Elimination-Aromatization Route

As summarized in the scheme below, we planned to perform a 1,2-reduction of enone 112 to produce allylic alcohol 302. We anticipated that a mixture of diastereomers might be obtained from the reduction reaction. Dehydration of allylic alcohol 302 would then be expected to afford a dihydrocyclopenta[a]phenalene such as 272, which upon dehydrogenation would lead to cyclopenta[a]phenalene (4).
A. 1,2-Reduction of Enone 112

With the goal of preparing allylic alcohol 302 from α,β-unsaturated ketone 112, we sought a reagent which would show good chemoselectivity for 1,2- rather than 1,4-reduction. Some reagents which have been reported to effect 1,2-reductions of enones include the combination of cerium (III) chloride and sodium borohydride developed by Luche,215 DIBAL,216 lithium aluminum hydride,217 and borane reagents218 such as 9-borabicyclo[3.3.1]nonane (9-BBN).219 We found that treatment of enone 112 with 1.2 equivalents of DIBAL in benzene at 0-5 °C followed by aqueous workup using a solution of Rochelle's salt produced a 16:1 mixture of allylic alcohols 302a and 302b as shiny orange-yellow flakes in excellent yield (eq 87). This reaction was extremely clean, and purification of the reaction mixture was not necessary.

\[
\text{112} \xrightarrow{1.2 \text{ equiv DIBAL, PhH, 0-5 °C, 10 min}} 302a + 302b (87) \quad (16:1)
\]

The stereochemical assignment of the structures of allylic alcohols 302a and 302b was based primarily on examples of DIBAL reductions of similar fused systems in the literature. Because DIBAL is a bulky hydride reagent, it typically adds to the convex face of polycyclic ketones. For example, Fiaud and Legros found that reduction of the enone shown below afforded the endo alcohol exclusively.\textsuperscript{216b} In the $^1$H NMR spectrum,

\[
\begin{align*}
\text{1.5 equiv DIBAL} & \quad \text{hexane, 0 °C, 2 h} \\
\text{65%}
\end{align*}
\]

the vinylic proton of major isomer 302a had a chemical shift of 6.19 ppm, while a broad hydroxyl stretch at 3330 cm$^{-1}$ was observed in the infrared spectrum.

Reduction of 112 following the method of Luche\textsuperscript{220} also predominantly produced allylic alcohol 302a, but with lower diastereoselectivity. As shown below, enone 112 when treated with cerium (III) chloride heptahydrate and sodium borohydride in methanol at 0 °C produced a 7:1 ratio of diastereomers 302a and 302b (eq 88). The reaction was slightly less clean than the DIBAL reduction, and the allylic alcohols 302a and 302b were contaminated with ca. 5% of unidentified byproducts.

\[
\begin{align*}
\text{1.0 equiv CeCl}_3\cdot7\text{H}_2\text{O} & \quad \text{5.0 equiv NaBH}_4 \\
\text{MeOH, 0 °C, 10 min} & \quad \text{ca. 95%}
\end{align*}
\]

\[302a + 302b \quad (7:1)\]

B. Attempts to Dehydrate Allylic Alcohols 302a and 302b

Our efforts to dehydrate the mixture of allylic alcohols 302a and 302b met with little success. Table 14 summarizes some of the methods which were employed. All of these reaction conditions had previously been examined in our attempts to dehydrate lactol 241, as described in Part Three of this dissertation. Pyridinium p-toluenesulfonate (PPTS) (entry 1) has been employed by Heathcock and coworkers for the dehydration of an allylic secondary alcohol.\textsuperscript{167} Triflic anhydride and 2,6-lutidine (entry 2) have been used by Naruta et al. for dehydration of an allylic alcohol.\textsuperscript{171} Gleiter has reported elimination of an allylic alcohol using methyltriphenylophosphonium iodide (MTPI) in hexamethylphosphorous triamide (HMPT) (entry 3).\textsuperscript{173} The most encouraging results were observed in the MTPI and Burgess reagent reactions. In both cases (entries 3 and 4) a nonpolar product was produced cleanly, but attempts to isolate the new compound were not successful. \textsuperscript{1}H NMR analysis of this compound after purification by flash chromatography was complicated (see below). The integration of the aliphatic region of the spectrum seems to indicate that a dimeric compound has been produced. Low resolution gas chromatography-mass spectral analysis of the product of the reaction with the Burgess reagent gave inconclusive results.

Figure 1. \textsuperscript{1}H NMR spectrum of the product of reaction of 302 with the Burgess reagent
Table 14. Attempted Dehydration of Allylic Alcohol 302a and 302b

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^{167})</td>
<td>cat. PPTS&lt;br&gt;dichloroethane, (\Delta), 1 h</td>
<td>decomposition</td>
</tr>
<tr>
<td>2(^{171})</td>
<td>4.5 equiv lutidine&lt;br&gt;1.0 equiv Tf(_2)O&lt;br(CH(_2)Cl(_2), 0 °C)</td>
<td>complex mixture by (^1)H NMR analysis</td>
</tr>
<tr>
<td>3(^{175})</td>
<td>2.0 equiv MTPI&lt;br&gt;HMPA, 100 °C, 1 h</td>
<td>nonpolar product by TLC</td>
</tr>
<tr>
<td>4(^{176})</td>
<td>2.0 equiv Burgess reagent&lt;br&gt;PhH, (\Delta), 1 h</td>
<td>nonpolar product by TLC</td>
</tr>
</tbody>
</table>

We questioned the stability of the dihydroaromatic product(s) ostensibly obtained from dehydration of 302, and were particularly concerned about the potential of 272 and isomers thereof to undergo dimerization or oligomerization reactions upon concentration. In an effort to prevent undesired side reactions of 272, we therefore next attempted to perform the dehydration and then to effect aromatization immediately after workup of the dehydration reaction of 203.
C. Dehydrogenation of Putative Dihydrocyclopenta[a]phenalene 272

Oxidation of hydroaromatic precursors is frequently the last step in the synthesis of polycyclic aromatic hydrocarbons, and we hoped that this process would produce cyclopenta[a]phenalene (4) from the putative dihydrocyclopenta[a]phenalene 272. Classical methods for aromatization include the use of reagents such as sulfur, selenium, palladium, and platinum, frequently under harsh reaction conditions. Some methods for dehydrogenation of aromatic precursors under milder conditions involve the use of high potential quinones such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or chloranil, reaction using trityl salts, and bromination with N-bromosuccinimide (NBS) followed by dehydrobromination. As a rule of thumb, as the number of hydrogen atoms which must be removed decreases, the milder the reaction conditions become.

After surveying the general literature regarding aromatization reactions, we focused our search on examples of dehydrogenation of dihydroazulenes because we reasoned that such aromatization reactions would be good models for our desired reaction, the preparation of 4 from dihydrocyclopenta[a]phenalene 272. One particularly encouraging example is the preparation of benz[a]azulenes 308 and 309 from the dihydroaromatic compounds 306 and 307 reported by Oda and coworkers in 1984 (eq

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221 For reviews of dehydrogenation reactions, see:
Treatment of 306 and 307 with palladium on carbon in refluxing ethylene glycol furnished the benz[a]azulenes 308 and 309 in moderate yield.

![Chemical structure](image)

Another pertinent example comes from the indeno[2,1-a]phenalene work of D. H. Reid. Reid has reported that a dihydroindeno[2,1-a]phenalene (as represented by structure 310 out of four possible structures) was aromatized to indeno[2,1-a]phenalene (42) by treatment with 20% palladium on charcoal in acetic acid (eq 90). The dehydrogenation reaction occurred slowly at room temperature, but required only a few minutes in refluxing acetic acid. No yield was reported for this aromatization reaction.

![Chemical structure](image)

We performed a number of small scale aromatization attempts on the dehydration product derived from allylic alcohol 203 with the Burgess reagent in refluxing benzene. A summary of these experiments is shown in Table 15. Under most of the reaction conditions examined, the compound tentatively assigned as 272 appeared to undergo decomposition. Basic alumina (entry 4) and nitrobenzene in pyridine (entry 5) were the

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most promising reaction conditions because the reactions appeared to be clean by TLC. However, attempts to isolate and identify the products of these two reactions were not successful.

Table 15. Attempted Aromatization of the Putative Cyclopentadiene 272

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1224</td>
<td>5% Pd/C PhH, Δ, 0.5 h</td>
<td>decomposition</td>
</tr>
<tr>
<td>220a</td>
<td>5% Pd/C CH₃CO₂H, rt</td>
<td>decomposition</td>
</tr>
<tr>
<td>3225</td>
<td>excess DDQ PhH, rt</td>
<td>immediate decomposition</td>
</tr>
<tr>
<td>4226</td>
<td>excess chloranil PhH, Δ, 16 h</td>
<td>complex mixture</td>
</tr>
<tr>
<td>5219c</td>
<td>basic Al₂O₃ PhH, Δ, 0.5 h</td>
<td>unidentified products</td>
</tr>
<tr>
<td>6227</td>
<td>excess PhNO₂ pyridine, Δ, 0.5 h</td>
<td>unidentified products</td>
</tr>
<tr>
<td>7228</td>
<td>1.1 equiv NBS cat. benzoyl peroxide CCl₄, Δ, 2 h</td>
<td>smear</td>
</tr>
<tr>
<td>863</td>
<td>Ph₃C⁺BF₄⁻ PhH, rt, 2 h</td>
<td>decomposition</td>
</tr>
</tbody>
</table>

Other Attempts to Prepare Cyclopenta[α]phenalene from Enone 112

A handful of other strategies for the preparation of 4 from cyclopentenone 112 were investigated, and the results of our studies are briefly summarized here. As shown in the scheme below, we considered preparing an enol triflate such as 303, which could then be reductively cleaved to generate a dihydrocyclopenta[α]phenalene such as 272.

To this end (eq 91), we treated 112 with 1.2 equivalents of lithium diisopropylamide and attempted to trap the enolate with N-(5-chloro-2-pyridyl)triflimide (292), a reagent recently introduced by Comins. This reaction produced several products according to TLC analysis, but after workup none of the desired enol triflate 303 was observed. Enone 112 was recovered in ca. 40% yield.

Another strategy which we studied briefly involved benzylic oxidation of 112 to generate a molecule such as 304, in which X is a heteroatom such as bromine.
Reduction of 304 was expected to produce 305, from which 4 could be obtained by elimination of HX and H₂O. We attempted to effect benzylic bromination of 112 using N-bromosuccinimide²²⁹ with benzoyl peroxide as initiator (eq 92). That the reaction produced a slew of products is not surprising, because in addition to benzylic bromination, allylic bromination of 112 is also possible, and furthermore, isomerization of the radical intermediates and the bromide products of the reaction can occur under the reaction conditions.

The last strategy which we investigated briefly for the preparation of 4 from 112 is adapted from Scott's azulene synthesis²³⁰ and is particularly titillating because 4 would be obtained directly from 112 in one operation. As suggested in the scheme below, keto-enol tautomerization of 112, followed by 1,5-hydrogen shift and dehydration, could

²²⁹Ref. 184 and references therein.
produce 4. Scott and coworkers have reported that treatment of trienone 313 with the reagent obtained from mixing phosphorous pentoxide with methanesulfonic acid\(^{231}\) directly produced azulene (31) in moderate yield (eq 93).

\[
\text{excess P}_2\text{O}_5\text{-MsOH} \quad 60^\circ \text{C, 8 h} \quad 30-50\%
\]

We found that upon treatment of enone 112 with the same reagent combination (eq 94), no reaction was observed after 1 h. The reaction mixture was heated to 60 °C and then gradually to 100 °C and the starting material was gradually consumed according to TLC analysis. Workup of the reaction using cold water produced intractable black solids, indicating that decomposition of enone 112 had likely occurred.

\[
1:10 \text{ P}_2\text{O}_5\text{-MeOH} \quad \text{rt, 1 h then } \Delta, 4 \text{ h}
\]

We shifted gears and began to work on the synthesis of cyclopenta[a]phenalene (4) by a modified Pauson-Khand route, in which the enyne has an added hydroxyl function compared to the substrate of our original Pauson-Khand route. Thus, in our second intramolecular Pauson-Khand route, aromatization of a dihydroaromatic precursor is no longer required. This work is described in the remainder of this dissertation.
As outlined in the above scheme, our modified Pauson-Khand route for the preparation of cyclopenta[a]phenalene (4) employs the hydroxy-substituted enyne 315 for a Pauson-Khand reaction to produce cyclopentenone 314. We envisioned that the hydroxy compound 314 would be a versatile synthetic intermediate for the construction of target molecule 4. In contrast to the enyne substrate in our first intramolecular Pauson-Khand route, this substrate has an added hydroxyl group, and aromatization of a dihydrocyclopenta[a]phenalene precursor to 4 is thus obviated. We envisioned that the Pauson-Khand substrate, allylic alcohol 315, could be readily prepared from 1,8-diiodonaphthalene, which we had already employed as a starting material in earlier routes for the synthesis of 4.

Many examples of Pauson-Khand reactions of substrates bearing free hydroxyl groups have been reported. Smit has observed that for Pauson-Khand reactions of hydroxy-substituted substrates, "dry state" conditions in which the substrate is applied to silica gel and gently warmed are superior to standard solution-phase thermolysis conditions.\textsuperscript{198a} For example, using dry state conditions, allylic alcohol 316 underwent the Pauson-Khand reaction to produce 317 in good yield (eq 95). Similarly, cyclopentenone
319 was obtained in 40% yield from 318 (eq 96). However, when Pauson-Khand reactions of allylic alcohols 316 and 318 were carried out under standard solution-phase, thermal conditions, competing polymerization caused the enones 317 and 319 to be isolated in less than 10% yield.

Tertiary amine N-oxide promotion has also been applied to Pauson-Khand reactions of allylic alcohol substrates. Jeong and coworkers performed an intermolecular Pauson-Khand reaction with phenylacetylene (320) and allyl alcohol (321) using trimethylamine N-oxide (TMANO) promotion and obtained a 2:1 mixture of regioisomers 322 and 323 in good yield (eq 97). Because our desired Pauson-Khand reaction is an intramolecular reaction, regioselectivity was not anticipated to be a concern.
Preparation of Enyne 313, A Substrate for the Key Pauson-Khand Reaction

We envisioned two general strategies for the preparation of enyne 315 from 1,8-diiodonaphthalene, differing only with respect to the order in which the substituents are introduced. In route $a$, allylic alcohol 324 may be prepared by monolithiation of 120 and reaction with acrolein. The alkyne might then be installed by a coupling reaction such as the Castro-Stephens or Stille coupling reaction. In route $b$, the order of the steps is reversed, and selective introduction of one acetylene group to produce an alkyne such as 325 was envisioned. Then, installation of the allylic alcohol by lithium-halogen exchange and reaction with acrolein would be expected to produce 315.

A. Access to Enyne 315 from Allylic Alcohol 324

We first investigated route $a$ for the preparation of 324 as summarized in the following scheme. After reaction of the monolithium derivative of 120 with acrolein, compound 326 ($R = H$) was expected to be obtained. If necessary, the alcohol could then be protected. Transition metal-mediated cross-coupling would produce alkyne 327. Liberation of the terminal alkyne, if a protected alkyne had been employed, and
deprotection of the alcohol, if necessary, would then produce the Pauson-Khand substrate 315.

Monolithium-halogen exchange of 1,8-diiodonaphthalene (120) was performed following the procedure of Katz. Reaction of the naphthyllithium intermediate with excess freshly distilled acrolein produced the allylic alcohol 324 in 47-52% yield (eq 98). Allylic alcohol 324 was purified by column chromatography on silica gel and was found to be a viscous yellow oil.

Installation of a (trimethylsilyl)acetylene substituent onto iodide 324 using the Sonogashira modification of the Castro-Stephens reaction proceeded in extremely poor yield. Treatment of 324 with catalytic amounts of dichlorobis(triphenylphosphine)-palladium and copper iodide and three portions of (trimethylsilyl)acetylene (a total of three equivalents) in triethylamine produced less than 20% of the desired product.
silylalkyne 328 (eq 99). A side product, ketone 329, was obtained in ca. 10-20% yield, and is probably produced via a 5-**exo** intramolecular Heck-type process as shown in the following scheme.

We wondered what role, if any, the free hydroxyl group was playing in the Sonogashira reaction and prepared two protected derivatives of allylic alcohol 324. Tert-butyldimethylsilyl (TBDMS) ether 333 was prepared in good yield using the commercially available silyl triflate reagent TBDMSOTf and a hindered base (eq 101).232 Methyl ether 334 was prepared in 78% yield by treatment of 324 with silver (I) oxide and calcium sulfate in methyl iodide (eq 102).233 Methyl ether 334 was also prepared using

---


the reagent combination of KOH, DMSO, and methyl iodide, but the yield using this method\(^{234}\) was only 51%.

\[
\text{HO} \quad 1.5 \text{ equiv 2,6-lutidine} \\
\text{324} \\
\text{CH}_2\text{Cl}_2, -20 ^\circ \text{C}, 20 \text{ min} \\
\text{1.2 equiv t-BuMe}_2\text{SiOTf} \\
\text{65\%} \\
\text{HO} \\
\text{324} \\
\text{MeO} \\
\text{334} \\
\text{78\%}
\]

Treatment of ethers 333 and 334 with excess (trimethylsilyl)acetylene under Sonogashira reaction conditions failed to produce usable amounts of the respective alkyne products. Silyl alkyne 335 was obtained in ca. 19\% yield (eq 103), while only a trace of the methyl ether 336 was produced (eq 104) from the coupling reaction of 324. In both cases, Heck products were observed by TLC analysis. We believe that the bulky ethers may actually promote intramolecular Heck reactions because as the oxygen substituent becomes more bulky, the allyl substituent is more likely to adopt in a conformation in which it is close to the palladium while the ether group lies on the opposite side to avoid unfavorable steric interactions with the \textit{peri} substituent.

\[\text{HO} \quad 0.05 \text{ equiv Pd(PPh}_3)_2\text{Cl}_2 \\
\text{333} \\
\text{Et}_3\text{N}, \text{rt}, 16 \text{ h} \\
\text{0.10 equiv Cul} \\
\text{0.10 equiv t-BuMe}_2\text{SiOTf} \\
\text{3.0 equiv Et}_3\text{N} \\
\text{SIMe}_3 \\
\text{335 (ca. 19\%)}
\]

\(^{234}\text{Johnstone, R. A. W.; Rose, M. E. Tetrahedron 1979, 35, 2169.}\)
Discouraged by these results, we set aside this route for the preparation of enyne 315 and began to investigate route $b$, in which the acetylene is installed before the allylic alcohol. Route $b$ gave much better results!

B. Preparation of Enyne 315 via Alkynylsilane 337

In method $b$, our plan was to selectively substitute an alkynyl group for one of the iodines of 1,8-diiodonaphthalene (120), thus producing a compound such as alkyne 337. We then planned to perform lithium-iodine exchange and to treat the resulting naphthyllithium intermediate with acrolein to produce allylic alcohol 326. From 326, enyne substrate 315 would be easily prepared by deprotection of the terminal acetylene.

We were excited to find literature precedent for the selective mono-coupling reactions of aryl diiodides. Grissom and coworkers have reported that 1,2-diiodobenzene (338) selectively undergoes a single coupling reaction when treated with 1.0 equivalent of 4-pentynol (339) under Sonogashira conditions to afford alkyne 340 in very good yield.
(eq 105). Upon treatment of diiodide 120 with a slight excess of (trimethylsilyl)acetylene and catalytic amounts of palladium reagent and copper iodide, we obtained mono-coupled product 337 in good yield (eq 106). Approximately 7% of 1,8-diiodonaphthalene (120) was recovered from this reaction. Alkyne 337, a yellow-orange oil, was isolated by chromatography on silica gel.

\[
\begin{align*}
\text{I} & \text{I} \\
\text{338} & \xrightarrow{\text{0.05 equiv Pd(PPh}_3\text{)4, 0.10 equiv Cul, Et}_2\text{N, rt, 16 h}} \text{339 OH} \\
& \quad \uparrow \\
& \quad \text{74%} \\
\text{I} & \equiv \\
\text{OH} & \xrightarrow{\text{339}} \text{340} \\
\end{align*}
\]

\[
\begin{align*}
\text{I} & \text{I} \\
\text{120} & \xrightarrow{\text{0.04 equiv Pd(PPh}_3\text{)2Cl}_2, 0.08 equiv Cul, 1.2 equiv SIMe}_3 \text{Et}_2\text{N, rt, 16 h}} \text{337} \\
& \quad \uparrow \\
& \quad \text{65-66%} \\
\end{align*}
\]

Allylic alcohol 326 was then prepared from iodide 337 by lithiation and reaction with acrolein. As shown in the scheme below, treatment of 337 with 1.1 equivalents of \(n\)-BuLi in diethyl ether at -30 °C produces the naphthyllithium intermediate 341, which was cooled to -78 °C before addition of excess freshly distilled acrolein. Aqueous workup yielded allylic alcohol 326 in very good yield. Allylic alcohol 326 could be purified by column chromatography on silica gel.

\[
\begin{align*}
\text{I} & \equiv \\
\text{SIMe}_3 & \xrightarrow{1.1 \text{ equiv } n\text{-BuLi, Et}_2\text{O, -30 °C, 10 min}} \text{341} \\
\text{I} & \equiv \\
\text{SIMe}_3 & \xrightarrow{2.0 \text{ equiv acrolein, -78 °C, 20 min}} \text{326} \\
& \quad \uparrow \\
& \quad \text{63-75%} \\
\end{align*}
\]

Desilylation of alkyne 326 to produce 315 was performed using a catalytic amount of potassium carbonate in methanol (eq 107). Immediate purification of the reaction mixture by column chromatography on silica gel was necessary, as the mixture began to undergo decomposition to high Rf products even upon initial concentration of the crude reaction mixture. We believe that 315 reacts with residual base to produce ether byproducts. Treatment of 326 with aqueous potassium hydroxide solution and methanol, the method used in our first-generation Pauson-Khand route, produced 315 in less than 35% yield, and decomposition of the substrate was evident. We later found that purification of the silylacetylene 326 starting material was not necessary, and that treatment of crude 326 with potassium carbonate and methanol produced 315 in 53-78% overall yield from iodide 337.

This facile three-step route to Pauson-Khand substrate 315 from 1,8-diiodonaphthalene (120) lent itself well to preparation of 315 on a large scale. Enyne 315, a waxy gold solid, mp 46.5-47 °C, was stable once it had been purified by chromatography. We next examined the Pauson-Khand reaction of our new hydroxy-substituted enyne.

---

Pauson-Khand Reaction of Enyne 315 to Produce Cyclopentenone 314

Pauson-Khand reaction of enyne 315 under NMO-promotion conditions similar to those employed in our first Pauson-Khand route produced the diastereomeric enones 314a and 314b in ca. 52-75% yield (the enones were contaminated with ca. 10% NMO as estimated by $^1$H NMR analysis). We attempted to remove NMO using an aqueous workup procedure and also by column chromatography using 30% ethyl acetate-hexanes or 100% diethyl ether, but the NMO was surprisingly difficult to separate from 314a and 314b. Enones 314a and 314b have a free hydroxyl group and consequently are very polar. Recrystallization of a small amount of 314a and 314b from chloroform provided a gold solid, mp 146-147 °C (sharp).

\[
\begin{align*}
\text{HO} \quad \text{315} & & 1.0 \text{ equiv \text{ Co}_2(\text{CO})_8 (274)} \nonumber \\
\text{CH}_2\text{Cl}_2, \text{rt, 2-3 h} & & + \text{4 x 2.0 equiv NMO} \nonumber \\
0 \degree \text{C} \to \text{rt, 5 h} & & \text{ca. 52-75% (ca. 90% pure)} \nonumber \\
\text{ca. 52-75% (ca. 90% pure)} & & \text{314a} \nonumber \\
\text{+} & & \text{314b} \nonumber \\
\text{(4-7:1)} & & \text{(108)}
\end{align*}
\]

Major diastereomer 314a and minor diastereomer 314b were obtained in a 4-7:1 ratio. The ratio of products appeared to be dependent on the quality of the air- and moisture-sensitive Co$_2$(CO)$_8$ reagent, as higher diastereoselectivity was obtained when a new bottle of the reagent had been employed.

The relative stereochemistry was assigned by comparison of $^1$H NMR coupling constant data. In the major isomer the coupling constant between $H_a$ and $H_c$ is 11.5 Hz, which is consistent with the large dihedral angle (estimated to be ca. 180° based on inspection of models) between these protons. In the minor isomer, the smaller $H_a$-$H_c$ coupling constant of 5.3 Hz is consistent of the estimated dihedral angle of 60°.
There is literature precedent for similar stereoselectivity in intramolecular Pauson-Khand reactions of similar substrates. Magnus has observed that a Pauson-Khand reaction of allylic alcohol \(342\) produced a ca. 3:1 ratio of diastereomers \(343a\) and \(343b\) (eq 109).\(^{237}\) Major product \(343a\), in which the C-3 substituent is exo to the bicyclic system, is believed to result from an intermediate such as \(344\). Pseudodiaxial interactions between the C-3 substituent and the substituent at the alkyne terminus disfavors intermediate \(345\), from which minor isomer \(343b\) arises. When the hydroxyl group of \(342\) was protected a bulky MOM ether, the MOM derivative corresponding to diastereomer \(343a\) was obtained as the sole product of the Pauson-Khand reaction in 68% yield.

Strategies for the Preparation of Cyclopenta[a]phenalene from Cyclopentenone 314

With the carbon skeleton of our target molecule, cyclopenta[a]phenalene (4), in hand, we next needed to consider functional group modification strategies for the generation of 4 from cyclopentenone 314. Two general strategies are shown in the scheme below. Route a begins by 1,2-reduction of the enone to produce a mixture of stereoisomeric diols 347, which we anticipated would undergo a double dehydration to produce cyclopenta[a]phenalene (4). If direct dehydration of 347 using the Burgess reagent or the Martin sulfurane, for example, was not possible, then other elimination strategies could be examined. Alternatively, diols 347 could be converted to the corresponding dibromide-, dimesylate-, or diacetate derivative, and we expected that 4 could be obtained from these derivatives using elimination chemistry. Strategy a is exciting because it has the potential to produce the target molecule very quickly, but on the other hand, this route is risky, especially because the double elimination might be a difficult task.

Route a' is a tempered variant of strategy a. In this modified route, alcohol 314 is first converted to the methyl ether 348. Then, in parallel to route a, 1,2-reduction of the
enone would be expected to produce allylic alcohol 349, and successive elimination of water and methanol would generate 4. In route b, the first step is dehydration of 314 to produce dienone 350, which might exist as its enol tautomer. 1,2-Reduction of dienone 350 would produce the alcohol 351, which would be expected to undergo a facile dehydration to produce 4. We were particularly interested in exploring the technique of flash vacuum thermolysis to effect acetate eliminations to produce 4 (e.g., diol 347 → diacetate → 4, or alcohol 351 → acetate → 4), and a discussion of flash vacuum thermolysis techniques for reactions in the gas phase follows.
Gas-phase reactions were employed chemists (and alchemists!) as early as the 15th century and were an important and routine method for the study of chemical structure and reactivity until the late 1800's. Since then, gas-phase thermolysis reactions have been used for a variety of applications, including preparative organic synthesis and the study of transient reaction intermediates and reaction kinetics. We hoped to use flash vacuum thermolysis to perform elimination reactions of acetate esters (and related derivatives) for the synthesis of cyclopenta[a]phenalene. Some advantages of gas-phase reactions that made this approach attractive include the ability to minimize intermolecular reactions and the potential to isolate relatively unstable products.

β-Elimination reactions of esters are well known. These reactions are predominantly cis eliminations, and involve a six-membered cyclic transition state, as shown below. It has been theorized that under some conditions (e.g., 450-550 °C) that these β-elimination reactions may be surface-catalyzed and involve a surface ion pair (see below).

---

238 For a monograph and reviews of gas-phase pyrolysis, see:

240 Ref 236a, p 85.
Elimination of acetate esters is a practical synthetic method. For example, thermolysis of acetate 352 yielded olefins 353 and 354 in a 70:30 ratio (as determined by GC analysis). The yield of 77% was based on recovery of the acetic acid liberated in the elimination (eq 110).

\[ \text{OAc} \xrightarrow{400 \degree C} \text{pyrex helices} \] 
\[ \begin{array}{c}
352 \\
\end{array} \xrightarrow{77\%} \begin{array}{c}
353 \\
354 \\
\end{array} \] (70:30) (110)

The pyrolysis of xanthate esters (the Chugaev reaction) is an analogous reaction which also provides a useful route to alkenes. Xanthate esters undergo thermal elimination reactions under milder conditions (typically 100-250 \(^\circ\)C) than do carboxylic esters, and one advantage of the milder reaction conditions is that isomerization of the olefinic products is minimized. Eq 111 depicts a xanthate ester elimination reaction which was reported by Bordwell and coworkers (no yield was reported for this transformation).

\[ \text{S}_200 \degree C, 1h \xrightarrow{200 \degree C, 1 h} \] 
\[ \begin{array}{c}
\text{355} \\
\end{array} \xrightarrow{200 \degree C, 1 h} \begin{array}{c}
\text{O} = \text{C} = \text{S} + \text{MeSH} \\
\end{array} \] (111)

---

242 Ref. 237 and Nace, H. R. Org. React. 1962, 12, 57.
Route a: A Double Elimination Strategy

The "double elimination" strategy for the synthesis of cyclopenta[a]phenalene (4) from enone 314 is gutsy and direct. As shown in the following scheme, 1,2-reduction of enone 314 should produce a mixture of diols 347; double dehydration reaction would then provide 4 directly. Alternatively, the hydroxyl groups could be functionalized to form the corresponding mesylates, acetates, or related derivatives, and double elimination of HOR from 356 would be expected to produce target molecule 4.

The route begins with selective reduction of the ketone group of 8-hydroxy enone 314. We found that this reaction could be carried out with either DIBAL or L-Selectride (lithium tri-sec-butylborohydride), as shown in Table 16. L-Selectride gave a cleaner reaction than DIBAL. Workup of the L-Selectride reaction mixture involved treatment of the reaction mixture with 6 M aqueous sodium hydroxide solution and 30% hydrogen peroxide solution. Excellent diastereoselectivity was observed in this reduction. L-Selectride typically approaches the substrate from the less hindered direction\(^{242}\) and thus

\(^{242}\) See ref. 218, p. 141.
347a results from reduction of major diastereomer 314a, while 347c results from reduction of minor diastereomer 314b.

Table 16. 1,2-Reduction of Enone 314

<table>
<thead>
<tr>
<th>Entry</th>
<th>314a:314b</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4:1</td>
<td>2.0 equiv DIBAL</td>
<td>mixture of mainly 3 isomers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PhH, 0 °C, 10 min</td>
<td>47% mass recovery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Na⁺K⁺ tartrate workup</td>
<td>messy reaction mixture</td>
</tr>
<tr>
<td>2</td>
<td>7:1</td>
<td>2.4 equiv DIBAL</td>
<td>same as above</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH₂Cl₂, -78 °C → -40 °C, 1 h</td>
<td>ca. 60% mass recovery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Na⁺K⁺ tartrate workup</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>7:1</td>
<td>1.1 equiv Lix-Bu₃BH</td>
<td>7:1 ratio of 347a:347c</td>
</tr>
<tr>
<td></td>
<td></td>
<td>THF, -78 °C, 10 min</td>
<td>ca. 64% yield (90% purity)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NaOH-H₂O₂ workup</td>
<td></td>
</tr>
</tbody>
</table>

¹H NMR data for the products of the L-Selectride reduction (entry 3, above) is presented in the following table. The ¹H NMR spectrum of the mixture 347a and 347c, an orange solid of mp 140-152 °C, was taken in acetone-d₆ because the diol mixture was
relatively insoluble in chloroform. The mixture of 347a and 347c had a broad hydroxyl peak in the infrared spectrum at 3300 cm\(^{-1}\).

![Chemical structures of 347a and 347c](image)

<table>
<thead>
<tr>
<th>Proton</th>
<th>(\delta)</th>
<th>m</th>
<th>coupling (Hz)</th>
<th>(\delta)</th>
<th>m</th>
<th>coupling (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ha</td>
<td>4.67</td>
<td>dd</td>
<td>(J_{ab} = 7.5) Hz</td>
<td>4.67</td>
<td>(obscured)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(J_{ac} = 8.9) Hz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb</td>
<td>4.83</td>
<td>d</td>
<td>(J_{ab} = 7.5) Hz</td>
<td>4.15</td>
<td>q</td>
<td>(J_{bc} = 4.1) Hz</td>
</tr>
<tr>
<td>Hc</td>
<td>2.84-2.86</td>
<td>m</td>
<td>(J_{fg} = 6.1) Hz</td>
<td>3.65</td>
<td>d</td>
<td>(J_{fg} = 9.1) Hz</td>
</tr>
<tr>
<td>Hd, He</td>
<td>2.84-2.86</td>
<td>m</td>
<td></td>
<td>1.74-1.86</td>
<td>m</td>
<td></td>
</tr>
<tr>
<td>Hf</td>
<td>4.07</td>
<td>d</td>
<td>(J_{fg} = 6.1) Hz</td>
<td>4.91-4.94</td>
<td>m</td>
<td></td>
</tr>
<tr>
<td>Hg</td>
<td>5.02-5.10</td>
<td>m</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

We next attempted to perform a double dehydration of the diol mixture 347a and 347c under a number of reaction conditions, as shown in Table 17. The Burgess reagent, (methoxycarbonylsulfamoyl)triethylammonium hydroxide (259), appeared to produce polymeric products (entry 1). Reaction of diols 347 with bis[\(\alpha,\alpha\)-bis(trifluoromethyl)-benzenemethanolate]diphenylsulfur (357) (entry 2), a sulfurane dehydrating reagent introduced by Martin,\(^{243}\) produced material of high \(R_f\) by TLC analysis, but we were


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unable to identify any of the products of this reaction. We also attempted to prepare the
dimesylate derivative of 347 and to effect mesylate elimination with potassium \( t \)-butoxide (entry 3) and found that decomposition occurred.\(^{244b}\)

Table 17. Attempted Double Dehydration of Diols 347a and 347c

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.5 equiv Burgess reagent PhH, ( \Delta ), 20 min</td>
<td>low ( R_f ) decomposition products</td>
</tr>
<tr>
<td>2</td>
<td>excess Martin sulfurane CH(_2)Cl(_2), rt, 16 h</td>
<td>poor mass recovery of high ( R_f ) products</td>
</tr>
<tr>
<td>( ^{244} )</td>
<td>2.2 equiv MsCl 4.0 equiv Et(_3)N THF, 0 °C then 3 equiv ( t )-BuOK, THF, 0 °C ( \rightarrow ) rt</td>
<td>low ( R_f ) decomposition products</td>
</tr>
</tbody>
</table>

We also sought to convert diol 347 to a dibromide, with the intention of performing a
dehydrohalogenation reaction to produce 4. To this end, we treated 347 with \( N \)-bromo-
succinimide and dimethylsulfide in an attempt to prepare dibromide 358 by a Corey-Kim
reaction,\(^{245}\) but none of the desired product was obtained. Instead, decomposition of the
starting material was observed by TLC analysis.


Formation of the diacetate derivative (359), however, proceeded smoothly when 347 was treated with excess acetic anhydride in pyridine containing a catalytic amount of 4-dimethylaminopyridine (DMAP) (eq 113).^{236b}

We were interested in producing 4 by performing acetate elimination from 359 and considered using palladium catalysis to effect this reaction. Trost^{246} and Tsuji^{247} have independently reported that allylic acetates and carbonates undergo palladium-catalyzed elimination reactions under mild conditions to afford 1,3-dienes. For example, Trost has effected acetate elimination from the allylic acetate 360 under palladium catalysis and obtained diene 361 in good yield (eq 114). Tsuji has shown that carbonate 362 undergoes elimination upon treatment with palladium (II) acetate and tributylphosphine in THF at room temperature to produce a 12.5:1 ratio of dienes 363 and 364 in 93% yield (eq 115).

---


We found, however, that no reaction occurred upon treatment of diacetate 359 with catalytic amounts of palladium (II) acetate and tributylphosphate in refluxing toluene (eq 116).

We plan to submit diacetate 359 to flash vacuum thermolysis and believe that cyclopenta[a]phenalene (4) should be obtained from β-acetate elimination (eq 117).
Some of the difficulties we encountered in our attempts to produce cyclopenta[α]phenalene (4) from diol 347 are reminiscent of problematic elimination reactions reported by Semmelhack and coworkers in their investigation of the synthesis of spiro[4.4]nonatetraene (365).\textsuperscript{248} Compound 365 is of theoretical interest, especially for investigations regarding spiroconjugation. Semmelhack and coworkers synthesized 365 after exploring many routes which had seemed reasonable but failed in the laboratory. It was found, for example, that base-induced elimination reactions of ditosylate 366 produced only unidentified products (eq 118). Gas phase thermolysis reactions of diacetate 367 and dixanthate 368 produced indene (369), ostensibly via rearrangement of the target molecule 365 (eq 119).

\[ \text{366} \xrightarrow{\text{unidentified products (118)}} \]

\[ \text{367} R = \text{Ac} \quad \text{368} R = \text{CS}_2\text{Me} \]

The route which Semmelhack and coworkers ultimately found successful is depicted in the below scheme. 1,2-Reduction of the spirocyclopentenone 370 produced the allylic diol 371 in 30% yield.\textsuperscript{249} Conversion to dichloride 372 and a subsequent double


\textsuperscript{249} Semmelhack has noted that other reagents, including DIBAL, failed to produce diol 371.
elimination reaction using potassium t-butoxide produced 365 in 23% overall yield from diol 371.

Route a': Preparation of 4 by Successive Elimination Reactions

Having encountered problems in the direct double elimination approach to 4, we next began work on route a', the modified, more conservative version of route a.

In this strategy, successive eliminations of H$_2$O and HOMe from 349, rather than a double elimination of H$_2$O or HOR, would be the key steps in the preparation of cyclopenta[a]phenalene (4). The 8-hydroxyl group of 314 is protected as a methyl ether, and 1,2-reduction of the resulting enone 348 then produces compound 349, in which the
oxygen functionalities have been differentiated. From compound 349, dehydration and elimination of methanol were anticipated to produce 4.

The route begins with the preparation of methyl ether 348, which was readily obtained from alcohol 314 following the method of Pearlman. Upon treatment of a 3:2 mixture of diastereomeric alcohols 314 with methyl iodide, silver (I) oxide, and calcium sulfate, methyl ether 348 was obtained as a 3:2 mixture of diastereomeric ethers in 65% yield (eq 120). The product was easily purified by chromatography on silica gel, and was obtained as a stable yellow solid with mp 113-115°C. The carbonyl stretch in the infrared spectrum of 348 was at 1701 cm⁻¹.

We then performed 1,2-reduction of enone 348 using the same methods we had examined for reduction of the hydroxy compound 314. This work is summarized in the table below. We did not determine the relative stereochemistry of the reduction products because the 1H NMR spectra were complicated by the many isomers and byproducts of the reduction reactions. For this transformation, there was no clear advantage to using DIBAL or L-Selectride as the reducing agent. The reduction of the methoxy compound 314 seems to occur with poor stereoselectivity compared to the reduction of the hydroxy compounds (see Table 16, above) but one must bear in mind that the ratio of diastereomers in the enone starting materials was lower in the reduction of the methoxy compounds than in the hydroxy counterparts.
Table 18. 1,2-Reduction of Enone 348

<table>
<thead>
<tr>
<th>Entry</th>
<th>348a:348b</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3:1</td>
<td>1.5 equiv DIBAL</td>
<td>3:1 ratio of 2 diastereomers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PhH, 0 °C, 15 min</td>
<td>ca. 75% yield (90% pure)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Na⁺K⁺ tartrate workup</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4:1</td>
<td>1.3 equiv Lir-Bu₃BH</td>
<td>3:1:1 ratio of 3 diastereomers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH₂Cl₂, -78 °C → -40 °C, 1 h</td>
<td>ca. 98% yield (90% pure)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Na⁺K⁺ tartrate workup</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.5:1</td>
<td>1.2 equiv Lir-Bu₃BH</td>
<td>2:1:1 ratio of diastereomers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>THF, -78 °C, 10 min</td>
<td>ca. 64% yield (90% pure)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NaOH-H₂O₂ workup</td>
<td></td>
</tr>
</tbody>
</table>

We then treated alcohol 349 (as a mixture of unidentified diastereomers) with the Burgess reagent in benzene at room temperature with the intent of producing a cyclopentadiene such as 373 (eq 121). This dehydration reaction could produce a number of cyclopentadiene isomers. We were excited to observe that by TLC analysis of the reaction mixture, a clean conversion of alcohol 349 to a high R_f material had occurred!
The product of this small-scale reaction was a yellow solid which when stored as a degassed, frozen benzene solution was stable for at least one month. We performed spectral analysis of the high Rf product and unfortunately, we could not conclusively determine if 373 or isomers thereof had been obtained. A proton NMR spectrum (in deuterobenzene) of the product is shown below. A Diels-Alder dimer is a good possibility for the structure of our product. Low-resolution mass spectral analysis of the product did not give conclusive data; however, stability of the product to the conditions of the GC/MS analysis could have been a problem.

Figure 2. $^1$H NMR spectrum of the product of reaction of 349 with the Burgess reagent
On the off chance that the product of the dehydration reaction was indeed a cyclopentadiene such as 373, we attempted to perform the elimination of methanol to produce cyclopenta[a]phenalene (4). The product of eq 121 was treated with excess DBU in refluxing deuterobenzene for 6 hours (eq 122). No reaction was observed. With this result, we concluded that the product of the dehydration reaction was probably not the desired cyclopentadiene 373.

In the remainder of this chapter we will discuss work on route b, in which elimination of the hydroxyl group from δ-hydroxy enone 314 is the first step in this strategy for the preparation of 4 from 314.

Route b: Preparation of Cyclopenta[a]phenalene via Dienone 350
As shown in the previous scheme, this simple and elegant strategy for the synthesis of 4 from enone 314, the product of our second-generation Pauson-Khand reaction, begins with elimination of water from δ-hydroxy enone 314 to produce dienone 350. Note that the enol tautomer of 350 is 9-hydroxycyclopenta[a]phenalene (374)\(^\text{250}\). 1,2-Reduction of dienone 350 is expected to produce the allylic alcohol 351. The synthesis of cyclopenta[a]phenalene by route \( b \) would conclude with the dehydration of alcohol 351. As in the previous route, flash vacuum thermolysis of the acetate derivative of alcohol 351 would be an attractive means for achieving the last step.

A Digression: Preparation of 4 via a Shapiro Reaction

We stumbled upon a method for the dehydration of δ-hydroxy enone 314 by accident in the course of preparing a trisylhydrazone derivative of this ketone for the synthesis of 4 via a Shapiro reaction. Our Shapiro strategy is shown in the following scheme. This route is refreshingly different from our other strategies for the preparation

\[\text{MeO} \quad \text{348} \quad \text{MeO} \quad \text{375} \quad \text{Li} \quad \text{376} \quad \text{MeO} \quad \text{377} \]

\[\text{Shapiro reaction}\]

\[\text{348} \rightarrow \text{375} \quad \text{375} \rightarrow \text{376} \quad \text{376} \rightarrow \text{377} \]

of 4, and involves preparation of trisylhydrazone 375 from methyl ether 348. We thought that upon treatment with excess n-BuLi, 375 would undergo a Shapiro reaction to produce the alkyl lithium intermediate 376. Proton transfer was anticipated to produce the cyclopentadienyl anion 377, from which elimination of methoxide would produce our target molecule 4.

To our surprise, when methyl ester 348 was treated with one equivalent of trisylhydrazine in the presence of a catalytic amount of concentrated hydrochloric acid in methanol, the product was not methyl ether 375 but diene 378. With hindsight, we reasoned that the formation of 378 from 348 was not completely unexpected, as in the acidic reaction medium, the methoxy group could become protonated and ionize to produce a stabilized benzylic cation.

![Chemical Reaction Diagram]

Trisylhydrazone 378, a brown solid with mp 90-100 °C (dec.) has a beautiful 1H NMR spectrum in which all of the peaks are resolved even in the 300 MHz spectrum. The two vinylic protons are singlets at 6.84 and 6.71 ppm, and the methylene protons are a singlet at 3.31 ppm. Two isomers of trisylhydrazone 378 having different geometries
about the C=N group were formed from this reaction in a 7:1 ratio and we have not
determined whether the trisyl group is syn to the double bond or the methylene group in
the major isomer. Because the less sterically hindered product is typically obtained, the Z
isomer (with respect to the olefin) is probably the major product.

With trisylhydrazone 378 in hand, we were eager to perform a Shapiro reaction
which we envisioned would produce 4 by the pathway shown in the following scheme.

The "syn-dianion effect" must be mentioned here. As shown above, the first
equivalent of base deprotonates the hydrazone to produce intermediate 379. The second
equivalent of base then deprotonates the α-carbon of the hydrazone derivative to produce
a dianion represented by structure 380. It has been observed with unsymmetrical,
saturated ketone derivatives, that a syn-dianion is usually obtained as a result of direction
from the nitrogen-centered anion. One might think that this phenomenon would disfavor
the second deprotonation for our Shapiro reaction if the major isomer of 378 has the trisyl
group Z with respect to the olefin rather than the methylene group. However, the "syn-

\[ \text{378} \xrightarrow{nBuLi} \text{379} \xrightarrow{nBuLi} \text{380} \xrightarrow{H^+} \text{381} \xrightarrow{-N_2} \text{382} \xrightarrow{H^+} \text{378} \]

dianion effect" is both solvent- and substrate-dependent. The "syn-dianion effect" has been observed in both hydrocarbon and ether solvents, but in strongly coordinating solvents such as TMEDA, direction of the site of the second deprotonation by nitrogen is not observed. Furthermore, the "syn-dianion effect" does not apply to α,β-unsaturated ketone derivatives such as our substrate (378).243,252

The Shapiro reaction of 378 was attempted under two different reaction conditions (Table 19). None of the desired cyclopenta[a]phenalene (4) was obtained. In THF (entry 1), no reaction was observed by TLC analysis and the starting material was recovered in ca. 90% yield. Using the solvent combination of TMEDA-hexane (entry 2) and excess n-BuLi, several spots, including starting material, were observed by TLC analysis.

**Table 19. Attempts to Prepare 4 from Trisylhydrazone 378 by Shapiro Reaction**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.2 equiv n-BuLi THF, -78 °C → 0 °C, 20 min 0 °C, 20 min</td>
<td>recovered starting material (ca. 90%)</td>
</tr>
<tr>
<td>2</td>
<td>3.0 equiv n-BuLi TMEDA-hexane, -78 °C → 0 °C, 1 h 0 °C, 30 min</td>
<td>several spots by TLC, including unreacted starting material</td>
</tr>
</tbody>
</table>

252 For examples of Shapiro reactions of α,β-unsaturated ketones, see:
In light of the surprising reluctance of the starting material to undergo a Shapiro reaction and upon further consideration of the reaction mechanism, we decided that the Shapiro reaction may be doomed after the first deprotonation. As shown in the scheme below, the downfall of the desired transformation may result from delocalization of the nitrogen-centered anion through the conjugated system, ultimately producing a phenalenyl anion represented by structure 382. This anion is predicted to be extremely stable and the methylene protons are no longer activated for the second deprotonation reaction.

Return to Route b: Dienone 350 as an Intermediate for the Synthesis of 4

Dienone 350 is the first intermediate in this final route to cyclopenta[a]phenalene (4). In light of our discovery that the methoxy compound underwent elimination and hydrazone formation upon treatment with a catalytic amount of protic acid, trisylhydrazine, and methanol, we expected that treatment of methyl ether 348 (or better
yet, the alcohol 314) with hydrochloric acid in methanol would similarly effect elimination of methanol (or water) to produce 350. Indeed, we found that upon exposure of a methanolic solution of alcohol 314 to concentrated hydrochloric acid that enone 350 was obtained (eq 123).

\[
\text{HO} \quad \text{cat. conc. HCl} \quad \text{MeOH, rt, 18 h} \quad 45\%
\]

314 \quad 350

Preliminary attempts to perform a 1,2-reduction of 350 to produce allylic alcohol 351 met with disappointing results. As shown in the table below, treatment of 350 with DIBAL, cerium (III) chloride with sodium borohydride (Luche reduction) and LS-Selectride (lithium trisiamylborohydride) failed to produce allylic alcohol 351. DIBAL appeared to produce several products upon reaction with dienone 350, and surprisingly, starting material was visible by TLC analysis despite the use of excess reducing agent. Exposure of dienone 350 to Luche reduction conditions (entry 2) and LS-Selectride (entry 3) seem to have led to the products of 1,4- or 1,6-reduction rather than the desired 1,2-reduction.

Table 21. Attempted 1,2-Reduction of Dienone 350
### Reaction Conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5 equiv DIBAL CH₂Cl₂, -40 °C → 0 °C, 1 h</td>
<td>streak, including unreacted starting material by TLC</td>
</tr>
<tr>
<td>2215</td>
<td>1.0 equiv CeCl₃·7H₂O 5.0 equiv NaBH₄ MeOH, 0 °C, 1 h</td>
<td>one new spot of same Rf as starting material; 1,4- or 1,6-reduction?</td>
</tr>
<tr>
<td>3253</td>
<td>1.2 equiv Li trisiamylborohydride THF, -78 °C → rt, 1 h</td>
<td>two spots of same Rf as starting material; 1,4- and 1,6-reduction?</td>
</tr>
</tbody>
</table>

### Conclusion

We are optimistic that target molecule 4 will be synthesized. Over the course of over three years we have explored three general synthetic routes with the preparation of the new non-alternant aromatic hydrocarbon cyclopenta[a]phenalene (4) as our goal. Our work on these very different routes allowed us to explore a rich variety of chemical reactions, including transition-metal mediated cross coupling reactions, radical cyclizations, elimination reactions, the intramolecular Pauson-Khand reaction, and much more. We believe that with our second-generation Pauson-Khand strategy, we are closer than ever to the synthesis of 4. The key reactions which we plan to carry out, as depicted below, are flash vacuum thermolysis of diacetate 359 to produce 4 (eq 124) and 1,2-

![Reaction Diagram](image)

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253 See ref. 218, pp 152-153 for a representative experimental procedure.
reduction of 350, acetylation of allylic alcohol 351, and β-elimination of acetate from 384. The attainment of target molecule 4 would be a happy ending to the story of our work towards the first synthesis of cyclopenta[a]phenalene.
Part V

Experimental Section
General Procedures

All reactions were performed in flame-dried glassware under a positive pressure of argon. Reaction mixtures were stirred magnetically unless otherwise indicated. Air and/or moisture sensitive reagents and solutions were transferred via syringe or cannula and were introduced into reaction vessels through rubber septa. Reaction product solutions were concentrated with a Büchi rotary evaporatory at approximately 20 mmHg unless otherwise indicated.

Materials

Commercial grade reagents and solvents were used without further purification except as indicated below.

Distilled under nitrogen, argon or vacuum from calcium hydride: diazabicyclo[5.4.0]undec-7-ene, dichloromethane, lutidine, N-methylpyrrolidinone, N,N,N',N'-tetramethylethylene diamine, and triethylamine.

Distilled under argon or vacuum from sodium benzophenone ketyl or dianion: benzene, diethyl ether, tetrahydrofuran, and toluene.

Distilled under argon or vacuum: acetic anhydride, allyl bromide, cyclopentanone, methyl chloroformate, tributyltin hydride and trimethylsilylacetylene.

Pyrrolidine was distilled from barium oxide.

1,8-Diaminonaphthalene was distilled from Zn dust under vacuum.

DMF was sequentially dried in three portions over activated 3 Å molecular sieves.\textsuperscript{87}

N-Methylformanilide was distilled from P\textsubscript{2}O\textsubscript{5} onto activated 4 Å molecular sieves.

Methyl iodide was filtered through neutral alumina immediately before use.
Copper (I) iodide was continuously extracted with THF for 18 h.\textsuperscript{255}

\textit{N}-Bromosuccinimide was recrystallized from water.\textsuperscript{184}

Dichlorobis(triphenylphosphine)palladium (II) was prepared according to the method of Heck\textsuperscript{256} and was recrystallized from chloroform.

Alkyllithium reagents were titrated in tetrahydrofuran at 0 °C with sec-butanol or menthol using 1,10-phenanthroline as an indicator.\textsuperscript{257}

Diazomethane was generated from Diazald using a Mini Diazald apparatus according to the procedure of Black.\textsuperscript{258}

\section*{Chromatography}

Analytical thin-layer chromatography (TLC) was performed on Merck pre-coated glass-backed silica gel 60 F-254 0.25 mm plates. Visualization of spots was effected by one or more of the following techniques: (a) ultraviolet irradiation, (b) exposure to iodine vapor, (c) immersion of the plate in a 10\% solution of phosphomolybdic acid in ethanol followed by heating to ca. 200 °C, (d) immersion of the plate in an ethanolic solution of 3\% \textit{p}-anisaldehyde containing 0.5\% concentrated sulfuric acid followed by heating to ca. 200 °C, (e) immersion of the plate in an ethanolic solution of 3\% \textit{p}-vanillin containing 0.5\% concentrated sulfuric acid followed by heating to ca. 200 °C, and (f) immersion of the plate in an aqueous solution of 1\% potassium permanganate containing 7\% potassium carbonate and 5\% sodium hydroxide followed by heating to ca. 200 °C.

Column chromatography was performed by using 230-400 mesh Merck or Baker silica gel.


Instrumentation

Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Boiling points are uncorrected.

Infrared spectra (IR) were recording using a Perkin-Elmer 1320 grating spectrophotometer.

$^1$H NMR spectra were recorded with a Varian XL-300 (300 MHz) and a Bruker AC-250 (250 MHz) spectrophotometer. Chemical shifts are expressed in parts per million (δ), relative to tetramethylsilane (with the CHCl$_3$ peak at 7.24 ppm used as a standard).

$^{13}$C NMR spectra were determined on a Varian XL-300 (75 MHz) spectrophotometer. Chemical shifts are reported in parts per million (δ), relative to tetramethylsilane (with the central peak of CDCl$_3$ at 77.0 ppm used as a standard).
1,8-Diiodonaphthalene (120).\textsuperscript{259}

A 1-L, three-necked, round-bottomed flask equipped with an internal low-temperature thermometer, a mechanical stirrer with a jacketed adapter, and a 60-mL pressure-equalizing addition funnel fitted with an argon inlet adapter was charged with 1,8-diaminonaphthalene (16.0 g, 100 mmol) and 170 mL of 6.9 M aqueous sulfuric acid. Using a dry ice-acetone bath, the internal temperature was lowered to -20 °C and the mixture became a white suspension. A solution of sodium nitrite (20.7 g, 300 mmol) in 70 mL of H\(_2\)O was added dropwise over 30 min, and the temperature of the thick, foamy light brown reaction mixture was maintained at -15 to -20 °C. Immediately after the addition was complete, the addition funnel was replaced with a second one, and a solution of potassium iodide (99.6 g, 600 mmol) in 100 mL H\(_2\)O was added dropwise over 45 min while the internal temperature was maintained between -15 and -20 °C. The reaction mixture turned dark brown, and gas evolution was observed. After the addition was complete, the low-temperature thermometer was replaced with a standard mercury thermometer, the addition funnel was replaced with a Friedrich condenser, and the cold bath was replaced with a heating mantle which had been prewarmed to approximately 100 °C. The reaction mixture was quickly heated to 80 °C and its consistency became syrupy. The reaction mixture was cooled to 25 °C and neutralized to pH 7 by the addition of solid NaOH (ca. 40 g). The resulting clear solution containing tarry black solids and white salts was filtered using a Buchner funnel and the solids were washed.

\textsuperscript{259}House, H. O.; Koepsell, D. G.; Campbell, W. J. \textit{J. Org. Chem.} 1972, \textit{37}, 1003
with 200 mL of water. Using a mortar and pestle, the solids were pulverized, and then were transferred to a 500-mL one-necked round-bottomed flask. Ether (400 mL) was added, and the mixture was stirred using a mechanical stirrer for 1 h. The solids were separated by filtration and the ether extraction process was repeated. The combined ether extracts were washed with three 200-mL portions of saturated aqueous Na$_2$S$_2$O$_3$ solution, three 200-mL portions of 3% NaOH solution, and 200 mL of saturated aqueous NaCl solution, dried over MgSO$_4$, filtered, and concentrated to afford 21.3 g (56%) of red crystals, mp 107-109 °C. A 1.5 g portion was deposited onto 5 g of silica gel and purified by column chromatography on a mixture of 5 g of silica gel and 5 g of carbon lampblack (elution with petroleum ether). (Note: The charcoal-silica gel column was found to be extremely slow. Purification by flash chromatography on silica gel with petroleum ether as eluent was acceptable, but a high ratio of silica gel was required.) After concentration, the resulting solids were washed with ca. 30 mL of cold petroleum ether to produce 1.01 g of 120 as pale yellow crystals, mp 110-111.5 °C [lit.259 108.5-110 °C] with spectral data consistent with that previously reported for this compound.259

$^1$H NMR (300 MHz, CDCl$_3$): 8.40 (dd, $J = 7.5, 1.3$ Hz, 2 H), 7.80 (d, $J = 7.5, 1.3$ Hz, 2 H), and 7.05 (t, $J = 7.5$ Hz, 2 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 144.0, 135.8, 132.2, 131.0, 126.9, and 96.0.

IR (CCl$_4$): 3060, 1530, 1350, 1320, 1180, and 1140 cm$^{-1}$. 

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8-Iodo-1-naphthaldehyde (109).

A 250-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, pressure-equalizing addition funnel, and rubber septum was charged with 1,8-diiodonaphthalene (2.0 g, 5.26 mmol) and 130 mL of diethyl ether. The pale yellow solution was cooled to -30 °C using a dry ice-acetone bath while n-butyllithium (2.05 mL of a 2.56 M solution in hexane, 5.26 mmol) was added rapidly dropwise over ca. 3 min. After 30 min, the resulting orange-yellow solution was cooled to -78 °C, and a solution of N,N-dimethylformamide (0.61 mL, 0.58 g, 7.90 mmol) in 20 mL of Et₂O was added dropwise from the addition funnel over 10 min. The reaction mixture was allowed to warm to 25 °C over 5.5 h, and then was poured into 75 mL of 10% aqueous HCl solution and stirred vigorously for 10 min. The aqueous layer was separated and extracted with three 50-mL portions of Et₂O. The combined organic phases were washed with 150 mL of H₂O and 150 mL of saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated to afford 1.58 g of an olive green oil. The crude mixture was deposited on silica gel and purified by column chromatography on silica gel (elution with 5% ethyl acetate-hexane) to afford 0.79 g (53%) of 109 as a yellow crystalline solid, mp 73 -74 °C (lit. 260 73-74 °C).

1H NMR (300 MHz, CDCl₃): 11.66 (s, 1 H), 8.22 (dd, J = 8.2, 1.8 Hz, 1 H), 7.93 (dd, J = 8.2, 1.8 Hz, 1 H), 7.89 (dd, J = 8.3, 1.9 Hz, 1 H), 7.85 (dd, J = 7.4, 1.7 Hz, 1 H), 7.51 (t, J = 8.0 Hz, 1 H), and 7.19 (t, J = 7.2 Hz, 1 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 191.5, 141.2, 136.5, 135.6, 134.1, 133.6, 130.1, 129.7, 127.6, 125.9, and 89.8.

IR (CCl$_4$): 3050, 2840, 1685, 1605, 1490, 1440, 1390, 1340, 1230, 1195, 1160, 1140, 1060, 1010, and 770 cm$^{-1}$. 
1-(8-Iodonaphthyl)fulvene (108).

A 50-mL, one-necked, round-bottomed flask equipped with a rubber septum was charged with 8-iodo-1-naphthaldehyde (0.79 g, 2.8 mmol) and 20 mL of methanol and gently warmed in a water bath until the aldehyde dissolved completely to afford a pale yellow solution. Freshly cracked cyclopentadiene (0.57 mL, 0.46 g, 7.0 mmol) was added in one portion via syringe, and pyrrolidine (0.35 mL, 0.30 g, 4.2 mmol) was then added dropwise by syringe over ca. 1 min. Within minutes the reaction mixture turned clear orange. After 20 min, glacial acetic acid (two drops) was added, and after 5 min further the resulting mixture was diluted with 50 mL of Et\textsubscript{2}O and poured into a separatory funnel containing 50 mL of H\textsubscript{2}O. The aqueous layer was separated and extracted with two 25-mL portions of Et\textsubscript{2}O. The combined organic phases were washed with 50 mL of H\textsubscript{2}O and 50 mL of saturated aqueous NaCl solution, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated to afford 0.95 g of 108 as a red oil. Column chromatography on silica gel (elution with 10% CH\textsubscript{2}Cl\textsubscript{2}-hexane) produced 0.75 g of an orange glass (ca. 90% pure by \textsuperscript{1}H NMR, estimated 74% yield) contaminated with traces of dichloromethane. [The product was unstable and began to decompose upon prolonged storage at room temperature under vacuum.] The product was stored in the freezer as a degassed, frozen benzene solution, but was best used immediately after purification.

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): 8.61 (s, 1 H), 8.25 (dd, J =7.7, 1.3 Hz, 1 H), 7.87-7.82 (m, 2 H), 7.43-7.50 (m, 2 H), 7.11 (t, J = 7.7 Hz, 1 H),
$^{13}$C NMR (75 MHz, CDCl$_3$):

6.60-6.63 (m, 2 H), 6.47-6.50 (m, 1 H), and 6.42-6.44 (m, 1 H).

144.0, 141.5, 140.5, 135.4, 134.2, 133.8, 132.9, 131.7, 130.7, 129.9, 127.1, 125.7, 125.5, 121.9, and 92.2.

IR (CCl$_4$):

3045, 2910, 1615, 1600, 1470, 1350, 1335, 1190, 1150, 1070, 1015, 900, and 875 cm$^{-1}$. 
1-(Methyl 8-naphthoyl)fulvene (182).

A 50-mL, one-necked, round-bottomed flask equipped with a rubber septum was charged with 1-(8-iodonaphthyl)fulvene (0.32 g, 0.97 mmol) and 25 mL of diethyl ether. The orange solution was cooled to -78 °C and n-butyllithium (0.56 mL of a 2.06 M solution in hexane, 1.16 mmol) was added via syringe over ca. 2 min. The resulting orange-red solution was stirred for 30 min and methyl chloroformate (0.15 mL, 0.18 g, 1.94 mmol) was added in one portion via syringe. The brown mixture was stirred at -78 °C for 15 min, and was then quenched with 20 mL of H2O. The cold bath was removed and the mixture was stirred at 25 °C for approximately 15 min. The aqueous layer was separated and extracted with two 25-mL portions of Et2O. The combined organic phases were washed with 50 mL of H2O and 50 mL of saturated aqueous NaCl solution, dried over Na2SO4, filtered, and concentrated to afford 0.27 g of a viscous brown oil. The crude material was deposited on silica gel and purified by column chromatography on silica gel (elution with 5% ethyl acetate-hexane) to produce 0.17 g (66%) of 182 as an orange oil.

1H NMR (300 MHz, CDCl3): 7.72 (dd, J = 8.2, 1.3 Hz, 1 H), 7.63 (dd, J = 7.7, 1.6 Hz, 1 H), 7.49 (dd, J = 7.1, 1.3 Hz, 1 H), 7.25-7.34 (m, 4 H), 6.41 (dt, J = 5.3, 1.7 Hz, 1H), 6.36 (d, J = 5.1 Hz, 1 H), 6.23 (d, J = 5.3 Hz, 1 H), 6.19 (dt, J = 5.2, 1.7 Hz, 1 H) and 3.43 (s, 3 H).
$^{13}\text{C} \text{NMR (75 MHz, CDCl}_3\text{)}$: 171.3, 145.5, 137.1, 134.6, 133.9, 133.5, 132.3, 131.9, 131.5, 131.1, 129.4, 128.5, 127.9, 125.8, 125.6, 125.0, 121.2 and 51.8.

IR (CCl$_4$): 3020, 2990, 2940, 1720, 1625, 1470, 1430, 1350, 1330, 1280, 1240, 1190, 1140, 1080, 1000 and 890 cm$^{-1}$. 
Anhydro-8-(hydroxymercuri)-1-naphthoic acid (165).²⁶¹

A 500-mL, three-necked, round-bottomed flask equipped with a glass stopper, a mechanical stirrer with a jacketed adapter, and a Friedrich condenser fitted with an argon inlet adapter was charged with 1,8-naphthalic anhydride (9.9 g, 50 mmol) and a solution of sodium hydroxide (7.0 g, 180 mmol) in 300 mL of H₂O. Using a 80-100 °C oil bath, the reaction mixture was heated for ca. 30 min to afford a dark brown solution. The oil bath was removed, 5 mL of glacial acetic acid was added via pipette, and a brownish-pink mixture was obtained. A solution of mercuric acetate (15.9 g, 50 mmol) in 50 mL of H₂O and 20 mL of acetic acid was then added, and a tan precipitate formed immediately. The resulting mixture was heated at reflux for 30 min, cooled to 25 °C, treated with 9 mL of acetic acid, and heated at reflux for 2 days. The reaction mixture was next cooled to 25 °C and the solids were separated using a Buchner funnel under aspirator pressure and were washed with 100 mL of H₂O. The resulting beige paste was transferred to a 24/40 one-necked 200 mL recovery flask and dried in an 80 °C oil bath at 0.5 mmHg for 24 h to afford 14.5 g of 165 as a crusty beige solid, used in the next step without purification.

8-Iodo-1-naphthoic acid (166).\textsuperscript{261}

A three-necked, 250-mL, round-bottomed flask equipped with an argon inlet adapter, Friedrich condenser, and glass stopper was charged with 14.0 g of anhydromercurinaphthoic acid from the previous reaction (pulverized with a mortar and pestle) and a solution of potassium iodide (27.0 g, 81.2 mmol) in 120 mL of H\textsubscript{2}O. The mixture was warmed in a ca. 60 °C water bath, affording a dark brown solution containing traces of a fine beige solid. Iodine (10.0 g, 39.6 mmol) was added in one portion, and the resulting mixture was heated at reflux in a 120-130 °C oil bath for 18 h. The reaction mixture was cooled to 25 °C, the solids were separated by filtration using a Buchner funnel with aspirator pressure, and the tan filtrate was washed with 100 mL of H\textsubscript{2}O. A solution of sodium thiosulfate (2 g) in 10 mL of H\textsubscript{2}O was added to the filtrate, and the resulting mixture was then acidified to pH 1 with concentrated hydrochloric acid to afford a mixture of white crystalline precipitate and a sticky orange glass. The mixture was filtered using a Buchner with fast speed filter paper and the solids were dissolved in 200 mL of acetone, dried over MgSO\textsubscript{4}, filtered, and concentrated to afford 8.85 g (approx. 79%) of 166 as a crusty yellow solid, mp 152-153 °C dec. [lit.\textsuperscript{255} 163.5-164.5 °C] (approximately 90% pure by \textsuperscript{1}H NMR analysis), which was suitable for use in the following esterification reaction.

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): 11.15 (br s, 1 H), 8.24 (d, J = 7.0- Hz, 1 H), 7.86-7.91 (m, 3 H), 7.48 (apparent t, J = 7.6 Hz, 1 H), and 7.19 (apparent t, J = 7.7 Hz, 1 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 175.4, 141.9, 135.4, 132.6, 131.3, 129.6, 129.5, 127.5, 125.0, 124.5, and 93.0.

IR (KBr) 2900 (br), 1670, 1490, 1445, 1400, 1280, 1190, 1140, 990, 895, 810 and 750 cm$^{-1}$. 
Methyl 8-iodo-1-naphthoate (167).\textsuperscript{261}

A 250-mL, one-necked, round-bottomed flask (note: clearseal joint) equipped with a magnetic stir bar was charged with 8-iodo-1-naphthoic acid (4.0 g, 13.4 mmol, ca. 90% pure) and 60 mL of methanol. The pale orange solution was cooled to -20 °C in an ice-salt bath and a solution of diazomethane (ca. 30 mmol, generated from Diazald (9.6 g, 44.1 mmol)) in 125 mL of diethyl ether was carefully added carefully over 15 min using a flame-polished 5-mL pipette. The resulting bright yellow solution was allowed to slowly warm to 25 °C over 2 h and then was stirred at 25 °C for 1 h. The reaction mixture was dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated to afford 3.6 g of a pale orange glass which was purified by column chromatography on silica gel (elution with 10% ethyl acetate-hexane) to afford 2.96 g (44% overall yield from 1,8-naphthalic anhydride) of 167 as a yellow oil.

\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}):} & \quad 8.21 \, (dd, \, J = 7.4, \, 1.2 \text{ Hz}, \, 1 \text{ H}), \quad 7.85 \, (dd, \, J = 8.3, \, 1.1 \text{ Hz}, \, 1 \text{ H}), \quad 7.84 \, (dd, \, J = 8.3, \, 1.2 \text{ Hz}, \, 1 \text{ H}), \quad 7.69 \, (dd, \, J = 7.4, \, 1.6 \text{ Hz}, \, 1 \text{ H}), \quad 7.45 \, (dd, \, J = 8.3, \, 8.2 \text{ Hz}, \, 1 \text{ H}), \quad 7.14 \, (dd, \, J = 8.3, \, 8.3 \text{ Hz}, \, 1 \text{ H}) \text{ and } 3.99 \, (s, \, 3 \text{ H}). \\
\text{\textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}):} & \quad 170.0, \, 141.5, \, 135.3, \, 134.2, \, 131.9, \, 131.2, \, 129.6, \, 129.1, \, 127.2, \, 125.2, \, 92.5 \text{ and } 52.9. \\
\text{IR (CCl\textsubscript{4}):} & \quad 3050, \, 2980, \, 2945, \, 2830, \, 1720, \, 1485, \, 1440, \, 1425, \, 1360, \, 1340, \, 1260, \, 1180, \, 1140, \, 1070, \, 1050, \, 1005 \text{ and } 940 \, \text{cm}^{-1}.
\end{align*}

Methyl 8-(1-cyclopentenyl)-1-naphthoate (222).

A 50-mL, one-necked, round-bottomed flask equipped with a rubber septum and needle inlet was charged with methyl 8-iodo-1-naphthoate (2.3 g, 7.37 mmol), 30 mL of 1-methyl-2-pyrrolidinone, tris(dibenzylideneacetone)-dipalladium (0.17 g, 0.18 mmol), and triphenylarsine (0.23 g, 0.74 mmol). The reaction mixture was degassed under a stream of argon for 5 min, (1-cyclopentenyl)tributylstannane (3.35 mL, 8.84 mmol, approximately 90% pure; contaminated with tributyltin chloride) was added via syringe over ca. 3 min, and the resulting mixture was heated at 70 °C for 3 h. The dark mixture was then cooled to 25 °C, poured into 50 mL of 1 M aqueous potassium fluoride dihydrate, stirred for 15 min, and then filtered through Celite (two 15-mL portions of diethyl ether were used to wash the Celite). The aqueous phase was separated and extracted with two 50-mL portions of diethyl ether and the combined organic phases were washed with 150 mL of water and 150 mL of saturated aqueous sodium chloride solution, dried over Na₂SO₄, filtered, and concentrated to afford 3.9 g of a brown oil. Purification by column chromatography on silica gel (elution with 5% ethyl acetate-hexane) yielded 1.51 g (81%) of 222 as a yellow oil.

¹H NMR (300 MHz, CDCl₃): 7.89 (dd, J = 8.4, 2.6 Hz, 1 H), 7.74 (dd, J = 6.7, 2.5 Hz, 1 H), 7.66 (dd, J = 7.6, 1.6 Hz, 1 H), 7.40-7.47 (m, 3 H), 5.59 (t, J=1.8 Hz, 1 H), 3.84 (s, 3H), 2.93 (td, J = 7.8, 2.4 Hz, 2 H), 2.66 (td, J = 7.7, 2.5 Hz, 2 H), and 2.11 (q, J = 7.5, 2 H).
$^{13}$C NMR (75 MHz, CDCl$_3$): 170.6, 143.5, 136.6, 134.6, 131.6, 131.4, 130.0, 128.9, 128.0, 127.3, 125.8, 125.7, 124.4, 52.1, 36.3, 33.7, and 23.1.

IR (thin film): 3050, 2950, 2840, 1720, 1500, 1455, 1430, 1370, 1330, 1270, 1195, 1160, 1110, 1050, 1015, 950, 905, 820, 770, and 730 cm$^{-1}$. 
Bromolactone 237.

A 50-mL, one-necked, round-bottomed flask equipped with a rubber septum with needle inlet was charged with ester 222 (0.82 g, 3.2 mmol) and 30 mL of chloroform. The pale yellow solution was cooled to 0 °C and the needle inlet was removed from the argon line and connected to a water bubbler to trap HBr. Bromine (0.25 mL, 0.78 g, 4.9 mmol) was added dropwise via syringe over ca. 1 min, and after 20 min, the ice bath was removed and 20 mL of saturated aqueous sodium bisulfate solution was added to the red reaction mixture. The aqueous phase was separated and extracted with two 20-mL portions of chloroform, and the combined chloroform phases were washed with 20 mL of water and 20 mL of saturated aqueous sodium chloride solution, dried over Na2SO4, filtered, and concentrated to afford 1.09 g of a beige glass which crystallized upon standing. Purification by column chromatography on silica gel (elution with 15% ethyl acetate-hexane) yielded 0.82 g (80%) of 237 as a beige solid, mp 99-99.5 °C (sharp).

1H NMR (300 MHz, CDCl3): 8.40 (d, J = 7.3, 1 H), 8.11 (d, J = 8.2 Hz, 1 H), 7.88 (dd, J = 7.6, 1.2 Hz, 1 H), 6.64-7.54 (m, 3 H), 4.38 (t, J = 4.5 Hz, 1 H), 2.79-2.89 (m, 2H), 2.42-2.47 (q, 6.5 Hz, 1 H) and 2.14-2.31 (m, 2 H).

13C NMR (75 MHz, CDCl3): 163.8, 134.1, 131.8, 129.5, 129.5, 128.5, 128.2, 126.1, 125.7, 125.5, 120.2, 111.8, 94.7, 60.4, 34.9, and 20.8.

IR (CCl4): 3040, 2950, 1725, 1580, 1505, 1460, 1430, 1390, 1340, 1315, 1295, 1250, 1200, 1170, 1140, 1110, 1045, 1010, 960, and 905 cm⁻¹.
Lactone 240.

A 50-mL, one-necked, round-bottomed flask equipped with a rubber septum with needle inlet was charged with bromide 237 (0.72 g, 2.27 mmol) and 20 mL of toluene. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (0.68 mL, 0.75 g, 4.53 mmol) was added via syringe in one portion and the resulting mixture was heated at reflux for 6 d. The resulting dark mixture was cooled to 25 °C and then poured into a mixture of 50 mL of 5% aqueous sulfuric acid solution and ca. 25 g of ice. The aqueous phase was separated and extracted with three 100-mL portions of diethyl ether. The combined organic phases were washed with 150 mL of water and 150 mL of saturated aqueous sodium chloride solution, dried over K₂CO₃, filtered, and concentrated to afford 0.467 g of a red oil. Purification by column chromatography on silica gel (elution with 15% ethyl acetate-hexane) yielded 0.447 g (84%) of 240 as an off-white solid, mp 102-105 °C.

¹H NMR (300 MHz, CDCl₃):  8.44 (dd, J = 7.4, 0.8 Hz, 1 H), 8.11 (dd, J = 8.6, 1.1 Hz, 1 H), 7.84 (d, J = 8.6 Hz, 1 H), 7.64 (t, J = 7.6, 1 H), 7.55 (dd, J = 7.4, 7.3, 1 H), 7.33 (dd, J = 7.2, 0.8 Hz, 1 H), 6.28-6.31 (m, 1 H), 5.90-5.94 (m, 1 H), 2.84-2.91 (m, 1 H), 2.54-2.70 (m, 2 H), 2.28-2.36 (m, 1 H).

¹³C NMR (75 MHz, CDCl₃):  163.8, 137.2, 134.6, 133.3, 133.0, 131.7, 128.7, 127.1, 126.7, 126.5, 126.0, 122.6, 122.2, 96.7, 42.3, and 31.4.

IR (CCl₄):  3050, 2930, 2840, 1720, 1510, 1401, 1350, 1300, 1250, 1180, 1150, 1120, 1030, and 960 cm⁻¹.
Lactols 241a and 241b.

A 150-mL, three-necked, round-bottomed flask equipped with a glass stopper, argon inlet adapter, and rubber septum was charged with lactone 223 (0.50 g, 2.1 mmol) and 20 mL of dichloromethane. The pale yellow solution was cooled to -78 °C and diisobutylaluminum hydride (4.2 mL of a 1.0 M solution in hexane, 4.2 mmol) was added dropwise via syringe over ca. 8 min. After 30 min, 20 mL of saturated aqueous sodium potassium tartrate was added and the suspension was vigorously stirred for 1.5 h. The aqueous phase was separated and extracted with two 50-mL portions of dichloromethane. The combined organic phases were washed with 80 mL of saturated sodium potassium tartrate solution, 80 mL of water, and 80 mL of saturated aqueous sodium chloride solution, dried over Na$_2$SO$_4$, filtered, and concentrated to afford 0.505 g of a pale orange glass. This material was deposited on silica gel and purified by column chromatography on silica gel (elution with 20% ethyl acetate-hexane) to produce 0.401 g (80%) of a 2:1 mixture of the lactols as a sand-colored solid, mp 102-106 °C.

$^1$H NMR (300 MHz, CDCl$_3$):
major isomer: 7.80 (d, J = 8.9 Hz, 1 H), 7.73 (d, J = 8.2 Hz, 1 H), 7.56 (d, J = 7.0 Hz, 1 H), 7.46 (t, J = 8.2 Hz, 1 H), 7.43 (t, J = 7.2 Hz, 1 H), 7.16 (dd, J = 7.2, 1.1 Hz, 1 H), 6.32 (d, J = 7.8 Hz, 1 H), 6.17-6.21 (m, 1 H), 5.96-6.00 (m, 1 H), 4.12 (d, J = 7.8 Hz, 1 H), 2.51-2.67 (m, 3 H) and 2.22-2.26 (m, 1 H).

minor isomer: 7.18 (dd, J = 7.1, 1.1 Hz, 1 H), 6.36 (d, J = 6.2 Hz, 1 H), 6.17-6.21 (m, 1 H), 5.88-5.92 (m, 1 H), 3.95 (d, J =
6.2 Hz, 1 H), 2.51-2.67 (m, 3 H) and 2.47-2.51 (m, 1 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 137.7, 136.0, 135.5, 135.0, 134.9, 133.3, 132.6, 132.6, 128.0, 127.9, 126.5, 126.4, 125.9, 125.6, 125.3, 122.6, 121.6, 121.3, 121.1, 92.1, 91.5, 90.1, 89.4, 40.9, 38.7, 31.9 and 31.4.

IR (CCl$_4$): 3380 (br), 3050, 2940, 2850, 1930, 1598, 1505, 1420, 1360, 1270, 1170, 1125, 1080, and 1040 cm$^{-1}$. 

222
Allylic bromides 243a and 243b.

A 50-mL, one-necked, round-bottomed flask equipped with an argon inlet adapter was charged with lactone 240 (0.22 g, 0.93 mmol) and 20 mL of carbon tetrachloride. To the pale yellow solution was added N-bromosuccinimide (0.17 g, 0.98 mmol) and ca. 10 mg of benzoyl peroxide. The flask was fitted with a reflux condenser and the reaction mixture was heated at reflux for 30 min, cooled to 25 °C, and then filtered through Celite. The Celite was washed with two 10-mL portions of carbon tetrachloride and the combined filtrates then concentrated to afford 0.358 g of a mixture of white solid and nearly colorless oil, which by 1H NMR analysis consisted of a 3:1 mixture of diastereomers 243a and 243b. Purification by column chromatography on silica gel yielded 0.18 g (62%) of the major isomer (243a) as a mixture of white solid and oil and 0.067 g (ca. 23%) of the minor isomer (243b), also as a mixture of white solid and oil, contaminated with ca. 10% of the major isomer.

**major isomer (243a):**

$^1$H NMR (300 MHz, CDCl$_3$): 8.39 (dd, J = 7.4, 2.7 Hz, 1 H), 8.09 (dd, J = 8.3, 1.8 Hz, 1 H), 7.85 (dd, J = 7.7, 2.5 Hz, 1 H), 7.53-7.64 (m, 3 H), 6.28 (dd, J = 5.4, 1.7 Hz, 1 H), 5.95 (dd, J = 5.4, 1.7 Hz, 1 H), 5.24-5.28 (m, 1 H), 3.33 (dd, J = 15.5, 7.2 Hz, 1 H) and 2.81 (dd, J = 15.5, 2.6 Hz, 1 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 163.5, 138.1, 135.8, 133.9, 132.8, 132.0, 129.5, 127.7, 127.2, 127.0, 126.5, 123.9, 119.8, 95.7, 53.2 and 50.5.
IR (CCl₄): 3050, 2930, 1720, 1610, 1580, 1305, 1460, 1420, 1400, 1350, 1295, 1240, 1180, 1140, 1120, 1015 and 920 cm⁻¹.

Minor isomer (243b):

¹H NMR (300 MHz, CDCl₃): 8.46 (d, J = 7.1 Hz, 1 H), 8.14 (d, J = 8.1 Hz, 1 H), 7.88 (d, J = 8.3 Hz, 1 H), 7.68 (apparent t, J = 7.8 Hz, 1 H), 7.53 (apparent t, J = 7.8 Hz, 1 H), 7.18 (d, J = 7.3 Hz, 1 H), 6.36 (dd, J = 5.4 Hz, 2.1 Hz, 1 H), 6.08 (d, J = 5.4 Hz, 1 H), 5.11 (br s, 1 H) and 3.06-3.09 (m, 2 H).

¹³C NMR (75 MHz, CDCl₃): 164.2, 137.6, 135.0, 133.6, 133.3, 132.1, 129.1, 127.4, 127.0, 126.7, 126.3, 122.9, 120.5, 97.1, 42.6 and 31.7.

IR (CCl₄): 3050, 1730, 1520, 1410, 1355, 1310, 1250, 1190, 1160, 1050 and 1030 cm⁻¹.
Triisopropylbenzenesulfonylhydrazine (206)\textsuperscript{262}

A 250-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, glass stopper, and rubber septum was charged with triisopropylbenzenesulfonyl chloride (20.0 g, 66 mmol) and 40 mL of THF. The resulting mixture was cooled to -10 °C using an ice-salt bath and hydrazine hydrate (55% hydrazine, 8.0 mL, 8.23 g, 140 mmol) was added by syringe over 5 min. The pale yellow solution was stirred at 0 °C for 3 h and was then treated with 40 mL of water and 40 mL of diethyl ether. The aqueous phase was separated and extracted with three 50-mL portions of diethyl ether. The combined organic phases were washed with two 50-mL portions of cold brine, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated to afford 18.8 g of a white solid. The solid mass was crushed using a spatula and washed with ca. 20 mL of petroleum ether. Filtration and removal of residual solvent in vacuo yielded 18.8 g (95%) of 206 as a white solid, mp 108-112 °C dec. [lit.\textsuperscript{262} 118-120 °C].

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): 7.20 (s, 2 H), 5.60 (br s, 1 H), 4.16 (quintet, \(J = 6.7\) Hz, 2 H), 3.72 (br s, 2 H), 2.92 (quintet, \(J = 6.8\) Hz, 1 H), 1.27 (d, \(J = 6.7\) Hz, 12 H), and 1.26 (d, \(J = 6.8\) Hz, 6 H).

\textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): 153.8, 151.8, 128.6, 124.0, 34.2, 29.8, 24.9 and 23.5.

IR (CCl\textsubscript{4}): 3360, 3320, 2950, 2920, 2840, 1595, 1460, 1420, 1380, 1360, 1330, 1260, 1150, 920 and 860 cm\textsuperscript{-1}.

\textsuperscript{262}Cusack, N. J.; Reese, C. B.; Risius, A. C.; Roozpeikar, B. Tetrahedron 1976, 32, 2157.
Cyclopentenone triisopropylbenzenesulfonylhydrazone (207).

A 200-mL, one-necked, round-bottomed flask equipped with a rubber septum, needle inlet, and stir bar was charged with triisopropylbenzenesulfonylhydrazine (18.8 g, 63 mmol) and 60 mL of methanol. The white suspension was stirred vigorously as freshly distilled cyclopentanone (5.6 mL, 5.3 g, 63 mmol) was added dropwise by syringe over 10 min. After 5 min, concentrated hydrochloric acid (ca. 1 mL) was added via disposable pipette. The mixture was stirred for 10 min and a white crystalline solid began to precipitate. The flask was placed in a refrigerator overnight, and the resulting white solids were filtered and washed with 25 mL of cold methanol to produce 16.1 g (70%) of 207 as white crystals, mp 144-146 °C dec. [lit.263 133-134 °C dec.]. Trituration of the supernatant with H2O produced an additional 4.1 g (18%) of pale orange solids, mp 137-145 °C dec. which were combined with the first crop of crystals.

1H NMR (300 MHz, CDCl3): 7.14 (s, 2 H), 7.00 (br s, 1 H), 4.21 (quintet, J = 7.1 Hz, 2 H), 3.47 (quintet, J = 7.1 Hz, 1 H), 2.32 (t, J = 7.2 Hz, 2 H), 2.12 (t, J = 7.4 Hz, 2 H), 1.80 (quintet, J = 6.9 Hz, 2 H), 1.68 (quintet, J = 6.3 Hz, 2 H), and 1.24 (m, 18 H).

13C NMR (75 MHz, CDCl3): 166.3, 153.0, 151.3, 131.5, 123.7, 34.1, 33.3, 30.0, 27.5, 24.8, 24.7, 23.5, and 12.2.

IR (CCl4): 3200, 2960, 2870, 1595, 1570, 1450, 1420, 1380, 1360, 1320, 1150, 1025 and 920 cm⁻¹.

1-

Tributylstannylcyclopentene (204).264

A 500-mL, three-necked, round-bottomed flask equipped with argon inlet adapter, pressure-equalizing addition funnel, and rubber septum was charged with trisylhydrazone 207 (16.0 g, 43.9 mmol), 120 mL of hexane, and 120 mL of \( N,N,N'N' \)-tetramethylethylenediamine (TMEDA). The pale yellow suspension was cooled to -78 °C and \( n \)-butyllithium (2.49 M solution in hexane, 44 mL, 109.8 mmol) was added dropwise from the addition funnel over 15 min. The red solution was stirred at -78 °C for 30 min, and then was allowed to warm to 0 °C over 30 min, and finally was stirred at that temperature for 30 min. The yellow solution was treated with tributyltin chloride (13.0 mL, 15.7 g, 48.3 mmol) which was added rapidly via syringe. The resulting mixture was stirred at 25 °C for 2 h and was then poured into 250 mL of \( H_2O \). The aqueous phase was extracted with two 150-mL portions of petroleum ether and the combined organic phases were washed with three 150-mL portions of water, two 100-mL portions of saturated aqueous copper sulfate solution, and 150 mL of brine, dried over \( K_2CO_3 \), filtered, and concentrated to afford 17 g of an amber oil which was purified by distillation to produce 204 as a pale yellow oil, bp 100-110 °C/0.5 mmHg (lit.265 115-125 °C/0.06 mmHg). The product was contaminated with ca 5% of tributyltin chloride and the yield was estimated to be 93% by \(^1\)H NMR.


$^1$H NMR (300 MHz, CDCl$_3$): 5.85 (t, $J = 2.2$ Hz, 1 H), 2.32-2.40 (m, 4H), 1.75 (quintet, $J = 7.3$ Hz, 2 H), 1.40-1.49 (m, 6 H), 1.23-1.34 (m, 12 H) and 0.85-0.89 (t, $J = 7.3$ Hz, 9 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 140.6, 39.6, 34.3, 29.3, 27.5, 27.4, 23.5, 13.8 and 9.3.

IR (thin film): 2970, 2930, 2860, 1580, 1460, 1420, 1370, 1350, 1290, 1250, 1170, 1160, 1070, 1040, 990, 970, 870 and 660 cm$^{-1}$. 
1-Iodo-8-allylnaphthalene.

A 1-L, three-necked, round-bottomed flask wrapped in aluminum foil and equipped with a vacuum adapter, rubber septum, and glass stopper was charged with 1,8-diiodonaphthalene (6.00 g, 15.8 mmol) and 360 mL of diethyl ether. [The lights in the hood were turned off.] The pale yellow solution was cooled to 0 °C while n-butyllithium solution (2.56 M in hexanes, 6.48 mL, 16.6 mmol) was added dropwise by syringe over 10 min. After 30 min, allyl bromide (2.73 mL, 31.6 mmol) was added dropwise via syringe over ca. 2 min to the bright yellow solution. Sodium iodide (1.18 g, 7.90 mmol) was added in one portion, and the reaction mixture was then stirred at 25 °C. After 1 h, 200 mL of 10% aqueous HCl was added, and the mixture was stirred for 30 min. The aqueous phase was separated and extracted with two 150-mL portions of diethyl ether. The combined organic phases were washed with three 200-mL portions of water and three 200-mL portions of saturated aqueous NaCl solution, dried over MgSO4, filtered, and concentrated to afford a brownish yellow oil (5.64 g). The oil was purified in two portions by column chromatography on silica gel (elution with hexane) to afford 2.40 g (52%) of 291 as a yellow oil.

1H NMR (300 MHz, CDCl3): 8.29 (d, J = 7.0 Hz, 1 H), 7.82 (d, J = 8.1 Hz, 1 H), 7.73 (dd, J = 7.4, 1.9 Hz, 1 H), 7.38-7.46 (m, 2 H), 7.0 (t, J = 7.7 Hz, 1 H), 6.22 (ddd, J = 17.1, 10.1, 6.0 Hz, 1 H), 5.12 (d, J = 10.1 Hz, 1 H), 4.90 (dd, J = 17.1, 1.7 Hz, 1 H) and 4.42 (d, J = 5.8 Hz, 2 H).
$^{13}$C NMR (75 MHz, CDCl$_3$): 142.6, 138.7, 136.4, 136.0, 132.3, 130.6, 130.4, 129.0, 126.0, 125.7, 115.8, 89.4 and 39.5.

IR (thin film): 3000, 2930, 2900, 2870, 2820, 2790, 1920, 1830, 1710, 1630, 1560, 1500, 1450, 1420, 1360, 1240, 1200, 1100, 910, 810 and 750 cm$^{-1}$. 
1-[(Trimethylsilyl)ethynyl]-8-allylnaphthalene (292).

A 100-mL, one-necked, round-bottomed flask wrapped in aluminum foil and equipped with a rubber septum was charged with 1-iodo-8-allyl-naphthalene (291) (1.50 g, 5.10 mmol) and 23 mL of degassed triethylamine in the dark. Trimethylsilylacetylene (1.13 mL, 0.79 g, 5.10 mmol) was added in one portion via syringe. Dichlorobis(triphenylphosphine)palladium (140 mg, 0.20 mmol) and copper (I) iodide (78 mg, 0.41 mmol) were added and the mixture became opaque and orange-colored. After 30 min, additional (trimethylsilyl)acetylene (1.13 mL, 5.10 mmol) was added in one portion via syringe to the orange mixture. An additional portion of (trimethylsilyl)acetylene (1.13 mL, 0.79 g, 5.10 mmol) was added 30 min later and the dark brown mixture was stirred at 25 °C for 4 h. The reaction mixture was filtered through Celite and the solids were washed with 200 mL of diethyl ether. Concentration yielded 1.70 g of a dark brown oil which was deposited onto silica gel and purified by column chromatography on silica gel (elution with hexanes) to produce 0.80 g (59%) of 292 as a yellow oil.

\[ ^{1}H \text{NMR (300 MHz, CDCl}_3\text{)}: \]
\[
7.81 (d, J = 8.0 \text{ Hz, } 1 \text{H}), 7.79 (d, J = 7.2 \text{ Hz, } 1 \text{H}), 7.71 (dd, J = 7.3, 1.3 \text{ Hz, } 1 \text{H}), 7.33-7.43 (m, 3 \text{H}), 6.21-6.30 (m, 1 \text{H}), 5.06 (dd, J = 10.2, 1.4 \text{ Hz, } 1 \text{H}), 4.98 (dd, J = 17.1, 1.7 \text{ Hz, } 1 \text{H}), 4.46 (d, J = 6.2, 2 \text{H}), \text{ and } 0.30 (s, 9 \text{H}).
\]

\[ ^{13}C \text{NMR (75 MHz, CDCl}_3\text{)}: \]
\[
139.0, 137.1, 135.4, 134.8, 131.3, 130.6, 129.3, 128.0, 125.9, 124.5, 119.2, 114.8, 107.5, 99.2, 39.5, \text{ and } -0.3.
\]
IR (thin film): 3070, 2980, 2150, 1650, 1580, 1510, 1460, 1420, 1260, 1010, 930, 860, and 770 cm$^{-1}$. 
1-Ethynyl-8-allylnaphthalene (113).

A 50-mL, one-necked round-bottomed flask equipped with a rubber septum was charged with 1-[(trimethylsilyl)ethynyl]-8-allyl-naphthalene (292) (0.800 g, 3.03 mmol) and 15 mL of methanol. To the yellow solution was added 3 mL of a 1M aqueous solution of potassium hydroxide via pipette, and the reaction mixture turned milky yellow. After 1 h, the reaction mixture was treated with 15 mL of 10% aqueous hydrochloric acid solution. The aqueous phase was extracted with three 25-mL portions of diethyl ether. The combined organic phases were washed with 50 mL of water and 50 mL of saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated to afford 0.528 g (91%) of 113 as a yellow oil.

\(^1\)H NMR (300 MHz, CDCl₃): 7.83-7.88 (m, 2 H), 7.75 (d, J = 7.7 Hz, 1 H), 7.37-7.47 (m, 3 H), 6.29 (ddd, J = 17.1, 10.1, 4.0 Hz, 1 H), 5.12 (dd, J = 10.1, 1.5 Hz, 1 H), 5.01 (dd, J = 17.1, 1.5 Hz, 1 H), 4.47 (d, J = 6.0 Hz, 2 H), and 3.46 (s, 1 H).

\(^13\)C NMR (75 MHz, CDCl₃): 138.8, 137.4, 135.8, 134.7, 130.8, 129.4, 128.1, 126.0, 124.5, 118.2, 115.1, 85.9, 82.2, 82.2, and 39.2.

IR (thin film): 3290, 3050, 2970, 2910, 2860, 2090, 1940, 1815, 1640, 1570, 1505, 1440, 1370, 1330, 1280, 1260, 1220, 1170, 1110, 990, 910, 820, and 800 cm\(^{-1}\).
Cyclopentenone 112.

A three-necked, 100-mL round-bottomed flask equipped with an argon inlet adapter, glass stopper, and rubber septum was charged via cannula with a solution of 1-ethynyl-8-allyl-naphthalene (0.421 g, 2.19 mmol) in 40 mL of methylene chloride. The resulting pale yellow solution was degassed with argon for 5 min. Dicobalt octacarbonyl (0.805 g, 93% pure, moistened with hexane, 2.19 mmol) was added in one portion and the resulting dark brown reaction mixture was stirred at 25 °C for 1.5 h. The reaction mixture was then cooled to 0 °C and N-methylmorpholine N-oxide (NMO) (0.513 g, 4.38 mmol) was added, and the ice bath was removed after 5 min. The cycle of cooling to 0 °C, addition of NMO, and stirring at room temperature was repeated hourly until four portions of NMO had been added. The resulting mixture was stirred for 12 h at room temperature, and then was filtered through Celite. The solids were washed with two 20-mL portions of dichloromethane. Concentration yielded a dark brown solid which was deposited on silica gel and purified by column chromatography (elution with 30% ethyl acetate-hexane) to afford 0.370 g (77%) of 112 as a brownish-orange solid, mp 107-108 °C.

$^1$H NMR (300 MHz, CDCl$_3$): 7.94 (d, J = 8.1 Hz, 1 H), 7.81 (d, J = 7.1 Hz, 1 H), 7.75 (d, J = 8.1 Hz, 1 H), 7.53 (apparent t, J = 7.7 Hz, 1 H), 7.46 (apparent t, J = 7.6 Hz, 1 H), 7.36 (d, J = 7.0 Hz, 1 H), 6.54 (d, J = 1.7 Hz, 1 H), 3.47 (dd, J = 14.8, 5.7 Hz, 1 H), 3.29-3.34 (m, 1 H), 2.94 (apparent t, J = 14.5 Hz, 1 H), 2.88 (dd, J = 18.5, 6.5 Hz, 1 H), and 2.29 (dd, J = 18.5, 3.1 Hz, 1 H).
$^{13}$C NMR (75 MHz, CDCl$_3$): 174.6, 133.8, 133.5, 131.7, 129.0, 128.2, 126.6, 126.3, 126.0, 125.6, 124.5, 124.3, 42.4, 38.4 and 36.6.

IR (thin film): 3050, 2950, 2840, 1720, 1500, 1455, 1430, 1370, 1330, 1270, 1195, 1160, 1110, 1050, 1015, 950, 905, 820, 770, and 730 cm$^{-1}$. 
Allylic alcohols 302a and 302b.

A one-necked, 25-mL, round-bottomed flask equipped with a septum and needle inlet was charged with cyclopentenone 112 (0.076 g, 0.35 mmol) and benzene (10 mL). The yellow solution was cooled to 0-5 °C in an ice-water bath and diisobutylaluminum hydride (0.28 mL of a 1.5 M solution in toluene, 0.41 mmol) was added dropwise via syringe over 1 min. Ten minutes later, two drops of methanol were added via disposable pipette, the ice bath was removed, and 10 mL of saturated aqueous sodium potassium tartrate (Rochelle's salt) solution was added and the resulting suspension was stirred vigorously for 1 h. The aqueous phase was separated and extracted with two 15-mL portions of diethyl ether. The organic phases were washed with 30-mL portions of water and brine, dried over sodium sulfate, filtered, and concentrated to afford 75 mg (97%) of an orange glass which solidified under vacuum to produce shiny, orange-yellow flakes, mp 109-112 °C of a 16:1 ratio of 302a and 302b.

$^1$H NMR (300 MHz, CDCl$_3$): 7.73 (d, J = 8.3 Hz, 1 H), 7.65 (d, J = 8.4, Hz, 1 H), 7.60 (d, J = 7.3 Hz, 1 H), 7.36 (apparent q, J = 8.3 Hz, 2 H), 7.19 (d, J = 7.4 Hz, 1 H), 6.19 (s, 1 H), 5.05 (t, J = 6.8 Hz, 1 H), 3.25 (dd, J = 14.2, 4.7 Hz, 1 H), 2.74-2.94 (m, 3 H), 2.33 (br s, 1 H) and 1.44 (dt, J = 11.8, 7.3, 1 H).

$^1$H NMR (300 MHz, C$_6$D$_6$): 7.60 (d, J = 8.4 Hz, 1 H), 7.54 (d, J = 78.4 Hz, 2 H), 7.25 (apparent t, J = 7.7 Hz, 1 H), 7.24 (apparent t, J = 7.5 Hz, 1 H), 7.03 (d, J = 6.9 Hz, 1 H), 6.08 (d, J = 2.0
$^{13}$C NMR (75 MHz, CDCl$_3$):

$\text{Hz, 1 H}, 4.84 (t, J = 6.7 \text{ Hz, 1 H}), 2.94 (dd, J = 12.8, 3.3 \text{ Hz, 1 H}), 2.61-2.68 (m, 2 \text{ H}), 2.48-2.60 (m, 1 \text{ H}), 1.40 (s, 1 \text{ H}) \text{ and 1.24-1.33 (m, 1 H).}$

IR (CCl$_4$):

3600, 3330 (br), 3060, 2970, 2930, 2880, 2860, 2050, 1930, 1590, 1500, 1440, 1380, 1320, 1130, 1070, 1040, 905, and 720 cm$^{-1}$. 

144.5, 136.0, 134.6, 130.7, 128.9, 128.1, 126.9, 126.7, 126.4, 126.2, 125.3, 122.3, 77.8, 43.0, 41.7, and 39.5.
1-Iodo-8-(1'-hydroxy-2'propenyl)naphthalene (324).

A 250-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, rubber septum, and a pressure-equalizing addition funnel fitted with a septum was charged with a solution of 1,8-diiodonaphthalene (2.04 g, 5.37 mmol) in 50 mL of diethyl ether via cannula in the dark. An additional 60 mL of diethyl ether was used to rinse the flask. The pale yellow solution was cooled to 0 °C while n-butyllithium solution (2.54 M in hexanes, 2.22 mL, 5.64 mmol) was added dropwise by syringe over 5 min. After 30 min, the orange solution was cooled to -78 °C and a solution of acrolein (0.54 mL, 0.45 g, 8.05 mmol) in 10 mL of diethyl ether was added dropwise via the addition funnel over 20 min. The bath was allowed to warm to -40 °C over 2 h and the resulting yellow mixture was quenched by the addition of 75 mL of 5% aqueous HCl solution. The aqueous phase was separated and extracted with three 40-mL portions of diethyl ether. The combined organic phases were washed with 100 mL of water and 100 mL of saturated aqueous NaCl solution, dried over Na₂SO₄, filtered, and concentrated to afford a light brown oil (2.11 g).

This material was deposited on silica gel and purified by column chromatography on silica gel (elution with 10% ethyl acetate-hexanes) to afford 0.778 g (47%) of 324 as a viscous yellow oil.

1H NMR (300 MHz, CDCl₃): 8.30 (d, J = 7.3 Hz, 1 H), 7.85 (d, J = 7.5 Hz, 1 H), 7.83 (d, J = 7.4 Hz, 1 H), 7.75 (d, J = 8.4 Hz, 1 H), 7.48 (apparent t, J = 7.5 Hz, 1 H), 7.29 (br s, 1 H), 7.04 (apparent t, J = 7.5 Hz, 1 H), 6.25 (ddd, J = 17.0, 10.0,
3.9 Hz, 1 H), 5.43 (d, J = 17.0 Hz, 1 H), 5.28 (J = 10.0 Hz, 1 H), and 2.37 (s, 1H).

\[ \text{\(^{13}\text{C NMR (75 MHz, CDCl}_3\): } 142.9, 140.1, 138.4, 135.8, 131.4, 130.5, 130.0, 128.2, 126.0, 125.7, 114.5, 87.8, \text{ and 67.3.} \]

\[ \text{IR (thin film): } 3560, 3380 \text{ (br), 3060, 3005, 2995, 2930, 1945, 1860, 1730, 1640, 1600, 1560, 1495, 1410, 1360, 1345, 1230, 1195, 1150, 1110, 970, 930, 820 \text{ and 760 cm}^{-1}.\]
1-Iodo-8-(1'-tert-butyldimethylsilyloxy-2'-propenyl)naphthalene (333).

A 10-mL, two-necked, round-bottomed flask equipped with a septum and argon inlet adapter was charged via cannula with a solution of alcohol 324 (0.143 g, 0.46 mmol) in 6 mL of dichloromethane. The pale yellow solution was treated with freshly distilled lutidine (80 mL, 0.69 mmol) and the reaction mixture was then cooled to -20 °C. Tert-butyldimethylsilyl trifluoromethane sulfonate (0.13 mL, 0.56 mmol) was added via syringe. After 30 min, the reaction mixture was poured into 15 mL of saturated aqueous sodium bicarbonate solution. The aqueous phase was separated and extracted with three 15-mL portions of dichloromethane. The organic extracts were washed with 20 mL of cold 5% aqueous HCl, 20 mL of water, and 20 mL of saturated aqueous NaCl solution, dried over Na₂SO₄, filtered, and concentrated to afford 0.189 g of a pale peach solid which was deposited on silica gel and purified by column chromatography on silica gel (elution with hexanes) to afford 0.106 g (65%) of 333 as an off-white waxy solid, mp 40-42 °C.

\[ ^1H \text{ NMR (300 MHz, CDCl}_3\]: 8.30 (dd, \( J = 7.3, 1.1 \text{ Hz, 1 H} \)), 8.06 (dd, \( J = 7.1, 1.1 \text{ Hz, 1 H} \)), 7.85 (d, \( J = 8.1 \text{ Hz, 1 H} \)), 7.73 (dd, \( J = 8.1, 1.1 \text{ Hz, 1 H} \)), 7.55 (s, 1 H), 7.53 (t, \( J = 7.7 \text{ Hz, 1 H} \)), 7.02 (t, \( J = 7.7 \text{ Hz, 1 H} \)), 6.30 (ddd, \( J = 16.0, 10.4, 3.4 \text{ Hz, 1 H} \)), 5.26 (dt, \( J = 16.9, 1.8 \text{ Hz, 1 H} \)), 5.07 (dt, \( J = 10.4, 1.8 \text{ Hz, 1 H} \)), 0.95 (s, 9 H), 0.13 (s, 3 H) and 0.91 (s, 3 H).

\[ ^13C \text{ NMR (75 MHz, CDCl}_3\]: 143.0, 142.0, 140.1, 135.8, 130.8, 130.7, 129.1, 127.4, 126.0, 125.8, 112.6, 87.7, 68.4, 26.0, 18.4 and -4.6.}
IR (CCL₄):
3060, 2960, 2940, 2890, 2860, 1640, 1595, 1560, 1495, 1470, 1390, 1360, 1330, 1250, 1190, 1160, 1130, 1030, 920, 860, 830, 760, and 670 cm⁻¹.
1-Iodo-8-(1-methoxy-2-propenyl)-naphthalene (334).

Alcohol 324 (0.083 g, 0.27 mmol) was dissolved in 1 mL of methyl iodide in a 5-mL, one-necked, round-bottomed flask equipped with a vacuum adapter in the dark. Calcium sulfate (0.146 g, 1.07 mmol) and silver (I) oxide (0.099 g, 0.43 mmol) were added and the resulting dark brown heterogeneous mixture was stirred for 17 h at room temperature. The reaction mixture was filtered through a plug of Celite and 1 mL of dichloromethane was used to rinse the solids. Concentration yielded a yellow orange oil which was deposited on silica gel and purified by column chromatography on silica gel (elution with 5% ethyl acetate-hexanes) to produce 0.068 g (78%) of 334 as a yellow oil.

$^1$H NMR (300 MHz, CDCl$_3$): 8.30 (dd, $J = 7.4$, 1.3 Hz, 1 H), 7.88 ($J = 7.4$, 1.3 Hz, 1 H), 7.84 (dd, $J = 8.1$, 1.2 Hz, 1 H), 7.75 (dd, $J = 8.1$, 1.3 Hz, 1 H), 7.53 ($t$, $J = 7.7$ Hz, 1 H), 7.00-7.06 (m, 2 H), 6.29 (ddd, $J = 17.1$, 10.7, 4.8 Hz, 1 H), 5.25 (dt, $J = 4.8$, 1.5 Hz, 1 H), 5.21 (dt, $J = 11.2$, 1.5 Hz, 1 H) and 3.34 (s, 3 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 143.1, 139.4, 137.1, 138.9, 133.2, 130.9, 130.7, 129.7, 127.8, 126.0, 125.9, 116.3, 87.8 and 56.5.

IR (thin film): 3060, 2990, 2930, 2820, 1640, 1590, 1560, 1490, 1440, 1400, 1320, 1260, 1190, 1070, 980, 920, 850, 690 and 760 cm$^{-1}$. 

253
**1-Iodo-8-(trimethylsilyl)alkynylnaphthalene (337).**

A 100-mL, one-necked, round-bottomed flask equipped with an argon inlet adapter was charged with a solution of 1,8-diiodonaphthalene (3.0 g, 7.90 mmol) and 60 mL of degassed triethylamine in the dark. To the resulting pale yellow solution was added trimethylsilylacetylene (1.34 mL, 0.93 g, 9.48 mmol) via syringe over ca. 1 min. Dichlorobis(triphenylphosphine)palladium (222 mg, 0.04 mmol) and copper iodide (120 mg, 0.08 mmol) were added, and the heterogeneous mixture was stirred at room temperature for 16 h. The color of the reaction mixture changed from yellow to orange, and the mixture became very thick (*use of an efficient stirrer is recommended*). The pumpkin-colored mixture was filtered using Celite and the solids were washed with 50 mL of diethyl ether. Concentration yielded 3.15 g of a viscous red oil which was deposited on silica gel and purified by chromatography on silica gel (elution with hexanes) to afford 1.80 g (65%) of 337 as a yellow-orange oil.

$^1$H NMR (300 MHz, CDCl$_3$): 8.25 (dd, $J = 7.4$, 1.2 Hz, 1 H), 7.86 (dd, $J = 7.2$, 1.4 Hz, 1 H), 7.78 (dd, $J = 8.1$, 1.4 Hz, 1 H), 7.77 (dd, $J = 8.1$, 1.3 Hz, 1 H), 7.37 (apparent t, $J = 7.6$ Hz, 1 H), 7.06 (t, $J = 7.8$ Hz, 1 H) and 0.28 (s, 9 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 142.8, 137.2, 134.7, 130.6, 130.5, 130.1, 127.0, 125.3, 104.2, 93.1 and -0.5.

IR (thin film): 3050, 2960, 2900, 2140, 1550, 1495, 1420, 1410, 1360, 1345, 1250, 1195, 1020, 900, 850, 820, 750, 690 and 650 cm$^{-1}$. 

255
1-(1-hydroxy-2-propenyl)-8-[(trimethylsilyl)ethynyl]-naphthalene (326).

A 250-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, pressure-equalizing addition funnel fitted with a septum, and a rubber septum was charged via cannula with a solution of iodide 337 (0.76 g, 1.93 mmol) in 40 mL of diethyl ether via cannula in the dark. An additional 10 mL of diethyl ether was used to rinse the flask. The pale yellow solution was cooled at -30 °C while n-butyllithium solution (2.39 M in hexanes, 0.89 mL, 2.12 mmol) was added dropwise by syringe over 5 min. After 10 min, the orange-yellow solution was cooled to -78 °C and a solution of acrolein (0.26 mL, 0.22 g, 3.86 mmol) in 5 mL of diethyl ether was added dropwise via the addition funnel over 5 min. The yellow reaction mixture was stirred for 20 min and was quenched by the addition of 40 mL of 5% aqueous HCl solution. The aqueous phase was separated and extracted with three 40-mL portions of diethyl ether. The combined organic phases were washed with 80 mL of water and 80 mL of saturated aqueous NaCl solution, dried over Na₂SO₄, filtered, and concentrated to afford an orange oil which was deposited onto silica gel and purified by column chromatography on silica gel (elution with 5% ethyl acetate-hexanes) to afford 0.407 g (75%) of 326 as an orange oil.

¹H NMR (300 MHz, CDCl₃): 7.83 (apparent td, J = 7.4, 1.7 Hz, 2 H), 7.75 (apparent td, J = 7.6, 1.7 Hz, 2 H), 7.46 (apparent t, J = 7.8 Hz, 1 H), 7.38 (apparent t, J = 7.5 Hz, 1 H), 7.18 (br s, 1 H), 6.30 (ddd, J = 17.0, 10.9, 2.0 Hz, 1 H), 5.48 (dd, J = 17.0, 3.0 Hz, 1 H), 5.28 (dt, J = 10.9, 2.0 Hz, 1 H), 2.85 (d, J = 4.0 Hz, 1 H) and 0.31 (s, 9 H).
$^{13}$C NMR (75 MHz, CDCl$_3$): 140.0, 139.8, 135.8, 134.7, 131.1, 130.4, 129.5, 127.0, 126.0, 124.6, 117.7, 114.0, 107.2, 99.1, 69.2 and -0.25.

IR (thin film): 3420 (br), 3050, 3960, 3900, 2140, 1405, 1370, 1320, 1250, 1120, 1010, 980, 910, 850 and 760 cm$^{-1}$. 
1-(1-Hydroxy-2-propenyl)-8-ethynyl-naphthalene (315).

A solution of silyl enyne 326 (2.59, 9.20 mmol) in 230 mL of methanol in a 500 mL, one-necked, round-bottomed flask equipped with an argon inlet adapter was treated with potassium carbonate (0.12 g, 0.92 mmol) and stirred vigorously for 2 h at room temperature. The solvent was removed under reduced pressure (using the rotary evaporator and, for ca. 10 min, the vacuum pump) and the residue was immediately purified by column chromatography on silica gel (elution with 5% ethyl acetate-petroleum ether) to afford 1.76 g (94%) of 315 as a gold solid, mp 46.5-47 °C.

$^1$H NMR (300 MHz, CDCl$_3$): 7.85 (apparent t, J = 8.4 Hz, 2 H), 7.78 (d, J = 7.7 Hz, 2 H), 7.47 (apparent t, J = 7.7 Hz, 1 H), 7.40 (apparent t, J = 7.7 Hz, 1 H), 7.21 (br s, 1 H), 6.29 (ddd, J = 17.3, 10.5, 4.1 Hz, 1 H), 5.47 (d, J = 17.3 Hz, 1 H), 5.28 (d, J = 10.5 Hz, 1 H), 3.50 (s, 1 H) and 2.69 (d, J = 4.4 Hz, 1 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 140.1, 139.5, 136.3, 134.6, 131.2, 130.3, 129.5, 127.0, 126.0, 124.6, 116.6, 114.1, 85.6 and 69.0.

IR (thin film): 3560, 3400 (br), 3300, 3060, 3020, 2930, 2670, 2250, 2090, 1940, 1860, 1830, 1760, 1620, 1600, 1580, 1500, 1410, 1350, 1240, 1170, 1120, 960, 910, 800, 770 and 730 cm$^{-1}$.
Hydroxy cyclopentenones 314a and 314b.

A 100-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, glass stopper, and rubber septum was charged with a solution of enyne 315 (0.330 g, 1.63 mmol) in 30 mL of dichloromethane via cannula. An additional 10 mL of dichloromethane was used to rinse the flask. The yellow solution was degassed for 10 min, and dicobalt octacarbonyl (~93% pure, moistened with hexanes, 0.558 g, 1.63 mmol) was added in one portion, and the resulting dark brown mixture was stirred at room temperature for 2.75 h. The mixture was cooled to 0 °C, N-methylmorpholine N-oxide (NMO) (0.380 g, 3.26 mmol) was added, and the ice bath was removed after 5 min. The cycle of cooling to 0 °C, addition of NMO, and stirring at room temperature was repeated hourly until NMO had been added four times. The mixture was stirred at room temperature for one additional hour, and then was filtered through Celite. The solids were washed with two 30-mL portions of dichloromethane. The supernatant was transferred to a separatory funnel and was washed with 75 mL of water and 75 mL of brine, and was dried over Na₂SO₄, filtered, and concentrated to afford an orange solid which was deposited on silica gel and purified by column chromatography (elution with diethyl ether) to afford a 5:1 mixture of 314a and 314b as an orange-yellow solid, 0.290 g (~75% yield, 90% pure as estimated by ¹H NMR analysis). Recrystallization of a small portion of the product from
chloroform produced orange-yellow crystals, mp 146-147 °C (sharp), which by \textsuperscript{1}H NMR analysis was a 5:1 mixture of diastereomers 314a and 314b.

major isomer (314a):
\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): 7.97 (dd, J = 8.3, 2.0 Hz, 1 H), 7.81-7.89 (m, 3 H), 7.51-7.62 (m, 2 H), 6.59 (d, J = 2.8 Hz, 1 H), 4.83 (dd, J = 11.5, 7.6 Hz, 1 H), 3.26-3.34 (m, 1 H), 2.92 (dd, J = 18.5, 6.3 Hz, 1 H), 2.74 (d, J = 7.6 Hz, 1 H) and 2.62 (dd, J = 19.2, 2.9 Hz, 1 H).

\textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): 184.9, 137.6, 133.6, 131.7, 127.6, 126.6, 126.0, 125.8, 124.6, 123.1, 74.6, 47.4, 40.5 and 39.1.

IR (CH\textsubscript{2}Cl\textsubscript{2}): 3560, 3360 (br), 2870, 1670, 1595, 1490, 1360, 1300, 1170, 1160, 1120, 1090, 1010, 980, 905 and 830 cm\textsuperscript{-1}. 

263
Diols 347a and 347c.

A mixture of enones 314a and 314b (7:1 ratio, 0.115 g, 0.38 mmol) was dissolved in 6 mL of THF in a one-necked, 25-mL, round-bottom flask equipped with a septum and needle inlet. The yellow-orange solution was cooled to -78 °C and L-Selectride (0.42 mL of a 1.0 M solution in THF, 0.42 mmol) was added dropwise via syringe over ca 30 sec. The reaction mixture turned olive-green. After 10 min, 5 drops of H2O and 10 drops of absolute ethanol were added and the reaction mixture was allowed to warm to 25 °C. Next, 3 mL of a 6 M aqueous solution of sodium hydroxide and 3 mL of 30% aqueous H2O2 solution were added and the resulting mixture was stirred at 25 °C for 2 h. The reaction mixture was then diluted with 10 mL of H2O and the aqueous phase was saturated with solid K2CO3 and extracted with three 15-mL portions of ether. The combined organic phases were washed with brine, dried over Na2SO4, filtered, and concentrated to give 0.096 g of an orange-brown solid which was deposited on silica gel and purified by column chromatography on silica gel (elution with 66% ethyl acetate-hexane) to produce 0.070 g of a 7:1 mixture of 347a and 347c as an orange solid, mp 140-142 °C. By 1H NMR analysis, the products were ~90% pure, contaminated with ca 10% sec-butyl alcohol, and the yield was estimated to be 54%. Diols 347a and 347c were relatively insoluble in most common organic solvents.
major isomer (347a):

\(^1\text{H} \text{NMR (300 MHz, acetone-}d_6\)): 7.76-7.87 (m, 4 H), 7.46-7.55 (m, 2 H), 6.38 (t, J = 1.8 Hz, 1 H), 5.02-5.10 (m, 1 H), 4.83 (d, J = 7.5 Hz, 1 H), 4.67 (dd, J = 8.9, 7.5 Hz, 1 H), 4.07 (d, J = 6.1 Hz, 1 H), 2.84-2.96 (m, 1 H) and 1.74-1.86 (m, 1 H).

mixture:

IR (KBr): 3300 (br), 3030, 1625, 1490, 1395, 1360, 1330, 1290, 1250, 1220, 1160, 1120, 1090, 1050, 980, 960, 810 and 760 cm\(^{-1}\).
Diacetate 359.

Diol 347 (0.050 g, 0.21 mmol) was dissolved in 1 mL of pyridine in a one-necked, 10-mL, round-bottom flask equipped with an argon inlet adapter. Acetic anhydride (0.4 mL, 4.2 mmol) was added via syringe in one portion to the brown solution. Dimethylaminopyridine (DMAP) (ca. 2 mg) was added to the reaction mixture and the resulting brown mixture was stirred at 25 °C. After 3 h, the reaction mixture was poured into 10 mL of H₂O. The aqueous phase was extracted with three 15-mL portions of diethyl ether. The combined organic phases were washed with 15 mL of H₂O and 15 mL of brine, dried over Na₂SO₄, filtered, and concentrated to afford a pale brown oil which was purified by column chromatography on silica gel (elution with 10% ethyl acetate-hexane) to afford 0.056 g (76%) of 359 as a pale beige solid, mp 134-136 °C.

\( ^1H \) NMR (300 MHz, CDCl₃): 7.81 (d, \( J = 8.0 \) Hz, 1 H), 7.77 (d, \( J = 8.2 \) Hz, 1 H), 7.72 (d, \( J = 7.1 \) Hz, 1 H), 7.47 (overlapping t, \( J = 8.2, 7.2 \) Hz, 2 H), 7.26 (d, \( J = 7.2 \) Hz, 1 H), 6.33 (t, \( J = 2.1 \) Hz, 1 H), 6.20 (d, \( J = 11.1 \) Hz, 1 H), 5.89 (td, \( J = 6.1, 1.6 \) Hz, 1 H), 3.18-3.22 (m, 1 H), 2.88 (dt, \( J = 13.8, 7.7 \) Hz, 1 H), 2.31 (s, 3 H), 2.08 (s, 3 H) and 1.86-1.93 (m, 1 H).

\( ^{13}C \) NMR (75 MHz, CDCl₃): 171.2, 171.1, 143.5, 133.8, 133.6, 128.8, 128.4, 128.3, 127.6, 125.8, 125.7, 123.4, 122.8, 122.3, 121.7, 79.6, 76.4, 46.9, 35.8, 21.3 and 21.2.

IR (CCl₄): 3040, 2920, 2860, 1750, 1440, 1370, 1238, 1060, 1020, 930 and 910 cm⁻¹.
Methoxy cyclopentenones 348a and 348b.

A 3:2 mixture of alcohols 314a and 314b (0.415 g, 1.76 mmol) was dissolved in 20 mL of methyl iodide in a one-necked, 50-mL, round-bottomed flask equipped with an argon inlet adapter. The flask was covered with aluminum foil to protect the reaction mixture from light. Calcium sulfate (0.96 g, 7.03 mmol) and silver (I) oxide (0.65 g, 2.81 mmol) were added, and the resulting dark brown mixture was stirred at 25 °C for 10 h. Additional portions of calcium sulfate (0.10 g, 0.70 mmol) and silver (I) oxide (0.07 g, 0.28 mmol) were then added and the mixture was stirred for 14 h. The dark brown mixture was then filtered through Celite, and the solids were washed with two 20-mL portions of dichloromethane. Reduction of the supernatant afforded a dark brown oil which was deposited on silica gel and purified by column chromatography on silica gel (elution with 75% diethyl ether-petroleum ether) to produce 0.285 g (65%) of a mixture of 348a and 348b as a yellow solid, mp 113-115 °C, as an approximately 3:2 ratio of diastereomers by 1H NMR analysis.

major isomer:
1H NMR (300 MHz, CDCl3): 7.94 (J = 8.1 Hz, 1 H), 7.78-7.82 (m, 2 H), 7.72 (d, J = 7.2 Hz, 1 H), 7.50-7.59 (m, 2 H), 6.58 (d, J = 2.0 Hz, 1 H), 4.58 (d, J = 11.8 Hz, 1 H), 3.67 (s, 3 H), 3.40-3.46 (m, 1 H), 2.90 (dd, J = 18.7, 6.3 Hz, 1 H) and 2.60 (dd, J = 18.7, 3.2 Hz, 1 H).
$^{13}$C NMR (75 MHz, CDCl$_3$): 207.3, 172.5, 135.2, 133.6, 131.6, 131.5, 129.1, 128.6, 127.8, 127.5, 127.4, 126.5, 125.9, 125.6, 125.5, 125.0, 124.4, 123.3, 82.7, 78.5, 57.4, 56.1, 44.2, 40.5 and 37.3.

IR (CCl$_4$): 3050, 2980, 2930, 2880, 2820, 1701, 1601, 1490, 1460, 1440, 1410, 1370, 1360, 1330, 1290, 1260, 1170, 1150, 1110, 1060 and 905 cm$^{-1}$. 
Trisyl hydrazone 376.

Methyl ether 348 (0.049 g, 0.20 mmol) was dissolved in 10 mL of mround-bottomed flask equipped with an argon inlet adapter. Triisopropylsulfonylhydrazine (0.128 g, 0.43 mmol) was added in one portion. Next, one drop of concentrated hydrochloric acid was added via pipette. The red reaction mixture was stirred for 2 h at 25 °C and then was reduced to a volume of ca. 0.5 mL using a rotary evaporator. The dark red oil was diluted with 25 mL of dichloromethane and washed with 20 mL of H2O. The aqueous phase was back-extracted with 25 mL of dichloromethane, and the combined organic extracts were washed with brine, dried over Na2SO4, filtered, and concentrated to afford a brown solid which was deposited on silica gel and purified by column chromatography on silica gel (elution with 10% ethyl acetate-hexane) to afford 0.096 g (98%) of 376 as a brown solid, mp 90-100 °C dec.

$^1$H NMR (300 MHz, CDCl3): 7.92 (d, J = 7.4 Hz, 1 H), 7.77 (d, J = 8.1 Hz, 1 H), 7.58 (d, J = 8.1 Hz, 1 H), 7.46 (t, J = 7.8 Hz, 1 H), 7.35 (t, J = 8.1 Hz, 1 H), 7.24 (d, J = 7.0 Hz, 1 H), 7.20 (s, 2 H), 6.84 (s, 1 H), 6.71 (s, 1 H), 4.35 (quintet, J = 6.7 Hz, 1 H), 3.31 (s, 2 H), 2.91 (quintet, J = 6.7 Hz, 1 H), 1.33 (d, J = 6.9 Hz, 12 H) and 1.26 (d, J = 7.0 Hz, 6 H).

$^{13}$C NMR (75 MHz, CDCl3): 161.3, 153.2, 151.4, 149.7, 139.6, 133.6, 132.3, 131.5, 129.9, 127.6, 127.4, 127.3, 126.9, 126.5, 125.8, 124.3, 123.9, 120.6, 34.2, 30.8, 29.9, 24.9 and 23.5.

IR (CCl4): 3150, 2910, 2850, 1595, 1490, 1420, 1380, 1320, 1290, 1150, 1040, and 850 cm$^{-1}$. 
Dienone 350.

Hydroxycyclopentenone 314 (0.198 g, 0.46 mmol) was dissolved in 15 mL of methanol in a one-necked 25-mL round-bottomed flask equipped with an argon inlet adapter. Concentrated hydrochloric acid (3 drops) was added via pipette and the resulting brown reaction mixture was stirred for 4 h. Additional hydrochloric acid (3 drops) were added and the mixture was stirred for 12 hours. The mixture was then concentrated and the black residue was dissolved in dichloromethane and deposited on silica gel. Purification by column chromatography on silica gel (elution with 20% ethyl acetate-petroleum ether) produced 0.045 g (45%) of 350 as a brown solid, mp 166-169 °C dec.

$^1$H NMR (300 MHz, CDCl$_3$): 7.94 (J = 8.1 Hz, 1 H), 7.78-7.82 (m, 2 H), 7.72 (d, J = 7.2 Hz, 1 H), 7.50-7.59 (m, 2 H), 6.58 (d, J = 2.0 Hz, 1 H), 4.58 (d, J = 11.8 Hz, 1 H), 3.67 (s, 3 H), 3.40-3.46 (m, 1 H), 2.90 (dd, J = 18.7, 6.3 Hz, 1H) and 2.60 (dd, J = 18.7, 3.2 Hz, 1 H).

$^{13}$C NMR (75 MHz, CDCl$_3$): 207.3, 172.5, 135.2, 133.6, 131.6, 131.5, 129.1, 128.6, 127.8, 127.5, 127.4, 126.5, 125.9, 125.6, 125.5, 125.0, 124.4, 123.3, 82.7, 78.5, 57.4, 56.1, 44.2, 40.5 and 37.3.

IR (CCl$_4$): 3050, 2980, 2930, 2880, 2820, 1701, 1601, 1490, 1460, 1440, 1410, 1370, 1360, 1330, 1290, 1260, 1170, 1150, 1110, 1060 and 905 cm$^{-1}$. 

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