Palladium-catalyzed annulation of alkynes and ADMET polymerization of soybean oil

Qingping Tian
Iowa State University
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UMI
Palladium-catalyzed annulation of alkynes
and ADMET polymerization of soybean oil

by

Qingping Tian

A dissertation submitted to the graduate faculty
in partial fulfillment of the requirements for the degree of
DOCTOR OF PHILOSOPHY

Major: Organic Chemistry
Major Professor: Richard C. Larock

Iowa State University
Ames, Iowa
1998
Graduate College
Iowa State University

This is to certify the Doctoral dissertation of

Qingping Tian

has met the dissertation requirement of Iowa State University

Signature was redacted for privacy.

Major Professor

Signature was redacted for privacy.

For the Major Program

Signature was redacted for privacy.

For the Graduate College
To my parents, my wife and my son
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LIST OF ABBREVIATIONS

Ac  acetyl
ADMET  acyclic diene metathesis
APCI  atmospheric pressure chemical ionization
aq  aqueous
br  broad
Bu  butyl
cat.  catalytic
concd  concentrated
dd  doublet of doublets
DMA  $N.N$-dimethylacetamide
DMF  $N.N$-dimethylformamide
DMSO  dimethyl sulfoxide
dt  doublet of triplets
eq  equation
equiv  equivalent
Et  ethyl
h  hour(s)
HRMS  high resolution mass spectroscopy
Hz  Hertz
IR  infrared
Me  methyl
min  minute(s)
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</tr>
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<td>$M_n$</td>
<td>number average molecular weight</td>
</tr>
<tr>
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<td>mole(s)</td>
</tr>
<tr>
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</tr>
<tr>
<td>MS</td>
<td>mass spectrometry</td>
</tr>
<tr>
<td>$M_w$</td>
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<td>number of repeating units</td>
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<td>normal</td>
</tr>
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<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>o</td>
<td>ortho</td>
</tr>
<tr>
<td>p</td>
<td>para</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>q</td>
<td>quartet</td>
</tr>
<tr>
<td>r</td>
<td>the integration ratio of the $^1$H NMR spectral peaks corresponding to $\text{OCH}_2\text{CHCH}_2\text{O}$ over $\text{CH}_3$ protons</td>
</tr>
<tr>
<td>t</td>
<td>tertiary</td>
</tr>
<tr>
<td>t</td>
<td>triplet</td>
</tr>
<tr>
<td>s</td>
<td>singlet</td>
</tr>
<tr>
<td>UV</td>
<td>ultraviolet</td>
</tr>
<tr>
<td>vac.</td>
<td>vacuum</td>
</tr>
</tbody>
</table>
ABSTRACT

A novel synthetic methodology for 9-alkylidene-9H-fluorenes by the palladium-catalyzed cascade reaction of aryl iodides and internal alkynes has been developed. This methodology has been extended to a number of aryl iodides and internal alkynes. The synthesis of a 9-alkylidene-9H-fluorene has also been achieved from a vinylic iodide. It has been demonstrated that this unusual cascade migration/coupling process also provides an efficient synthetic route to polycyclic aromatic hydrocarbons.

We have also investigated the palladium-catalyzed reaction of internal alkynes and (2-iodophenyl)acetonitrile or 2-iodobenzonitrile. (2-Iodophenyl)acetonitrile reacts with diphenylacetylene in the presence of a palladium catalyst to afford 2-amino-3.4-diphenylnapthalene in 83% yield. This is the first example of a cyano group actually participating in an organopalladium addition reaction. An unusual product 2-amino-3-{(E)-1-propenyl}-4-propynaphthalene has been obtained as the sole product in the reaction of 4-octyne. The formation of this unusual product has been rationalized by a mechanism similar to the palladium-catalyzed cyclization of enynes. The reaction of 2-iodobenzonitrile and diphenylacetylene affords 2,3-diphenylindenone in 30% yield.

The acyclic diene metathesis (ADMET) polymerization of soybean oil has been studied in this thesis. The polymerization of ethylene glycol dioleate afforded the isomerized $E,E$-dioleate (27%), dimer (18%), trimer (13%), tetramer (7%), pentamer (5%), hexamer (4%), heptamer (4%) and 9-octadecene (21%). Only a trace amount of the intramolecular cyclized compound (0.1%) was formed in the reaction. Under the same conditions, glyceryl trioleate undergoes ADMET polymerization to produce dimer, trimer, tetramer, pentamer and monocyclic oligomers, with monocyclic oligomers predominating. A variety of materials, from sticky oils to rubbers, have been prepared from the ADMET
polymerization of soybean oil under different conditions. These materials are very likely to be biodegradable and have potential applications in paints, lubricants, coatings and adhesives.
GENERAL INTRODUCTION

Annulation processes are extremely important in organic synthesis for the construction of heterocycles and carbocycles. The palladium-mediated annulation of alkynes has proven a useful route for the synthesis of heterocycles and carbocycles.

The Larock group has recently developed a novel palladium-catalyzed annulation of internal alkynes by aryl iodides containing a nucleophilic substituent in the ortho position. This methodology has been further investigated in this thesis.

Acyclic diene metathesis (ADMET) polymerization has emerged as a very useful process for polymer synthesis. This dissertation records our success in the ADMET polymerization of soybean oil.

Dissertation Organization

This dissertation is divided into three chapters. Each chapter is a journal paper presented with its own introduction, result and discussion, experimental section, conclusion, acknowledgment and references. Following the last chapter is a general conclusion.

Chapter I describes the synthesis of 9-alkylidene-9H-fluorenes by a novel palladium-catalyzed cascade reaction of aryl iodides and internal alkynes. This type of reaction has been extended to a number of aryl iodides and internal alkynes. We have proposed a mechanism for this reaction and the stereochemistry of this reaction has been addressed. This unusual cascade migration/coupling process has been successfully employed in the synthesis of even more complicated polycyclic aromatic hydrocarbons, such as benzo[b]fluoranthene.
Chapter 2 deals with the palladium-catalyzed reaction of internal alkynes with (2-iodophenyl)acetonitrile and 2-iodobenzonitrile. 2-Amino-3.4-diphenylnaphthalene has been isolated as the sole product from the reaction of (2-iodophenyl)acetonitrile and diphenylacetylene in 83% yield. This is the first example of a cyano group actually participating in an organopalladium addition reaction. An unusual product 2-amino-3-((E)-1-propenyl)-4-propynaphthalene has been obtained as the sole product in the reaction of 4-octyne. The formation of this unusual product has been rationalized by a mechanism similar to the palladium-catalyzed cyclization of enynes. The reaction of 2-iodobenzonitrile and diphenylacetylene affords 2.3-diphenylindenone in 30% yield.

Chapter 3 presents our work on the ADMET polymerization of soybean oil. Our model system studies have focused on the metathesis reaction of ethylene glycol dioleate, glyceryl trioleate and glyceryl trilinoleate. The composition of the products from these reactions has been fully investigated by $^1$H and $^{13}$C NMR spectral analysis and MS spectrometry. It has been shown that the metathesis reactions of the model systems do follow the ADMET polymerization mechanism. Based on our experience with the model systems, we have succeeded in the ADMET polymerization of soybean oil. A variety of materials, from sticky oils to rubbers, have been prepared from soybean oil.
CHAPTER 1. SYNTHESIS OF 9-ALKYLDENE-9H-FLUORENES BY A NOVEL PALLADIUM-CATALYZED CASCADE REACTION OF ARYL IODIDES AND INTERNAL ALKYNES

A paper to be submitted to the Journal of Organic Chemistry

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Abstract

In the presence of a palladium catalyst, aryl iodides react with internal aryl alkynes to afford 9-alkyldene-9H-fluorenes in good yields. 9-Alkyldene-9H-fluorenes can also be prepared by the Pd-catalyzed rearrangement of 1-iodo-2,2-diarylalkenes. This process appears to involve (1) oxidative addition of the aryl iodide to Pd(0), (2) alkyne insertion, (3) rearrangement to an arylpalladium intermediate, and (4) aryl-aryl coupling.

Introduction

Annulation processes are extremely important in organic synthesis for the construction of heterocycles and carbocycles. Palladium-mediated annulation has drawn particular attention recently. Among these processes, the annulation of alkynes, which often involves cascade insertion processes, has proven a useful route for the synthesis of heterocycles and carbocycles from simple synthetic building blocks.
For example, the intermolecular-intramolecular cascade reaction of a 1,6-enyne with \( \beta \)-bromostyrene affords the endo product 1 (eq 1). This reaction was successfully applied to the synthesis of a vitamin D analog.

\[
\begin{align*}
\text{E} = \text{CO}_2\text{CH}_3
\end{align*}
\]

Intramolecular cyclization can be used for the synthesis of polycyclics. In the Pd-catalyzed cascade carbopalladation of a polyalkyne, a steroid skeleton is constructed from the linear diynetriene 2 (eq 2).

\[
\begin{align*}
\text{E} = \text{CO}_2\text{Et}
\end{align*}
\]

The tris-cyclization of compound 3 afforded the polyfused heterocycle 4 (eq 3). This reaction constitutes an example of \([2 + 2 + 2]\) cyclization.
Negishi et al. have reported the synthesis of a highly substituted benzene derivative 5 by an intermolecular-intramolecular cascade carbopalladation process (eq 4).^n

\[
\text{cat. Pd(PPh}_3\text{)}_4 \quad \text{Et}_3\text{N, MeCN} \\
100^\circ\text{C, 6 d} \\
n-\text{Hex} + n-\text{Hex} = n-C_6H_{13} \\
5 (65\%) 
\]

The formation of disubstituted alkynes by coupling of terminal alkynes and aryl or vinylic substrates, followed by intramolecular cyclization of a phenol or amine, is employed for the synthesis of benzofurans and indoles. Benzo[b]furans can be prepared easily by the reaction of \(\alpha\)-iodophenol with terminal alkynes (eq 5).^7 An alternative, more versatile methodology has been reported recently.^5 The palladium-catalyzed reaction of \(\alpha\)-ethynylphenol with a wide variety of unsaturated halides or triflates gives 2-vinylic- or 2-arylbenzo[b]furans (eq 6).^8

\[
\begin{align*}
\text{cat. Pd(OAc)}_2(PPh}_3\text{)}_2 \quad \text{cat. Cul, piperidine} \\
\text{RX} \\
\text{DMF, 80 }^\circ\text{C} \\
R = \text{aryl, vinylic}
\end{align*}
\]
The synthesis of 2-substituted indoles has been achieved by the coupling of 2-ethynylaniline with aryl and vinylic halides, followed by Pd(II)-catalyzed cyclization (eq 7). As an alternative method, the 2,3-disubstituted indole is obtained directly by the coupling of the o-alkynyl trifluoroacetanilide with aryl and vinylic halides or triflates (eq 8).

Similarly, o-iodobenzoic acid reacts with various terminal acetylenes in the presence of Pd(PPh₃)₄, Et₃N, and ZnCl₂ in DMF to give the corresponding 3-substituted isocoumarins in fair to excellent yields (eq 9).
Recently, Larock and Yum have developed a conceptually and experimentally simple, but novel, approach to indoles involving the palladium-catalyzed heteroannulation of internal alkynes using \( \sigma \)-iodoaniline and its derivatives (eq 10). This process is highly regioselective and has also been successfully extended to the synthesis of 2,3-disubstituted benzo[b]furans (eq 11), isocoumarins (eq 12) and indenones (eq 13).
The N-methylbenzo[d,e]quinoline 6 was prepared by the annihilation of an internal alkyne with a tertiary dimethylamine (eq 14). One methyl group is eliminated during the reaction. The dimethylaminonaphthalene-Pd complex 7 is an active catalyst, but other Pd complexes are inactive.

The synthesis of substituted fulvenes can be achieved by the cross-coupling of terminal alkynes and vinylic halides or triflates (eq 15). The reaction can be explained by the intermolecular insertion of two alkynes, followed by cyclization back onto the original vinylic group, and β-hydrogen elimination to form the fulvene. The annihilation of internal alkynes has also been employed in the synthesis of a fulvene. Thus, 1,2,3,4,5-pentaphenyfulvene was obtained from the reaction of diphenylacetylene and (Z)-1-bromo-2-phenylethylene (eq 16).
The intermolecular reaction of 2-iodonaphthalene with diphenylacetylene affords compound 8 (eq 17). Heck et al. have reported the synthesis of 9,10-diphenylphenanthrene from 2-iodobiphenyl and diphenylacetylene by a palladium-catalyzed annulation process; however, the yield was only 14% (eq 18). Larock et al. subsequently optimized reaction conditions and extended this process to a wide variety of internal acetylenes and 2-iodobiaryls, as well as vinylic halides and triflates bearing aryl groups in the 2-position (eq 19).
Heck also reported the formation of a substituted naphthalene as a 1:2 adduct from the reaction of iodobenzene and diphenylacetylene (eq 20). Dyker made a minor change in the reaction conditions and observed a totally new product, the substituted phenanthrene 9, which is a 2:1 adduct from the same starting materials (eq 21). In addition, Cacchi has obtained triphenylethylene utilizing slightly different reaction conditions (eq 22).
With our ongoing interests in developing methodology for the synthesis of heterocycles and carbocycles, we have investigated the reaction of iodobenzene and diphenylacetylene by employing our standard palladium reaction conditions. An unusual 1:1 adduct, 9-benzylidene-9H-fluorene (10), has been observed (eq 23). This result encouraged us to further investigate this reaction. Herein we wish to report our improved reaction conditions for this reaction and our effort to extend this reaction to a variety of aryl iodides and internal alkynes.

Results and Discussion

The original reaction did not afford a good yield of 9-benzylidene-9H-fluorene (23 %, eq 23). Obviously, the reaction conditions needed to be optimized before further testing.
the scope and limitations of the reaction. The effect of various bases, the chloride source and the ligand (PPh₃) were therefore examined. The results are summarized in Table 1.

As indicated in eq 23, the formation of product 10 is the result of a 1:1 adduct of iodobenzene and diphenylacetylene; therefore, only 1 equiv of diphenylacetylene is actually required in the reaction. Indeed, we found that the yield of the reaction was improved when only 1 equiv of diphenylacetylene was employed in the reaction (compare entries 1 and 2).

In an attempt to further improve the yield of the reaction, we examined the use of PPh₃ in the reaction. The addition of 10 mol % PPh₃, which presumably behaves as a ligand for palladium, showed a significant effect on the reaction. Good yields were obtained when the reactions were exposed to only catalytic amounts of PPh₃ (entries 4, 5 and 7).

An appropriate chloride source is also important for the reaction. Without chloride present, the reaction did not afford a good yield (37%, entry 5). The addition of LiCl slightly improved the yield (41%, entry 4). The use of n-Bu₄NCl as the chloride source further improved the yield (62%, entry 7). Different amounts of n-Bu₄NCl were employed in the reaction, but no big difference has been observed (entries 7-9). One equiv of n-Bu₄NCl appears to be enough.

Like much of our previous palladium chemistry,¹²⁻¹⁴ the choice of base is critical to the reaction. Without any base, no reaction has been observed (entry 6). Thus, a number of bases have been examined in the reaction. When NaOAc was used as the base, compound 10 was the only product obtained from the reaction (entries 1-9). However, a mixture of products of 9 and 10 was obtained when the reaction was exposed to other bases (entries 10-13). Under reaction conditions similar to Dyker's¹¹ (only replacing n-Bu₄NBr with n-Bu₄NCl), the reaction afforded 9 as the major product (entry 11). This
<table>
<thead>
<tr>
<th>entry</th>
<th>alkyne (equiv)</th>
<th>base (equiv)</th>
<th>chloride source (equiv)</th>
<th>PPh3 (equiv)</th>
<th>time (h)</th>
<th>isolated yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NaOAc (2)</td>
<td>LiCl (1)</td>
<td></td>
<td>17</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>NaOAc (2)</td>
<td>LiCl (1)</td>
<td></td>
<td>30</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>NaOAc (2)</td>
<td>n-BuNCl (1)</td>
<td></td>
<td>24</td>
<td>44</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>NaOAc (2)</td>
<td>LiCl (1)</td>
<td>10</td>
<td>8</td>
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<td>1</td>
<td>NaOAc (2)</td>
<td>-</td>
<td>10</td>
<td>24</td>
<td>37</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>-</td>
<td>n-BuNCl (1)</td>
<td>10</td>
<td>24</td>
<td>no reaction</td>
</tr>
<tr>
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<td>1</td>
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<td>n-BuNCl (1)</td>
<td>10</td>
<td>24</td>
<td>62</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>NaOAc (2)</td>
<td>n-BuNCl (2)</td>
<td>10</td>
<td>24</td>
<td>61</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>NaOAc (2)</td>
<td>n-BuNCl (3)</td>
<td>10</td>
<td>24</td>
<td>57</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>Na2CO3 (2)</td>
<td>n-BuNCl (1)</td>
<td>10</td>
<td>48</td>
<td>30 20</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
<td>K2CO3 (2)</td>
<td>n-BuNCl (1)</td>
<td>10</td>
<td>48</td>
<td>71 8</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
<td>KOAc (2)</td>
<td>n-BuNCl (1)</td>
<td>10</td>
<td>24</td>
<td>12 42</td>
</tr>
</tbody>
</table>

*All reactions were run in the presence of 5 mol % Pd(OAc)$_2$ in DMF at 100 °C.*
result is dramatically different from that observed when NaOAc was employed as the base in the reaction (entry 7).

This investigation led to the following standard reaction procedure: 1 equiv of aryl halide, 1 equiv of alkyne, 5 mol % of Pd(OAc)$_2$, 10 mol % PPh$_3$, 2 equiv of NaOAc, 1 equiv of $n$-Bu$_3$NCl in DMF at 100 ºC.

With this standard procedure in hand, we next set out to explore the scope and limitations of the reaction by first examining other alkynes. As shown in Table 2, the alkynes which have been successful in this reaction have a phenyl group and another sterically hindered group, such as a phenyl, $t$-butyl or similar group (entries 1-3). The structural requirements required of the alkyne can be rationalized by the proposed mechanism of the reaction as shown below.

Based on the structure of the products from this reaction (Table 2) and our present understanding of organopalladium chemistry, especially the active role of Pd(IV) as an intermediate in organopalladium chemistry, we propose the following mechanism for this reaction (Scheme 1). The mechanism involves the formation, transformation and reductive elimination of Pd(IV) intermediates. The oxidative addition of Pd(0) to iodobenzene produces an arylpalladium intermediate 11, which rapidly inserts alkyne to produce a vinylic palladium species 12. This in turn undergoes oxidative addition to the neighboring aryl C-H bond to generate a Pd(IV) intermediate 13, which isomerizes to afford a new Pd(IV) intermediate 14. Reductive elimination of 14 leads to Pd(II) intermediate 15, which undergoes further oxidative addition to the neighboring phenyl ring to afford Pd(IV) intermediate 16. Two consecutive reductive eliminations finally afford the product and HI, and regenerate the Pd(0) catalyst.
### Table 2. Palladium-catalyzed Reaction of Iodobenzene and Internal Alkynes.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>alkyne</th>
<th>time (h)</th>
<th>product</th>
<th>isolated % yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph—=—Ph</td>
<td>12</td>
<td>![Product Image]</td>
<td>62</td>
</tr>
<tr>
<td>2</td>
<td>Ph—=—t-Bu</td>
<td>20</td>
<td>![Product Image]</td>
<td>61</td>
</tr>
<tr>
<td>3</td>
<td>Ph—=—OH</td>
<td>20</td>
<td>![Product Image]</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>Ph—=—SiMe(_3)</td>
<td>20</td>
<td>![Product Image]</td>
<td>66(^b)</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: 5 mol % Pd(OAc)\(_2\), 10 mol % PPh\(_3\), 1 equiv of alkyne, 2 equiv of NaOAc and 1 equiv of \(n\)-Bu\(_4\)NCl in DMF at 100 °C. \(^b\) The yield is based upon the consumption of iodobenzene.
According to the proposed mechanism, it is obvious that the alkyne must have an aryl group at one end of the triple bond. Since the arylpalladium intermediate 11 must insert the aryl group next to the aryl group already present in the alkyne, the other group attached to the triple bond must be more sterically hindered than the aryl group of the alkyne in order to afford the desired regiochemistry. since our previous research\textsuperscript{12-14} has proven that the arylpalladium complexes prefer to insert the aryl moiety on the less hindered end of the triple bond.
The proposed mechanism also explains the formation of 10 from the reaction of iodo benzene and 1-phenyl-2-(trimethylsilyl)acetylene (entry 4, Table 2). As shown in Scheme 2, the reaction may involve the formation of intermediate 18, followed by desilylation and subsequently cross-coupling with iodo benzene. An alternative route to compound 10 might start with the desilylation of 1-phenyl-2-(trimethylsilyl)acetylene, followed by cross-coupling with 2-iodobenzene. The resultant diphenylacetylene can then react with 2-iodobenzene to give the final product 10 (Scheme 3).

Scheme 2

Scheme 3
Compound 9 was obtained in some cases (Table 1, 10-12). As Dyker proposed,\textsuperscript{21} reductive elimination of intermediate 13 afford a Pd(II) species. This then undergoes an oxidative addition to iodobenzene to generate a Pd(IV) intermediate, followed by reductive elimination and subsequent aryl-aryl coupling to afford compound 9.

In order to further examine the scope of this type of reaction, a variety of aryl iodides were employed in the reaction. The results are summarized in Table 3.

Various substituted aryl iodides generally work as well as iodobenzene. The functional group can be either an electron-donating or electron-withdrawing group. Aryl iodides bearing a substituent in the ortho position, including 2-iodobenzotrifluoride (entry 2), 2-iodobenzonitrile (entry 3) and 1-tert-butyl-2-iodobenzene (entry 4), afforded the expected \(E\) isomers. However, other substrates, such as 2-iodotoluene (entry 5) and 2-iodoanisole (entry 6), produced mixtures of \(Z\) and \(E\) isomers. Furthermore, aryl iodides bearing functional groups in the para position also afforded mixtures of \(Z\) and \(E\) isomers (entries 7-9).

The structural assignment of the \(Z\) and \(E\) isomers is based on 1D and 2D NMR spectra. 2D NOESY\textsuperscript{24} is a powerful tool to identify the structure of these isomers. For example, the 2D NOESY spectra of 19 (entry 4) clearly shows a crosspeak between the protons of the tert-butyl group and the vinylic proton H-10. This confirms that 19 exists in the \(E\) configuration. In some cases, 1D \(^1\text{H}\) NMR spectra provide sufficient information to assign the stereochemistry. For example, the \(^1\text{H}\) NMR spectra of compounds 20 and 21 (entry 8) exhibit doublets for proton H-4 at 8.37 and 8.39 ppm. In the \(Z\) isomer 20, the benzene ring present on the vinylic carbon C-10 could exhibit an anisotropic effect\textsuperscript{25} on the ring which bears the \(\text{CO}_2\text{Et}\) group. This interaction may shield the protons on that ring, and as a result, the chemical shift of proton H-4 on that ring should appear at higher field. No such anisotropic interaction can exist in the \(E\) isomer 21.
Table 3. Pd-Catalyzed Coupling of Various Aryl Iodides and Diphenylacetylene.\

<table>
<thead>
<tr>
<th>entry</th>
<th>aryl iodide</th>
<th>time (h)</th>
<th>product(s)</th>
<th>isolated % yield (Z:E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
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<td><img src="image1" alt="Product 1" /></td>
<td>62</td>
</tr>
<tr>
<td>2</td>
<td>CF₃Ph</td>
<td>48</td>
<td><img src="image2" alt="Product 2" /></td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>CN</td>
<td>10</td>
<td><img src="image3" alt="Product 3" /></td>
<td>63</td>
</tr>
<tr>
<td>4</td>
<td>t-Bu</td>
<td>96</td>
<td><img src="image4" alt="Product 4" /></td>
<td>35</td>
</tr>
<tr>
<td>5</td>
<td>Me</td>
<td>12</td>
<td><img src="image5" alt="Product 5" /> + <img src="image6" alt="Product 6" /></td>
<td>61 (40:60)</td>
</tr>
<tr>
<td>6</td>
<td>OMe</td>
<td>158</td>
<td><img src="image7" alt="Product 7" /> + <img src="image8" alt="Product 8" /></td>
<td>25 (42:58)</td>
</tr>
</tbody>
</table>
Table 3. (continued)

<table>
<thead>
<tr>
<th>entry</th>
<th>aryl iodide</th>
<th>time (h)</th>
<th>product(s)</th>
<th>isolated % yield (Z:E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>MeO-I</td>
<td>18</td>
<td><img src="image" alt="Product 20 and 21" /></td>
<td>45 (40:60)</td>
</tr>
<tr>
<td>8</td>
<td>EtO₂C-I</td>
<td>15</td>
<td><img src="image" alt="Product 20 and 21" /></td>
<td>45 (40:60)</td>
</tr>
<tr>
<td>9</td>
<td>Me-I</td>
<td>20</td>
<td><img src="image" alt="Product 20 and 21" /></td>
<td>60 (40:60)</td>
</tr>
<tr>
<td>10</td>
<td>Py-I</td>
<td>48</td>
<td><img src="image" alt="Product 20 and 21" /></td>
<td>76 (19:14 40:27)</td>
</tr>
</tbody>
</table>
and the signal for H-4 should appear at lower field. Therefore, the configuration of 20 and 21 is tentatively assigned as Z and E, respectively.

The reactions of 1-tert-butyl-2-iodobenzene and 2-iodoanisole deserve special mention here. Dyker has reported that 1-tert-butyl-2-iodobenzene reacts with a palladium catalyst to give the strained 1,2-dihydrocyclobutabenzene derivative 23 in 75% yield (eq 24). Employing two equivalents of 2-iodoanisole under the same reaction conditions affords the substituted dibenzopyran 24 (eq 25). Under our reaction conditions, we only observe fluorene products (Table 3, entries 4 and 6). Clearly, addition of an alkyne completely changes the nature of the reaction. As shown in entry 6, the reaction of 2-iodoanisole did not afford a good yield even after a long reaction time (158 h). GC-MS analysis of the reaction indicated that a significant amount of 2-iodoanisole still had not participated in the reaction. On the other hand, 4-iodoanisole reacted with diphenylacetylene much faster and also gave a much better yield (entry 7).
Heteroaromatic iodides have also been examined in the reaction. The reaction of 3-iodopyridine afforded a good yield of a mixture of regioisomers and Z/E isomers (entry 10). All these isomers are known compounds and the structural assignment is thus based on the literature. On the other hand, only one isomer 22 was obtained from the reaction of iodothiophene, although the yield was low (entry 11).

As one can see from Table 3, in most cases, the E isomers are the sole or predominant products in the reaction. Previous literature has shown that these types of fluorene compounds undergo interconversions when heated to 140 °C in decalin. Therefore, we suspect that the formation of isomers is due to thermal isomerization of the initially formed E isomer, which is expected by our mechanism to be produced in the reaction. This has been proved by the following experiments.

We were able to separate the Z and E isomers (20 and 21) from the reaction of ethyl 4-iodobenzoate and diphenylacetylene by preparative TLC (entry 8). When submitted to the standard palladium reaction conditions, both isomers 20 and 21 gave a mixture of...
20 and 21 and the ratio of isomers (40:60) was exactly the same as that obtained from the original reaction of ethyl 4-iodobenzoate and diphenylacetylene. However, without Pd(OAc)$_2$ present, simple heating of the $E$ isomer 21 for the same period of time in DMF generated a 12:88 mixture of isomers 20 and 21. This indicates that Pd(OAc)$_2$ or perhaps reduced Pd(0) may play an important role in the isomerization process.

We have also examined the effects of temperature and reaction time on the isomerization process. The results are shown in Table 4.

Table 4. Effects of temperature and reaction time on the reaction of ethyl 4-iodobenzoate and diphenylacetylene.$^a$

<table>
<thead>
<tr>
<th>entry</th>
<th>temp. ($^\circ$C)</th>
<th>rxn time (h)</th>
<th>isolated % yield$^b$</th>
<th>ratio 20 : 21</th>
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<tr>
<td>1</td>
<td>80</td>
<td>4</td>
<td>5</td>
<td>21 : 79</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>8</td>
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<td>37 : 63</td>
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<td>42 : 58</td>
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<td>100</td>
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<td>32 : 68</td>
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<td>42 : 58</td>
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<tr>
<td>8</td>
<td>100</td>
<td>32</td>
<td>44</td>
<td>39 : 61</td>
</tr>
<tr>
<td>9</td>
<td>100</td>
<td>72</td>
<td>44</td>
<td>40 : 60</td>
</tr>
</tbody>
</table>

$^a$ All reactions were run in the presence of 5 mol % Pd(OAc)$_2$, 10 mol % PPh$_3$, 2 equiv of NaOAc and 1 equiv of $n$-Bu$_3$NCl in DMF at 100 $^\circ$C. $^b$ The yield was determined by $^1$H NMR spectroscopy using undecane as an internal standard.
From Table 4, one can see that different ratios were observed at different reaction times. At the beginning of the reaction, the percentage of \( E \) isomer \( 21 \) in the mixture was relatively high, presumably because there had been insufficient time to effect significant isomerization. After a period of time (16 h for the reaction at 80°C or 8 h for the reaction at 100°C), the ratio levels out at approximately 40:60 and little further isomerization is observed (entries 7-9). We have also found that the actual temperature is very important for the isomerization process. Higher temperatures (100°C) accelerate the process. After the same period of time (4 h), the reaction at the higher temperature (100°C) afforded a higher percentage of isomer \( 20 \) in the mixture than that at the lower temperature (80°C) (compare entries 1 and 5). We have observed, however, that the higher temperature (100°C) is necessary for the reaction to reach completion. The reaction failed to reach completion at 80°C even after several days (entry 4).

The mechanism of the isomerization process about the exocyclic double bond in the fluorene system has not been fully elucidated. However, examination of the resonance structures for the \( E \) isomer \( 21 \) reveals particularly favorable resonance structures \( 25 \) and \( 26 \) (Figure 1). In resonance structure \( 25 \), the two \( \pi \)-electrons of the exocyclic double bond are shifted to the 5-membered ring of the fluorene ring system to give a stable 6 \( \pi \)-electron arrangement, which is similar to that of fulvene.\(^9\) Resonance structure \( 26 \) is also particularly favorable due to the electron-withdrawing effect of the ester group. We suggest that due to the resonance contributions of \( 25 \) and \( 26 \), the exocyclic double bond may be of low enough energy to allow for thermal isomerization to the \( Z \) isomer \( 20 \). We suspect that the Pd(0) catalyst may also form an olefin complex further weakening the double bond and thus accelerating the isomerization process.
Figure 1. Resonance structures for the $E$ isomer 21.

As shown in the proposed mechanism (Scheme 1), vinylic palladium intermediate 12 is a proposed intermediate in the reaction. Since intermediate 12 should be easily generated by the oxidative addition of Pd(0) to the corresponding iodide, 1,2,2-triphenyl-1-iodoethylene, we might expect to observe the formation of product 10 from this vinylic iodide under our reaction conditions. Indeed, this turned out to be true. The expected product 10 was obtained from the reaction in 70% yield (eq 26).

Inspired by this result, we have also examined the reaction of 1-iodo-2,2-diphenylethylene. This compound gave the annulated pentafulvene 33 in 69% yield (Scheme 4). This is the same product that Dyker obtained from the same starting material under similar reaction conditions. This reaction might go through intermediate 27. Instead of forming the fluorene product 28, intermediate 27 apparently undergoes
oxidative addition to the terminal olefinic C-H bond to generate a Pd(IV) intermediate 29, followed by reductive elimination to produce a new Pd(II) species 30. Oxidative addition of the starting iodide Ph$_2$C=CHI to 30 generates a Pd(IV) intermediate 31. Reductive elimination of 31 affords a Pd(II) intermediate 32, which cyclizes to the final product 33 (Scheme 4).

Benzo[b]fluoranthene (34) is a ubiquitous environmental contaminant, as well as a moderately potent tumor initiator. Recent increased interest in compound 34, inspired by the report of favorable antitumor activity by a fluoranthene derivative in clinical trials, has
encouraged us to examine our fluorene methodology as a potentially very efficient synthetic route to benzo[b]fluoranthenes.

A few synthetic approaches have been developed to benzo[b]fluoranthane and its derivatives. For example, Rice et al. have recently reported a convenient approach to 34 using a Pd-catalyzed arene-aryl triflate coupling (Scheme 5). Unfortunately, the synthesis of triflate 35 required several steps.

**Scheme 5**

![Scheme 5 Diagram](image-url)

We wish now to report a more efficient strategy for the synthesis of benzo[b]fluoranthenes (Scheme 6). Our recently reported methodology for the palladium-catalyzed carboannulation of an alkyne afforded the silyl-substituted phenanthrene 36, which was subsequently converted to the corresponding iodide 37 by exposure to ICl. Utilizing our standard conditions, iodide 37 undergoes a cascade process involving intermediates 38 and 39 to afford the final product 34 (Scheme 6). This example nicely demonstrates that this type of cascade cyclization reaction provides a very powerful and convenient synthetic route to polycyclic aromatic hydrocarbons.
The Pd-catalyzed coupling of iodobenzene and diphenylacetylene has been examined. An unusual product, 9-benzylidene-9H-fluorene (10), has been obtained in 62% yield. This type of reaction has been extended to a number of other aryl iodides and internal alkynes, providing an efficient synthetic route to 9-alkylidene-9H-fluorenes. Based on the proposed mechanism for this reaction, the synthesis of 9-alkylidene-9H-fluorene has also been achieved from a vinylic iodide. Indeed, this unusual cascade migration/coupling process appears applicable to the synthesis of even more complicated polycyclic aromatic hydrocarbons, such as benzo[b]fluoranthene (34).
Experimental Section

**General.** All $^1$H and $^{13}$C NMR spectra were recorded at 300 and 75.5 MHz respectively. Thin-layer chromatography (TLC) was performed using commercially prepared 60 mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm), or basic KMnO$_4$ solution (3 g KMnO$_4$ + 20 g K$_2$CO$_3$ + 5 mL NaOH (5%) + 300 mL H$_2$O).

**Reagents.** All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of NaOAc, LiCl, DMF, CH$_2$Cl$_2$, hexanes and ethyl acetate were purchased from Fisher Scientific. Pd(OAc)$_2$ was donated by Johnson Matthey, Inc. and Kawaken Fine Chemicals Co., Ltd. Iodobenzene, 2-iodobenzotri fluoride, 2-iodotoluene, 2-iodoanisole, 4-iodoanisole, 2-iodothiophene, triphenylphosphine, 1-phenyl-2-(trimethylsilyl)acetylene and diphenylacetylene were obtained from Aldrich Chemical Co., Inc. Ethyl 4-iodobenzoate and n-Bu$_3$NCl were purchased from Lancaster Synthesis Inc. 2-Iodobenzonitrile was purchased from Trans World Chemicals, Inc. 4-Phenyl-2-methyl-3-butyn-2-ol was obtained from Farchan Scientific Co. 3,3-Dimethyl-1-phenyl-1-butyne,$^{14}$ 3-iodopyridine,$^{15}$ 1-tert.-butyl-2-iodobenzene,$^{16}$ 1-iodo-1,2,2-triphenylethylene,$^{17}$ and 1-iodo-2,2-diphenylethylene$^{18}$ were prepared according to previous literature procedures.

**General Procedure for the Palladium-catalyzed Reaction of Aryl Iodides and Internal Alkynes.** Palladium acetate (2.8 mg, 0.0125 mmol), PPh$_3$ (6.7 mg, 0.0250 mmol), sodium acetate (42 mg, 0.5 mmol), n-Bu$_3$NCl (70 mg, 0.25 mmol), the aryl iodide (0.25 mmol), the alkyne (0.25 mmol), and 5 mL of DMF (or appropriate modifications) were placed in a 4 dram vial, which was heated in an oil bath at 100 °C for the period of time indicated in Tables 1-3. The reaction mixture was cooled, diluted with
ether, washed with saturated NH$_4$Cl, dried over anhydrous MgSO$_4$, and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography or preparative TLC.

The following compounds were prepared by the above procedure.

**9-Benzylidene-9H-fluorene (10)** (Tables 2 and 3, entry 1). Obtained as a white solid in 62% yield from the reaction of 2-iodobenzene and diphenylacetylene after purification by column chromatography (hexanes): mp 73-74 °C (lit$^{39}$, mp 73-74 °C); $^1$H NMR (CDCl$_3$) $\delta$ 7.06 (dt, $J$ = 1.2, 7.5 Hz, 1 H), 7.29-7.50 (m, 6 H), 7.54-7.61 (m, 3 H), 7.70-7.74 (m, 3 H), 7.78-7.82 (m, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 119.6, 119.7, 120.2, 124.4, 126.7, 127.0, 127.3, 128.1, 128.2, 128.6, 129.3, 136.5, 136.6, 136.9, 139.2, 139.5, 141.3 (one sp$^2$ C missing due to overlap); IR (CDCl$_3$) 3053, 1490 cm$^{-1}$; HRMS m/z 254.1088 (calcd for C$_{20}$H$_{14}$, 254.1096).

**9-(2,2-Dimethylpropylidene)-9H-fluorene** (Table 2, entry 2). Obtained as a light yellow oil in 61% yield from the reaction of 2-iodobenzene and 3,3-dimethyl-1-phenyl-1-butyne$^{14}$ after purification by column chromatography (hexanes): $^1$H NMR (CDCl$_3$) $\delta$ 1.52 (s, 9 H), 6.95 (s, 1 H), 7.27-7.40 (m, 4 H), 7.66-7.80 (m, 3 H), 8.05-8.08 (m, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 30.4, 32.4, 119.2, 119.5, 119.7, 126.4, 126.9, 127.4, 127.6, 127.7, 134.8, 135.4, 138.2, 140.8, 141.7, 141.9; IR (CDCl$_3$) 3053, 2958, 1448 cm$^{-1}$; HRMS m/z 234.1412 (calcd for C$_{18}$H$_{14}$, 234.1408).

**9-(2-Hydroxy-2-methylpropylidene)-9H-fluorene** (Table 2, entry 3). Obtained as a yellow oil in 55% yield from the reaction of 2-iodobenzene and 2-methyl-4-phenyl-3-butyln-2-ol after purification by column chromatography (20:1 hexanes/EtOAc): $^1$H NMR (CDCl$_3$) $\delta$ 1.68 (s, 6 H), 6.82 (s, 1 H), 7.27-7.45 (m, 4 H), 7.62-7.73 (m, 3 H), 8.64 (d, $J$ = 6.9 Hz, 1 H) (OH missing due to exchange); $^{13}$C NMR (CDCl$_3$) $\delta$ 30.7, 71.1, 119.4, 119.9, 126.9, 127.0, 128.1, 128.4, 129.0, 135.4, 135.5, 136.4, 139.1.
9-Benzylidene-1-trifluoromethyl-9H-fluorene (Table 3, entry 2). Obtained as a light yellow oil in 75% yield from the reaction of 2-iodobenzotrifluoride and diphenylacetylene after purification by column chromatography (hexanes): $^1$H NMR (CDCl$_3$) $\delta$ 7.02 (dt, $J = 1.2, 7.2$ Hz, 1 H), 7.19 (d, $J = 7.2$ Hz, 1 H), 7.31 (dt, $J = 1.2, 7.5$ Hz, 1 H), 7.41-7.52 (m, 6 H), 7.66 (d, $J = 7.2$ Hz, 1 H), 7.72 (d, $J = 7.2$ Hz, 1 H), 7.93 (d, $J = 7.2$ Hz, 1 H), 8.16 (s, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 119.4, 123.0, 124.5 (q, $\gamma^{a}C.F = 271.5$ Hz, CF$_3$), 124.9, 125.0, 125.1, 127.4, 127.7, 128.2, 128.3, 128.7, 128.8, 131.6, 135.2 (q, $J_{c,F} = 6.4$ Hz), 137.1, 137.5, 139.2, 142.1 (one sp$^2$ C missing due to overlap); IR (CDCl$_3$) 3058, 4026, 1492 cm$^{-1}$; HRMS m/z 322.0965 (calcd for C$_{21}$H$_{13}$F$_{3}$, 322.0969).

9-Benzylidene-1-cyano-9H-fluorene (Table 3, entry 3). Obtained as a yellow solid in 63% yield from the reaction of 2-iodobenzonitrile and diphenylacetylene after purification by column chromatography using 30:1 hexanes/EtOAc as eluant: mp 145-146°C (hexane/EtOAc); $^1$H NMR (CDCl$_3$) $\delta$ 7.10 (dt, $J = 1.0, 7.8$ Hz, 1 H), 7.33 (dt, $J = 1.0, 7.5$ Hz, 1 H), 7.41-7.51 (m, 5 H), 7.56-7.63 (m, 3 H), 7.92 (d, $J = 7.5$ Hz, 1 H), 7.93 (dd, $J = 1.0, 7.5$ Hz, 1 H), 8.65 (s, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 105.1, 118.6, 119.8, 123.7, 124.7, 127.8, 128.5, 128.6, 128.7, 129.1, 132.1, 133.5, 135.0, 136.3, 136.5, 138.6, 139.3, 140.8 (one sp$^2$ C missing due to overlap); IR (CDCl$_3$) 3076, 2215 (CN), 1573 cm$^{-1}$; HRMS m/z 279.1035 (calcd for C$_{21}$H$_{13}$N, 279.1048).

9-Benzylidene-1-tert.-butyl-9H-fluorene (Table 3, entry 4). Obtained as a yellow liquid in 35% yield from the reaction of 1-tert.-butyl-2-iodobenzene and diphenylacetylene after purification by column chromatography (hexanes): $^1$H NMR (CDCl$_3$) $\delta$ 1.67 (s, 9 H), 6.91 (dt, $J = 1.0, 7.8$ Hz, 1 H), 7.00 (d, $J = 7.8$ Hz, 1 H), 7.20-
7.48 (m, 8 H), 7.65-7.68 (m, 2 H), 8.12 (s, 1 H); $^1$C NMR (CDCl$_3$) δ 30.9, 35.5, 117.8, 118.9, 125.0, 125.9, 126.3, 127.7, 127.8, 128.3, 128.7, 128.8, 135.8, 136.6, 137.4, 138.4, 138.5, 140.6, 141.9, 148.1; IR (CDCl$_3$) 3056, 2957, 1598 cm$^{-1}$; HRMS m/z 310.1719 (calcd for 310.1721).

(Z/E)-9-Benzylidene-1-methyl-9H-fluorene (Table 3, entry 5). A yellow solid obtained in 61% yield as an inseparable mixture of Z/E isomers (40:60) from the reaction of 2-iodotoluene and diphenylacetylene after purification by column chromatography (hexanes). The assignment of isomers is based upon the presence of a singlet at δ 2.41 (CH$_3$) for the Z isomer and a singlet at δ 2.48 (CH$_3$) for the E isomer. Spectral data for the product mixture: $^1$H NMR (CDCl$_3$) δ 2.41 (s, 3 H), 2.48 (s, 3 H), 6.89 (d, J = 8.1 Hz, 1 H), 7.06 (dt, J = 1.0, 7.8, Hz, 1 H), 7.15 (d, J = 7.5 Hz, 1 H), 7.28-7.72 (m, 22 H), 7.79 (d, J = 7.0 Hz, 1 H); $^1$C NMR (CDCl$_3$) δ 21.7, 21.8, 119.4, 119.6, 120.0, 120.2, 120.3, 120.4, 124.2, 124.4, 126.3, 126.4, 126.6, 126.9, 127.6, 127.9, 128.0, 128.1, 128.4, 128.5, 129.3, 129.4, 134.0, 136.3, 136.4, 136.9, 137.0, 137.1, 138.2, 138.6, 139.2, 139.3, 140.0, 141.3, 141.5 (3 sp$^2$ C missing due to overlap); IR (CDCl$_3$) 3053, 3019, 2916, 1492, 1445 cm$^{-1}$; HRMS m/z 268.1247 (calcd for C$_{21}$H$_{16}$, 268.1252).

(Z)-9-Benzylidene-1-methoxy-9H-fluorene and (E)-9-benzylidene-1-methoxy-9H-fluorene (Table 3, entry 6). A yellow oil obtained in 25% yield (42:58 Z/E isomers) from the reaction of 2-iodoanisole and diphenylacetylene after purification by column chromatography (30:1 hexanes/EtOAc). The Z/E isomers were further separated by preparative TLC. (Z)-9-Benzylidene-1-methoxy-9H-fluorene: $R_f$ = 0.38 (30:1 hexanes/EtOAc); $^1$H NMR (CDCl$_3$) δ 4.02 (s, 3 H), 6.91 (dd, J = 1.2, 8.1 Hz, 1 H), 7.01 (dt, J = 1.2, 7.5 Hz, 1 H), 7.24-7.47 (m, 7 H), 7.53-7.56 (m, 2 H), 7.70 (d, J = 7.5 Hz, 1 H), 8.39 (s, 1 H); $^1$C NMR (CDCl$_3$) δ 55.3, 109.8, 112.4, 119.7, 124.5, 125.5,
$^{1}H$ NMR (CDCl$_3$) $\delta$ 3.34 (s, 3 H), 6.75 (dd, $J = 1.2, 7.8$ Hz, 1 H), 7.31-7.44 (m, 9 H), 7.73-7.76 (m, 1 H), 7.78 (s, 1 H); $^{13}C$ NMR (CDCl$_3$) $\delta$ 54.2, 109.5, 112.4, 119.8, 120.0, 124.0, 126.6, 126.9, 127.0, 127.6, 127.7, 130.0, 130.1, 134.6, 138.7, 139.3, 141.2, 143.5, 156.0; IR (CDCl$_3$) 3055, 2922, 1607, 1488 cm$^{-1}$; HRMS $m/z$ 284.1197 (calcd for C$_{21}$H$_{16}$O. 284.1201).

**(E)-9-Benzylidene-1-methoxy-9H-fluorene:** $R_f = 0.32$ (30:1 hexanes/EtOAc); $^{1}H$ NMR (CDCl$_3$) $\delta$ 3.34 (s, 3 H), 6.75 (dd, $J = 1.2, 7.8$ Hz, 1 H), 7.31-7.44 (m, 9 H), 7.73-7.76 (m, 1 H), 7.78 (s, 1 H); $^{13}C$ NMR (CDCl$_3$) $\delta$ 54.2, 109.5, 112.4, 119.8, 120.0, 124.0, 126.6, 126.9, 127.0, 127.6, 127.7, 130.0, 130.1, 134.6, 138.7, 139.3, 141.2, 143.5, 156.0; IR (CDCl$_3$) 3055, 2922, 1607, 1488 cm$^{-1}$; HRMS $m/z$ 284.1197 (calcd for C$_{21}$H$_{16}$O. 284.1201).

**(Z)-9-Benzylidene-3-methoxy-9H-fluorene and (E)-9-benzylidene-3-methoxy-9H-fluorene** (Table 3, entry 7). A yellow oil obtained in 45% yield (40:60 $Z/E$ isomers) from the reaction of 4-iodoanisole and diphenylacetylene after purification by column chromatography (30:1 hexanes/EtOAc). The $Z/E$ isomers were further separated by preparative TLC. **(Z)-9-Benzylidene-3-methoxy-9H-fluorene:** $R_f = 0.36$ (30:1 hexanes/EtOAc); $^{1}H$ NMR (CDCl$_3$) $\delta$ 3.87 (s, 3 H), 6.61 (dd, $J = 2.4, 8.1$ Hz, 1 H), 7.23 (d, $J = 2.4, 1$ Hz), 7.31-7.50 (m, 6 H), 7.56-7.60 (m, 3 H), 7.67-7.70 (m, 1 H), 7.76-7.80 (m, 1 H); $^{13}C$ NMR (CDCl$_3$) $\delta$ 55.5, 104.8, 112.7, 119.5, 120.2, 125.1, 125.4, 127.1, 127.8, 128.1, 128.5, 129.4, 129.5, 136.0, 127.1, 128.9, 140.5, 143.1, 160.5; IR (CDCl$_3$) 3050, 2951, 1607, 1455 cm$^{-1}$; HRMS $m/z$ 284.1201 (calcd for C$_{21}$H$_{16}$O. 284.1201).

**(E)-9-Benzylidene-3-methoxy-9H-fluorene:** $R_f = 0.31$ (30:1 hexanes/EtOAc); $^{1}H$ NMR (CDCl$_3$) $\delta$ 3.92 (s, 3 H), 6.89 (dd, $J = 2.4, 8.4$ Hz, 1 H), 7.06 (dt, $J = 1.2, 7.5$ Hz, 1 H), 7.24 (d, $J = 2.4$ Hz, 1 H), 7.31 (dt, $J = 0.9, 7.5$ Hz, 1 H), 7.40-7.48 (m, 3 H), 7.56-7.60 (m, 4 H), 7.66-7.71 (m, 2 H); $^{13}C$ NMR (CDCl$_3$) $\delta$ 55.6, 104.5, 113.4, 119.6, 121.3, 124.4, 125.6, 126.8, 127.8, 128.4, 128.5, 129.3, 132.4, 136.0, 137.1, 137.4, 140.7, 140.9, 160.5; IR (CDCl$_3$) 3051, 2952, 1607, 1454 cm$^{-1}$; HRMS $m/z$ 284.1200 (calcd for C$_{21}$H$_{16}$O. 284.1201).
Compounds 20 and 21 (Table 3, entry 8). A yellow solid obtained in 45% yield (40:60 Z/E isomers) from the reaction of ethyl 4-iodobenzoate and diphenylacetylene after purification by column chromatography (50:1 hexanes/EtOAc). The Z/E isomers were further separated by preparative TLC. Compound 20: mp 124-125 °C (hexanes/EtOAc): $^1$H NMR (CDCl$_3$) $\delta$ 1.41 (t, $J$ = 1.2 Hz, 3 H), 4.41 (q, $J$ = 1.2 Hz, 2 H), 7.37-7.50 (m, 5 H), 7.57-7.61 (m, 3 H), 7.75-7.83 (m, 4 H), 8.37 (d, $J$ = 1.0 Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.4, 61.0, 120.0, 120.2, 120.8, 124.0, 127.5, 128.0, 128.4, 128.5, 128.6, 129.3, 129.5, 130.2, 135.9, 136.4, 138.4, 139.5, 140.5, 141.3, 166.6; IR (CDCl$_3$) 3053, 2977, 2924, 1712, 1609, 1492 cm$^{-1}$; HRMS m/z 326.1304 (calcd for C$_{25}$H$_{18}$O$_2$, 326.1307). Compound 21: mp 104-105 °C; $^1$H NMR (CDCl$_3$) $\delta$ 1.46 (t, $J$ = 1.2 Hz, 3 H), 4.46 (q, $J$ = 1.2 Hz, 2 H), 7.10 (dt, $J$ = 1.0, 7.5 Hz, 1 H), 7.33-7.51 (m, 4 H), 7.59-7.62 (m, 3 H), 7.79-7.84 (m, 3 H), 8.04 (dd, $J$ = 1.2, 7.5 Hz, 1 H), 8.39 (d, $J$ = 1.2 Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.4, 61.1, 120.0, 120.1, 120.9, 124.4, 127.2, 128.4, 128.4, 128.6, 128.9, 129.2, 129.6, 130.1, 135.9, 136.4, 136.6, 139.2, 140.5, 143.6, 166.8; IR (CDCl$_3$) 3052, 2976, 2922, 1713, 1609, 1423 cm$^{-1}$; HRMS m/z 326.1304 (calcd for C$_{25}$H$_{18}$O$_2$, 326.1307).

(Z/E)-9-Benzylidene-3-methyl-9H-fluorene (Table 3, entry 9). A yellow solid obtained in 60% yield as an inseparable mixture of Z/E isomers (40:60) from the reaction of 4-iodotoluene and diphenylacetylene after purification by column chromatography (hexanes). The assignment of isomers is based upon the presence of a singlet at $\delta$ 2.42 (CH$_3$) for the Z isomer and a singlet at $\delta$ 2.48 (CH$_3$) for the E isomer. Spectral data for the product mixture: $^1$H NMR (CDCl$_3$) $\delta$ 2.42 (s, 3 H), 2.48 (s, 3 H), 6.88 (d, $J$ = 7.2 Hz, 1 H), 7.05 (dt, $J$ = 1.2, 7.2 Hz, 1 H), 7.15 (d, $J$ = 7.8 Hz, 1 H), 7.28-7.49 (m, 9 H), 7.54-7.71 (m, 13 H), 7.78 (dt, $J$ = 1.2, 6.6 Hz, 1 H); $^{13}$C NMR
(Z)-9-Benzylidene-4-azafluorene, (E)-9-benzylidene-4-azafluorene.

(Z)-9-Benzylidene-2-azafluorene and (E)-9-benzylidene-2-azafluorene (Table 3, entry 10). A yellow solid obtained in 76% yield as a mixture of regioisomers and Z/E isomers (19:14:40:27) from the reaction of 3-iodopyridine and diphenylacetylene after purification by column chromatography using 2:1 hexanes/EtOAc as eluant. The isomers were further separated by preparative TLC. The melting points and $^1$H NMR spectra of these isomers match those in the literature.$^{28}$ (Z)-9-Benzylidene-4-azafluorene: mp 64-65 °C (lit.$^{32b}$ mp 62-63 °C); $^1$H NMR (CDCl$_3$) $\delta$ 6.98 (dd, $J$ = 4.8, 7.5 Hz, 1 H), 7.42-7.51 (m, 4 H), 7.61-7.64 (m, 3 H), 7.70 (s, 1 H), 8.04 (dt, $J$ = 1.5, 7.5 Hz, 2 H), 8.59 (dd, $J$ = 1.5, 4.8 Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 120.6, 121.5, 124.3, 127.4, 128.5, 128.6, 128.7, 129.2, 129.3, 133.4, 133.7, 136.4, 137.0, 140.2, 149.2, 158.3 (one sp$^2$ C missing due to overlap).

(E)-9-Benzylidene-4-azafluorene: mp 99-100 °C (lit.$^{28b}$ mp 96-98 °C); $^1$H NMR (CDCl$_3$) $\delta$ 7.16-7.25 (m, 2 H), 7.42-7.51 (m, 4 H), 7.61-7.64 (m, 3 H), 7.70 (s, 1 H), 8.04 (dt, $J$ = 1.5, 7.5 Hz, 2 H), 8.59 (dd, $J$ = 1.5, 4.8 Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 120.6, 121.5, 124.3, 127.4, 128.5, 128.6, 128.7, 129.2, 129.3, 133.4, 133.7, 136.4, 137.0, 140.2, 149.2, 158.3 (one sp$^2$ C missing due to overlap).

(Z)-9-Benzylidene-2-azafluorene: mp 164-165 °C (lit.$^{28a}$ mp 165-166 °C); $^1$H NMR (CDCl$_3$) $\delta$ 7.41-7.51 (m, 5 H), 7.59-7.63 (m, 3 H), 7.80-7.88 (m, 3 H), 8.52 (d, $J$ = 5.1 Hz, 1 H), 8.83 (s, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 114.6, 114.6, 120.7, 121.1, 128.5, 128.7,
128.8, 129.3, 129.5, 131.9, 134.7, 136.4, 136.8, 140.0, 145.6, 147.8, 149.0; HRMS m/z 255.1047 (calcd for C\textsubscript{18}H\textsubscript{11}N, 255.1048). \textit{(E)-9-Benzylidene-2-azafluorene}: mp 83-84 °C (lit.\textsuperscript{28a} mp 82-83 °C); \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta \) 7.19-7.36 (m, 1 H), 7.36-7.51 (m, 4 H), 7.59-7.66 (m, 4 H), 7.80-7.84 (m, 2 H), 8.60 (d, \( J = 5.1 \) Hz, 1 H), 9.06 (s, 1 H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \( \delta \) 114.4, 121.3, 124.8, 128.6, 128.7, 128.9, 129.1, 129.2, 129.6, 134.6, 136.2, 137.1, 138.8, 142.2, 145.9, 148.7 (one sp\textsuperscript{2} C missing due to overlap); HRMS m/z 255.1034 (calcd for C\textsubscript{18}H\textsubscript{11}N, 255.1048).

8H-Indeno[2,1-b]thiophene (22) (Table 3. entry 11). Obtained as a yellow oil in 24% yield from the reaction of 2-iodothiophene and diphenylacetylene after purification by column chromatography (hexanes): \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta \) 7.21-7.51 (m, 9 H), 7.73 (d, \( J = 7.5 \) Hz, 3 H); \textsuperscript{1}H NMR (CD\textsubscript{3}OD) \( \delta \) 6.70 (d, \( J = 4.8 \) Hz, 1 H), 6.86 (d, \( J = 5.1 \) Hz, 1 H), 7.03-7.24 (m, 7 H), 7.42 (d, \( J = 7.5 \) Hz, 1 H), 7.53 (d, \( J = 7.5 \) Hz, 2 H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \( \delta \) 118.9, 119.0, 120.1, 125.0, 125.1, 127.9, 128.6, 128.8, 128.9, 133.2, 136.5, 136.7, 137.5, 142.4, 149.6; IR (CDCl\textsubscript{3}) 3053, 2922, 1624, 1491 cm\textsuperscript{-1}; HRMS m/z 260.0664 (calcd for C\textsubscript{18}H\textsubscript{12}S, 260.0666).

The following compounds were prepared using the general procedure reported earlier, except that no alkynes were employed.

9-Benzylidene-9H-fluorene (10) (eq 26). Obtained as a white solid in 70% yield from the reaction of 1-iodo-1,2,2-triphenylethylene\textsuperscript{17} after purification by column chromatography (hexanes). The melting point and \textsuperscript{1}H and \textsuperscript{13}C NMR spectra were identical to those in the literature.\textsuperscript{19}

Compound 33 (Scheme 4). Obtained as an orange solid in 69% yield from the reaction of 1-iodo-2,2-diphenylethylene\textsuperscript{18} after purification by column chromatography (hexanes). The melting point and \textsuperscript{1}H and \textsuperscript{13}C NMR spectra match those in the literature.\textsuperscript{20}
9-Iodo-10-phenylphenanthrene (37) (Scheme 6). 9-Iodo-10-phenylphenanthrene was prepared from 9-phenyl-10-(trimethylsilyl)phenanthrene using an iodination procedure from the literature. An ICl solution in CH$_2$Cl$_2$ (1 M, 0.48 mL, 0.48 mmol) was slowly added to a solution of 9-phenyl-10-(trimethylsilyl)phenanthrene (133 mg, 0.40 mmol) in CH$_2$Cl$_2$ (1.0 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 2 h. Then, the mixture was quenched by adding excess ether, washed with Na$_2$S$_2$O$_4$ solution, water and brine, dried (MgSO$_4$) and filtered. The mixture was concentrated, purified by column chromatography. A white solid (112 mg, 0.29 mmol, 73%) was obtained: mp 118-120 °C (CH$_2$Cl$_2$/MeOH); $^1$H NMR (CDCl$_3$) δ 7.33 (dd, $J = 1.8, 6.0$ Hz, 2 H), 7.44 (d, $J = 3.9$ Hz, 2 H), 7.54-7.61 (m, 3 H), 7.62-7.73 (m, 3 H), 8.49-8.52 (m, 1 H), 8.68-8.76 (m, 2 H); $^{13}$C NMR (CDCl$_3$) δ 106.6, 122.6, 122.7, 127.0, 127.1, 127.5, 127.8, 128.1, 128.5, 128.7, 130.0, 130.3, 130.6, 132.3, 132.4, 134.7, 145.3, 145.4; IR (CDCl$_3$) 3064, 3025, 1481 cm$^{-1}$; HRMS m/z 380.0062 (calcd for C$_{29}$H$_{19}$I, 380.0062).

Benzo[b]fluoranthene (34) (Scheme 6). Obtained as a white solid in 55% yield from the reaction of 37 after purification by column chromatography (hexanes). The melting point and $^1$H and $^{13}$C NMR spectra were identical to those already in the literature.

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References


CHAPTER 2. FIRST PALLADIUM-CATALYZED ANNULATION OF AN ALKYNE ONTO A CYANO GROUP: SYNTHESIS OF 3,4-DISUBSTITUTED 2-AMINONAPHTHALENES AND 3,4-DIPHENYLINDENONE

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Abstract

The palladium-catalyzed reaction of internal alkynes and (2-iodophenyl)acetonitrile or 2-iodobenzonitrile has been investigated. (2-Iodophenyl)acetonitrile reacts with diphenylacetylene in the presence of a palladium catalyst to afford 2-amino-3,4-diphenylnaphthalene in 83% yield. This is the first example of a cyano group actually participating in an organopalladium addition reaction. The reaction has been extended to other internal alkynes. An unusual product 2-amino-3-\{(E)-1-propenyl\}-4-propylnaphthalene has been obtained as the sole product in the reaction of 4-octyne. The formation of this unusual product has been rationalized by a mechanism similar to the palladium-catalyzed cyclization of enynes. On the other hand, the reaction of 2-iodobenzonitrile and diphenylacetylene affords 2,3-diphenylindenone in 30% yield.
Introduction

The development of new annulation processes is one of the most challenging and important quests in organic synthesis. The cyano group (CN) has been employed as a reactive moiety in the synthesis of numerous organic compounds. The possibility of incorporating the cyano group into a ring system has been a very attractive idea to synthetic chemists. Metal-mediated approaches have provided efficient ways to realize this possibility.

Janz et al. have extensively investigated the cycloaddition of dienes to nitriles. The latter functions as a dienophile only at elevated temperatures (200-400 °C) in the gas-phase with the aid of an acidic surface (eq 1). The heterocycle is formed only in the presence of an acidic catalyst: in its absence, cyclohexene is the sole product.

\[ \text{Al}_{2}O_{3} / Cr_{2}O_{3} \quad \text{[catalyst]} \quad \rightarrow \quad \text{[heterocycle]} \quad \text{[loss of H₂]} \quad \rightarrow \quad \text{pyridine} \]

The synthesis of pyridine derivatives can also be achieved by the co-cyclization of alkynes with nitriles. This approach was explored first in 1877 by Ramsay, who observed the formation of pyridine in moderate yields by passing a mixture of acetylene and hydrogen cyanide through a red-hot glass tube. In 1973, Wakatsuki and Yamazaki first reported the homogeneous catalytic cycloaddition of alkynes and nitriles using a phosphine-stabilized cobalt(III) complex (eq 2). Since then, a variety of cobalt-based systems have been found to be active catalysts for this reaction. This methodology has also been extended to other substrates. For example, Vollhardt et al. reported the coupling of \( α, ω \)-diynes and nitriles (eq 3). Research has also indicated that catalysts other than Co
can also be employed in this general process. Ingrosso observed that some Rh(I) complexes were excellent long-lived catalyst precursors for the pyridine synthesis.\(^a\)

\[
2 \text{HC} = \text{CH} + \text{N} = \text{CR} \xrightarrow{[\text{Co}]} \text{R}
\]

\[
\begin{align*}
\text{C} = \text{CH} \\
\text{(CH}_2\text{n)} \\
\text{C} = \text{CH}
\end{align*} + \text{N} = \text{CR} \xrightarrow{[\text{Co}]} \text{(CH}_2\text{n)}
\]

The cyclotrimerisation reaction of organic nitriles can be induced by \(n\)-butyllithium.\(^8\) This reaction is highly solvent dependent. A 3:1 molar mixture of benzonitrile and \(n\)-butyllithium in hexane solution afforded 2,4,6-triphenyl-1,3,5-triazine as the final product (eq 4). However, when hexane was replaced by THF in the \(n\)-butyllithium solution, a dihydrotriazine product was formed (eq 5).

\[
3 \text{PhC} \equiv \text{N} \xrightarrow{\text{n-BuLi (hexane)}} \text{Ph}
\]

\[
3 \text{PhC} \equiv \text{N} \xrightarrow{\text{n-BuLi (THF)}} \text{Ph}
\]
Nitriles can also serve as suitable precursors for the intramolecular Barbier reaction. Thus, the intramolecular reductive cyclization of 5-iodo-2-phenylpentanenitrile afforded 2-phenylcyclopentanone in 55% yield (eq 6).

\[ \text{CN} \quad \text{Ph} \quad \text{SmI}_2 \quad \text{H}_3\text{O}^+ \quad 55\% \]

The rhodium-catalyzed reaction of diazo dicarbonyl compounds with nitriles provides very direct access to functionalized 1,3-oxazoles (Scheme 1). Presumably, the reaction proceeds via formation of electrophilic rhodium carbene complex 1 as the key intermediate.

**Scheme 1**

The reaction of titanocene methyldiene complex Cp,Ti=CH, with nitriles produces intermediate 2. Further treatment with Na$_2$SO$_4$$\cdot$10 H$_2$O gives 4-amino-4-azadienes in a
one-pot procedure (Scheme 2). In this reaction, \( \text{Cp}_2\text{Ti}=\text{CH}_2 \) is generated in situ from \( \text{Cp}_2\text{TiMe}_2 \) by gentle heating.

\[
\begin{align*}
\text{Cp}_2\text{Ti}=\text{CH}_2 + 2 \text{RCN} & \xrightarrow{60 \, ^\circ\text{C}} \text{Cp}_2\text{Ti}(\text{N=NR})(\text{N=NR})_2 \xrightarrow{\text{Na}_2\text{SO}_4\cdot10\,\text{H}_2\text{O}} \text{NH}_2
\end{align*}
\]

A low-valent titanium reagent prepared from \( \text{TiCl}_4 \) and zinc powder induced the intramolecular reductive coupling of a cyano group with a nitro group. Thus, the reaction of \( \gamma \)-nitronitriles (3), derived from \( \alpha,\beta \)-unsaturated nitriles and nitroethane, gave the cyclic amidines 4 (eq 7).

\[
\begin{align*}
\text{Me} & \quad \text{CN} & \quad \text{R}^1 \quad \text{R}^2 \\
\text{NO}_2 & \quad 1. \text{TiCl}_4/\text{Zn/THF} \quad 2. 10\% \, \text{aq} \, \text{K}_2\text{CO}_3 & \quad \text{R}^1 \quad \text{R}^2 \\
3 & \quad & \quad 4
\end{align*}
\]

Cyano groups attached to an aryl ring can sometimes react with neighboring functional groups. In the case of the \((\alpha\text{-cyanoaryl})\text{allenes} 5\), zinc ions initiate an enamine-to-nitrile cyclization. After an aqueous acidic workup, 2-acylindenones (6) are obtained as the sole product (Scheme 3).
In the reaction of 4-octyne with Et₂ZrCp₂, followed by treatment with PhCN and I₂, the corresponding imine 7 was the product. The imine 7 could be carbonylated to produce a lactam 8 as the final product (Scheme 4)."
Benzonitrile and acetonitrile are commonly employed as ligands for PdCl₂. In fact, PdCl₂(PhCN)₂ and PdCl₂(MeCN)₂ are widely used catalysts in palladium-mediated reactions. Acetonitrile has also been utilized as a solvent in numerous palladium reactions. In these cases, benzonitrile and acetonitrile simply serve as ligands or the solvents in these reactions, and are not incorporated into the molecular structure of the products. In other cases, substrates bearing a cyano group can undergo palladium-catalyzed processes to produce the products in which the cyano group is present. The following are some examples.

In the presence of KCN, cyanocarbonylation of iodobenzene takes place to form benzoyl cyanide (eq 8).\(^\text{17}\)

\[
\text{PhC} = \text{CH} + \text{CO} + \text{KCN} \xrightarrow{\text{cat. Pd(PPh₃)₄}} \text{PhC} = \text{COCN}
\]

(8)

The reaction of trimethylsilyl cyanide (Me₃SiCN) with acetylenes in the presence of a palladium catalyst has been investigated by Chatani and co-workers.\(^\text{18}\) The PdCl₂/pyridine catalyzed reaction of phenylacetylene and other terminal acetylenes with Me₃SiCN results in the addition of Me₃SiCN to the carbon-carbon triple bond (eq 9). When an excess of Me₃SiCN was employed without solvent and in the presence of a Ni catalyst, a 2-amino-5-cyanopyrrole was obtained (eq 10).
There are numerous palladium-catalyzed reactions in which cyano groups are left completely untouched during the process. For example, the cyanomethylation of aryl halides can be carried out by a palladium-catalyzed cross-coupling reaction (eq 11).\textsuperscript{19}

\[
\text{PhBr} + \text{Bu}_3\text{SnCH}_2\text{CN} \xrightarrow{\text{cat. PdCl}_2[\text{P(o-tol)}_3]\_2} \text{PhCH}_2\text{CN}
\] (11)

\textit{p}-Iodobenzonitrile has been employed in a different type of palladium-catalyzed coupling reaction. The reaction with 3,3,3-triethoxy-1-propyne gave 1-aryl-3,3,3-triethoxy-1-propyne, which was converted to the corresponding ethyl arylpropiolate (eq 12).\textsuperscript{10} Even when water is used as the solvent, \textit{p}-iodobenzonitrile undergoes coupling with terminal acetylenes in the presence of a palladium catalyst (eq 13).\textsuperscript{21}

\[
\text{NC}^-\text{I} + \text{HC}=\text{C}(_2\text{OEt})_3 \xrightarrow{\text{1. cat. PdCl}_2(\text{PPh}_3)_2} \text{NC}^-\text{I} \xrightarrow{\text{2. TsOH, PhH}} \text{NC}^-\text{I} \xrightarrow{\text{1\% PdCl}_2(\text{PPh}_3)_2} \text{74%}
\] (12)

\[
\text{NC}^-\text{I} + \text{PhC}≡\text{H} \xrightarrow{\text{1\% PdCl}_2(\text{PPh}_3)_2} \text{NC}^-\text{I} \xrightarrow{\text{2\% CuI, K}_2\text{CO}_3} \text{96%}
\] (13)
$o$-Cyanoaryl halides have been employed in a number of palladium-catalyzed coupling reactions. $^{22}$ $o$-Iodobenzonitrile reacted with Knochel’s borylmethylzinc reagent $^9$ to give benzylic boronate $^10$ (eq 14). $^{22a}$ In another case, 3-bromo-4,6-dimethyl-2-pyridinecarbonitrile ($^{11}$) was heated with phenylacetylene in Et$_3$N in the presence of PdCl$_2$(PPh$_3$)$_2$ and Cul, to give 4,6-dimethyl-3-phenylethynyl-2-pyridinecarbonitrile ($^{12}$) in 60% yield (eq 15). $^{22b}$

$$\begin{align*}
\text{PhCN} & + \text{IZnCH}_2\text{B} & \xrightarrow{\text{cat. PdCl}_2(\text{PPh}_3)_2} & \text{PhCH}_2\text{B} \quad \text{(eq 14)} \\
& & \text{cat. PdCl}_2(\text{PPh}_3)_2 & \text{67}\% \\
\end{align*}$$

$$\begin{align*}
\text{MeN}^- & + \equiv \text{Ph} & \xrightarrow{\text{cat. PdCl}_2(\text{PPh}_3)_2, \text{CuI, Et}_3\text{N}} & \text{MeN}^- \equiv \text{Ph} \\
& & \text{cat. PdCl}_2(\text{PPh}_3)_2, \text{CuI, Et}_3\text{N} & \text{100 $^\circ$C, 24 h} \\
& & & \text{60}\% \\
\end{align*}$$

In none of these palladium-catalyzed reactions (eqs 8-15), does the carbon-nitrogen triple bond of the cyano group become involved in the reactions themselves. In fact, the nitrile group is generally considered inert towards Pd-C bonds. On the other hand, in the presence of other metals, such as Co (eqs 2-3), Sm (eq 6), Rh (Scheme 1), Ti (Scheme 2 and eq 7), Zn (Scheme 3) and Zr (Scheme 4), insertion of the carbon-nitrogen triple bond is the key step in the process. To the best of our knowledge, there are no reports of organopalladium compounds adding to the carbon-nitrogen triple bond of a nitrile in the absence of other metals. However, it has been clearly established that aryl and vinylpalladium complexes can readily insert into various other multiple bonds, such as
those present in alkenes, conjugated dienes, alkynes, CO₂, and carbonyl groups. An example of addition to a carbon-nitrogen double bond has been demonstrated in Scheme 4. Thus, it appears possible that the carbon-nitrogen triple bond might undergo insertion reactions by aryl or vinylpalladium complexes under appropriate reaction conditions.

Recently, convenient palladium-alkyne annulation methodology has been developed in this group, which offers useful routes to indoles, indenones, benzofurans and isocoumarins (eq 16). These reactions involve the insertion of an internal alkyne into an arylpalladium intermediate and subsequent cyclization onto the functional group present in the ortho position. The indenone synthesis provides an interesting example of the intramolecular reaction of a functional group, an aldehyde, normally inert towards organopalladium species. We envisioned that a cyano or cyanomethyl group might serve as the neighboring functional group in the above reaction and that the vinylpalladium intermediates might insert into the carbon-nitrogen triple bond. To our delight, we have succeeded in realizing, for the first time, the insertion of an organopalladium intermediate into a carbon-nitrogen triple bond. Herein, we would like to report our investigation of the palladium-catalyzed cross-coupling of (2-iodophenyl)acetonitrile or 2-iodobenzonitrile with diphenylacetylene and other internal alkynes.
Results and Discussion

We chose the reaction of (2-iodophenyl)acetonitrile and diphenylacetylene as a model system for our initial investigation. First of all, the standard reaction conditions used in much of our previous palladium annulation chemistry were employed in the reaction. As hoped for, the carbon-nitrogen triple bond of the cyano group participated in the reaction and 2-amino-3,4-diphenylnapthalene was obtained in 34% yield (eq 17).

\[
\begin{align*}
\text{PhCN} & + \text{Ph} & \longrightarrow & \text{Ph} \\
\text{Ph} & \text{Ph} & \text{Ph} & \text{Ph} \\
2 \text{equiv} & 5\% \text{Pd(OAc)}_2 & \text{2 equiv NaOAc} & \text{1 equiv LiCl} \\
& \text{DMF, 100 °C, 11 h} & & \\
& & & 34% \\
\end{align*}
\]

Since the yield of the reaction was low, considerable effort has been carried out to optimize the reaction conditions so as to improve the yields. First, different reaction times and palladium catalysts were examined in the reaction (Table 1). Using Pd(OAc)$_2$, GC-MS analysis indicated that the reaction had not reached completion even after 11 h (entries 1 and 2). Thus, longer reaction times were employed. According to GC-MS analysis, the reaction was complete after 48 h and higher yields were observed (entries 3 and 4). Other palladium catalysts, such as Pd(dba)$_2$ and Pd(PPh$_3$)$_2$, did not afford good yields. Pd(OAc)$_2$ appears to be the best catalyst. Somewhat surprising was the observation that 5 mol % Pd(OAc)$_2$ is as effective as 20 mol % of the catalyst (compare entries 1 and 2, 3 and 4).
Table 1. Effect of reaction time and catalyst on the Pd-catalyzed reaction of (2-iodophenyl)acetonitrile and diphenylacetylene (eq 17).a

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>rxn time (h)</th>
<th>% isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5% Pd(OAc)$_2$</td>
<td>11</td>
<td>34</td>
</tr>
<tr>
<td>2</td>
<td>20% Pd(OAc)$_2$</td>
<td>11</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>5% Pd(OAc)$_2$</td>
<td>48</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>20% Pd(OAc)$_2$</td>
<td>48</td>
<td>51</td>
</tr>
<tr>
<td>5</td>
<td>5% Pd(dba)$_2$</td>
<td>11</td>
<td>19</td>
</tr>
<tr>
<td>6</td>
<td>5% Pd(dba)$_2$</td>
<td>72</td>
<td>30</td>
</tr>
<tr>
<td>7</td>
<td>5% Pd(PPh$_3$)$_4$</td>
<td>32</td>
<td>32</td>
</tr>
</tbody>
</table>

a All reactions were run in DMF in the presence of 2 equiv of diphenylacetylene, 2 equiv of NaOAc and 1 equiv of LiCl at 100 °C for the specified period of time.

The next variable examined was the solvent (Table 2). The use of DMF as the solvent is crucial to the success of this reaction (Table 2, entry 1). The reaction was also carried out in 9:1 DMF/H$_2$O, although the yield was considerably lower (entry 2). Other solvents, including DMSO, CH$_3$NO$_2$, DMA and CH$_3$CN were inefficient and none of the desired product was observed (entries 3-6). The failure of DMA is particularly striking, since it usually behaves very similar to DMF as one might expect with such similar structures.

The next task was to find the best base for the reaction. As shown in Table 3, a series of inorganic bases (Table 3, entries 1-5) were examined first and NaOAc was observed to furnish the highest yield (entry 1). After careful consideration of the possible mechanism of the reaction (vide infra), we realized that a hydrogen source is required for
Table 2. Effect of solvent on the Pd-catalyzed reaction of (2-iodophenyl)acetonitrile and diphenylacetylene (eq 17).

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>rxn time (h)</th>
<th>% isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DMF</td>
<td>48</td>
<td>52</td>
</tr>
<tr>
<td>2</td>
<td>9:1 DMF/H₂O</td>
<td>24</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>DMSO</td>
<td>21</td>
<td>-b</td>
</tr>
<tr>
<td>4</td>
<td>CH₃NO₂</td>
<td>21</td>
<td>-b</td>
</tr>
<tr>
<td>5</td>
<td>DMA</td>
<td>21</td>
<td>-b</td>
</tr>
<tr>
<td>6</td>
<td>CH₃CN</td>
<td>96</td>
<td>-c</td>
</tr>
</tbody>
</table>

*a* All reactions were run in DMF in the presence of 5 mol % Pd(OAc)₂, 2 equiv of diphenylacetylene, 2 equiv of NaOAc and 1 equiv of LiCl at 100 °C for the specified period of time.  

*b* (2-Iodophenyl)acetonitrile disappeared, but none of the desired product was obtained.  

*c* (2-Iodophenyl)acetonitrile did not react completely and only a trace of the desired product was observed.

The reaction. With this in mind, NaH and HCOONa, were examined as bases (entries 7 and 8). The latter base might serve not only as a carboxylate base, but also as a reducing agent.  

However, neither reaction afforded the desired product. It was known that tertiary amines containing an α-hydrogen could provide a hydride to palladium through insertion of the palladium into the C-H bond adjacent to nitrogen.  

Therefore, Et₃N was examined in the reaction and the yield of the reaction was significantly improved (entry 8). It was also noticed that employing n-Bu₂NCl as the chloride source afforded better yields than LiCl (compare entries 1 and 9, 8 and 10). Another tertiary amine, i-Pr₂NEt, was also examined in the reaction and a high yield was obtained (entry 11). However, the
Table 3. Effect of base on the Pd-catalyzed reaction of (2-iodophenyl)acetonitrile and diphenylacetylene (eq 17).a

<table>
<thead>
<tr>
<th>entry</th>
<th>base (equiv)</th>
<th>Cl⁻ source (1 equiv)</th>
<th>rxn time (h)</th>
<th>% isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaOAc (2)</td>
<td>LiCl</td>
<td>48</td>
<td>52</td>
</tr>
<tr>
<td>2</td>
<td>Na₂CO₃ (2)</td>
<td>LiCl</td>
<td>48</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>K₂CO₃ (2)</td>
<td>LiCl</td>
<td>48</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>KOAc (2)</td>
<td>LiCl</td>
<td>48</td>
<td>42</td>
</tr>
<tr>
<td>5</td>
<td>NaHCO₃ (2)</td>
<td>LiCl</td>
<td>48</td>
<td>32</td>
</tr>
<tr>
<td>6</td>
<td>NaH (2)</td>
<td>LiCl</td>
<td>48</td>
<td>.b</td>
</tr>
<tr>
<td>7</td>
<td>HCOONa (2)</td>
<td>LiCl</td>
<td>48</td>
<td>.b</td>
</tr>
<tr>
<td>8</td>
<td>Et₃N (3)</td>
<td>LiCl</td>
<td>48</td>
<td>73</td>
</tr>
<tr>
<td>9</td>
<td>NaOAc (2)</td>
<td>n-Bu₄NCl</td>
<td>48</td>
<td>63</td>
</tr>
<tr>
<td>10</td>
<td>Et₃N (3)</td>
<td>n-Bu₄NCl</td>
<td>48</td>
<td>76</td>
</tr>
<tr>
<td>11</td>
<td>i-Pr₂NEt (3)</td>
<td>n-Bu₄NCl</td>
<td>48</td>
<td>75</td>
</tr>
<tr>
<td>12</td>
<td>Et₃NH (3)</td>
<td>n-Bu₄NCl</td>
<td>48</td>
<td>.b</td>
</tr>
<tr>
<td>13</td>
<td>i-Pr₂NH (3)</td>
<td>n-Bu₄NCl</td>
<td>48</td>
<td>51</td>
</tr>
<tr>
<td>14</td>
<td>Et₃N (3)</td>
<td>n-Bu₄NCl</td>
<td>72</td>
<td>76</td>
</tr>
<tr>
<td>15</td>
<td>Et₃N (3)</td>
<td>n-Bu₄NCl</td>
<td>120</td>
<td>77</td>
</tr>
</tbody>
</table>

a All reactions were run in DMF in the presence of 5 mol % Pd(OAc)₂ and 2 equiv of diphenylacetylene at 100 °C for the specified period of time. b Only a trace of the desired product was observed.
corresponding secondary amines did not furnish good yields (entries 12 and 13). We also confirmed again that a reaction time of 48 h is enough for the reaction, since no improvement in yield was observed after 48 h (compare entries 10, 14 and 15).

In a continued effort to optimize the reaction conditions, the effects of phosphines and Lewis acids were explored (Table 4). It was observed that the addition of the Lewis

Table 4. Effects of phosphines and Lewis acids on the Pd-catalyzed reaction of (2-iodophenyl)acetonitrile and diphenylacetylene (eq 17).^a

<table>
<thead>
<tr>
<th>entry</th>
<th>additive</th>
<th>base (equiv)</th>
<th>$n$-Bu$_4$NCl equiv</th>
<th>rxn time (h)</th>
<th>% isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>NaOAc (2)</td>
<td>3</td>
<td>24</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>Zn(OAc)$_2$ (1 equiv)</td>
<td>NaOAc (2)</td>
<td>3</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>ZnCl$_2$ (1 equiv)</td>
<td>NaOAc (2)</td>
<td>3</td>
<td>21</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>Et$_3$N (3)</td>
<td>1</td>
<td>48</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>PPh$_3$ (10 mol %)</td>
<td>Et$_3$N (3)</td>
<td>1</td>
<td>72</td>
<td>77</td>
</tr>
<tr>
<td>6</td>
<td>P(o-tolyl)$_3$ (10 mol %)</td>
<td>Et$_3$N (3)</td>
<td>1</td>
<td>72</td>
<td>78</td>
</tr>
<tr>
<td>7</td>
<td>PAR$_b$ (10 mol %)</td>
<td>Et$_3$N (3)</td>
<td>1</td>
<td>96</td>
<td>66</td>
</tr>
</tbody>
</table>

^a All reactions were run in DMF in the presence of 5 mol % Pd(OAc)$_2$ and 2 equiv of diphenylacetylene at 100 °C for the specified period of time. ^b Ar = 2,6-dimethoxyphenyl.
acids Zn(OAc)$_2$ and ZnCl$_2$ only made the reaction worse (compare entries 1-3). The addition of catalytic amounts of phosphines, such as PPh$_3$, P(o-tolyl)$_3$, and tris(2,6-dimethoxyphenyl)phosphine, did not improve the yield and longer reaction times were required for the reactions to reach completion (entries 4-7).

Having established the optimal solvent, reaction time, catalyst and base, our attention was turned towards the amount of the base Et$_3$N. Varying amounts of Et$_3$N from 1 to 5 molar equivalents were examined (Table 5). The results indicate that 2 equiv of Et$_3$N afforded the best yield of naphthylamine product (Table 5, entry 2).

**Table 5. Effect of the amount of Et$_3$N on the Pd-catalyzed reaction of (2-iodophenyl)acetonitrile and diphenylacetylene (eq 17).**

<table>
<thead>
<tr>
<th>entry</th>
<th>Et$_3$N equivs</th>
<th>% isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>71</td>
</tr>
</tbody>
</table>

*All reactions were run in DMF in the presence of 5 mol % Pd(OAc)$_2$, 2 equiv of diphenylacetylene, and 1 equiv of n-Bu$_4$NCl at 100 °C for 48 h.*

The final variable examined was the stoichiometry of the diphenylacetylene. Different amounts of diphenylacetylene were employed in the reaction (Table 6). The highest yield was obtained when 3 equiv of diphenylacetylene was utilized (entry 3).

Based on the above investigation, the optimal conditions for this reaction are as follows: 5 mol % Pd(OAc)$_2$, 3 equiv of diphenylacetylene, 2 equiv of Et$_3$N, 1 equiv of n-
Table 6. Effect of the amount of diphenylacetylene on the Pd-catalyzed reaction of (2-iodophenyl)acetonitrile and diphenylacetylene (eq 17).\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>diphenylacetylene equivs</th>
<th>% isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>76</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>83</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>74</td>
</tr>
</tbody>
</table>

\(^a\) All reactions were run in DMF in the presence of 5 mol % Pd(OAc)$_2$, 2 equiv of Et$_3$N, and 1 equiv of $n$-Bu$_4$NCl at 100 °C for 48 h.

With these optimal conditions in hand, other alkynes were employed in the reaction. The results are summarized in Table 7. This reaction works reasonably well for other internal alkynes. For 1-phenyl-1-propyne and 4,4-dimethyl-2-pentyne, the desired products were obtained in high yields (Table 7, entries 2-4). It was also noticed that these reactions provided only a single regioisomer as shown in Table 6 (entries 2-4). The regiochemistry of these products could be determined by 1D and 2D NMR spectral analysis. The reaction of 3,3-dimethyl-1-phenyl-1-butyne afforded the desired product 13 in 27% yield and the further cyclized product 14 in 15% yield (entry 5). When 1-phenyl-1-butyne was employed as the alkyne, the anticipated product 15 was observed in 37% yield. However, an unexpected product 16 was also obtained in 17% yield (entry 6).
Table 7. The Pd-catalyzed reaction of (2-iodophenyl)acetonitrile and internal alkynes.\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>alkyne</th>
<th>product(s)</th>
<th>% isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph$\equiv$Ph</td>
<td><img src="image1" alt="Product 1" /></td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>Ph$\equiv$Me</td>
<td><img src="image2" alt="Product 2" /></td>
<td>65</td>
</tr>
<tr>
<td>3</td>
<td>Me$\equiv$CMe\textsubscript{3}</td>
<td><img src="image3" alt="Product 3" /></td>
<td>61\textsuperscript{b}</td>
</tr>
<tr>
<td>4</td>
<td>Ph$\equiv$CMe\textsubscript{3}</td>
<td><img src="image4" alt="Product 4" /> + <img src="image5" alt="Product 5" /></td>
<td>75\textsuperscript{b,c}</td>
</tr>
<tr>
<td>5</td>
<td>Ph$\equiv$Et</td>
<td><img src="image6" alt="Product 6" /> + <img src="image7" alt="Product 7" /></td>
<td>27 + 15</td>
</tr>
<tr>
<td>6</td>
<td>n-Pr$\equiv$n-Pr</td>
<td><img src="image8" alt="Product 8" /></td>
<td>37 + 17</td>
</tr>
<tr>
<td>7</td>
<td>Ph$\equiv$SiMe\textsubscript{3}</td>
<td><img src="image9" alt="Product 9" /></td>
<td>30\textsuperscript{b}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} All reactions were run in DMF in the presence of 5 mol \% Pd(OAc)$_2$, 3 equiv of alkyne, 2 equiv of Et\textsubscript{3}N, 1 equiv of n-Bu\textsubscript{4}NCl at 100 °C for 48 h unless otherwise indicated. \textsuperscript{b} Five equiv of alkyne were used in the reaction. \textsuperscript{c} Two equiv of H\textsubscript{2}O were employed in the reaction.
Similarly, the unusual product 17 was produced as the sole product in the reaction of 4-octyne (entry 7). The (E)-stereochemistry of products 16 and 17 was established from the $^1$H NMR coupling constants between the olefinic hydrogens ($J = 16.2$ Hz), and fully confirmed by 2D NOESY spectroscopy. As shown in entry 8, the reaction of (2-iodophenyl)acetonitrile with 1-phenyl-2-(trimethylsilyl)acetylene afforded the simple coupling product 18 and none of the desired naphthalene product was observed. This reaction presumably proceeds by desilylation of the acetylene to produce phenylacetylene, which undergoes coupling with (2-iodophenyl)acetonitrile to give 18.

The mechanism of this naphthalene synthesis has not been fully elucidated, but based upon our previous research on alkyne annulation chemistry$^{23-25}$ as well as structural analysis of the products, especially the regiochemistry (Table 7, entries 2-6), we tentatively propose the following mechanism for this process (Scheme 5). Presumably, this process starts with the reduction of Pd(OAc)$_2$ to the actual catalyst Pd(0). The oxidative addition of Pd(0) to (2-iodophenyl)acetonitrile produces an arylpalladium intermediate 19, which rapidly inserts the alkyne to produce a vinylic palladium species 20. This may subsequently undergo addition to the neighboring CN triple bond to generate the intermediate 21, followed by tautomerization to the new Pd(II) intermediate 22 (path 1). An alternative path might involve formation of ketenimine 23$^{28}$ in the presence of the base and subsequent syn addition of the vinylpalladium species to the C=N double bond to generate intermediate 22 (path 2). We have no evidence which allows us to chose between these two paths. In the next step, palladium complex 22 is somehow reduced to the final product, accompanied by the regeneration of the Pd(0) catalyst. We can only speculate as to how this occurs. It may be that the base Et$_3$N or the solvent DMF provides a source of "hydride" for the reduction. As mentioned earlier, employing Et$_3$N as the base furnishes the highest yields, so one might suspect that Et$_3$N is serving as the hydrogen source.$^{27}$
DMF, which is the solvent, could also be the hydrogen source, since the yield of the desired product was sharply reduced when other solvents, such as DMSO, DMA and CH$_3$CN, were used in the reaction (Table 2, entries 1, 3, 5 and 6). Negishi et al. have reported that H$_2$O was an external hydrogen source in his palladium carbonylation reaction (Scheme 4). Therefore, we used 2 equiv of H$_2$O in some reactions and the yield was significantly improved (Table 7, compare entries 3 and 4). This indicates that adventitious water may be the hydrogen source. Water also may be simply protonating the species 21.
or 22 to generate Pd(II), which is subsequently reduced to Pd(0) by other species present in the reaction.

The regioselectivity of the reaction can be nicely explained by the proposed mechanism. As seen in our previous research,\textsuperscript{23-25} the aryl group of an arylpalladium intermediate such as 19 would be expected to add to the less hindered end of the alkyne placing the palladium moiety on the more hindered end of the original triple bond. As a result, the more sterically hindered group present in the alkyne should end up in the 3 position of the naphthalene product and the less hindered group in the 4 position (Table 7, entries 2-4). This is indeed observed.

Compound 13 is the anticipated product from the reaction of (2-iodophenyl)-acetonitrile and 3,3-dimethyl-1-phenyl-1-butyne (Table 7, entry 5). The formation of compound 14 was completely unexpected. We can only surmise that the arene-arene coupling of product 13 in the presence of a Pd(II) catalyst is producing product 14. This type of palladium(II)-promoted aryl-aryl coupling is known\textsuperscript{30}, but it is surprising that sufficient Pd(II) salts would exist under the reducing conditions of our reaction to be able to effect this cross-coupling.

The formation of the unusual products 16 and 17 might be rationalized by a mechanism similar to the palladium-catalyzed cyclization of enynes.\textsuperscript{10} Trost et al.\textsuperscript{10a-c} have extensively studied the palladium-catalyzed reductive cyclization of 1,6-enynes (Scheme 6). In this process, the Pd-hydride produced from the reaction of Pd(0) with HOAc preferentially adds to the alkyne, followed by intramolecular alkene insertion and subsequent β-hydrogen elimination to furnish either the 1,4-diene or 1,3-diene (Scheme 6).\textsuperscript{10c}
In analogy with the palladium-catalyzed 1,6-enyne chemistry, we propose the following mechanism for the formation of products 16 and 17 (Scheme 7). Oxidative addition of (2-iodophenyl)acetonitrile to Pd(0) and subsequent insertion of 4-octyne furnishes intermediate 25. This species then undergoes a β-hydrogen elimination to produce an allene intermediate 26, which subsequently isomerizes to intermediate 27 in which the hydride is now syn to the nitrile in the square planar Pd intermediate. Addition of the Pd-H to the carbon-nitrogen triple bond generates intermediate 28, an acyl-like organopalladium intermediate, which in turn can add to the allene to furnish intermediate 29, a π-allylic or π-benzylic (after imine tautomerization) intermediate, which might be expected to eliminate HPdX to generate the new carbon-carbon double bond and eventually regenerate the Pd(0) catalyst. Intermediate 30 would be expected to tautomerize to the final product 17 (Scheme 7).
Scheme 7

The reaction of 2-iodobenzonitrile with diphenylacetylene was also investigated under several different reaction conditions. The results are shown in Table 8. Under the standard reaction conditions established in our previous research (see chapter 1), the fluorene product 31 was obtained in 63% yield (Table 8, entry 1). In the absence of PPh₃, the reaction furnished 31 in 56% yield (entry 2). When the solvent was changed from DMF to 9:1 DMF/H₂O, the major product was 3,4-diphenylindenone 32 in 28% yield (entry 3). The same indenone product 32 was also the major product (30%) under the optimal conditions developed for the reaction of (2-iodophenyl)acetonitrile and diphenylacetylene (entry 4). When 2 equiv of water was added, the reaction afforded 32 in 25% yield (entry 5). Further optimization of this reaction is in progress.
Table 8. The Pd-catalyzed reaction of 2-iodobenzonitrile and diphenylacetylene.<sup>a</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>alkyne (equiv)</th>
<th>base source (equiv)</th>
<th>Cl&lt;sup&gt;-&lt;/sup&gt; source (1 equiv)</th>
<th>PPh&lt;sub&gt;3&lt;/sub&gt;</th>
<th>solvent</th>
<th>rxn time (h)</th>
<th>product</th>
<th>% isolated yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>NaOAc (2)</td>
<td>n-Bu&lt;sub&gt;4&lt;/sub&gt;NCl 10%</td>
<td>DMF</td>
<td>10</td>
<td>31</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>NaOAc (2)</td>
<td>LiCl</td>
<td>DMF</td>
<td>11</td>
<td>56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>NaOAc (2)</td>
<td>LiCl</td>
<td>9:1 DMF/H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>10</td>
<td>32</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>Et&lt;sub&gt;2&lt;/sub&gt;N (3)</td>
<td>n-Bu&lt;sub&gt;4&lt;/sub&gt;NCl</td>
<td>DMF</td>
<td>48</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>Et&lt;sub&gt;2&lt;/sub&gt;N (3)</td>
<td>n-Bu&lt;sub&gt;4&lt;/sub&gt;NCl</td>
<td>DMF</td>
<td>48</td>
<td>25&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> All reactions were run in DMF in the presence of 5 mol % Pd(OAc)<sub>2</sub> at 100 °C for the specified period of time. <sup>b</sup> Two equiv of H<sub>2</sub>O were employed in the reaction.
A possible mechanism for the formation of 32 is proposed in Scheme 8. The initial step is the oxidative addition of Pd(0) to 2-iodobenzonitrile and the resultant arylpalladium complex adds to diphenylacetylene to generate intermediate 33. This in turn undergoes an intramolecular insertion into the carbon-nitrogen triple bond to furnish intermediate 34, which is converted to intermediate 35 by protonolysis. Further hydrolysis of the imine affords the observed indenone. To make the reaction catalytic in palladium, the Pd(II) salt formed upon initial hydrolysis of 34 must be reduced back to Pd(0).

Scheme 8

Conclusion

For the first time, the carbon-nitrogen triple bond has been observed to participate in an organopalladium addition reaction. Reactions of (2-iodophenyl)acetonitrile with diphenylacetylene and other internal alkynes afford 3,4-disubstituted 2-aminonaphthalenes in moderate to good yields. Similarly, 2-iodobenzonitrile reacts with diphenylacetylene to produce 3,4-diphenylindenone in low, unoptimized yield. The addition of a vinylpalladium
intermediate to the carbon-nitrogen triple bond is assumed to be the key step in both of these reactions.

**Experimental Section**

**General.** All $^1$H and $^{13}$C NMR spectra were recorded at 300 and 75.5 MHz respectively. Thin-layer chromatography (TLC) was performed using commercially prepared 60 mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm), or basic KMnO$_4$ solution [3 g KMnO$_4$ + 20 g K$_2$CO$_3$, + 5 mL NaOH (5%) + 300 mL H$_2$O].

**Reagents.** All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of NaOAc, LiCl, DMF, CH$_2$Cl$_2$, hexanes and ethyl acetate were purchased from Fisher Scientific. Pd(OAc)$_2$ was donated by Johnson Mathey Inc. and Kawaken Fine Chemicals Co., Ltd. 1-Phenyl-2-(trimethylsilyl)acetylene, 4-octyne and diphenylacetylene were obtained from Aldrich Chemical Co., Inc. (2-Iodophenyl)acetonitrile, 4,4-dimethyl-2-pentyne and $n$-Bu$_4$NCl were purchased from Lancaster Synthesis Inc. 2-Iodobenzonitrile was purchased from Trans World Chemicals, Inc. 1-Phenyl-1-propyne and 1-phenyl-l-butyne were obtained from Farchan Scientific Co. 3,3-Dimethyl-1-phenyl-l-butyne was prepared according to a previous literature procedure.$^{24}$

**General Procedure for the Palladium-catalyzed Reaction of (2-Iodophenyl)acetonitrile or 2-Iodobenzonitrile and Internal Alkynes.** Palladium acetate (2.8 mg, 0.0125 mmol), Et$_3$N (50.5 mg, 0.5 mmol), $n$-Bu$_4$NCl (70 mg, 0.25 mmol), (2-iodophenyl)acetonitrile (60.8 mg, 0.25 mmol) or 2-iodobenzonitrile (57.3 mg, 0.25 mmol), the alkyne (0.75 mmol), and 5 mL of DMF were placed in a 4 dram vial.
which was heated in an oil bath at 100 °C for 48 h unless otherwise indicated. The reaction mixture was cooled, diluted with ether, washed with saturated NH₄Cl, dried over anhydrous MgSO₄, and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography or preparative TLC. The following compounds were prepared by the above procedure.

2-Amino-3,4-diphenynaphthalene (Table 7, entry 1). Obtained as a brown solid in 83% yield from the reaction of (2-iodophenyl)acetonitrile and diphenylacetylene after purification by column chromatography (15:1 hexanes/EtOAc): mp 158-160 °C (hexanes/EtOAc); ¹H NMR (CDCl₃) δ 3.74 (br s, 2 H), 7.09-7.24 (m, 12 H), 7.33-7.37 (m, 2 H), 7.65 (d, J = 6.3 Hz, 1 H); ¹³C NMR (CDCl₃) δ 108.3, 122.5, 125.6, 126.2, 126.4, 126.9, 127.0, 127.3, 127.5, 128.3, 130.0, 130.6, 130.9, 134.4, 137.6, 139.2, 139.8, 142.4; IR (CDCl₃) 3465, 3371, 3052, 1618 cm⁻¹; HRMS m/z 295.1360 (calcd for C₂₂H₁₇N, 295.1361).

2-Amino-4-methyl-3-phenynaphthalene (Table 7, entry 2). Obtained as a red oil in 65% yield from the reaction of (2-iodophenyl)acetonitrile and 1-phenyl-1-propyne after purification by column chromatography (15:1 hexanes/EtOAc): ¹H NMR (CDCl₃) δ 2.37 (s, 3 H), 3.62 (br s, 2 H), 7.00 (s, 1 H), 7.26-7.54 (m, 7 H), 7.63 (d, J = 8.1 Hz, 1 H), 7.92 (d, J = 8.4 Hz, 1 H); ¹³C NMR (CDCl₃) δ 16.5, 106.8, 122.4, 124.5, 126.0, 126.2, 127.2, 127.5, 129.1, 130.0, 130.4, 132.8, 134.4, 138.6, 152.5; IR (CDCl₃) 3471, 3378, 3054, 2859, 1623 cm⁻¹; HRMS m/z 233.1205 (calcd for C₁₇H₁₅N).

2-Amino-3-tert-butyl-4-methynaphthalene (Table 7, entries 3 an 4). Obtained as an orange oil from the reaction of (2-iodophenyl)acetonitrile and 4,4-dimethyl-2-pentyne after purification by column chromatography (15:1 hexanes/EtOAc): ¹H NMR (CDCl₃) δ 1.68 (s, 9 H), 2.82 (s, 3 H), 3.95 (br s, 2 H), 6.87 (s, 1 H), 7.19-7.33 (m, 2
H), 7.50 (dd, \( J = 1.5, 8.7 \) Hz, 1 H), 7.92 (d, \( J = 8.7 \) Hz, 1 H); \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \) 20.3, 33.1, 37.8, 110.8, 122.4, 124.1, 125.3, 129.5, 132.7, 133.6, 135.5, 144.3 (one \( sp^2 \) carbon missing due to overlap); IR (CDCl\(_3\)) 3497, 3381, 3064, 2955, 1621 cm\(^{-1}\); HRMS \( m/z \) 213.1522 (calcd for C\(_{15}\)H\(_{19}\)N, 213.1518).

2-Amino-3-tert-butyl-4-phenyl-naphthalene (13) (Table 7, entry 5). Obtained as a light orange solid in 21% yield from the reaction of (2-iodophenyl)acetonitrile and 3,3-dimethyl-1-phenyl-1-butyne after purification by column chromatography (15:1 hexanes/EtOAc): mp 164-165 °C (hexanes/EtOAc); \(^1\)H NMR (CDCl\(_3\)) \( \delta \) 1.31 (s, 9 H), 4.14 (br s, 2 H), 6.92 (d, \( J = 8.4 \) Hz, 1 H), 6.97 (dt, \( J = 1.2 \), 6.6 Hz, 1 H), 7.24-7.40 (m, 7 H), 7.53 (d, \( J = 8.1 \) Hz, 1 H); \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \) 32.9, 37.4, 112.4, 122.2, 124.6, 125.6, 126.7, 127.2, 127.3, 129.4, 131.4, 132.6, 134.1, 138.7, 142.8, 144.1; IR (CDCl\(_3\)) 3478, 3367, 3061, 2956, 1618 cm\(^{-1}\); HRMS \( m/z \) 275.1680 (calcd for C\(_{20}\)H\(_{21}\)N, 275.1674).

2-Amino-1-tert-butylfluoranthene (14) (Table 7, entry 5). Obtained as a light yellow solid in 15% yield from the reaction of (2-iodophenyl)acetonitrile and 3,3-dimethyl-1-phenyl-1-butyne after purification by column chromatography (15:1 hexanes/EtOAc): mp 95-96 °C (hexanes/EtOAc); \(^1\)H NMR (CDCl\(_3\)) \( \delta \) 1.55 (s, 9 H), 4.08 (br s, 2 H), 6.80 (s, 1 H), 7.32-7.39 (m, 4 H), 7.73-7.78 (m, 2 H), 8.04 (m, 1 H); \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \) 30.6, 33.3, 117.1, 119.7, 124.6, 126.8, 127.6, 127.8, 127.9, 129.4, 135.4, 137.1, 137.5, 140.2, 140.8, 147.1 (two \( sp^2 \) carbon missing due to overlap); IR (CDCl\(_3\)) 3467, 3374, 3063, 2930, 1622 cm\(^{-1}\); HRMS \( m/z \) 273.1512 (calcd for C\(_{20}\)H\(_{19}\)N, 293.1518).

2-Amino-4-ethyl-3-phenyl-naphthalene (15) (Table 7, entry 6). Obtained as a light brown solid in 37% yield from the reaction of (2-iodophenyl)acetonitrile and 1-phenyl-1-propyne after purification by column chromatography (15:1 hexanes/EtOAc): mp
131-132 °C (hexanes/EtOAc); $^1$H NMR (CDCl$_3$) $\delta$ 1.14 (t, $J = 7.5$ Hz, 3 H), 2.78 (q, $J = 7.5$ Hz, 2 H), 3.55 (br s, 2 H), 6.98 (s, 1 H), 7.25-7.54 (m, 7 H), 7.63 (d, $J = 7.8$ Hz, 1 H), 7.95 (d, $J = 8.4$ Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 15.5, 23.0, 107.0, 122.4, 124.5, 125.9, 126.1, 126.4, 127.6, 129.1, 129.9, 134.9, 138.4, 139.1, 142.6 (one sp$^2$ carbon missing due to overlap); IR (CDCl$_3$) 3427, 3304, 3065, 2980, 1621 cm$^{-1}$; HRMS m/z 247.1315 (calcd for C$_{19}$H$_{19}$N, 247.1361).

2-Amino-3-ethenyl-4-phenyl naphthalene (16) (Table 7, entry 6). Obtained as an orange solid in 17% yield from the reaction of (2-iodophenyl)acetonitrile and 1-phenyl-1-propyne after purification by column chromatography (15:1 hexanes/EtOAc): mp 128-130 °C (hexanes/EtOAc); $^1$H NMR (CDCl$_3$) $\delta$ 4.14 (br s, 2 H), 5.40 (dd, $J = 1.8$, 11.7 Hz, 1 H), 5.47 (dd, $J = 1.8$, 18.3 Hz, 1 H), 6.42 (dd, $J = 11.7$, 18.0 Hz, 1 H), 7.05-7.10 (m, 2 H), 7.24-7.50 (m, 7 H), 7.59 (d, $J = 8.1$ Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 108.9, 120.0, 122.5, 125.5, 125.6, 126.2, 126.7, 127.0, 127.4, 128.1, 130.7, 134.0, 134.1, 139.4, 139.6, 142.0; IR (CDCl$_3$) 3444, 3375, 3051, 2961, 1624 cm$^{-1}$; HRMS m/z 245.1202 (calcd for C$_{18}$H$_{15}$N, 245.1204).

2-Amino-3-((E)-1-propenyl)-4-propyl naphthalene (17) (Table 7, entry 7). Obtained as a red oil in 30% yield from the reaction of (2-iodophenyl)acetonitrile and 4-octyne after purification by column chromatography (15:1 hexanes/EtOAc): $^1$H NMR (CDCl$_3$) $\delta$ 1.07 (t, $J = 7.5$ Hz, 3 H), 1.57-1.66 (m, 3 H), 1.97-2.00 (m, 2 H), 2.97-3.03 (m, 2 H), 3.96 (br s, 2 H), 5.86-5.93 (m, 1 H), 6.45 (dd, $J = 1.8$, 16.2 Hz, 1 H), 6.91 (s, 1 H), 7.20-7.34 (m, 2 H), 7.55 (d, $J = 8.1$ Hz, 1 H), 7.87 (d, $J = 8.1$ Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 12.7, 18.9, 23.9, 31.8, 107.1, 122.2, 124.3, 125.5, 126.2, 126.4, 126.5, 126.7, 132.2, 134.3, 137.7, 142.5; IR (CDCl$_3$) 3474, 3378, 3065, 2955, 1563 cm$^{-1}$; HRMS m/z 225.1520 (calcd for C$_{18}$H$_{19}$N, 225.1518).
**{2-(Phenylethynyl)phenyl}acetonitrile (18)** (Table 7. entry 8). Obtained as a red oil in 58% yield from the reaction of (2-iodophenyl)acetonitrile and 1-phenyl-2-(trimethylsilyl)acetylene after purification by column chromatography (30:1 hexanes/EtOAc): $^1H$ NMR (CDCl$_3$) $\delta$ 3.98 (s, 2 H), 7.32-7.42 (m, 5 H), 7.50-7.62 (m, 4 H); $^{13}C$ NMR (CDCl$_3$) $\delta$ 22.9, 86.1, 95.8, 117.5, 122.6, 122.9, 128.3, 128.5, 128.6, 129.0, 129.1, 131.7, 131.8, 132.5; IR (CDCl$_3$) 3059, 2925, 2248 (CN), 2214, 1599 cm$^{-1}$; HRMS m/z 217.0891 (calcd for C$_{16}$H$_{12}$N, 217.0892).

**9-Benzylidene-1-cyano-9H-fluorene (31)** (Table 8, entries 1 and 2). Obtained as a yellow solid from the reaction of 2-iodobenzonitrile and diphenylacetylene under the indicated conditions after purification by column chromatography using 30:1 hexanes/EtOAc as eluant: mp 145-146 °C (hexane/EtOAc); $^1H$ NMR (CDCl$_3$) $\delta$ 7.10 (dt, $J$ = 1.0, 7.8 Hz, 1 H), 7.33 (dt, $J$ = 1.0, 7.5, Hz, 1 H), 7.41-7.51 (m, 5 H), 7.56-7.63 (m, 3 H), 7.92 (d, $J$ = 7.5 Hz, 1 H), 7.93 (dd, $J$ = 1.0, 7.5 Hz, 1 H), 8.65 (s, 1 H); $^{13}C$ NMR (CDCl$_3$) $\delta$ 105.1, 118.6, 119.8, 123.7, 124.7, 127.8, 128.5, 128.6, 128.7, 129.1, 132.1, 133.5, 135.0, 136.3, 136.5, 138.6, 139.3, 140.8 (one sp$^2$ C missing due to overlap); IR (CDCl$_3$) 3076, 2215 (CN), 1573 cm$^{-1}$; HRMS m/z 279.1035 (calcd for C$_{21}$H$_{13}$N, 279.1048).

**2,3-Diphenylindenone (32)** (Table 8, entries 3-5). Obtained as a red solid from the reaction of 2-iodobenzonitrile and diphenylacetylene under the indicated conditions after purification by column chromatography using 30:1 hexanes/EtOAc as eluant. The $^1H$ and $^{13}C$ NMR spectra were identical to those in the literature.$^{24}$

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References


CHAPTER 3. PREPARATION OF BIODEGRADABLE POLYMERS BY ADMET POLYMERIZATION OF SOYBEAN OIL

A paper to be submitted to the Journal of American Oil Chemists' Society
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Abstract

Grubbs' recently developed ruthenium catalyst 2 has been employed in the acyclic diene metathesis (ADMET) polymerization of 1,9-decadiene and 5-hexenyl 4-pentenoate and proven more efficient than Schrock's previously used molybdenum catalyst 1. In the presence of 0.1 mol % of catalyst 2, the ADMET polymerization of ethylene glycol dioleate afforded the isomerized (E)-dioleate (27%), dimer (18%), trimer (13%), tetramer (7%), pentamer (5%), hexamer (4%), heptamer (4%) and 9-octadecene (21%). Only a trace amount of the intramolecular cyclized compound (0.1%) was formed in the reaction. Under the same conditions, glyceryl trioleate undergoes ADMET polymerization to produce dimer, trimer, tetramer, pentamer and monocyclic oligomers, with monocyclic oligomers predominating. The high number of repeating units of the monocyclic oligomers (n ~ 6, 10 and 21) indicates that crosslinking occurs readily in this process. Based on our model system studies, we have examined the ADMET polymerization of soybean oil and succeeded in producing polymer materials. A variety of materials, from sticky oils to rubbers, have been prepared from soybean oil. These materials are very likely to be biodegradable.
Introduction

Olefin metathesis is a reaction in which olefins are formally fragmented at their carbon-carbon double bonds and new olefin molecules result by recombination of the fragments.\(^1\) For example, the reversible metathesis of 2-pentene to form 2-butene and 3-hexene is shown in eq 1.

\[
2 \text{CH}_3\text{CH}==\text{CHCH}_3 \xrightleftharpoons{\text{catalyst}} \text{CH}_3\text{CH}==\text{CHCH}_3 + \text{C}_2\text{H}_5\text{CH}==\text{CHCH}_3
\]  (1)

Metathesis chemistry requires the action of a catalyst. A wide variety of transition metal compounds may be used as the catalyst, but the most widely used, in order of importance, are tungsten (W), molybdenum (Mo), rhenium (Re) and ruthenium (Ru). Among these catalysts, the most widely used and also most convenient catalyst systems are based upon WCl\(_6\) as catalyst and an alkylmetal or a Lewis acid as the co-catalyst.

The olefin metathesis of esters of unsaturated fatty acids has been reported. In 1972, Boelhouwer and his co-workers succeeded in the olefin metathesis of methyl oleate, an ester of one of the main fatty acids present in soybean oil, and obtained the expected mixture of olefins by using the classical metathesis catalyst WCl\(_6/\text{Me}_4\text{Sn}\) (eq 2).\(^2\) The more highly unsaturated esters of linoleic acid and linolenic acid, the other two most abundant fatty acids in soybean oil, were found to be less reactive than the oleic acid esters towards the WCl\(_6/\text{Me}_4\text{Sn}\) catalyst, but at higher temperatures they were observed to react to give the expected multitude of products.\(^3\)
Kohashi and Foglia have also examined the co-metathesis reactions of methyl oleate with other unsaturated diesters by employing the same catalyst WCl₆/Me₄Sn. The conversion of equimolar amounts of methyl oleate and esters of the type MeO₂C(CH₃)ₙCH=CH(CH₂)ₙCO₂Me proceeded smoothly when n = 1 (esters of 3-hexenedioic acid). However, poor yields were observed for esters of 4-octenedioic acid (n = 2).

Schuchart investigated the co-metathesis of methyl oleate and ethylene. In the presence of 1% Re₂O₇/SiO₂•Al₂O₃ (24.3%) /B₂O₃ (6%), the principal products are 1-decene (35%) and methyl 9-decanoate (45%). The remaining 20% of the products are self-metathesis products 9-octadecene and dimethyl 9-octadecenedioate-1.18 (eq 3). The ethenolysis of methyl linoleate under the same conditions afforded 1-heptene (12%), 1.4-decadiene (17%), methyl 9-decanoate (30%), and methyl 9,12-tridecadienoate (22%) as the principal products. The remaining 19% of the products were self-metathesis and secondary ethenolysis products.
The WCl₅/Me₄Sn-catalyzed metathesis of soybean oil, which consists mostly of the triglycerides of oleic (23%), linoleic (51%) and linolenic acids (7%), afforded the expected low boiling, volatile products, but the cross-linked higher boiling, more viscous products, so called "stand oils", have not been closely examined, though their drying properties are more pronounced than the corresponding thermally-polymerized oils containing fewer carbon-carbon double bonds.³

Finkel'shtein et al. also examined the co-metathesis of synthetic and natural oils (soybean oil, sunflower oil and safflower oil).⁹ Employing a considerable excess of a symmetrical olefin leads to the complete suppression of inter- and intramolecular metathesis of the di- and polytriglycerides. The metathesis equilibrium is shifted to intermolecular metathesis of triglycerides and olefin to afford the resultant, new glycerides. It is also found that the order of the metathesis reactivity is linolenic > linolenic > oleic.

Olefin metathesis has also been employed in the synthesis of polymers. Thus, in the case of cyclic olefins, cleavage of the ring leads to the formation of a difunctional moiety, which effectively forms the building block for the polymer chain. This is called ring-opening metathesis polymerization (ROMP). The ROMP of norbornene is shown in eq 4.

\[ \begin{align*} \text{n} & \quad \text{catalyst} & \quad \text{n} \\
\end{align*} \]

Recently, acyclic dienes have been employed in metathesis polymerization by Wagener.⁷ As shown in eq 5, this process allows the molecular weight of the product to be controlled if the olefinic by-product (ethylene) is selectively removed during the reaction. This process is called acyclic diene metathesis (ADMET) polymerization.
The choice of catalyst has proven very important in ADMET polymerization. Wagener et al. have found that the classical metathesis catalyst utilizing Lewis acid components, such as WCl₆/EtAlCl₂, are not very effective in ADMET polymerization due to competing acid-catalyzed olefin addition and C=C bond migration. Nubel and co-workers have exploited a modified classical catalyst, WCl₆/SnMe₃/PrOAc, which appears capable of doing ADMET chemistry. However, this catalyst requires high reaction temperatures (80 °C) and long reaction times due to the low activity of the catalyst.

Wagener et al. have demonstrated in model compound studies that by employing a Lewis acid-free catalyst system, ADMET polymerization is quantitative; the competing olefin addition chemistry is completely eliminated. Thus, Schrock’s well-defined tungsten and molybdenum alkylidenes (1) and more recently Grubbs’ ruthenium alkylidene complex (2) have been successfully employed in ADMET polymerization. These Lewis acid-free catalysts show higher activities in ADMET polymerization than the classical metathesis catalysts and the reaction can be carried out at room temperature in

\[
\text{n H}_2\text{C} = \text{CH}-\text{R}-\text{CH}=\text{CH}_2 \xrightarrow{\text{catalyst}} \frac{\text{H}_2\text{C} = \text{CH}-\text{R}-\text{CH}=\text{H}}{\text{n}} + (\text{n}-1) \text{H}_2\text{C} = \text{CH}_2
\]
short reaction times. More importantly, these catalysts are tolerant of certain organic
functional groups, including ester, ether, ketone, carbonate, thioether, and aromatic amine
functionalities.\textsuperscript{12}

We envisioned that the ADMET process could be employed in the polymerization of
soybean oil. Since the ADMET process proceeds as a step polymerization, the ADMET
polymerization of soybean oil should be better controlled than the previously used, thermal
polymerization process.\textsuperscript{13} It was our hope that this process would convert soybean oil to
useful, new biodegradable materials.

\textbf{Results and Discussion}

\textbf{Evaluation of ADMET polymerization catalysts}

Since the catalyst is very important in ADMET polymerization, our initial work has
focused on an evaluation of the catalysts. Two catalysts, Mo-based catalyst 1 and Ru-
based catalyst 2 have been widely employed in ADMET or ring-opening polymerizations
and have proven very efficient.\textsuperscript{10,11} Thus, our evaluation was limited to these two
catalysts.

Two representative dienes, 1,9-decadiene (3) and 5-hexenyl 4-pentenoate (4), were
chosen as the monomers (eqs 6 and 7). The results of their polymerizations using catalysts
1 and 2 are summarized in Table 1. When diene 3 was allowed to react with catalyst 1,
rapid evolution of ethylene (violent bubbling) was observed. However, the polymerization
did not proceed completely even after 4 days and a liquid was obtained (entry 1). The \textsuperscript{1}H
NMR spectrum of the product showed two clearly separated peaks for the terminal olefinic
protons (δ = 4.97) and the newly formed internal olefinic protons (δ = 5.40). End group
analysis\textsuperscript{10b} based on the integration of these two types of olefinic protons indicated that the
number of the repeating unit (X_n) was 3 and the average molecular weight (M_n) was 358
(entry 1). On the other hand, when catalyst 2 was employed, the reaction started relatively slowly, since only a few bubbles were observed when catalyst 2 was mixed with 3. but the reaction proceeded more completely and solidified after 4 days. End group analysis indicated $X_n = 142$ and $M_n = 15620$ (entry 2).

\[
\text{Table 1. Evaluation of catalysts 1 and 2 in the polymerization of dienes 3 and 4.}^a
\]

<table>
<thead>
<tr>
<th>entry</th>
<th>diene</th>
<th>catalyst</th>
<th>product</th>
<th>$X_n^{b}$</th>
<th>$M_n^{b}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>1</td>
<td>liquid</td>
<td>3</td>
<td>358</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>2</td>
<td>solid</td>
<td>142</td>
<td>15620</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>1</td>
<td>oil</td>
<td>20</td>
<td>2840</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>2</td>
<td>very sticky oil</td>
<td>150</td>
<td>14200</td>
</tr>
</tbody>
</table>

$^a$ All reactions were run in the presence of 0.5 mol % catalyst under Ar for 4 days. $^b$ All $X_n$ and $M_n$ were determined by end group analysis from $^1$H NMR spectral analysis.
Similar results were observed for the reactions of diene 4 (eq 7). In the presence of catalyst 1, a sticky oil was obtained. According to end group analysis, $X_n$ was 20 and $M_n$ was 2840 (Table 1, entry 3). When catalyst 2 was used, the reaction afforded a very sticky oil, which had substantially higher $X_n$ (100) and $M_n$ (14200) values (entry 4).

These results indicate that catalyst 1 is more reactive than catalyst 2, but catalyst 2 affords higher molecular weight polymers. This can be explained by the extreme instability of catalyst 1. Catalyst 1 is very sensitive to moisture and oxygen. Trace impurities in the monomer will destroy the catalyst.\textsuperscript{9b} On the other hand, catalyst 2 is only mildly sensitive to oxygen and very stable to water, alcohols and most organic solvents.\textsuperscript{14} The good stability allows catalyst 2 to stay alive for a long time and afford polymer with higher $X_n$ and $M_n$. Therefore, catalyst 2 appears to be the better catalyst for ADMET polymerization. We have therefore employed this catalyst in the following experiments.

**Polymerization of ethylene glycol dioleate**

After the successful ADMET polymerization of terminal dienes 3 and 4, our attention turned towards the ADMET polymerization of the internal diene ethylene glycol dioleate (5). Dioleate 5 was prepared from oleic acid and ethylene glycol (eq 8).\textsuperscript{15}
The ADMET polymerization of dioleate 5 was conducted by employing 0.1 mol % catalyst 2 at 55 °C under vacuum for 24 h (eq 9).

\[
\begin{align*}
\text{CH}_3\text{(CH}_2\text{)}_7\text{CH}=&\text{CH}\text{(CH}_2\text{)}_7\text{CO}_2\text{CH}_2 \\
\text{CH}_3\text{(CH}_2\text{)}_7\text{CH}=&\text{CH}\text{(CH}_2\text{)}_7\text{CO}_2\text{CH}_2 & 0.1 \text{ mol % catalyst 2} & 55 \text{ °C, vacuum, 24 h} \\
\left[\text{CH}_3\text{(CH}_2\text{)}_7\text{CO}_2\text{CH}_2\right]_n + (n-1) \text{CH}_3\text{(CH}_2\text{)}_7\text{CH}=&\text{CH}\text{(CH}_2\text{)}_7\text{CH}_3 & 9\text{-octadecene}
\end{align*}
\]

After work-up, two fractions, a light brown oil (48 w/w %) and a white waxy solid (50 w/w %), were obtained. Each fraction was then further partitioned by flash chromatography. The composition of each fraction is shown in Figure 1.

It turned out that the major components of the first fraction (a light brown oil) are compound A, 9-octadecene (39 w/w %), which is the product expected to accompany formation of the polymer, and compound B, the \(E,E\)-isomer of the starting dioleate (42 w/w %). Only a trace amount of the intramolecular cyclization product, compound C (0.3 w/w %), was isolated from this fraction. This indicates that the reaction does not proceed to a significant extent by intramolecular cyclization, but does follow the anticipated ADMET process to produce oligomers. On the other hand, the second fraction (the white waxy solid) is mainly composed of dimer (22 w/w %), trimer (22 w/w %) and tetramer (14 w/w %). It is very interesting that even pure heptamer was isolated from this fraction.

The overall product composition of the ADMET polymerization of the dioleate was determined by combining the isolated masses of each component from both fractions. These combined masses were used to calculate an overall isolated percent yield for each component. Thus, 27% of the starting dioleate was converted to the \(E,E\)-isomer B. The
A = \text{CH}_3(\text{CH}_2)_{7}\text{CH=CH(CH}_2)_7\text{CH}_3

B = \text{E},\text{E-CH}_3(\text{CH}_2)_{7}\text{CH=CH(CH}_2)_7\text{C}_02\text{CH}_2\text{CH}_2\text{O}_2\text{C(CH}_2)_7\text{CH=CH(CH}_2)_7\text{CH}_3

C = \text{intramolecular cyclization product:}

\begin{align*}
\text{Oligomer: } & (\text{Z/E-CH}_3(\text{CH}_2)_{7}\text{CH=CH(CH}_2)_7\text{C}_02\text{CH}_2\text{CH}_2\text{O}_2\text{C(CH}_2)_7\text{CH=CH(CH}_2)_7\text{CH}_3

\text{Dimer: } & n = 2; \text{Trimer: } n = 3; \text{Tetramer: } n = 4; \text{Pentamer: } n = 5; \text{Hexamer: } n = 6; \text{Heptamer: } n = 7.

\text{Figure 1. Composition of the two fractions.}

remaining dioleate (73%) undergoes ADMET polymerization to afford the following components: dimer (18%), trimer (13%), tetramer (7%), pentamer (5%), hexamer (4%), heptamer (4%) and 9-octadecene (21%).

All of these isolated compounds have been fully characterized by $^1$H and $^{13}$C NMR spectroscopy. APCI (Atmospheric Pressure Chemical Ionization) MS and GPC. The $^1$H NMR spectra match the molecular structures of the assigned compounds. For example. Table 3 shows the integration ratios for the $^1$H NMR spectrum of the dimer. The experimental values are consistent with the theoretical ones.
Table 3. Integration ratios of the $^1$H NMR spectrum of the dimer.

<table>
<thead>
<tr>
<th>proton</th>
<th>$\text{CH}=$CH</th>
<th>$\text{O}_2\text{CCH}_2$</th>
<th>$\text{CH}_2\text{-CH}=$</th>
<th>$\text{O}_2\text{CCH}_2\text{CH}_2$</th>
<th>other $\text{CH}_2$</th>
<th>$\text{CH}_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>theoretical</td>
<td>1.00</td>
<td>1.00</td>
<td>1.50</td>
<td>1.00</td>
<td>7.00</td>
<td>0.75</td>
</tr>
<tr>
<td>experimental</td>
<td>1.00</td>
<td>1.01</td>
<td>1.52</td>
<td>0.98</td>
<td>7.03</td>
<td>0.69</td>
</tr>
</tbody>
</table>

The $Z/E$ configuration of these components can be determined by $^{13}$C NMR spectral analysis. The olefinic carbons of the starting dioleate ($Z,Z$-configuration) appear at 129.7 and 130.0 ppm. Component B shows two olefinic carbon peaks at 130.1 and 130.5 ppm. Considering that trans olefinic carbons generally have higher chemical shifts than the corresponding cis olefinic carbons, we have tentatively assigned the $E,E$-configuration to compound B. It has also been observed that the $^{13}$C NMR spectra of all of the oligomers formed in the reaction show both cis olefinic carbon peaks ($\delta < 130.0$ ppm) and trans olefinic carbon peaks ($\delta > 130.0$ ppm), where the latter peaks are much more intense than the former ones. This indicates that the carbon-carbon double bonds in these oligomers have both $Z$ and $E$ configurations, with the $E$ configuration predominating.

As shown in Table 4, the results from mass spectrometry (APCI) match the corresponding formula weights (F.W.). However, there are differences between the GPC results and the formula weights. Presumably, this is due to the difference in the hydrodynamic volume of the polyester samples and the polystyrene standard utilized.$^{10b}$ Similar discrepancies are observed in all of the GPC experiments with oligomers prepared from glycercyl trioleate and soybean oil to be discussed later. As shown in entry 1, the $M_n/F.W.$ ratio for the dioleate is 2.18 and the other ratios are close to this value. This suggests that the $M_n$ is approximately linear with F.W. and $M_n$ can be corrected by dividing by approximately a factor of 2.
Table 4. Results from MS (APCI) and GPC.

<table>
<thead>
<tr>
<th>oligomer</th>
<th>F.W.</th>
<th>MS (APCI)</th>
<th>GPC (M&lt;sub&gt;n&lt;/sub&gt;)</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;/F.W.</th>
</tr>
</thead>
<tbody>
<tr>
<td>dioleate</td>
<td>590</td>
<td>591 (MH)&lt;sup&gt;*&lt;/sup&gt;</td>
<td>1289</td>
<td>2.18</td>
</tr>
<tr>
<td>dimer</td>
<td>929</td>
<td>930 (MH)&lt;sup&gt;*&lt;/sup&gt;</td>
<td>1796</td>
<td>1.93</td>
</tr>
<tr>
<td>trimer</td>
<td>1267</td>
<td>1268 (MH)&lt;sup&gt;*&lt;/sup&gt;</td>
<td>2385</td>
<td>1.88</td>
</tr>
<tr>
<td>tetramer</td>
<td>1604</td>
<td>1605 (MH)&lt;sup&gt;*&lt;/sup&gt;</td>
<td>2996</td>
<td>1.86</td>
</tr>
<tr>
<td>pentamer</td>
<td>1945</td>
<td>1946 (MH)&lt;sup&gt;*&lt;/sup&gt;</td>
<td>3542</td>
<td>1.82</td>
</tr>
<tr>
<td>hexamer</td>
<td>2282</td>
<td>2282 (M)&lt;sup&gt;*&lt;/sup&gt;</td>
<td>4443</td>
<td>1.95</td>
</tr>
<tr>
<td>heptamer</td>
<td>2621</td>
<td>2622 (MH)&lt;sup&gt;*&lt;/sup&gt;</td>
<td>6551</td>
<td>2.50</td>
</tr>
</tbody>
</table>

The polymerization reaction has also been run under a variety of reaction conditions in an effort to improving the yield of solid product and minimize the amount of the catalyst used (Table 5). It has been shown that a vacuum is necessary for the reaction to produce good yields of solid product (compare entries 1 and 3). The smallest amount of catalyst

Table 5. Optimization of the reaction conditions.

<table>
<thead>
<tr>
<th>entry</th>
<th>cat. (mol %)</th>
<th>vac./Ar</th>
<th>time (h)</th>
<th>light brown oil</th>
<th>white waxy solid</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.1</td>
<td>vac.</td>
<td>24</td>
<td>48</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>0.1</td>
<td>vac.</td>
<td>48</td>
<td>47</td>
<td>49</td>
</tr>
<tr>
<td>3</td>
<td>0.1</td>
<td>Ar</td>
<td>24</td>
<td>64</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>0.05</td>
<td>vac.</td>
<td>28</td>
<td>59</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>0.2</td>
<td>vac</td>
<td>24</td>
<td>62</td>
<td>38</td>
</tr>
<tr>
<td>6</td>
<td>0.5</td>
<td>vac.</td>
<td>24</td>
<td>63</td>
<td>43</td>
</tr>
<tr>
<td>7</td>
<td>1.0</td>
<td>vac.</td>
<td>43</td>
<td>57</td>
<td>44</td>
</tr>
</tbody>
</table>
used in the reaction has been 0.05 mol % (entry 4) and the reaction still affords a fair yield of solid product (40%). However, when more catalyst is employed, the yields of solid product do not increase accordingly (entries 5-7) and the best yield is obtained when 0.1 mol % catalyst is used (entry 1).

**Polymerization of glyceryl trioleate and glyceryl trilinoleate**

Glyceryl trioleate was prepared from oleic acid and glycerol (eq 10).

\[
\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CO}_2\text{H} + \text{HO—HO—HO—} \xrightarrow{4-(\text{Dimethylamino})\text{pyridine}} \xrightarrow{\text{N,N-dicyclohexylcarbodiimide}} \text{CCl}_4
\]

\[
\begin{align*}
\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CO}_2^- & + \text{HO—}\text{HO—}\text{HO—} \\
\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CO}_2^- & \xrightarrow{4-(\text{Dimethylamino})\text{pyridine}} \xrightarrow{\text{N,N-dicyclohexylcarbodiimide}} \text{CCl}_4 \\
\text{glyceryl trioleate} & \quad 51\%
\end{align*}
\]

Polymerization of the trioleate has been examined by employing the best conditions developed for the polymerization of the dioleate (eq 11). The resulting crude product (a very sticky oil) was dissolved in CH$_2$Cl$_2$ and then poured into an excess of MeOH (work-up procedure A). Thus, two fractions, a MeOH/CH$_2$Cl$_2$ soluble fraction (32 w/w %) and a MeOH/CH$_2$Cl$_2$ insoluble fraction (67 w/w %), were isolated. The MeOH/CH$_2$Cl$_2$ insoluble fraction was further partitioned by flash chromatography and eight components were isolated (Table 6).
\[
\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CO}_2 \quad \text{n} \quad \text{O}_2\text{C}(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CH}_3
\]

0.1 mol % catalyst

55 °C, vacuum

24 h

\[
(\text{CH}(\text{CH}_2)_7\text{CO}_2) - \text{O}_2\text{C}(\text{CH}_2)_7\text{CH} + x \text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CH}_3
\]

Table 6. Composition of the MeOH/CH\(_2\)Cl\(_2\) insoluble fraction.

<table>
<thead>
<tr>
<th>entry</th>
<th>w/w %</th>
<th>(r)</th>
<th>(r')</th>
<th>n</th>
<th>structural assignment</th>
<th>comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>0.39</td>
<td>0.44</td>
<td>1</td>
<td>isomerized trioleate</td>
<td>yellow oil</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>0.70</td>
<td>0.66</td>
<td>2</td>
<td>dimer</td>
<td>white wax</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>0.85</td>
<td>0.80</td>
<td>3</td>
<td>trimer</td>
<td>white oil</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>0.99</td>
<td>0.89</td>
<td>4</td>
<td>tetramer</td>
<td>white, sticky oil</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>1.08</td>
<td>0.95</td>
<td>5</td>
<td>pentamer</td>
<td>white, sticky oil</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>1.17</td>
<td>1.00</td>
<td>6</td>
<td>monocyclic oligomer</td>
<td>white, very sticky oil</td>
</tr>
<tr>
<td>7</td>
<td>17</td>
<td>1.28</td>
<td>1.04</td>
<td>7</td>
<td>monocyclic oligomer</td>
<td>very sticky oil</td>
</tr>
<tr>
<td>8</td>
<td>31</td>
<td>1.43</td>
<td>1.06</td>
<td>8</td>
<td>monocyclic oligomer</td>
<td>white, very sticky oil</td>
</tr>
</tbody>
</table>

\(^a\)The theoretical value of \(r\) is calculated as \(4n/(3n+6)\), while \(n\) is the number of repeating units (eq 11).

The structural assignment of these components (Table 6, entries 1-8) is based on \(^1\)H NMR spectral data. The \(^1\)H NMR spectra of these components are similar to the starting trioleate (see the attached spectra in Appendix C. pages 193-203), only differing in the peak integrations. Analysis of the peak integration data provides information about the structure of these components. Our attention has focused on the ratio of the \(^1\)H NMR spectral peaks corresponding to OCH\(_2\)CHCH\(_2\)O over the terminal CH\(_3\) protons. This ratio is defined as
"r". If the trioleates just link with each other in a straight chain with no intramolecular cyclization, the value of x in eq 11 should be equal to (n-1). Then, the ratio r can be described as $4n/(9n-6(n-1))$, i.e. $4n/(3n+6)$. According to this equation, the theoretical values of r for the acyclic oligomers, from monomer to octamer are recorded in column 4 of Table 6 (Table 6, entries 1-8, n = 1-8). A comparison of the experimental values of r (Table 6, column 3) and the theoretical ones (Table 6, column 4) suggests that components 1 to 5 can be tentatively assigned as isomerized trioleate, dimer, trimer, tetramer and pentamer. The $^{13}$C NMR spectrum of component 1 shows new peaks for the olefinic carbons ($\delta = 130.2, 130.5$ ppm), which presumably correspond to the E-isomer and suggests that component 1 is simply the isomerized $E,E,E$- trioleate. The olefinic carbons in compounds 2-8 show intense peaks at $\delta = 130.2-130.6$ ppm. This indicates that the carbon-carbon double bonds in these compounds are predominately the E configuration. This phenomenon is consistent with our observations made during our study of the oligomers formed in the ADMET polymerization of the ethylene glycol dioleate.

Note that there is a significant discrepancy between the experimental and theoretical values of r for components 6-8 (Table 6, compare column 3 and 4 of entries 6-8). This suggests the possibility of intramolecular cyclization. If only one intramolecular cyclic ring is formed in the oligomer, the value of x in eq 11 is expected to be n; thus, r can be calculated as $4n/(9n-6n)$, i.e. 1.33. This indicates that all monocyclic oligomers have the same value of r, regardless of the number of repeating units (n) in the polymer or the size of the cyclic ring. Since the experimental values of r (Table 6, entries 6-8) are close to 1.33, we have tentatively assigned components 6-8 as monocyclic oligomers. For component 8, the experimental value of r is 1.43. This is even higher than 1.33 and indicates the possibility of bicyclic oligomers in component 8, since the r value of the bicyclic oligomers can be calculated as $4n/(3n-6)$, which is bigger than 1.33.
The GPC results from analysis of the starting trioleate and the monocyclic components 6-8 are summarized in Table 7. A discrepancy between the formula weight of the trioleate (884) and its $M_n$ (1172) is observed (entry 1) and the ratio of $M_n$ over F.W. is 1.32. In analogy to our previous results on the dioleate, which suggested that $M_n$ is approximately linear with F.W., we have assumed that this linear relationship also exists for the trioleate system. Thus, $M_n$ in Table 7 is corrected by a factor of 1.32. The corresponding numbers of repeating units can be approximately calculated from these corrected $M_n$. According to eq 11, the molecular weight of the monocyclic oligomers should be the mass of the reactant (884 x n) minus the mass of 9-octadecene (252 x n): so the number average molecular weight is 632 x n. Then, $n = M_n/(1.32 \times 632)$. The results are summarized in Table 7. The average number of repeating units of component 6 is calculated as 6 and this appears to be reasonable, since the previous component (component 5) has been assigned as a pentamer ($n = 5$). As expected, the average number of repeating units of component 7 is even higher than that of component 6 ($n \approx 10$, Table 7, entry 3). It is very interesting that component 8, which is the major oligomer formed in the reaction, has a high average repeating unit number. This significantly higher degree of polymerization of the trioleate ($n \approx 6, 10, 21$) than that of the dioleate ($n = 2-4$) suggests

<table>
<thead>
<tr>
<th>entry</th>
<th>component</th>
<th>$M_n$</th>
<th>$M_w$</th>
<th>PDI</th>
<th>$n^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>trioleate</td>
<td>1172</td>
<td>1518</td>
<td>1.29</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>5375</td>
<td>7448</td>
<td>1.38</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>8182</td>
<td>11478</td>
<td>1.40</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>17459</td>
<td>27963</td>
<td>1.60</td>
<td>21</td>
</tr>
</tbody>
</table>

$^a$ The value of $n$ is calculated as $n = M_n/(1.32 \times 632)$. 

Table 7. GPC results for the monocyclic oligomers and the approximate number of repeating units.
that there has been additional polymerization by cross-linking. This is to be expected, since the trioleate, which has three double bonds, may behave as a trifunctional monomer to produce dendrimers. In the ideal case, after m generations, n can be calculated as $n = 1 + 3^m$. Thus, a second generation dendrimer affords $n = 10$ and the third generation dendrimer will yield $n = 28$.

Other experiments also confirm the existence of cross-linking polymerization. The polymerization of the trioleate has been examined in the presence of 1.6 mol% of catalyst 2 for 24 h. A brown rubber was obtained in 87% yield. This rubbery material did not dissolve in organic solvents, such as CH₂Cl₂, chloroform, toluene or benzene. Under the same conditions, the polymerization of glyceryl trilinoleate also produced a brown rubber, which was insoluble in organic solvents. We suspect that these rubbery materials are highly crosslinked polymers.

In summary, our model system studies suggest that polymerization of the dioleate and trioleate follow the expected ADMET mechanism. Polymerization of dioleate afforded a series of oligomers, from dimer to heptamer, with dimer and trimer predominating. On the other hand, polymerization of the trioleate produced monocyclic oligomers with much higher molecular weights, due to possible cross-linking polymerization.

**Polymerization of Soybean oil.**

Encouraged by the success of our model system studies, the polymerization of soybean oil has been examined. New Horizons soybean oil produced by Pioneer Hi-Bred Inc. was employed in the following reactions. The results are summarized in Table 8.

Depending on the reaction conditions, two types of products, a sticky oil and a rubbery material, have been observed. Accordingly, two efficient workup procedures, procedures A and B, have been developed for these two types of materials. In procedure A, which is applicable to the sticky oil, the crude product is dissolved in CH₂Cl₂ and then
Table 8. Polymerization of soybean oil.

| entry | oil (ml) | cat. (mol %) | temp. (°C) | vac./Ar | time (h) | crude product | isolated product  \\
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>fraction A</td>
<td>fraction B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(r)</td>
<td>(r)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1.5</td>
<td>r.t.</td>
<td>vac.</td>
<td>120</td>
<td>85% brown rubber</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1.4</td>
<td>r.t.</td>
<td>vac.</td>
<td>192</td>
<td>86% brown, sticky rubber</td>
<td>30% (0.36)</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1.4</td>
<td>r.t.</td>
<td>vac.</td>
<td>240</td>
<td>87% brown rubber</td>
<td>24% (0.29)</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>1.4</td>
<td>r.t.</td>
<td>Ar</td>
<td>240</td>
<td>99% dark brown oil</td>
<td>40% (0.29)</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>1.4</td>
<td></td>
<td>vac.</td>
<td>15</td>
<td>86% brown rubber</td>
<td>23% (0.31)</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>1.5</td>
<td></td>
<td>Ar</td>
<td>24</td>
<td>99% deep brown oil</td>
<td>37% (0.29)</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>0.2</td>
<td>r.t.</td>
<td>vac.</td>
<td>240</td>
<td>89% light brown oil</td>
<td>17% (0.21)</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>0.2</td>
<td>r.t.</td>
<td>Ar</td>
<td>240</td>
<td>100% brown oil</td>
<td>38% (0.27)</td>
</tr>
</tbody>
</table>
Table 8. (continued)

<table>
<thead>
<tr>
<th>entry</th>
<th>oil (ml)</th>
<th>cat. (mol %)</th>
<th>temp. (°C)</th>
<th>vac./Ar</th>
<th>time (h)</th>
<th>crude product</th>
<th>isolated product&lt;sup&gt;a&lt;/sup&gt;</th>
<th>fraction A</th>
<th>fraction B</th>
<th>fraction C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>fraction A (r)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>0.2</td>
<td>55</td>
<td>vac.</td>
<td>63</td>
<td>82% brown rubber</td>
<td>18% (0.30)</td>
<td>30% (1.10)</td>
<td>34%</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>0.2</td>
<td>55</td>
<td>Ar</td>
<td>62</td>
<td>99% brown oil</td>
<td>43% (0.28)</td>
<td>55% (1.05)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>0.1</td>
<td>55</td>
<td>vac.</td>
<td>192</td>
<td>81% brown rubber</td>
<td>24% (0.47)</td>
<td>31% (1.10)</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>2</td>
<td>0.1</td>
<td>55</td>
<td>vac.</td>
<td>24</td>
<td>90% brown oil</td>
<td>23% (0.31)</td>
<td>67% (1.19)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>2</td>
<td>0.1</td>
<td>55</td>
<td>Ar</td>
<td>24</td>
<td>98% brown oil</td>
<td>41% (0.33)</td>
<td>57% (0.85)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>2</td>
<td>0.01</td>
<td>55</td>
<td>vac.</td>
<td>168</td>
<td>100% light brown oil</td>
<td>100% (0.56)</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>2</td>
<td>0</td>
<td>55</td>
<td>vac.</td>
<td>212</td>
<td>99% brown oil</td>
<td>99% (0.56)</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> See the experimental section for the work-up procedure.
poured into an excess of MeOH. The MeOH solution and the residual material are collected as fraction A and fraction B, respectively. If the crude product is a rubbery material, procedure B is utilized for the work-up. Thus, the crude product is first worked up utilizing procedure A. The MeOH/CH₂Cl₂ soluble fraction is recorded as fraction A and the residual rubbery material is further partitioned by Soxhlet extraction. The CH₂Cl₂ solution is collected as fraction B and the remaining rubbery material is collected as fraction C. A "blank" work-up experiment in which soybean oil was processed using procedure A has shown that soybean oil is quantitatively recovered in fraction A.

As proven in our model system studies, ¹H NMR spectroscopy can provide valuable information about the structural makeup of the oligomers. Again, r, the ratio of the OCH₂CHCH₃O protons over the terminal CH₃ protons, has served as an important parameter in our understanding of the structure of the oligomers. The ¹H NMR spectra of soybean oil, and the fractions A and B obtained from the polymerization of soybean oil (see the attached spectra in Appendix C, pages 204-206) have all the same peaks, but the integrations are different. For the original soybean oil, r is equal to 0.56. The value of r for fraction A ranged from 0.21 to 0.47 depending on the reaction conditions. This is lower than that of soybean oil and consistent with our expectation that fraction A contains unreacted or isomerized soybean oil and long chain alkene by-product.

In fact, the GC-MS results obtained from the analysis of fraction A in Table 8, entry 4 showed peaks with masses of 102, 168, 208, 250, 290, and 330. All of these masses can be assigned to the alkenes expected from the ADMET reaction of the triglycerides in soybean oil. For example, mass 208 presumably comes from the alkene CH₃(CH₂)₇CH=CHCH₂CH=CHCH₂CH₃. The mass of CH₃CH₂CH=CHCH₂CH=CH-CH₂CH=CHCH₂CH=CH(OCH₂)CH₃ is 220. This product is expected to be formed by metathesis of the soybean oil and the ethyl vinyl ether used to quench the reaction. The
mass 250 can be assigned as CH\,(\text{CH}_2)\text{XH} = \text{CHCH}_2\text{CH} = \text{CH(\text{CH}_2)}\text{CH}.

GC-MS analysis of the fraction A from Table 8, entry 11 showed only three peaks with masses of 220, 250, 290. The other low molecular weight alkenes expected to be formed may have been removed by vacuum. The value of \( r \) for fraction B was found to be higher than that of soybean oil. This indicates the formation of oligomers. On the other hand, the rubbery materials of fraction C are presumably highly crosslinked polymers.

In the early stages of our investigation, a relatively high amount of catalyst 2 (1.5\%) was employed and the reaction afforded a brown rubber, which did not dissolve in any common organic solvent (Table 8, entry 1). Soybean oil purified by pretreatment with CaH\(_2\), MgSO\(_4\), or Ac\(_2\)O gave the same result as the original soybean oil. Thus, soybean oil taken directly from the bottle was used in the following reactions without any further purification.

The reactions proceeded very slowly at room temperature and long reaction times (5-10 days) were required (entries 1-4). The reaction time can be reduced substantially by increasing the temperature to 55 °C (Table 8, entry 5). The effect of vacuum was also examined. Under vacuum, the reaction afforded an insoluble rubber (entries 1, 3, and 5), but no rubbery material was obtained under Ar (Table 8, entry 4).

Less catalyst has also been employed. When 0.2 mol % catalyst 2 was employed, the reaction at room temperature afforded a brown oil after 240 h either under vacuum or Ar (entries 7 and 8). When the reaction was run with 0.2 mol % catalyst 2 at 55 °C, a rubbery material was obtained under vacuum (entry 9), but a brown oil was obtained under Ar (entry 10). A comparison of entries 3 and 7 indicates that a high amount of catalyst favors the formation of rubbery materials.

In the presence of 0.1 mol % catalyst under vacuum, a rubbery material was obtained after 192 h (entry 11). However, if the reaction was stopped earlier (24 h), a
brown oil was obtained in 90% yield (entry 12). The analogous reaction under Ar afforded a similar oily product (entry 13), but the yield of fraction B is not as good as that obtained when the reaction was run under vacuum (entry 12). The reaction with 0.01 mol % catalyst failed (entry 14). In entry 15, without any catalyst, soybean oil was quantitatively recovered in fraction A after the reaction was run under vacuum at 55 °C for 212 h. This indicates that no thermal polymerization occurred at 55 °C and no oil is lost due to the vacuum.

In summary, as observed in the ADMET polymerization of the dioleates, 0.1 mol % catalyst appears to give the best results. Under these conditions, the reaction affords either a rubbery material at long reaction times (entry 11) or a sticky oil at short reaction times (entry 12).

Copolymerization of soybean oil

Di-(4-pentenyl) 1,4-benzenedicarboxylate (6) was prepared according to a literature procedure. The polymerization of 6 was achieved using 0.5 mol % of catalyst 2. End group analysis indicated that $M_n = 3718$ and $X_n = 13$ (eq 12).

![Chemical Structure](image)

(12)

The copolymerization of soybean oil and diester 6 was investigated. In the presence of 0.5 mol % catalyst 2, a 50:50 (w/w) mixture of soybean oil and diester 6 produced a copolymer with 41% weight recovery. $^1$H NMR spectral data indicated that the molar ratio of diester 6 to soybean oil in the copolymer was 4.37, which was slightly higher than that in the reactant mixture (3.09). This slight difference may be due to a difference in the relative reactivities of diester 6 and soybean oil. As a terminal diene, diester 6 should be more reactive in ADMET polymerization than soybean oil, which
contains only internal carbon-carbon double bonds. Similar results have also been observed in the copolymerization of soybean oil and norbornene. This latter reaction is currently being studied further by other members of the Larock research group.

**Conclusion**

Our experiments on the ADMET polymerization of 1,9-decadiene and (5-hexenyl) 4-pentenoate have suggested that Grubbs’ ruthenium catalyst 2 is more efficient than Schrock’s molybdenum catalyst 1. In the presence of 0.1 mol % of catalyst 2, the ADMET polymerization of ethylene glycol dioleate afforded isomerized, E,E-dioleate and a series of oligomers, from dimer to heptamer. This is the first example of an internal diene participating in ADMET polymerization. Under the same conditions, glycercyl trioleate underwent ADMET polymerization to produce dimer, trimer, tetramer, pentamer and monocyclic oligomers, with the high molecular weight monocyclic oligomers predominating. We have also succeeded in the ADMET polymerization of soybean oil. A variety of materials, from sticky oils to rubbers, have been prepared from soybean oil. These materials are very likely to be biodegradable.

**Experimental Section**

**General.** All $^1$H and $^{13}$C NMR spectra were recorded at 300 and 75.5 MHz respectively. Gel permeation chromatography (GPC) analyses were carried out with the use of a Waters gel permeation system (410 refractive index detector) coupled with a Wyatt miniDawn. The chromatography system was equipped with three ultrastyragel columns (Waters HR 1.4 and 5). The molecular weights were calculated by calibration with polystyrene standards. THF was utilized as the solvent, and the flow rate was 1.0 ml/min., with the system equilibrated at 40 °C.
GC-MS spectrometry experiments were performed using a Finnigan Magnum Ion Trap Detector. The MS system was configured in the electron impact ionization mode with the automatic gain control feature turned on. DB5-ms was used in the experiments. MS (APCI) experiments were performed on a Finnigan TSQ 700 Mass Spectrometer equipped with a Finnigan APCI ion source.

Thin-layer chromatography (TLC) was performed using commercially prepared 60 mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm). or basic KMnO₄ solution [3 g KMnO₄ + 20 g K₂CO₃, + 5 mL NaOH (5%) + 300 mL H₂O].

**Reagents.** All reagents were used directly as obtained commercially unless otherwise noted. Ethylene glycol and glycerol were purchased from Fisher Scientific. 1,9-Decadiene, ethyl vinyl ether, 2,6-di-tert-butyl-4-methylphenol (BHT), N,N-dicyclohexylcarbodiimide, 4-(dimethylamino)pyridine and oleic acid were obtained from Aldrich Chemical Co., Inc. Catalyst 1 and 2 were provided by Professor K. B. Wagener (Department of Chemistry and Center for Macromolecular Science and Engineering at the University of Florida). Catalyst 2 was also purchased from Strem Chemicals, Inc. (5-Hexenyl) 4-pentenoate and di-(5-pentenyl) 1,4-benzenedicarboxylate were prepared according to previous literature procedures.¹⁰

**Ethylene glycol dioleate (5).** Ethylene glycol dioleate was prepared according to a literature procedure.¹⁵ Ethylene glycol (1.097 g, 17.7 mmol) was added to a solution of oleic acid (10 g, 35.4 mmol) in 50 ml of CCl₄ at 0 °C. This was followed by the addition of 4-(dimethylamino)pyridine (4.32 g, 35.4 mmol). Most of these components dissolved after stirring for 30 min. A solution of N,N-dicyclohexylcarbodiimide (7.31 g, 35.4 mmol) in dry CCl₄ was added to the mixture, which was then allowed to stir at room temperature for 5 h. The resulting mixture was filtered and the precipitate was washed with
Evaporation of the filtrate under reduced pressure gave the crude product, which was purified by flash chromatography (20:1 hexanes/EtOAc) to afford a colorless liquid (7.13 g, 12.1 mmol, 68%): $^1$H NMR (CDCl$_3$) $\delta$ 0.87 (t, $J = 6.2$ Hz, 6 H), 1.27 (m, 40 H), 1.61 (m, 4 H), 2.00 (m, 8 H), 2.31 (t, $J = 7.5$ Hz, 4 H), 4.26 (s, 4 H), 5.24-5.36 (m, 4 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.1, 22.7, 24.9, 27.1, 27.2, 29.1, 29.13, 29.2, 29.3, 29.6, 29.7, 29.8, 31.9, 34.1, 62.0, 129.7, 130.0, 173.5 (one sp$^3$ carbon missing due to overlap); IR (CDCl$_3$) 3002, 2952, 1742, 1456 cm$^{-1}$; MS (APCI) $m/\ell$ 591 (MH)$^+$. 

**Glyceryl trioleate.** Glycerol trioleate was prepared according to a literature procedure.$^{15}$ Glycerol (0.429 g, 4.66 mmol) was added to a solution of oleic acid (5.0 g, 17.7 mmol) in 25 ml of CCl$_4$ at 0 °C. This was followed by the addition of 4-(dimethylamino)pyridine (2.162 g, 17.7 mmol). Most of these components dissolved after stirring for 30 min. A solution of N,N-dicyclohexylcarbodiimide (3.652 g, 17.7 mmol) in 30 ml of dry CCl$_4$ was added to the mixture, which was then allowed to stir at room temperature for 6 h. The resulting mixture was filtered and the precipitate was washed with CCl$_4$. Evaporation of the filtrate under reduced pressure gave the crude product, which was purified by flash chromatography (20:1 hexanes/EtOAc) to afford a colorless liquid (2.10 g, 2.37 mmol, 51%): $^1$H NMR (CDCl$_3$) $\delta$ 0.87 (t, $J = 6.6$ Hz, 9 H), 1.28 (m, 60 H), 1.60 (m, 6 H), 1.99 (m, 12 H), 2.30 (dt, $J = 1.5$, 6.0 Hz, 6 H), 4.13 (dd, $J = 6.0$, 12.0 Hz, 2 H), 4.29 (dd, $J = 6.0$, 12 Hz, 2 H), 5.24-5.39 (m, 7 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.1, 22.7, 24.8, 24.9, 27.1, 27.2, 29.0, 29.10, 29.13, 29.2, 29.3, 29.5, 29.7, 29.8, 31.9, 34.1, 34.2, 62.1, 68.9, 129.6, 129.7, 130.0, 172.8, 173.3 (14 sp$^3$ carbons missing due to overlap); IR (CDCl$_3$) 3002, 2924, 1744, 1456 cm$^{-1}$; MS (APCI) $m/\ell$ 886 (MH)$^+$. 

**ADMET polymerization of ethylene glycol dioleate.** In a nitrogen-filled dry box, catalyst 2 (2.0 mg, 2.43 μmol) was weighed into a Schlenk tube with a magnetic stir bar. After being capped with a stopcock, the flask was removed from the dry box and
attached to a manifold. Another Schlenk flask loaded with ethylene glycol dioleate was also connected to the manifold. The manifold was evacuated and filled with argon three times. The two Schlenk flasks were then opened to the manifold. Under a steady flow of argon, ethylene glycol dioleate (1.5 ml, 1.39 g, 2.36 mmol) was transferred to the flask charged with the catalyst 2. The flask was then switched to the vacuum line and the reaction mixture was slowly warmed to 55 °C for 24 h while stirring. The flask was removed from the bath and allowed to cool. Then, CH₂Cl₂ (10 ml), ethyl vinyl ether (0.1 ml) and BHT (15 mg) were added to the flask. After 12 h of stirring, an additional 20 ml of CH₂Cl₂ was added to the solution, and the resulting solution was poured into 200 ml of rapidly stirring methanol at 0 °C. The white precipitate formed was then separated from the solvents by centrifugation, followed by decanting of the solvents, and then dried by pumping overnight. This procedure yielded a white solid (0.69 g, 50% weight recovery): mp 49-53 °C. The solvent portions were collected, concentrated and dried by pumping overnight, affording a light brown oil (0.66 g, 48% weight recovery). A portion of the white solid (0.2 g) was further partitioned by flash chromatography, yielding eight fractions (Figure 1). The light brown oil was also processed by flash chromatography, affording six fractions (Figure 1). The following are the spectral data for these fractions:

(Z) and (E)-9-Octadecene (Figure 1, A). ¹H NMR (CDCl₃) δ 0.89 (t, J = 6.9 Hz, 6 H), 1.20-1.33 (m, 24 H), 1.94-1.98 (m, 4 H), 5.35-5.41 (m, 2 H); ¹³C NMR (CDCl₃) δ 14.2, 22.8, 27.3, 29.2, 29.4, 29.6, 29.7, 29.8, 32.0, 32.7, 129.9, 130.4; IR (CDCl₃) 2952, 2849, 1463 cm⁻¹; HRMS m/z 252.2815 (calcd for C₁₈H₃₆, 252.2817).

E,E-Ethylene glycol dioleate (Figure 1, B). ¹H NMR (CDCl₃) δ 0.87 (t, J = 6.3 Hz, 6 H), 1.27 (m, 40 H), 1.59-1.64 (m, 4 H), 1.90-1.98 (m, 8 H), 2.32 (t, J = 7.5 Hz, 4 H), 4.26 (s, 4 H), 5.24-5.36 (m, 4 H); ¹³C NMR (CDCl₃) δ 14.2, 22.7, 24.9, 29.1.
29.12, 29.2, 29.3, 29.5, 29.6, 29.7, 31.9, 32.6, 34.1, 62.0, 130.1, 130.5, 173.6 (one sp\(^3\) carbon missing due to overlap); IR (CDCl\(_3\)) 3002, 2845, 1734, 1462 cm\(^{-1}\).

**Compound C** (Figure 1). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.20-1.40 (m, 20 H), 1.59-1.64 (m, 4 H), 1.90-2.10 (m, 4 H), 2.32 (t, \(J = 7.5\) Hz, 4 H), 4.30 (s, 4 H), 5.30-5.40 (m, 2 H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 24.7, 27.8, 28.7, 28.8, 28.9, 31.9, 34.3, 62.0, 130.8, 173.6; MS (APCI) \(m/z\) 339 (MH\(^+\)).

**Dimer** (Figure 1). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 0.87 (t, \(J = 6.3\) Hz, 6 H), 1.20-1.40 (m, 56 H), 1.59-1.64 (m, 8 H), 1.90-1.98 (m, 12 H), 2.31 (t, \(J = 7.5\) Hz, 8 H), 4.26 (s, 8 H), 5.24-5.42 (m, 6 H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 14.2, 22.7, 24.9, 27.2, 27.3, 29.0, 29.04, 29.1, 29.17, 29.2, 29.4, 29.5, 29.6, 29.7, 29.7, 29.7, 29.8, 31.9, 32.6, 34.1, 62.0, 129.7, 129.9, 130.1, 130.2, 130.3, 130.5, 173.6 (two sp\(^3\) carbons missing due to overlap); IR (CDCl\(_3\)) 3052, 2952, 1739, 1461 cm\(^{-1}\); MS (APCI) \(m/z\) 930 (MH\(^+\)).

**Trimer** (Figure 1). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 0.87 (t, \(J = 6.3\) Hz, 6 H), 1.20-1.40 (m, 72 H), 1.56-1.64 (m, 12 H), 1.90-2.01 (m, 16 H), 2.31 (t, \(J = 7.5\) Hz, 12 H), 4.26 (s, 12 H), 5.24-5.42 (m, 8 H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 14.1, 22.7, 24.9, 27.1, 27.2, 27.3, 28.9, 29.0, 29.1, 29.15, 29.2, 29.3, 29.5, 29.55, 29.6, 29.72, 29.8, 31.9, 32.5, 32.6, 34.1, 62.0, 129.7, 129.8, 130.0, 130.2, 130.3, 130.5, 173.6; IR (CDCl\(_3\)) 3052, 2920, 1739, 1462 cm\(^{-1}\); MS (APCI) \(m/z\) 1268 (MH\(^+\)).

**Tetramer** (Figure 1). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 0.87 (t, \(J = 6.3\) Hz, 6 H), 1.20-1.40 (m, 88 H), 1.56-1.64 (m, 16 H), 1.90-2.10 (m, 20 H), 2.31 (t, \(J = 7.5\) Hz, 16 H), 4.26 (s, 16 H), 5.24-5.42 (m, 10 H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 12.4, 14.1, 22.7, 24.9, 27.1, 27.2, 27.3, 28.9, 29.0, 29.1, 29.16, 29.2, 29.3, 29.5, 29.55, 29.6, 29.72, 29.8, 31.9, 32.5, 32.6, 34.1, 62.0, 129.7, 129.8, 130.0, 130.2, 130.3, 130.5, 173.6; IR (CDCl\(_3\)) 3052, 2920, 1738, 1461 cm\(^{-1}\); MS (APCI) \(m/z\) 1605 (M\(^+\)).
**Pentamer** (Figure 1). $^1$H NMR (CDCl$_3$) $\delta$ 0.87 (t. $J = 6.3$ Hz. 6 H), 1.20-1.40 (m. 104 H), 1.56-1.64 (m. 20 H), 1.90-2.10 (m. 24 H), 2.31 (t. $J = 7.5$ Hz. 20 H), 4.26 (s. 20 H), 5.24-5.42 (m. 12 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.2, 22.7, 24.9, 27.1, 27.2, 29.0, 29.1, 29.19, 29.2, 29.4, 29.5, 29.6, 29.6, 29.7, 29.75, 29.8, 31.9, 32.6, 34.1, 62.0, 129.8, 129.9, 130.0, 130.2, 130.3, 130.5, 173.6; IR (CDCl$_3$) 3051, 2921, 1738, 1462 cm$^{-1}$; MS (APCI) $m/z$ 1946 (MH)$^+$.  

**Hexamer** (Figure 1). $^1$H NMR (CDCl$_3$) $\delta$ 0.87 (t. $J = 6.3$ Hz. 6 H), 1.20-1.40 (m. 120 H), 1.56-1.64 (m. 24 H), 1.90-2.10 (m. 28 H), 2.31 (t. $J = 7.5$ Hz. 24 H), 4.26 (s. 24 H), 5.24-5.42 (m. 14 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.2, 22.8, 24.9, 27.2, 29.1, 29.16, 29.2, 29.3, 29.39, 29.4, 29.6, 29.7, 29.8, 32.0, 32.6, 32.7, 34.2, 62.0, 129.9, 130.2, 130.3, 130.6, 173.6; IR (CDCl$_3$) 3052, 2922, 1738. 1469 cm$^{-1}$; MS (APCI) $m/z$ 2282 (M)$^+$.  

**Heptamer** (Figure 1). $^1$H NMR (CDCl$_3$) $\delta$ 0.87 (t. $J = 6.3$ Hz. 6 H), 1.20-1.40 (m. 136 H), 1.56-1.64 (m. 28 H), 1.90-2.10 (m. 32 H), 2.31 (t. $J = 7.5$ Hz. 28 H), 4.26 (s. 28 H), 5.24-5.42 (m. 16 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.2, 22.7, 24.9, 29.0, 29.1, 29.18, 29.2, 29.3, 29.4, 29.51, 29.6, 29.71, 29.8, 31.9, 32.6, 32.7, 34.1, 62.0, 129.9, 130.2, 130.3, 130.5, 173.6; IR (CDCl$_3$) 3052, 2921, 1737. 1461 cm$^{-1}$; MS (APCI) $m/z$ 2622 (MH)$^+$.  

**ADMET polymerization of glyceryl trioleate or soybean oil.** In a nitrogen-filled dry box, catalyst 2 (2.0 mg, 2.43 μmol) was weighed into a Schlenk tube containing a magnetic stir bar. After being capped with a stopcock, the flask was removed from the dry box and attached to a manifold. Another Schlenk flask containing soybean oil was also connected to the manifold and the mixture degassed by three freeze-thaw cycles. The manifold was evacuated and filled with argon three times. The two Schlenk flasks were then opened to the manifold. Under a steady flow of argon, soybean oil (2 ml, 1.89
g. 2.14 mmol, assuming that the average molecular weight of soybean oil is 884) was transferred to the flask charged with the catalyst 2. The flask was then switched to the vacuum line and the reaction mixture was slowly warmed to 55 °C for the specified period of time while stirring. After that, the flask was then removed from the bath and allowed to cool. If the resulting polymer was a brown oil, procedure A was used to work up the reaction mixture. Procedure B was employed when the resulting product was a rubber.

**Procedure A:** To the reactant flask, CH₂Cl₂ (20 ml), ethyl vinyl ether (0.2 ml) and BHT (30 mg) are added. After 12 h of stirring, an additional 20 ml of CH₂Cl₂ is added to the solution, and the resulting solution is poured into 200 ml of rapidly stirring MeOH at 0 °C. The stirring is continued until the product appeared free of color. Then, the solvent is decanted off and the remaining solvent is evacuated. The residual material is then collected, dried by pumping overnight and recorded as MeOH/CH₂Cl₂ insoluble fraction B (Table 8). The MeOH solution is also concentrated, dried, and recorded as MeOH/CH₂Cl₂ soluble fraction A (Table 8).

**Procedure B:** The resulting rubber material is first processed utilizing procedure A. The soluble fraction is recorded as fraction A (Table 8) and the residual rubber is further partitioned by Soxhlet extraction using CH₂Cl₂ as the solvent. The CH₂Cl₂ solution was collected, dried and recorded as fraction B (Table 8). The remaining rubber is recorded as fraction C (Table 8).

The fraction B obtained from ADMET polymerization of glyceryl trioleate was further partitioned by flash chromatography and eight components were isolated. The following are the spectra data for these components:

**Component 1** (Table 6, entry 1). ¹H NMR (CDCl₃) δ 0.87 (m, 9 H), 1.20-1.42 (m, 60 H), 1.50-1.65 (m, 6 H), 1.90-2.10 (m, 12 H), 2.30 (dt, J = 1.5, 7.2 Hz, 6 H), 4.13 (dd, J = 6.0, 12.0 Hz, 2 H), 4.29 (dd, J = 6.0, 12.0 Hz, 2 H), 5.24-5.39 (m, 7 H):
$^{13}$C NMR (CDCl$_3$) $\delta$ 14.1, 22.7, 24.8, 24.9, 27.2, 29.0, 29.1, 29.13, 29.2, 29.25, 29.3, 29.5, 29.36, 29.6, 29.63, 29.7, 29.75, 29.8, 31.9, 32.6, 32.7, 34.1, 34.2, 62.1, 68.9, 129.7, 130.1, 130.2, 130.22, 130.5, 172.9, 173.3; IR (CDCl$_3$) 3002, 2921, 1744, 1461 cm$^{-1}$; MS (APCI) $m/z$ 886 (MH$^+$).

**Component 2** (Table 6, entry 2). $^1$H NMR (CDCl$_3$) $\delta$ 0.80-0.90 (m, 12 H), 1.20-1.42 (m, 96 H), 1.50-1.65 (m, 12 H), 1.90-2.10 (m, 20 H), 2.30 (dt, $J$ = 1.5, 7.5 Hz, 12 H), 4.13 (dd, $J$ = 6.0, 12.0 Hz, 4 H), 4.29 (dd, $J$ = 6.0, 12.0 Hz, 4 H). $^1$C NMR (CDCl$_3$) $\delta$ 14.1, 22.7, 24.8, 24.9, 29.0, 29.1, 29.12, 29.16, 29.18, 29.23, 29.3, 29.4, 29.5, 29.6, 29.62, 29.7, 29.75, 29.8, 31.9, 32.6, 32.7, 34.1, 34.2, 62.1, 68.9, 129.6, 129.7, 129.8, 130.1, 130.2, 130.22, 130.5, 172.8, 173.3; IR (CDCl$_3$) 3001, 2922, 1744 cm$^{-1}$.

**Component 3** (Table 6, entry 3). $^1$H NMR (CDCl$_3$) $\delta$ 0.80-0.90 (m, 15 H), 1.20-1.42 (m, 132 H), 1.50-1.65 (m, 18 H), 1.90-2.10 (m, 28 H), 2.30 (dt, $J$ = 1.5, 7.5 Hz, 18 H), 4.13 (dd, $J$ = 6.0, 12.0 Hz, 6 H), 4.29 (dd, $J$ = 6.0, 12.0 Hz, 6 H). $^1$C NMR (CDCl$_3$) $\delta$ 14.1, 22.7, 24.8, 24.9, 27.2, 27.3, 29.0, 29.1, 29.13, 29.2, 29.23, 29.3, 29.5, 29.6, 29.63, 29.66, 29.7, 29.75, 29.8, 31.9, 32.6, 32.7, 34.1, 34.2, 62.1, 68.9, 129.7, 129.8, 130.1, 130.2, 130.22, 130.5, 172.9, 173.3; IR (CDCl$_3$) 3002, 2922, 1744, 1461 cm$^{-1}$.

**Component 4** (Table 6, entry 4). $^1$H NMR (CDCl$_3$) $\delta$ 0.80-0.90 (m, 18 H), 1.20-1.42 (m, 168 H), 1.50-1.65 (m, 24 H), 1.90-2.10 (m, 36 H), 2.30 (dt, $J$ = 1.5, 7.5 Hz, 24 H), 4.13 (dd, $J$ = 6.0, 12.0 Hz, 8 H), 4.29 (dd, $J$ = 6.0, 12.0 Hz, 8 H). $^1$C NMR (CDCl$_3$) $\delta$ 14.1, 22.7, 24.8, 24.9, 27.2, 27.3, 29.0, 29.1, 29.12, 29.2, 29.24, 29.3, 29.5, 29.6, 29.63, 29.66, 29.7, 29.75, 29.8, 31.9, 32.6, 32.7, 34.1, 34.2, 62.1, 68.9, 129.8, 130.1, 130.2, 130.22, 130.3, 130.5, 172.9, 173.3. IR (CDCl$_3$) 3002, 2922, 1744, 1447 cm$^{-1}$. 

Component 5 (Table 6, entry 5). \( ^1H \text{NMR (CDCl}_3 \rangle \delta 0.80-0.90 \text{ m, 21 H).} \\
1.20-1.42 \text{ (m, 204 H), 1.50-1.65 \text{ (m, 30 H), 1.90-2.10 \text{ (m, 44 H), 2.30 \text{ (dt, J = 1.5. 7.5 Hz, 30 H). 4.13 \text{ (dd, J = 6.0, 12.0 Hz, 10 H). 4.29 \text{ (dd, J = 6.0, 12.0 Hz, 10 H). 5.24-5.39 \text{ (m, 27 H);}}}} \\
{^13C \text{NMR (CDCl}_3 \rangle \delta 14.2, 22.8, 24.9, 24.9, 27.2, 27.3, 29.0, 29.1, 29.15, 29.17, 29.2, 29.22, 29.26, 29.4, 29.5, 29.6, 29.66, 29.7, 29.72, 29.8, 31.9, 32.6, 32.7, 34.1, 34.2, 62.1, 68.9, 129.8, 130.1, 130.2, 130.4, 130.6, 172.9, 173.3; IR (CDCl}_3 \rangle 3002, 2949, 1739 \text{ cm}^{-1}.} \\
Component 6 (Table 6, entry 6). \( ^1H \text{NMR (CDCl}_3 \rangle \delta 0.80-0.90 \text{ (m, 3 H), 1.20-1.42 \text{ (m, 36 H), 1.50-1.65 \text{ (m, 6 H), 1.90-2.10 \text{ (m, 8 H), 2.30 \text{ (dt, J = 1.5, 7.5 Hz, 6 H). 4.13 \text{ (dd, J = 6.0, 12.0 Hz, 2 H), 4.29 \text{ (dd, J = 6.0, 12.0 Hz, 2 H) 5.24-5.39 \text{ (m, 5 H);}}}} \\
{^13C \text{NMR (CDCl}_3 \rangle \delta 14.1, 22.7, 24.8, 24.9, 27.2, 27.3, 29.0, 29.1, 29.14, 29.2, 29.23, 29.3, 29.5, 29.6, 29.67, 29.7, 29.75, 29.8, 31.9, 32.6, 32.7, 34.1, 34.2, 62.1, 68.9, 129.7, 129.8, 130.1, 130.2, 130.23, 130.5, 172.9, 173.3; IR (CDCl}_3 \rangle 2952, 1735, 1462 \text{ cm}^{-1}.} \\
Component 7 (Table 6, entry 7). \( ^1H \text{NMR (CDCl}_3 \rangle \delta 0.80-0.90 \text{ (m, 3 H), 1.19-1.42 \text{ (m, 36 H), 1.50-1.65 \text{ (m, 6 H), 1.90-2.10 \text{ (m, 8 H), 2.30 \text{ (dt, J = 1.5, 7.5 Hz, 6 H). 4.13 \text{ (dd, J = 6.0, 12.0 Hz, 2 H), 4.29 \text{ (dd, J = 6.0, 12.0 Hz, 2 H) 5.22-5.39 \text{ (m, 5 H);}}}} \\
{^13C \text{NMR (CDCl}_3 \rangle \delta 14.1, 22.7, 24.8, 24.9, 27.2, 27.3, 29.0, 29.1, 29.15, 29.2, 29.23, 29.4, 29.5, 29.6, 29.63, 29.7, 29.76, 29.8, 31.9, 32.6, 32.7, 34.1, 34.2, 62.1, 68.9, 129.6, 130.1, 130.2, 130.22, 130.5, 172.9, 173.3; IR (CDCl}_3 \rangle 2946, 1738, 1456 \text{ cm}^{-1}.} \\
Component 8 (Table 6, entry 8). \( ^1H \text{NMR (CDCl}_3 \rangle \delta 0.81-0.90 \text{ (m, 3 H), 1.20-1.42 \text{ (m, 36 H), 1.50-1.65 \text{ (m, 6 H), 1.90-2.10 \text{ (m, 8 H). 2.30 \text{ (dt, J = 1.5, 7.5 Hz, 6 H). 4.13 \text{ (dd, J = 6.0, 12.0 Hz, 2 H), 4.29 \text{ (dd, J = 6.0, 12.0 Hz, 2 H) 5.22-5.38 \text{ (m, 5 H);}}}} \\
{^13C \text{NMR (CDCl}_3 \rangle \delta 14.1, 22.7, 24.8, 24.9, 27.2, 27.3, 29.0, 29.1, 29.15, 29.2, 29.3, 29.5, 29.6, 29.63, 29.7, 29.76, 29.8, 31.9, 32.6, 32.7, 34.1, 34.2, 62.1, 68.9, 129.6, 130.1, 130.2, 130.22, 130.5, 172.9, 173.3; IR (CDCl}_3 \rangle 2946, 1738, 1456 \text{ cm}^{-1}.}
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References


GENERAL CONCLUSION

Two types of Pd-catalyzed annulation reaction of internal alkynes have been investigated. First, a novel palladium-catalyzed cascade reaction of aryl iodides and internal alkynes has been developed as an efficient synthetic route to 9-alkylidene-9H-fluorenes. This type of reaction has been extended to a number of aryl iodides and internal alkynes. The synthesis of a 9-alkylidene-9H-fluorenes has also been achieved from a vinylic iodide. This unusual cascade migration/coupling process appears applicable to the synthesis of even more complicated polycyclic aromatic hydrocarbons, such as benzo[b]fluoranthene.

The second type of alkyne annulation reaction studied in this thesis is the palladium-catalyzed reaction of internal alkynes and (2-iodophenyl)acetonitrile or 2-iodobenzonitrile. (2-Iodophenyl)acetonitrile reacts with diphenylacetylene in the presence of a palladium catalyst to afford 2-amino-3,4-diphenylnaphthalene in 83% yield. This is the first example of a cyano group actually participating in an organopalladium addition reaction. An unusual product 2-amino-3-\([(E)-1\text{-propenyl}\}]-4\text{-propylnaphthalene} has been obtained as the sole product in the reaction of 4-octyne. The formation of this unusual product has been rationalized by a mechanism similar to the palladium-catalyzed cyclization of enynes. The reaction of 2-iodobenzonitrile and diphenylacetylene affords 2,3-diphenylindenone in 30% yield.

The ADMET polymerization of soybean oil has also been achieved. Our model system studies have shown that the ADMET polymerization of ethylene glycol dioleate afforded the expected oligomers, from dimer to heptamer. Glyceryl trioleate undergoes ADMET polymerization to produce dimer, trimer, tetramer, pentamer and monocyclic oligomers, with monocyclic oligomers predominating. When a relatively high amount of catalyst was employed, rubbery materials were obtained from the polymerization of
glyceryl trioleate and glyceryl trilinoleate. The ADMET polymerization of soybean oil has produced polymeric materials. Using different reaction conditions, a variety of materials, from sticky oils to rubbers, have been prepared from soybean oil.
APPENDIX A. CHAPTER 1 $^1$H AND $^{13}$C NMR SPECTRA
2D NOESY SPECTRUM
APPENDIX B. CHAPTER 2 $^1$H AND $^{13}$C NMR SPECTRA
A 1H NMR spectrum of an organic compound. The spectrum shows peaks at various chemical shifts, with labels indicating the number of protons and their relative intensities. The peaks are labeled with integrals, with values ranging from 0.0 to 10.0. The spectrum is annotated with the date Sun Apr 7 21:54:38 1996.
\[
\text{NH}_2
\]
\[
\text{CMe}_3
\]
APPENDIX C. CHAPTER 3 ¹H AND ¹³C NMR SPECTRA
ethyleneglycol dioleate
ethylene glycol dioleate
Compound A: (Z)- and (E)-9-octadecene (Figure 1)
Compound A: (Z)- and (E)-9-octadecene (Figure 1)
Compound B: $E$, $E$-ethylene glycol dioleate (Figure 1)
Compound B: \(E, E\)-ethylene glycol dioleate (Figure 1)
Compound C: intramolecular cyclization (Figure 1)

\[
\begin{align*}
\text{CH} \quad \text{(CH}_2\text{)}_7 \text{C}=\text{O} \\
\text{CH} \quad \text{(CH}_2\text{)}_7 \text{C}=\text{O} \\
\text{C} \quad \text{O} \\
\end{align*}
\]
Compound C: intramolecular cyclization (Figure 1)
Dimer of ethylene glycol dioleate (Figure 1)
Dimer of ethylene glycol dioleate (Figure 1)
Trimer of ethylene glycol dioleate (Figure 1)
Trimer of ethylene glycol dioleate (Figure 1)
Tetramer of ethylene glycol dioleate (Figure 1)
Tetramer of ethylene glycol dioleate (Figure 1)
Pentamer of ethylene glycol dioleate (Figure 1)
Pentamer of ethylene glycol dioleate (Figure 1)
Hexamer of ethylene glycol dioleate (Figure 1)
Hexamer of ethylene glycol dioleate (Figure 1)
Heptamer of ethylene glycol dioleate (Figure 1)
Heptamer of ethylene glycol dioleate (Figure 1)
glyceryl trioleate
glyceryl trioleate
Component 1: isomerized glyceryl trioleate (Table 6, entry 1)
Component I: isomerized glyceryl trioleate (Table 6, entry 1)
Component 2: dimer of glyceryl trioleate (Table 6, entry 2)
Component 2: dimer of glyceryl trioleate (Table 6, entry 2)
Component 3: trimer of glyceryl trioleate (Table 6, entry 3)
Component 3: trimer of glyceryl trioleate (Table 6, entry 3)
Component 4: tetramer of glyceryl trioleate (Table 6, entry 4)
Component 4: tetramer of glyceryl trioleate (Table 6, entry 4)
Component 5: pentamer of glyceryl trioleate (Table 6, entry 5)
Component 5: pentamer of glyceryl trioleate (Table 6, entry 5)
Component 6: monocyclic oligomer (n = 6) (Table 6, entry 6)
Component 6: monocyclic oligomer (n = 6) (Table 6, entry 6)
Component 7: monocyclic oligomer (n = 10) (Table 6, entry 7)
Component 7: monocyclic oligomer (n = 10) (Table 6, entry 7)
Component 8: monocyclic oligomer (n = 21) (Table 6, entry 8)
Component 8: monocyclic oligomer \((n = 21)\) (Table 6, entry 8)
Fraction A: MeOH/CH$_2$Cl$_2$ soluble fraction obtained from polymerization of soybean oil (Table 8, entry 13)
Fraction B: MeOH/CH₂Cl₂ insoluble fraction obtained from polymerization of soybean oil (Table 8, entry 13)
H NMR spectrum of soybean oil

(New Horizons soybean oil produced by Pioneer Hi-Bred Inter. Inc.)
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