Advances in C-H activation by palladium: migration and cyclocarbonylation

Marino Andres Campo Molina
Iowa State University

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Advances in C-H activation by palladium: migration and cyclocarbonylation

by

Marino Andres Campo Molina

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

Major: Organic Chemistry

Program of Study Committee:
Richard C. Larock, Major Professor
Valerie Sheares Ashby
Keith Woo
Walter S. Trahanovsky
David Hoffman

Iowa State University
Ames, Iowa
2003

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This is to certify that the doctoral dissertation of
Marino Andres Campo Molina
has met the dissertation requirements of Iowa State University

Signature was redacted for privacy.

Major Professor

Signature was redacted for privacy.

For the Major Program
To all of those who believed in me.

Thank you, I could not have done it alone.
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<tr>
<td>Ts</td>
<td>\textit{p}-toluenesulfonyl</td>
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<td>tt</td>
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Palladium-catalyzed intramolecular C-H activation of \textit{o}-halobiaryls has been used to carry out important chemical transformations. For instance, in the presence of catalytic amounts of Pd(0), \textit{o}-halobiaryls are readily cyclocarbonylated under an atmosphere of CO to produce fluorenones in high yields with good regioselectivity. This methodology has been successfully applied to the preparation of polycyclic fluorenones and fluorenones containing fused isoquinoline, indole, pyrrole, thiophene, benzothiophene, and benzofuran rings.

A novel 1,4-Pd migration between the \textit{o}- and \textit{o}'-positions of biaryls has been observed in organopalladium intermediates derived from \textit{o}-halobiaryls. The organopalladium intermediates generated by this unique C-H activation-migration process have been trapped by way of a Heck reaction and Suzuki-Miyaura cross-coupling with aryloboronic acids. Similarly, organopalladium intermediates generated by 1,4-Pd migration have been trapped by intramolecular arylation to produce fused polycycles. This unique migration-arylation methodology have been used to prepare complex polycyclic compounds containing fused benzofuran, quinoline, oxepine, indole, phenanthrene, and naphthalene rings.
GENERAL INTRODUCTION

Palladium methodology is a powerful tool in organic synthesis due to the ability of this metal to catalyze a wide range of reactions. Most commonly, organopalladium intermediates are prepared in situ from the oxidative addition of organic halides or triflates to Pd(0). A more attractive approach to organopalladium intermediates involves C-H activation, which offers a more direct route to such intermediates as well as better atom economy.

Our own interest in Pd-catalyzed methodology involving C-H activation led us to examine intramolecular versions of this process in o-halobiaryls. First of all, we cyclocarbonylated o-halobiaryls to fluorenones using carbon monoxide. We have also discovered that palladium is able to migrate between the o- and o'-positions of these biaryls through a five-membered palladacycle intermediate. We have been able to show that such palladium migration is compatible with other Pd-catalyzed reactions, such as Heck, Suzuki, and alkyne annulation. Furthermore, we have developed a two step C-H activation process to transform o-halobiaryls into complex fused polycycles.

Dissertation Organization

This dissertation is divided into three chapters. Each of these chapters is written by the following guidelines for a full paper in the Journal of Organic Chemistry.

Chapter 1 describes the synthesis of fluoren-9-ones and other cyclic ketones by the palladium catalyzed cyclocarbonylation of o-halobiaryls. The regioselectivity and general scope of this methodology for preparing carbocyclic and heterocyclic ketones is examined in detailed in terms of electronic and steric effects.
Chapter 2 describes experimental results aimed to establish a 1,4-palladium migration in organopalladium intermediates derived from \( \alpha \)-halobiaryls. In order to accomplish this goal, the key arylpalladium intermediates generated by 1,4-palladium migration were trapped by Heck, Suzuki and alkyne annulation reactions. Our experimental results point to the intermediacy of an electrophilic palladium species, which prefers to reside in the more electron-rich position of the biaryl.

Chapter 3 describes the synthetic aspect of this 1,4-palladium migration. This methodology makes use of a palladium migration to generate key organopalladium intermediates, which undergo intramolecular arylation producing polycycles containing fused benzofuran, quinoline, oxepine, indole, phenanthrene, and naphthalene rings.

Finally, all the \( ^1 \text{H} \) and \( ^{13} \text{C} \) NMR spectra for the starting materials and the palladium-catalyzed reaction products have been compiled in appendices A-C.
CHAPTER 1. SYNTHESIS OF FLUOREN-9-ONES BY THE
PALLADIUM-CATALYZED CYCLOCARBONYLATION OF o-HALOBIARYLS

Based on a paper published in the Journal of Organic Chemistry
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Department of Chemistry, Iowa State University, Ames, IA 50011
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Abstract
The synthesis of various substituted fluoren-9-ones has been accomplished by the palladium-
catalyzed cyclocarbonylation of o-halobiaryls. The cyclocarbonylation of 4'-substituted 2-
iodobiphenyls produces very high yields of 2-substituted fluoren-9-ones bearing either
electron-donating or electron-withdrawing substituents. 3'-Substituted 2-iodobiphenyls
afford 3-substituted fluoren-9-ones in excellent yields with good regioselectivity. This
chemistry has been successfully extended to polycyclic fluorenones and fluorenones
containing fused isoquinoline, indole, pyrrole, thiophene, benzothiophene, and benzofuran
rings.

Introduction
Fluoren-9-ones are a family of natural products displaying a wide range of biological
activity,\(^1\) such as antibiotic\(^1a\) and inhibitory activity for human telomerase\(^1b\) and protein
kinase-C\(^1c\) (Figure 1). In recent years, fluorenones have attracted much interest because of
groundbreaking discoveries in the biomedical field, which include their use as probes for DNA redox chemistry. Furthermore, fluorenones have been prepared as key synthetic intermediates for the total synthesis of natural products, such as stealthin and prekinamycin.

![Chemical structures of biologically active fluoren-9-ones.](image)

**Figure 1.** Biologically active fluoren-9-ones.

The most useful syntheses of fluorenones include Friedel-Crafts ring closures of biarylcarboxylic acids and derivatives, intramolecular [4 + 2] cycloaddition reactions of conjugated enynes, oxidation of fluorenes, and remote metalation of 2-biphenylcarboxamides or 2-biphenyloxazolines. Unfortunately, these methods suffer some drawbacks, mainly because they employ harsh reaction conditions, such as a strong Lewis acid, heat, or a nucleophilic base, which do not tolerate many organic functional groups. Alternatively, fluorenones have been synthesized by the palladium-catalyzed cyclization of o-iodobenzophenones (Scheme 1). Although, this reported methodology employs relatively
mild reaction conditions, the o-iodobenzophenones used as starting materials are difficult to prepare and require the use of a synthetically limited Friedel-Crafts type reaction.

**Scheme 1**

![Scheme 1](image)

EDG: electron-donating group (OMe, OH)

Our interest in fluorenones has led to the development of a novel palladium-catalyzed cyclocarbonylation of readily available o-halobiaryls, which provides a highly efficient and direct route to the fluoren-9-one skeleton, as well as other related cyclic aromatic ketones (eq 1). Herein, we report the full details of this new fluorenone synthesis.

\[
\text{cat. Pd(0)} \quad \text{base} \quad \text{CO (1 atm)}
\]

**Results and Discussion**

In order to develop an optimum set of reaction conditions, we first studied the palladium-catalyzed cyclocarbonylation of commercially available 2-iodobiphenyl (1) to fluoren-9-one (2) as our model system. All of the optimization reactions have been carried out using 0.25 mmol of 2-iodobiphenyl (1) in DMF (6 mL) at 110 °C for 7 h under one atm of carbon monoxide. It is evident from the results listed in Table 1, that the base added, as well as the ligand present on palladium, are critical elements in this reaction. For instance, the use of chelating ligands, such as 1,2-bis(diphenylphosphino)ethane (dppe), 1,1'-
bis(diphenylphosphino)ferrocene (dppf), and 1,10-phenanthroline gave poor yields of the desired fluoren-9-one (2) (entries 1-3). Monodentate phosphine ligands have a major effect on the yield of the cyclocarbonylation reaction. Use of the electron-deficient ligands tri(p-fluorophenyl)phosphine and tri(p-chlorophenyl)phosphine gave low yields of fluoren-9-one (33 % and 37 % respectively), while the more electron-rich triphenylphosphine produced a 58 % yield (entries 4-6). Following this electronic trend, we have observed that the bulky, electron-rich ligand tricyclohexylphosphine was by far the most effective ligand, producing a quantitative yield of the desired compound 2 (entry 7). Finally, we explored the effect of different bases on the yield of fluoren-9-one and found that replacing the unusual cesium pivalate (CsPiv) base with NaOAc or Cs₂CO₃ was detrimental to the reaction (entries 8 and 9), the yield dropping from 100% to 92% and 82% respectively. The use of organic bases, such as pyridine and diisopropylethylamine, gave negligible yields of fluoren-9-one (entries 10 and 11).

The results of this optimization study have led to the development of a standard set of reaction conditions employing one atm of carbon monoxide, one equiv of the aryl halide (0.25 mmol), 5 mol % of commercially available Pd(PCy₃)₂, and 2 equiv of anhydrous cesium pivalate in DMF (6 ml) at 110 °C for 7 h. This procedure has been applied to a wide range of aryl halides (Table 2). 2-Iodobiphenyl produces fluoren-9-one (2) in a quantitative yield (entry 2). Under our reaction conditions, 2-bromobiphenyl is also converted to fluoren-9-one (2) in a quantitative yield (entry 1). However, biphenyl-2-yl trifluoromethanesulfonate fails to afford the desired product.
Table 1. Palladium-catalyzed cyclocarbonylation of 2-iodobiphenyl (1) to fluoren-9-one (2).a

<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>Pd catalyst</th>
<th>ligand (mol %)</th>
<th>time (h)</th>
<th>% isolated yield of 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CsPivb</td>
<td>Pd(OAc)2</td>
<td>dppe (5)</td>
<td>7</td>
<td>46</td>
</tr>
<tr>
<td>2</td>
<td>CsPiv</td>
<td>Pd(OAc)2</td>
<td>dppf (5)</td>
<td>7</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>CsPiv</td>
<td>Pd(OAc)2</td>
<td>1,10-phenanthroline (5)</td>
<td>7</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>4</td>
<td>CsPiv</td>
<td>Pd(OAc)2</td>
<td>$(p$-FC$_6$H$_5$)$_2$P (10)</td>
<td>7</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>CsPiv</td>
<td>Pd(OAc)2</td>
<td>$(p$-ClC$_6$H$_4$)$_2$P (10)</td>
<td>7</td>
<td>37</td>
</tr>
<tr>
<td>6</td>
<td>CsPiv</td>
<td>Pd(OAc)2</td>
<td>Ph$_3$P (10)</td>
<td>7</td>
<td>58 (38c)</td>
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<tr>
<td>7</td>
<td>CsPiv</td>
<td>Pd(PCy$_3$)$_2$</td>
<td>d</td>
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<td>8</td>
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<td>Pd(PCy$_3$)$_2$</td>
<td>d</td>
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<td>92</td>
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<td>84</td>
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<td>Pd(PCy$_3$)$_2$</td>
<td>d</td>
<td>24</td>
<td>&lt; 5</td>
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<tr>
<td>11</td>
<td>(i-Pr)$_2$NEt</td>
<td>Pd(PCy$_3$)$_2$</td>
<td>d</td>
<td>24</td>
<td>&lt; 5</td>
</tr>
</tbody>
</table>

aAll reactions were run with 0.25 mmol of 2-iodobiphenyl (1), 2 equiv of base, 5 mol % of Pd catalyst, and 5 or 10 mol % of an appropriate ligand in 6 mL of DMF at 110 °C for 7 h under one atm of CO. bCsPiv = cesium pivalate. cThe amount of DMF solvent was reduced from 6 mL to 1 mL. dThe palladium catalyst contains 10 mol % of tricyclohexylphosphate, so no further ligand was added to the reaction mixture.

The utility of this reaction for the synthesis of 2-substituted fluoren-9-ones has been assessed by studying the cyclocarbonylation of readily prepared 4'-substituted 2-iodobiphenyls (entries 2-6). As indicated, the reaction works well, tolerating both electron-donating, as well as electron-withdrawing substituents.

We have also addressed the question of regiochemistry in the cyclocarbonylation of 3'-substituted 2-iodobiphenyls (entries 7 and 8). Cyclocarbonylation of the electron-rich 2-iodo-3'-methylbiphenyl (12) and the electron-poor 3-(2-iodophenyl)benzaldehyde (15)
**Table 2.** Synthesis of fluoren-9-ones by the Pd-catalyzed cyclocarbonylation of o-halobisaryls.\(^a\)

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<th>entry</th>
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<th>% yield</th>
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<tr>
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<td><img src="image" alt="X=CHO (15)" /></td>
<td><img src="image" alt="16" /> + <img src="image" alt="17" /></td>
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<td><img src="image13" alt="structure" /></td>
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<td>55</td>
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*aAll reactions were carried out under the optimal conditions described in the text. The product ratio was determined by $^1$H NMR spectroscopic analysis. In order to keep the equivalents of aryl halide consistent, we employed 0.125 mmol of aryl dibromide 26. The reaction period was extended to 14 h. A 42 % yield of compound 47 was recovered at the end of the reaction.*

affords similar 9:1 regiochemical mixtures in excellent yields. In both cases, the predominant isomer arises from ring closure distal to the substituent. These experimental results seem to indicate that there is only a weak electronic effect during the cyclization process, and that a more important steric effect favors the less hindered isomers 13 and 16.
This cyclocarbonylation does not appear to be significantly affected by the presence of substituents ortho to the halo group. For example, the palladium-catalyzed reaction of 2-iodo-3-methoxybiphenyl\textsuperscript{10} (18) produces 1-methoxyfluoren-9-one (19) in 99\% yield (entry 9).

Interestingly, this palladium-catalyzed transformation can be readily employed on biaryl systems containing either polycyclic or heterocyclic rings. Thus, treatment of 9-iodo-10-phenylphenanthrene (20) with carbon monoxide under our standard reaction conditions produces indene[1,2-\textit{l}]phenanthren-13-one\textsuperscript{11} (21) in a 98\% yield (entry 10). Similarly, 2-bromo-1-phenylnaphthalene\textsuperscript{12} (22) produces a 96\% yield of benzo[\textit{c}]fluoren-7-one\textsuperscript{13} (23) (entry 11). Furthermore, cyclocarbonylation of the nitrogen-containing heterocycle 4-iodo-3-phenylisoquinoline\textsuperscript{14} (24) produces 11-oxoindeno[1,2-\textit{c}]isoquinoline\textsuperscript{15} (25) in a 95\% yield (entry 12).

This palladium reaction is also effective for the double cyclocarbonylation of 2,2'''-dibromo-p-quaterphenyl\textsuperscript{16} (26) (entry 13). Under our standard reaction conditions, but 14 h reaction time, substrate 26 produces the desired [2,2']bifluorenyl-9,9'''-dione\textsuperscript{17} (27) in 87 \% yield.

So far, we have demonstrated the utility of this chemistry by preparing a variety of fluorenones in high yields with good regioselectivity from o-halobiaryls containing six-membered ring aromatics, such as benzene, naphthalene, phenanthrene, etc. (Table 2, entries 1-13). We next turned our attention to applying this palladium methodology to o-halobiaryls in which one of the aromatic rings is a five-membered ring heterocycle, such as a benzofuran, a benzothiophene, a thiophene, a pyrrole or an indole (entries 14-24). We began
by studying the electronic effects of the cyclocarbonylation of o-iodobiaryls containing a benzofuran. When 3-iodo-2-phenylbenzofuran\(^\text{18}\) (28) was subjected to the standard reaction conditions, it failed to give any of the desired benz[b]indenof[2,1-d]furan-10-one (29) (entry 14). On the other hand, the cyclocarbonylation of 3-(2-iodophenyl)benzofuran (30), in which ring closure takes place onto the electron-rich benzofuran ring, produced the desired benz[b]indenof[1,2-d]furan-6-one (31) in 81% yield (entry 15). In these benzofuran-containing systems, cyclocarbonylation occurred onto the more reactive benzofuran moiety of the biaryl (entry 15), but failed to do so onto the less electron-rich phenyl ring of the biaryl (entry 14). Similar electronic effects have also been observed with o-halobiaryls containing either benzothiophene or thiophene rings. For instance, 3-iodo-2-phenylbenzothiophene\(^\text{19}\) (32) produced a 67% yield of 10-oxo-10H-benz[b]indenof[1,2-d]thiophene\(^\text{30}\) (33) (entry 16), while 3-(2-bromophenyl)thiophene\(^\text{21}\) (34) produced an 86% yield of indeno[2,1-d]thiophen-8-one\(^\text{22}\) (35) with excellent C-2 regioselectivity (entry 17). It is noteworthy that switching from the oxygen heterocycle of entry 14 to the sulfur analogue of entry 16 resulted in a substantial increase in yield. In like manner, the pyrrole derivative 1-(2-iodophenyl)pyrrole (36) gave a 96% yield of pyrrolo[1,2-a]indol-9-one\(^\text{23}\) (37) (entry 18).

The yield of the palladium-catalyzed cyclocarbonylation of o-halobiaryls containing an indole was not only dependent on electronic effects, but also on the nature of the protecting group on the indole nitrogen. To illustrate, 2-iodo-3-phenyl-1H-indole (38) and 3-iodo-2-phenyl-1H-indole\(^\text{24}\) (42), both of which have unprotected nitrogens, failed to give the desired indenoindolones under the standard reaction conditions (entries 19 and 21). However, the N-methyl substituted indole analogues 2-iodo-1-methyl-3-phenylindole (40)
and 3-iodo-1-methyl-2-phenylindole (44) produced the desired 5-methyl-5H-indeno[2,1-b]indol-6-one\(^{24,25}\) (41) and 5-methyl-5H-indeno[1,2-b]indol-10-one\(^{26}\) (45) in 49% and 21% yields respectively (entries 20 and 22). In an attempt to increase the yield of indeno[1,2-b]indol-10-one, 3-iodo-2-phenyl-1-(4-toluenesulfonyl)indole (46) was prepared and subsequently cyclocarbonylated under our standard reaction conditions to produce 5H-indeno[1,2-b]indol-10-one\(^{27}\) (43) in a 45% yield (entry 23). It is worth emphasizing that compound 46 led to the cyclocarbonylated product 43 in which the sulfonamide functionality had been removed under the relatively mild reaction conditions employed. This unusual deprotection was also observed in the cyclocarbonylation of 3-(2-bromophenyl)-1-(4-toluenesulfonyl)indole (47), which led to 5H-indeno[2,1-b]indol-6-one (39) in 55% yield (entry 24). Furthermore, 42% of the 3-(2-bromophenyl)-1-(4-toluenesulfonyl)indole (47) was recovered at the end of the reaction, which seems to indicate that removal of the sulfonamide functionality occurs during or after the cyclocarbonylation reaction, not before.

In summary, the synthesis of fluorenones have been accomplished in excellent yields with good regioselectivity by the cyclocarbonylation of o-halobiaryls containing six-membered ring aromatics (Table 2, entries 1-13). Similarly, this palladium-catalyzed reaction can also be used to prepare more strained fluorenones containing two fused five-membered rings (Table 2, entries 14-24). In the latter reactions, the yield of fluorenone is strongly dependent on electronic effects. This fact can be rationalized in terms of the ring strain of the palladium intermediates (see the latter mechanistic discussion and Scheme 2) leading to such fluorenones. The transformation is more favorable if cyclization occurs onto an electron-rich system, such as a benzofuran [81% yield (entry 15)], a thiophene [86% yield
(entry 17)], a pyrrole [96 % yield (entry 18)] or an indole [97 % yield based on percent conversion (entry 24)] versus cyclization onto a relatively unreactive phenyl group [0-67 % yields (entries 14, 16 and 19-23)].

Finally, this chemistry can also be applied to vinylic halides for the preparation of indenones. For instance, the cyclocarbonylation of commercially available 1-bromo-1,2,2-triphenylethene (48) led to 2,3-diphenyl-1-indenone (49) in 81 % yield (Table 3, entry 1); however, 1-iodo-1,2,2-triphenylethene\(^{28}\) (51) led to the desired product 49 in only a 61 % yield along with 24 % of triphenylethene (50) (entry 2). Furthermore, 5-iodo-6-phenyl dibenz[b,f]oxepine\(^{29}\) (52) produced indeno[5,6]dibenz-[b,f]oxepin-14-one (53) in 80 % yield (entry 3). Similar attempts to cyclocarbonylate 3-iodo-4-phenylisocoumarin (54) or 4-iodo-3-phenylisocoumarin (56) under our standard reaction conditions resulted in failure (entries 4 and 5). It is unclear why substrates 54 and 56 failed to successfully undergo the cyclocarbonylation reaction, but it is possibly due to unfavorable electronic effects during the cyclization process. Finally, the cyclocarbonylation of 1-iodo-2-phenylcyclohexene\(^{30}\) (58) produced 1,2,3,4-tetrahydrofluoren-9-one\(^{31}\) (59) in 34 % yield. This indicates that the palladium-catalyzed cyclocarbonylation of vinylic halides to indenones does not appear to be as general as the cyclocarbonylation of o-halobiarlyls to fluorenones. This observation can be rationalized in terms of unfavorable electronic effects during the cyclocarbonylation of vinylic halides or possibly the instability of the desired indenone products.

We propose a possible reaction mechanism for this palladium-catalyzed synthesis of fluorenones involving (1) oxidative addition of the aryl halide to Pd(0), (2) CO insertion to
Table 3. Palladium-catalyzed cyclocarbonylation of vinylic halides to indenones.\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product(s)</th>
<th>% yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(X = \text{Br} ) (48)</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 52</td>
<td>81\textsuperscript{b} + 0</td>
</tr>
<tr>
<td>2</td>
<td>(X = \text{I} ) (51)</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 49 + (\text{Ph} - \text{H} - \text{Ph} ) 50</td>
<td>61 + 24</td>
</tr>
<tr>
<td>3</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 52</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 53</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 54</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 55</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 56</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 57</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 58</td>
<td>(\text{Ph} - \text{O} - \text{Ph} ) 59</td>
<td>34</td>
</tr>
</tbody>
</table>

\textsuperscript{a}All reactions were carried out under the optimal conditions described in the text. \textsuperscript{b}The reaction time was extended to 24 h.

generate the acylpalladium intermediate A, (3) either oxidative addition of the neighboring aryl C-H to the acylpalladium to generate a Pd(IV) intermediate (path 1)\textsuperscript{22} or electrophilic
palladation (path 2)\textsuperscript{33} and subsequent elimination of HI to generate the neighboring aryl C-H to the acylpalladium to generate a Pd(IV) intermediate (path 1)\textsuperscript{32} or electrophilic palladation (path 2)\textsuperscript{33} and subsequent elimination of HI to generate intermediate B, and (4) reductive elimination of the ketone with simultaneous regeneration of the Pd(0) catalyst (Scheme 2).

**Scheme 2**

Finally, we have explored the use of our cyclocarbonylation methodology to prepare six-membered ring ketones. Unfortunately, treating 1-benzyl-2-iodobenzene\textsuperscript{34} (60) with CO under our standard reaction conditions failed to give the desired product 61a or tautomer 61b (Table 4, entry 1). Similarly, the more electron-rich (2-iodophenyl)phenyl ether\textsuperscript{39} (62) failed
to produce the desired xanthen-9-one (63) under our standard reaction conditions (entry 2).

A similar attempt to cyclocarbonylate 1-(2-bromobenzyl)indole\textsuperscript{35} (64) led exclusively to

\begin{table}[h]
\begin{center}
\begin{tabular}{cccc}
\hline
entry & substrate & product(s) & \% yield \\
\hline
1 & & & 0 \\
2 & & & 0 \\
3 & & & 70 + 0 \\
\hline
\end{tabular}
\end{center}
\caption{Palladium-catalyzed cyclocarbonylation of aryl halides to six-membered ring ketones.}\textsuperscript{a}
\end{table}

\textsuperscript{a}All reactions were carried out under the optimal conditions described in the text.

direct cyclization, without CO insertion, producing 6-\textit{H}-isoindolo[2,1-\textit{a}]indole\textsuperscript{36} (65) in 70 % yield and none of the desired cyclic ketone product 66a or tautomer 66b (entry 3). We speculate that the cyclocarbonylation of aryl halides to six-membered ring ketones is unfavorable due to the difficulty in forming a seven-membered ring organopalladium intermediate analogous to B, which would be required prior to cyclization (Scheme 2).
Therefore, we conclude that the preparation of six-membered ring ketones by this methodology is probably not feasible, at least under our present reaction conditions.

**Conclusion**

The palladium-catalyzed cyclocarbonylation of o-halobiaryls provides a short, straightforward route to a variety of substituted fluoren-9-ones under mild reaction conditions and short reaction times. Our success in extending this reaction to other biaryl systems, as well as some vinylic halides, indicates its potential for the synthesis of a wide variety of five-membered carbocyclic and heterocyclic aromatic ketones. We were unable to extend this chemistry to the preparation of six-membered cyclic ketones.

**Experimental Section**

**General procedures.** All $^1$H and $^{13}$C spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic KMnO$_4$ solution [3 g of KMnO$_4$ + 20 g of K$_2$CO$_3$ + 5 mL of NaOH (5 %) + 300 mL of H$_2$O]. All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV.

**Reagents.** All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of DME, THF, DMF, diethyl ether, ethyl acetate and hexanes were purchased from Fisher Scientific Co. 2-Iodobiphenyl (1), 2-idothioanisole and thiophene-3-
boronic acid were obtained from Lancaster Synthesis Ltd. 2-Iodoaniline, triphenylethene (50), 1,2,2-triphenyl-1-bromoethene (48), 2-bromobiphenyl (3), 1-bromo-2-iodobenzene, 4-bromotoluene, 3-bromotoluene, 2-fluoroanisole, 4-bromoanisole, 2,5-dihydro-2,5-dimethoxyfuran, 2-bromophenylboronic acid, 4,4’-diiodobiphenyl, phenyllithium, phenylacetylene, cesium carbonate, cesium fluoride, pivalic acid and triethylamine were obtained from Aldrich Chemical Co., Inc. Bis(tricyclohexylphosphine)palladium(0) was purchased from Strem Chemicals, Inc.

**Synthesis of the o-Halobiaryls**

2-Iodo-4'-methylbiphenyl (4). 2-Iodo-4'-methylbiphenyl (4) was prepared by a procedure reported by Hart. A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 4-methylphenylmagnesium bromide [prepared from 4-bromotoluene (1.71 g, 10.0 mmol) and Mg (0.246 g, 10.0 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I2 (3.8 g, 15.0 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I2 was destroyed by adding 10% aq NaHSO3 (35 mL); the organic layer was separated and rewashed with brine (20 mL). Finally, the organic layer was dried (MgSO4), filtered and the solvent removed under reduced pressure. The residue was chromatographed using 20:1 hexanes/ethyl acetate to afford 0.88 g (60 %) of the desired compound 3 as a colorless liquid with spectral properties identical to those previously reported.

2-Iodo-4'-methoxybiphenyl (6). This biphenyl was prepared by the same method used to prepare 4, but 4-bromoanisole (1.71 g, 10.0 mmol) was employed. The residue was
chromatographed using 20:1 hexanes/ethyl acetate to afford 0.610 g (39 %) of the desired compound 6 as a yellow solid. This compound was further purified by recrystallization from hexanes to yield a white solid: mp 58-60 °C; 

\[ \text{H NMR (CDCl}_3\text{) } \delta \text{ 3.86 (s, 3H), 6.94-7.02 (m, 3H), 7.26-7.30 (m, 3H), 7.36 (td, } J = 7.2, 0.9 \text{ Hz, 1H), 7.93 (dd, } J = 8.0, 0.9 \text{ Hz, 1H); } \]

\[ \text{C NMR (CDCl}_3\text{) } \delta \text{ 55.5, 99.4, 113.5, 128.4, 128.8, 130.4, 130.7, 137.0, 139.7, 146.5, 159.3; } \]

HRMS m/z 309.98594 (calcd for C_{13}H_{11}IO, 309.98547).

**2-Iodo-4'-'methoxymethylbiphenyl (8).** This iodobiphenyl was prepared in two steps from 2-iodo-4'-methylbiphenyl (4). Compound 4 was brominated by the procedure of Ponchant\(^{37}\) to afford 4'-bromomethyl-2-iodobiphenyl (67): 

\[ \text{H NMR (CDCl}_3\text{) } \delta \text{ 4.54 (s, 2H), 7.01-7.07 (m, 1H), 7.26-7.41 (m, 6H), 7.94-7.97 (m, 1H); } \]

\[ \text{C NMR (CDCl}_3\text{) } \delta \text{ 33.4, 98.2, 128.2, 128.3, 129.1, 129.4, 130.1, 130.2, 130.4, 137.5, 139.6, 144.6, 145.8} \]

A solution of 4'-bromomethyl-2-iodobiphenyl (67) (0.228 g, 0.611 mmol) and NaOMe (0.162 g, 3.0 mmol) in 10 mL of anhydrous methanol was stirred for 16 h at room temperature. The mixture was diluted with diethyl ether (50 mL) and washed with brine (25 ml). The organic layer was dried (MgSO\(_4\)), filtered, and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 7:1 hexanes/ethyl acetate to afford 0.172 g (87 %) of the desired compound 8 as a colorless oil: 

\[ \text{H NMR (CDCl}_3\text{) } \delta \text{ 3.44 (s, 3H), 4.51 (s, 2H), 6.99-7.04 (m, 1H), 7.26-7.41 (m, 6H), 7.94 (dd, } J = 8.1, 1.2 \text{ Hz, 1H); } \]

\[ \text{C NMR (CDCl}_3\text{) } \delta \text{ 58.6, 74.8, 98.8, 127.6, 128.4, 129.0, 129.6, 130.4, 137.9, 139.7, 143.8, 146.6; IR (CH}_2\text{Cl}_2\text{) } \text{3049, 2985, 1463 cm}^{-1}; \]

HRMS m/z 324.0016 (calcd for C_{14}H_{13}IO, 324.0011).

**4-(2-Iodophenyl)benzaldehyde (10).** Compound 67 was oxidized to aldehyde 10 using the following procedure: a solution of AgClO\(_4\) (0.29 g, 1.4 mmol) in DMSO (5 mL)
was added quickly with stirring to 4'-bromomethyl-2-iodobiphenyl (0.50 g, 1.3 mmol) in DMSO (2 mL). The resulting mixture was allowed to stand for 30 min at room temperature in the dark. At this point, triethylamine (0.81 g, 8.0 mmol) was added and the mixture stirred for an additional 20 min. The reaction mixture was quenched with brine (25 mL) and extracted with diethyl ether (60 mL). The aqueous layer was reextracted with diethyl ether (20 mL), and the organic layers were combined, dried (MgSO₄) and filtered. The solvent was removed under reduced pressure, and the resulting yellow oil was purified by column chromatography using 5:1 hexanes/ethyl acetate to afford 0.308 g (77 %) of 4-(2-iodophenyl)benzaldehyde (10) as a white solid: mp 79-80 °C (lit. mp 80-81 °C). The spectral properties were identical to those previously reported.²⁸

2-Iodo-3'-methylbiphenyl (12). This biphenyl was prepared by the same method used to prepare 4, but 3-bromotoluene (1.71 g, 10.0 mmol) was employed. It was obtained as a colorless liquid (0.84 g, 57 %): ¹H NMR (CDCl₃) δ 2.44 (s, 3H), 7.04 (td, J = 7.6, 2.0 Hz, 1H), 7.16-7.18 (m, 2H), 7.22-7.24 (m, 1H), 7.31-7.41 (m, 3H), 7.97 (dd, J = 8.0, 0.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 21.6, 98.8, 126.5, 127.9, 128.1, 128.4, 128.8, 130.1, 130.2, 137.6, 139.5, 144.2, 146.8; HRMS m/z 293.99093 (calcd for C₁₃H₁₁I, 293.99055).

3-(2-Iodophenyl)benzaldehyde (15). This aldehyde was prepared in two steps from 2-iodo-3'-methylbiphenyl (12) by the same method used to prepare 4-(2-iodophenyl)benzaldehyde (10). Bromination of 12 produced 3'-bromomethyl-2-iodo-biphenyl (68) in 70 % yield: ¹H NMR (CDCl₃) δ 4.54 (s, 2H), 7.04 (td, J = 8.55, 1.8 Hz, 1H), 7.26-7.42 (m, 6H), 7.95 (dd, J = 7.8, 1.2 Hz, 1H); ¹³C NMR (CDCl₃) δ 33.4, 98.6, 128.3, 128.4, 128.5, 129.1, 129.5, 130.1, 130.2, 137.5, 139.7, 144.7, 146.0. Oxidation of 68 (0.485 g, 1.3
mmol) using DMSO (7 mL) and AgClO₄ (0.29 g, 1.4 mmol) gave 0.300 g (75 %) of the desired product 15 as a clear oil: ¹H NMR (CDCl₃) δ 7.06 (td, J = 7.8, 1.8 Hz, 1H), 7.30 (dd, J = 7.8, 1.8 Hz, 1H), 7.41 (td, J = 7.4, 1.2 Hz, 1H), 7.56-7.64 (m, 2H), 7.85-7.86 (m, 1H), 7.91 (dt, J = 6.9, 1.8 Hz, 1H), 7.96 (dd, J = 7.8, 1.2 Hz, 1H), 10.06 (s, 1H); ¹³C NMR (CDCl₃) δ 98.3, 128.5, 128.8, 128.9, 129.5, 130.1, 130.8, 135.5, 136.3, 139.8, 145.0, 145.2, 192.1; IR (CHCl₃) 1698 cm⁻¹; HRMS m/z 307.97049 (calcd for C₁₃H₁₀IO, 307.96982).

2-Iodo-3-methoxybiphenyl (18). 1-Lithio-2-methoxybiphenyl was prepared in situ from 2-fluoroanisole (1.134 g, 9.0 mmol) and phenyllithium (10 mL of 1.8 M solution in hexanes) in diethyl ether (20 ml) by the procedure of Huisgen. The reaction mixture was cooled to 0 °C using an ice bath and I₂ (3.5 g, 13.8 mmol) was added slowly with constant stirring. The mixture was stirred for an additional 30 min, then the excess I₂ was destroyed by adding 10% aq NaHSO₃ (35 mL). The organic layer was rewashed with brine (20 mL), dried (MgSO₄) and filtered. Removal of solvent under reduced pressure gave a yellow oil that was purified by chromatography using 20:1 hexanes/ethyl acetate to afford 1.02 g (36 %) of the desired compound 18 as a yellow solid. Recrystallization from hexanes/ethyl acetate gave the desired product as a white solid: mp 83-84 °C; ¹H NMR (CDCl₃) δ 3.94 (s, 3H), 6.82 (dd, J = 8.2, 1.2 Hz, 1H), 6.92 (dd, J = 7.5, 1.2 Hz, 1H), 7.30-7.43 (m, 6H); ¹³C NMR (CDCl₃) δ 56.7, 91.4, 109.5, 122.8, 127.6, 127.9, 129.0, 129.4, 144.6, 148.9, 158.4; HRMS m/z 309.98594 (calcd for C₁₃H₁₁IO, 309.98547).

9-Iodo-10-phenylphenanthrene (20). This iodobiaryl was prepared from 9-phenyl-10-(trimethylsilyl)phenanthrene using an iodination procedure from the literature. To a solution of 9-phenyl-10-(trimethylsilyl)phenanthrene (0.133 g, 0.4 mmol) in CH₂Cl₂ (2 mL)
was added ICl (0.078 g, 0.48 mmol) in CH₂Cl₂ (2 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 1 h, then the excess ICl was destroyed by adding 10% aq Na₂S₂O₃ (10 mL). The organic layer was dried (MgSO₄), filtered and the solvent removed under reduced pressure. The remaining solid was recrystallized from methanol/CH₂Cl₂ to afford 0.13 g (85 %) of the desired compound 20 as a white solid: mp 118-120 °C; ¹H NMR (CDCl₃) δ 7.28 (dd, J = 6.0, 1.8 Hz, 2H), 7.38 (d, J = 3.9 Hz, 2H), 7.50-7.56 (m, 3H), 7.60-7.70 (m, 3H), 8.44-8.47 (m, 1H), 8.63-8.70 (m, 2H); ¹³C NMR (CDCl₃) 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 (CDCl₃) 3064, 3025, 1481 cm⁻¹; HRMS m/z 380.0062 (calcd for C₂₀H₁₃I, 380.0062).

2-Bromo-1-phenylnaphthalene (22). This starting material was prepared by the procedure of Wittig: ¹H NMR (CDCl₃) δ 7.27-7.31 (m, 2H), 7.32-7.36 (m, 1H), 7.41-7.52 (m, 5H), 7.65-7.72 (m, 2H), 7.79-7.82 (m, 1H); ¹³C NMR (CDCl₃) δ 121.8, 126.3, 127.0, 127.1, 128.1, 128.2, 128.6, 129.2, 130.2, 130.4, 132.6, 134.2, 139.9, 140.1.

4-Iodo-3-phenylisoquinoline (24). This aryl iodide was prepared by the procedure of Larock et al: ¹H NMR (CDCl₃) δ 7.45-7.53 (m, 3H), 7.61-7.71 (m, 3H), 7.83 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 9.17 (s, 1H); ¹³C NMR (CDCl₃) δ 98.2, 128.0, 128.1, 128.1, 128.4, 129.9, 132.4, 132.5, 138.7, 143.7, 152.1, 157.1 (one sp² carbon missing due to overlap); IR (neat) 3055, 1630, 1549 cm⁻¹; HRMS m/z 330.9852 (calcd for C₁₅H₁₀IₑN, 330.9858).

2,2'''-Dibromo-p-quaterphenyl (26). This aryl dibromide was prepared by a selective Suzuki-Miyaura cross-coupling reaction as follows. 4,4'-Diodobiphenyl (0.406 g, 1.0 mmol), 2-bromophenylboronic acid (0.44 g, 2.2 mmol), CsF (0.608 g, 4.0 mmol),
Pd(dba)$_2$ (0.0576 g, 0.10 mmol), and PPh$_3$ (0.052 g, 0.2 mmol) in 1,2-dimethoxyethane (DME) (5 mL) were stirred under Ar at 90 °C for 6 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (MgSO$_4$), filtered and the solvent removed under reduced pressure. The residue was purified by crystallization from ethanol/acetoneto afford 0.318 g (68 % yield) of the desired compound 26 as a yellow solid: mp 170-171 °C (lit$^{16}$ mp 174.8 °C); $^1$H NMR (CDCl$_3$) δ 7.21-7.26 (m, 1H), 7.39-7.41 (m, 2H), 7.51-7.55 (m, 2H), 7.70-7.76 (m, 3H); $^{13}$C NMR (CDCl$_3$) δ 122.9, 126.9, 127.7, 129.0, 130.1, 131.6, 133.5, 140.1, 140.4, 142.4; IR (CH$_2$Cl$_2$) 3054, 1466 cm$^{-1}$; HRMS m/z 463.9607 (calcd for C$_{26}$H$_{16}$Br$_2$: 463.9598).

3-Iodo-2-phenylbenzofuran (28). This compound was prepared by the procedure of Cacchi et al.$^{18}$ The spectral properties were identical to those previously reported.$^{18}$

3-(2-Iodophenyl)benzofuran (30). This starting material was prepared by the procedure of Jørgensen et al.$^{41}$ from 1-(2-iodophenyl)-2-phenoxyethanone$^{42}$ (69) [$^1$H NMR (CDCl$_3$) δ 5.10 (s, 1H), δ 6.91 (dd, $J$ = 7.5, 1.2 Hz, 2H), 6.98 (tt, $J$ = 7.4, 1.0 Hz, 1H) 7.14-7.18 (m, 1H), 7.25-7.30 (m, 2H), 7.40-7.44 (m, 2H), 7.92 (d, $J$ = 8.2 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 71.6, 91.7, 114.9, 121.9, 128.1, 128.7, 129.7, 132.4, 140.8, 141.5, 157.7, 199.9].

To a solution of 69 (0.2 g, 0.59 mmol) in CH$_2$Cl$_2$ (8 mL) was added methanesulfonic acid (0.39 mL, ~ 6 mmol). The resulting solution was stirred at 55 °C for 40 h. The reaction mixture was diluted with diethyl ether (30 mL) and washed with brine (30 mL). The organic layer was dried (MgSO$_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 18:1 hexanes/ethyl acetate to afford 0.122 g (64 %) of the desired compound 30 as a clear oil: $^1$H NMR (CDCl$_3$) δ 7.05-7.09 (m,
1H), 7.25 (td, J = 7.4, 1.2 Hz, 1H), 7.33 (td, J = 7.6, 1.2 Hz, 1H), 7.39-7.41 (m, 2H), 7.46 (d, J = 7.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.76 (s, 1H), 8.00 (d, J = 8.0 Hz, 1H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 99.8, 111.8, 121.0, 122.9, 124.2, 124.7, 127.1, 128.3, 129.5, 131.2, 136.8, 140.0, 143.0, 155.0; IR (CH\(_2\)Cl\(_2\)) 3049, 3068 cm\(^{-1}\); HRMS m/z 319.9702 (calcd for C\(_{14}\)H\(_9\)O, 319.9698).

3-Iodo-2-phenylbenzothiophene (32). This starting material was prepared in two steps from commercially available 2-iodothioanisole. To a solution of 2-iodothioanisole (1.53 g, 6.1 mmol) and phenylacetylene (0.75 g, 7.3 mmol) in Et\(_3\)N (25 mL) was added PdCl\(_2\)(PPh\(_3\))\(_2\) (86 mg, 2.0 mol %). The mixture was stirred for 5 min under Ar and Cul (11 mg, 1.0 mol %) was added. The resulting mixture was then heated under an Ar atmosphere at 60 °C for 2 h. The reaction mixture was allowed to cool to room temperature, and the ammonium iodide salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography using 20:1 hexanes/ethyl acetate to afford 1.26 g (92 %) of 2-(2-phenylethynyl)thioanisole (70) as a yellow oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.51 (s, 3H), 7.10 (td, J = 7.5, 1.2 Hz, 1H), 7.17 (dd, J = 7.8, 0.9 Hz, 1H), 7.27-7.37 (m, 4H), 7.48 (ddd, J = 7.5, 1.2, 0.6 Hz, 1H), 7.56-7.60 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 15.3, 87.1, 96.1, 123.4, 124.4, 124.5, 128.6, 128.6, 129.0, 131.8, 132.5, 141.9; IR (CH\(_2\)Cl\(_2\)) 1599, 1491 cm\(^{-1}\); HRMS m/z 224.06627 (calcd for C\(_{15}\)H\(_{12}\)S, 224.06597). 3-Chloromercurio-2-phenylbenzothiophene was prepared in situ from 70 by the procedure of Larock et al.\(^{19}\) To a suspension of Hg(OAc)\(_2\) (0.318 g, 1.0 mmol) in glacial HOAc (3 mL) at room temperature was added 2-(2-phenylethynyl)thioanisole (0.224 g, 1.0 mol), and the resulting solution was stirred at room temperature for 30 min. The reaction mixture was
quenched by adding I₂ (0.38 g, 1.5 mmol), and the mixture was stirred vigorously for an
additional 30 min. Excess I₂ was destroyed by adding 10% aq Na₂S₂O₃ (30 mL), and the
aqueous layer was extracted with diethyl ether (50 mL). The organic layer was dried
(MgSO₄), filtered and the solvent removed under reduced pressure. The residue was purified
by column chromatography using 30:1 hexanes/ethyl acetate to afford 0.304 g (90 %) of 3-
iodeo-2-phenylbenzothiophene as a yellow oil: ¹H NMR (CDCl₃) δ 7.34-7.40 (td, J = 7.5, 1.5
Hz, 1H), 7.42-7.50 (m, 4H), 7.66-7.69 (m, 2H), 7.75-7.78 (m, 1H), 7.81-7.84 (m, 1H); ¹³C
NMR (CDCl₃) δ 79.7, 122.4, 125.7, 125.8, 126.6, 128.8, 129.2, 130.3, 134.9, 139.2, 142.2,
142.4; IR (CH₂Cl₂) 3065, 1601, 1477, 1433 cm⁻¹; HRMS m/z 335.94745 (calcd for C₁₄H₁₃S,
335.94697).

3-(2-Bromophenyl)thiophene (34). This aryl bromide was prepared by a selective
Suzuki-Miyaura cross-coupling reaction as follows. 1-Bromo-2-iodobenzene (0.2829 g, 1.0
mmol), thiophene-3-boronic acid (0.140 g, 1.1 mmol), cesium fluoride (0.304 g, 2.0 mmol),
Pd(dba)₂ (0.0288 g, 0.05 mmol), and PPh₃ (0.026 g, 0.1 mmol) in DME (5 mL) were stirred
under Ar at 90 °C for 6 h. The reaction mixture was diluted with diethyl ether (50 mL) and
washed with brine (30 mL). The organic layer was dried (MgSO₄), filtered, and the solvent
removed under reduced pressure. The residue was purified by column chromatography using
hexanes to afford 0.210 g (88 %) of the desired compound 34 as a clear oil: ¹H NMR
(CDCl₃) δ 7.17 (td, J = 7.6, 0.4 Hz, 1H), 7.28-7.40 (m, 5H), 7.65 (d, J = 8.0 Hz, 1H); ¹³C
NMR (CDCl₃) δ 122.6, 124.0, 124.8, 127.4, 128.7, 129.0, 131.3, 133.4, 137.6, 141.1; IR
(CH₂Cl₂) 3112, 3048, 1468 cm⁻¹; HRMS m/z 237.9455 (calcd for C₁₀H₇BrS, 237.9452).
1-(2-Iodophenyl)pyrrole (36). This aryl iodide was prepared by the condensation of 2-iodoaniline with 2,5-dihydro-2,5-dimethoxyfuran. To a solution of citric acid monohydrate (4.2 g, 20 mmol) in water (20 mL) was added 2,5-dihydro-2,5-dimethoxyfuran (1.716 g, 13 mmol) and the mixture was stirred vigorously for approximately 8 min at room temperature. At this point a homogeneous solution was obtained, and the mixture was diluted with methanol (10 mL), followed by addition of 2-iodoaniline (2.19 g, 10 mmol) in methanol (20 mL). The mixture was stirred at room temperature for 14 h, then diluted with diethyl ether (75 mL) and washed with brine (75 mL). The aqueous layer was reextracted with diethyl ether (25 mL) and the organic layers were combined, dried (Na$_2$SO$_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 20:1 hexanes/ethyl acetate to afford 2.28 g (85 %) of the desired compound 36 as a clear oil:

$^1$H NMR (CDCl$_3$), $\delta$ 6.34 (t, $J = 2.0$ Hz, 2H), 6.81 (t, $J = 2.0$ Hz, 2H), 7.09 (td, $J = 7.6, 1.6$ Hz, 1H), 7.30 (dd, $J = 7.6, 1.6$ Hz, 1H), 7.40 (td, $J = 7.6, 1.2$ Hz, 1H), 7.94 (dd, $J = 7.6, 1.2$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 96.1, 109.4, 122.4, 128.3, 129.2, 129.6, 140.2, 144.2; IR (CH$_2$Cl$_2$) 3049, 1496 cm$^{-1}$; HRMS m/z 268.9705 (calcd for C$_{10}$H$_8$IN, 268.9702).

2-Iodo-3-phenyl-1H-indole (38). This indole derivative was prepared from 2-trimethylsilyl-3-phenyl-1H-indole$^{43}$ using an iodination procedure from the literature.$^{40}$ To a solution of 2-trimethylsilyl-3-phenyl-1H-indole (0.265 g, 1.0 mmol) in CH$_2$Cl$_2$ (2 mL) was added ICl (0.1785 g, 1.1 mmol) in CH$_2$Cl$_2$ (3 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 1 h. Then the excess ICl was destroyed by adding 10% aq Na$_2$S$_2$O$_3$ (15 mL). The organic layer was dried (MgSO$_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 7:1 hexanes/ethyl
acetate to afford 0.249 g (78%) of the desired compound 38 as a pale yellow oil: $^1$H NMR (CDCl$_3$) δ 7.06-7.18 (m, 2H), 7.25-7.28 (m, 1H), 7.32-7.38 (m, 1H), 7.44-7.50 (m, 2H), 7.56-7.63 (m, 3H), 8.02 (br s, 1H); $^{13}$C NMR (CDCl$_3$) δ 77.3, 110.5, 119.0, 120.6, 122.9, 123.8, 127.1, 127.3, 128.7, 129.9, 134.6, 139.8; IR (CH$_2$Cl$_2$) 3446, 3053, 1404 cm$^{-1}$; HRMS m/z 318.9862 (calcd for C$_{14}$H$_{10}$IN, 318.9858).

2-Iodo-1-methyl-3-phenylindole (40). This indole derivative was prepared in two steps from 3-phenyl-1H-indole. To a suspension of NaH (0.0528 g, 2.2 mmol) in DMF (4 mL) at 0 °C was added 3-phenyl-1H-indole (0.338 g, 1.7 mmol) in DMF (4 mL) and the mixture was stirred at room temperature for 30 min. At this point MeI (2.414 g, 17.0 mmol) in DMF (4 mL) was added and the reaction mixture stirred at room temperature for 14 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried (MgSO$_4$), and the solvent removed under reduced pressure. The residue was purified by column chromatography using 9:1 hexanes/ethyl acetate to afford 0.350 g (78%) of the desired 1-methyl-3-phenylindole (71) as a yellow oil with spectral properties identical to those previously reported.$^{44}$ To a solution of 71 (0.343 g, 1.61 mmol) in THF (10 mL) at 0 °C was added n-butyllithium (0.76 mL of 2.5 M in hexanes, 1.9 mmol) and the reaction mixture was stirred at 0 °C for 4 h and then for 40 min at room temperature. The reaction mixture was cooled again to 0 °C and I$_2$ (0.762 g, 3.0 mmol) was added slowly over a 5 min period and the stirring was continued for an additional 10 min. At this point, the reaction mixture was diluted with diethyl ether (35 mL) and excess I$_2$ was destroyed by adding 10% aq Na$_2$S$_2$O$_3$ (40 mL). The organic layer was dried (MgSO$_4$), filtered, and the solvent
removed under reduced pressure. The residue was purified by column chromatography using 18:1 hexanes/ethyl acetate to afford 0.383 g (70%) of the desired compound 40 as a clear oil:

$^1$H NMR (CDCl$_3$) $\delta$ 3.85 (s, 3H), 7.06-7.11 (m, 1H), 7.18-7.23 (m, 1H), 7.33-7.39 (m, 2H), 7.45-7.50 (m, 2H), 7.56-7.61 (m, 3H); $^{13}$C NMR (CDCl$_3$) $\delta$ 34.8, 87.0, 110.0, 119.2, 120.2, 122.5, 123.2, 127.1, 127.8, 128.6, 130.2, 135.4, 138.8; IR (CH$_2$Cl$_2$) 3048, 2941, 1460, 1323 cm$^{-1}$; HRMS m/z 333.0019 (calcd for C$_{15}$H$_{12}$IN, 333.0015).

3-Iodo-2-phenyl-1H-indole (42). This indole derivative was prepared by the procedure of Bocci and Palla.$^{24}$ The spectral properties were identical to those previously reported.$^{24}$

3-Iodo-1-methyl-2-phenylindole (44). This indole derivative was prepared from 42. To a suspension of NaH (0.031 g, 1.3 mmol) in DMF (2 mL) at 0°C was added 42 (0.320 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point, MeI (1.42 g, 10.0 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 14 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried (MgSO$_4$), and the solvent removed under reduced pressure. The residue was purified by column chromatography using 9:1 hexanes/ethyl acetate to afford 0.310 g (93%) of the desired 3-iido-1-methyl-2-phenylindole (44) as a clear oil: $^1$H NMR (CDCl$_3$) $\delta$ 3.65 (s, 1H), 7.21-7.25 (m, 1H), 7.29-7.30 (m, 2H), 7.44-7.51 (m, 6H); $^{13}$C NMR (CDCl$_3$) $\delta$ 32.1, 59.0, 109.9, 120.8, 121.5, 123.0, 128.5, 128.9, 130.5, 131.0, 131.7, 137.8, 141.8; IR (CH$_2$Cl$_2$) 3047, 2944, 1463 cm$^{-1}$; HRMS m/z 333.0019 (calcd for C$_{15}$H$_{12}$IN, 333.0015).
3-Iodo-2-phenyl-1-(4-toluenesulfonyl)indole (46). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added 3-iodo-2-phenyl-1H-indole (0.320 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point p-toluenesulfonyl chloride (0.305 g, 1.6 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 14 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried (MgSO$_4$), and the solvent removed under reduced pressure. The residue was purified by column chromatography using 5:1 hexanes/ethyl acetate to afford 0.30 g (68 %) of the desired compound 46 as a white solid: mp 118-120 °C; $^1$H NMR (CDCl$_3$) δ 2.32 (s, 3H), 7.07-7.10 (m, 2H), 7.30-7.50 (m, 10H), 8.30 (dt, $\delta$ = 8.1, 0.9 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 21.8, 76.0, 116.2, 122.4, 124.9, 126.3, 127.1, 127.7, 129.5, 129.7, 131.8, 132.0, 132.5, 135.3, 137.2, 141.3, 145.2; IR (CH$_2$Cl$_2$) 3065, 2982, 1377, 1260, 1178 cm$^{-1}$; HRMS m/z 472.9955 (calcd for C$_{15}$H$_{12}$O$_2$, 472.9946).

3-(2-Bromophenyl)-1-(4-toluenesulfonyl)indole (47). This indole derivative was prepared by a selective Suzuki-Miyaura cross-coupling reaction as follows. 2-Bromophenyboronic acid (0.221 g, 1.1 mmol), 3-iodo-1-(4-toluenesulfonyl)indole$^{45}$ (0.3974 g, 1.0 mmol) [mp 130-131 °C; $^1$H NMR (CDCl$_3$) δ 2.31 (s, 3H), 7.20 (d, $\delta$ = 8.0 Hz, 2H), 7.28-7.36 (m, 3H), 7.68 (s, 1H), δ 7.75-7.77 (m, 2H), 7.93-7.96 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 21.7, 66.9, 113.4, 122.0, 124.0, 125.7, 127.0, 129.8, 130.1, 132.5, 134.4, 134.9, 145.4], CsF (0.304 g, 2.0 mmol), Pd(dba)$_2$ (0.0288 g, 0.05 mmol), and PPh$_3$ (0.026 g, 0.1 mmol) in DME (5 mL) were stirred under Ar at 90 °C for 5 h. The reaction mixture was diluted with diethyl
ether (50 mL) and washed with brine (30 mL). The organic layer was dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 5:1 hexanes/ethyl acetate to afford 0.349 g (82%) of the desired compound 47 as a clear oil: ¹H NMR (CDCl₃) δ 2.32 (s, 3H), 7.20-7.25 (m, 4H), 7.34-7.42 (m, 4H), 7.71 (dd, J = 8.0, 1.2 Hz, 1H), 7.75 (s, 1H), 7.80-7.83 (m, 2H), 8.04 (d, J = 8.4 Hz, 1H); ¹³C NMR (CDCl₃) δ 21.6, 113.8, 120.8, 122.6, 123.5, 123.9, 124.9, 125.4, 127.0, 127.5, 129.4, 130.0, 130.1, 132.0, 133.5, 133.6, 134.8, 135.2, 145.1; IR (CH₂Cl₂) 3066, 2981, 1373, 1177 cm⁻¹; HRMS m/z 425.0091 (calcd for C₁₅H₁₂O₂, 425.0085).

2-Iodo-1,2,2-triphenylethene (51). This vinylic iodide was prepared by the procedure of Miller et al.²⁸

5-Iodo-6-phenyldibenz[6/|oxepme (52). This vinylic iodide was prepared by the procedure of Kitamura et al.²⁹ The spectral properties were identical to those previously reported.²⁹

4-Iodo-3-phenylisocoumarin (54). To a solution of methyl 2-(phenylethynyl)benzoate⁴⁶ (0.0708 g, 0.3 mmol) in CH₂Cl₂ (3 mL) under Ar was added ICl (0.0584 g, 0.36 mmol) in CH₂Cl₂ (0.5 mL) dropwise via syringe. The reaction was stirred for 30 min at room temperature then diluted with diethyl ether (50 mL), washed with 10 % aq Na₂S₂O₃ (25 mL), dried (MgSO₄), and filtered. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography using 10:1 hexanes/ethyl acetate to afford 94.6 mg (90%) of the indicated compound 54 as a white solid: mp 169-170 °C; ¹H NMR (CDCl₃) δ 7.47-7.49 (m, 3H), 7.59 (t, J = 7.8 Hz, 1H), 7.68-7.71 (m, 2H), 7.83-7.92 (m, 2H), 8.31 (d, J = 7.5 Hz, 1H); ¹³C NMR (CDCl₃) δ 76.7, 120.5, 128.3, 129.5, 129.9,
130.2, 130.4, 131.7, 135.4, 135.9, 138.4, 155.0, 161.7; IR (CH\textsubscript{2}Cl\textsubscript{2}) 1736 cm\textsuperscript{-1}; HRMS m/z 347.9652 (calcd for C\textsubscript{15}H\textsubscript{10}I\textsubscript{2}, 347.9647).

3-Iodo-4-phenylisocoumarin (56). To a solution of 4-phenyl-3-(trimethylsilyl)isocoumarin\textsuperscript{47} (0.441 g, 1.5 mL) and I\textsubscript{2} (1.14 g, 4.5 mmol) in CH\textsubscript{3}CN (15 mL) under Ar was added AgOTf (0.78 g, 3.0 mmol) in CH\textsubscript{3}CN (5 mL) at room temperature. The reaction mixture was stirred at 55 °C for 5 d. The mixture was allowed to cool to room temperature, diluted with diethyl ether (100 mL), and filtered. The filtrate was washed with 10 % aq Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} (25 mL) and the organic layer dried (MgSO\textsubscript{4}), and filtered. The solvent was evaporated under reduced pressure and the residue purified by column chromatography using 9:1 hexanes/ethyl acetate to afford 501 mg (96 %) of the indicated compound 56 as a white solid: mp 170-171 °C; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta \) 6.98 (d, \( J = 12.0 \) Hz, 1H), 7.27 (dd, \( J = 7.6, 2.0 \) Hz, 2H), 7.50-7.63 (m, 5H), 8.31 (dd, \( J = 8.0, 0.8 \) Hz, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \( \delta \) 107.9, 119.6, 125.6, 127.4, 128.7, 128.9, 129.1, 129.9, 130.5, 135.2, 137.0, 137.3, 161.2.

1-Iodo-2-phenylcyclohexene (58). This vinylic iodide was prepared by the procedure of Larock et al.\textsuperscript{30}

1-Benzyl-2-iodobenzene (60). To a solution of 2-iodobenzyl bromide (1.485 g, 5.0 mmol) in benzene (25 mL) was added AgClO\textsubscript{4} (2.07 g, 10 mmol) at room temperature and stirred for 7 h. The resulting mixture was filtered and diluted with Et\textsubscript{2}O (30 mL). The organic layer was washed twice with H\textsubscript{2}O (30 mL), dried (MgSO\textsubscript{4}), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 50:1 hexanes/ethyl acetate to obtain 1.529 g (86 %) of the desired product 60 as a clear oil with spectral properties identical to those previously reported.\textsuperscript{34}
(2-Iodophenyl)phenyl ether (62). Compound 62 was prepared by the procedure of Kitamura et al.29

1-(2-Bromobenzyl)indole (64). Compound 64 was prepared by the procedure of Kozikowski et al.35

General Procedure for the Pd-Catalyzed Cyclocarbonylation of o-Halobiaryls. DMF (6 mL), Pd(PCy3)2 (8.4 mg, 0.0125 mmol), anhydrous cesium pivalate (0.117 g, 0.5 mmol), and the o-halobiaryl (0.25 mmol) were stirred under an Ar atmosphere at room temperature for 5 min. The mixture was flushed with CO and fitted with a CO filled balloon. The reaction mixture was heated to 110 °C with vigorous stirring for 7 h. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO4), filtered and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

Fluoren-9-one (2). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 45.1 mg (100 %) of the indicated compound as a yellow solid: mp 82-83 °C. This compound was identified by comparing the 1H NMR and 13C NMR spectra and melting point with an authentic sample obtained from Aldrich Chemical Co., Inc.

2-Methyfluoren-9-one (5). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 47.1 mg (97 %) of the indicated compound as a yellow solid: mp 90-91 °C (lit.48 mp 92 °C); 1H NMR (CDCl3) δ 2.33 (s, 3H), 7.19-7.24 (m, 2H), 7.33 (d, J = 7.6 Hz, 1H), 7.04- 7.41 (m, 3H), 7.58 (d, J = 7.2 Hz, 1H); 13C NMR (CDCl3) δ 21.4, 120.0,
120.2, 124.2, 125.0, 128.6, 134.3, 134.4, 134.7, 135.1, 139.3, 141.8, 144.7, 194.2. The spectral properties were identical to those previously reported.

2-Methoxyfluoren-9-one (7). The reaction mixture was chromatographed using 6:1 hexanes/ethyl acetate to afford 52.6 mg (100 %) of the indicated compound as a yellow solid: mp 78-79 °C (lit. mp 78 °C); ¹H NMR (CDCl₃) δ 3.82 (s, 3H), 6.94 (dd, J = 8.4, 2.8 Hz, 1H), 7.14-7.18 (m, 2H), 7.34-7.41 (m, 3H), 7.56 (d, J = 7.6 Hz, 1H); IR (CH₂Cl₂) 1717 cm⁻¹. The spectral properties were identical to those previously reported.

2-Methoxymethylfluoren-9-one (9). The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 56.0 mg (100 %) of the indicated compound as a yellow oil: ¹H NMR (CDCl₃) δ 3.41 (s, 3H), 4.46 (s, 2H), 7.26-7.30 (m, 1H), 7.45-7.50 (m, 4H), 7.62-7.65 (m, 2H); ¹³C NMR (CDCl₃) δ 58.3, 74.1, 120.3, 123.6, 124.4, 129.1, 133.9, 134.4, 134.4, 134.8, 139.8, 143.9, 144.3, 193.8 (missing one sp² carbon due to overlap); IR (CH₂Cl₂) 3054, 2930, 1718 cm⁻¹; HRMS m/z 224.0840 (calcd for C₁₅H₁₂O₂, 224.0837).

9-Oxofluorene-2-carbaldehyde (11). The reaction mixture was chromatographed using 2:1 hexanes/ethyl acetate to afford 52.0 mg (100 %) of the indicated compound as a yellow solid: mp 204-205 °C (lit. mp 203-204 °C); ¹³C NMR (CDCl₃) δ 121.0, 121.7, 125.0, 130.8, 135.0, 135.1, 135.4, 136.4, 137.5, 143.3, 149.9, 190.8, 192.4. The spectral properties were identical to those previously reported.

3-Methylfluoren-9-one (13). The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 43.7 mg (90 %) of the indicated compound as a yellow solid: mp 66-67 °C (lit. mp 65 °C); ¹³C NMR (CDCl₃) δ 22.2, 120.1, 121.3, 124.2, 124.3, 129.0,
The other spectral properties were identical to those previously reported.\textsuperscript{52}

1-Methylfluoren-9-one (14). The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 4.9 mg (10\%) of the indicated compound as a yellow solid: mp 98-99 \degree C (lit.\textsuperscript{53} mp 98-99 \degree C). The spectral properties were identical to those previously reported.\textsuperscript{53}

9-Oxofluorene-3-carbaldehyde (16) and 9-oxofluorene-1-carbaldehyde (17). The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 48.9 mg (94\%) of the indicated compounds as a 9:1 inseparable mixture of isomers (the ratio was determined by \textsuperscript{1}H NMR spectroscopic analysis). 9-Oxofluorene-1-carbaldehyde (minor isomer): \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \delta 11.06 (s, 1H) (as a characteristic peak); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \delta 120.7, 124.9, 125.2, 126.3, 130.0, 133.6, 134.0, 134.7, 135.6, 143.8, 144.5, 145.0, 190.5, 194.4; IR (CH\textsubscript{2}Cl\textsubscript{2}) 1695, 1711 cm\textsuperscript{-1}; HRMS m/z 208.05281 (calcd for C\textsubscript{14}H\textsubscript{8}O\textsubscript{2}, 208.05243). 9-Oxofluorene-3-carbaldehyde (major isomer). This isomer was purified by recrystallization from hexanes/ethyl acetate to afford 29.2 mg (56\%) of the desired compound as a yellow solid: mp 148-149 \degree C (lit.\textsuperscript{54} mp 149-150 \degree C); \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \delta 7.37 (td, J = 7.5, 1.2 Hz, 1H), 7.57 (td, J = 7.5, 1.2 Hz, 1H), 7.62-7.64 (m, 1H), 7.71 (d, J = 7.5 Hz, 1H), 7.82-7.82 (m, 2H), 8.03 (t, J = 0.9, 1H), 10.10 (s, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \delta 119.7, 121.2, 124.8, 125.0, 130.1, 132.7, 134.4, 135.7, 138.8, 141.2, 143.6, 145.2, 191.7, 193.0; IR (CHCl\textsubscript{3}) 1719, 1701 cm\textsuperscript{-1}; HRMS m/z 208.05281 (calcd for C\textsubscript{14}H\textsubscript{8}O\textsubscript{2}, 208.05243).

1-Methoxyfluoren-9-one (19). The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 52.0 mg (99\%) of the indicated compound as a yellow solid:
mp 142-143 °C (lit.\textsuperscript{55} mp 141-142 °C); \textsuperscript{1}H NMR (CDCl\textsubscript{3}) δ 3.97 (s, 3H), 6.81 (d, J = 8.1 Hz, 1H), 7.11 (dd, J = 7.2, 0.6 Hz, 1H), 7.27 (td, J = 6.9, 1.2 Hz, 1H), 7.40-7.49 (m, 3H), 7.63 (dt, J = 7.2, 1.0 Hz, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 56.2, 113.1, 113.3, 120.3, 120.4, 124.1, 129.4, 134.1, 134.7, 137.0, 143.4, 146.7, 158.6, 187.5. The spectral properties were identical to those previously reported.\textsuperscript{55}

**Indene[1,2-f]phenanthrene-13-one (21).** The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 68.7 mg (98 %) of the indicated compound as an orange solid: mp 183-184 °C (ethanol/acetone) (lit.\textsuperscript{11} mp 185-187 °C); \textsuperscript{1}H NMR (CDCl\textsubscript{3}) δ 7.25-7.34 (m, 1H), 7.48 (td, J = 8.2, 1.2 Hz, 1H), 7.62-7.79 (m, 5H), 8.02 (d, J = 7.5 Hz, 1H), 8.57-8.63 (m, 2H), 8.70 (d, J = 8.1 Hz, 1H), 9.21-9.24 (m, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 122.8, 123.5, 123.7, 124.0, 125.5, 125.9, 126.2, 127.4, 127.5, 127.7, 127.8, 128.6, 129.0, 129.4, 131.2, 134.1, 134.5, 134.8, 144.0, 144.8, 196.0. The spectral properties were identical to those previously reported.\textsuperscript{11}

**Benzo[c]fluoren-7-one (23).** The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 55.3 mg (96 %) of the indicated compound as an orange solid: mp 160-161 °C (lit.\textsuperscript{13} mp 161-162 °C). The spectral properties were identical to those previously reported.\textsuperscript{13}

**11-Oxoindeno[1,2-c]isoquinoline (25).** The reaction mixture was chromatographed using 1:1 hexanes/ethyl acetate to afford 54.9 mg (95 %) of the indicated compound as a yellow solid: mp 198-200 °C (lit.\textsuperscript{14} mp 199-200 °C); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 119.8, 120.7, 123.6, 123.9, 127.7, 128.8, 129.3, 130.6, 132.6, 133.6, 134.7, 135.0, 143.9, 158.4, 162.5, 194.2. The spectral properties were identical to those previously reported.\textsuperscript{14}
[2,2']Bifluorenyl-9,9'-dione (27). In order to keep the equiv of aryl halide consistent, we employed 0.125 mmol of aryl dibromide 26 and the reaction period was extended to 14 h. The reaction mixture was diluted with water (20 mL) and a yellow solid crystallized from the reaction mixture. The solid was filtered and washed with water (10 mL) and then ethanol (5 mL) to yield 0.039 g (87%) of the desired compound 27. The indicated compound was further purified by crystallization from CHCl₃/toluene to afford a green-yellow solid: mp 295-296 °C (lit. mp 295-297 °C); ¹H NMR (CDCl₃) δ 7.33 (t, J = 7.2 Hz, 1H), 7.55-7.63 (m, 3H), 7.70 (d, J = 6.8 Hz, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.93 (s, 1H); ¹³C NMR and IR were not obtained for this compound due to its poor solubility in common organic solvents; HRMS m/z 358.1001 (calcd for C₂₆H₁₄O₂, 358.0994).

Benz[6]indeno[1,2-f]furan-6-one (31). The reaction mixture was chromatographed using 7:1 hexanes:ethyl acetate to afford 44.6 mg (81%) of the indicated compound as an orange solid: mp 109-110 °C; ¹H NMR (CDCl₃) δ 7.12-7.18 (m, 2H), 7.29-7.38 (m, 3H), 7.44 (td, J = 7.8, 1.2 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.71 (dd, J = 8.0, 0.4 Hz, 1H); ¹³C NMR (CDCl₃) δ 113.8, 120.3, 122.0, 124.1, 124.8, 128.6, 128.7, 133.9, 134.9, 136.0, 141.4, 154.6, 161.6, 180.7; IR (CH₂Cl₂) 3025, 1714 cm⁻¹; HRMS m/z 220.0526 (calcd for C₁₅H₈O₂, 220.0524).

10-Oxo-10-H-benz[b]inden[1,2-d]thiophene (33). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 39.6 mg (67%) of the indicated compound as an orange solid: mp 203-204 °C (lit. mp 205-206 °C); ¹H NMR (CDCl₃) δ 7.17-7.49 (m, 6H), 7.76-7.80 (m, 1H), 8.10-8.14 (m, 1H); ¹³C NMR (CDCl₃) δ 120.4, 123.1,
123.3, 123.7, 125.5, 126.8, 129.7, 132.6, 133.8, 135.0, 137.1, 138.8, 144.2, 162.4, 187.4; IR (CH₂Cl₂) 1718, 1697, 1608 cm⁻¹; HRMS m/z 236.03008 (calcd for C₁₃H₈OS, 236.02959).

**Indeno[2,1-d]thiophen-8-one (35).** The reaction period was extended to 14 h. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 40.1 mg (86 %) of the indicated compound as a yellow solid: mp 109-110 °C (lit. mp 107-110 °C); ¹³C NMR (CDCl₃) δ 119.7, 120.3, 124.1, 128.2, 133.8, 137.1, 138.0, 139.3, 139.8, 158.8, 185.7. The other spectral properties were identical to those previously reported.²²

**Pyrrolo[1,2-a]indol-9-one (37).** The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 40.5 mg (96 %) of the indicated compound as a yellow solid: mp 121-122 °C (lit. mp 119.5-121.5 °C); ¹³C NMR (CDCl₃) δ 110.5, 114.2, 116.2, 119.7, 124.7, 125.7, 130.5, 132.2, 134.4, 144.0, 179.9. The other spectral properties were identical to those previously reported.²³

**5H-Indeno[2,1-b]indol-6-one (39).** This compound was prepared from compound 47. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 30.6 mg (55 %) of the indicated compound as a purple solid: mp 259-260 °C; ¹H NMR (CDCl₃) δ 7.02 (t, J = 7.4 Hz, 1H), 7.15 (t, J = 7.4 Hz, 1H), 7.21 (d, J = 6.8 Hz, 1H), 7.25-7.38 (m, 4H), 7.83 (d, J = 8.0 Hz, 1H) (missing one proton due to exchange); ¹³C NMR (CDCl₃) δ 114.8, 119.9, 121.1, 121.9, 122.4, 123.6, 126.7, 127.2, 134.4, 134.8, 136.9, 140.6, 143.4, 184.1 (missing one sp² carbon due to overlap); IR (CH₂Cl₂) 3444, 3055, 1705 cm⁻¹; HRMS m/z 219.0686 (calcd for C₁₃H₈NO, 219.0684).

**5-Methyl-5H-indeno[2,1-b]indol-6-one (41).** The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 28.5 mg (49 %) of the indicated
compound as a dark red solid: mp 145-146 °C (lit.\textsuperscript{7b,25} mp 147-148 °C); \textsuperscript{1}H NMR (CDCl\textsubscript{3}) δ 3.87 (s, 3H), 6.94-6.99 (m, 1H), 7.08-7.10 (m, 1H), 7.14-7.20 (m, 1H), 7.22-7.30 (m, 4H), 7.65 (dt, $J = 8.1, 1.1$ Hz, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 30.8, 111.7, 119.2, 121.4, 121.9, 122.1, 123.7, 126.2, 126.6, 133.7, 134.1, 137.4, 140.6, 144.1, 147.2, 185.0; IR (CH\textsubscript{2}Cl\textsubscript{2}) 3054, 1704 cm\textsuperscript{-1}; HRMS m/z 233.0843 (calcd for C\textsubscript{16}H\textsubscript{14}NO, 233.0841).

**5H-Indeno[1,2-b]indol-10-one (43).** This compound was prepared from compound 46. The reaction mixture was chromatographed using 2:1 hexanes/ethyl acetate to afford 24.9 mg (45 %) of the indicated compound as a red solid: mp 334-336 °C (sublimes) (lit.\textsuperscript{27} mp 333-336 °C); \textsuperscript{13}C NMR (DMSO-d\textsubscript{6}) δ 114.4, 114.8, 119.8, 120.0, 123.1, 123.2, 123.6, 123.8, 130.5, 133.3, 135.3, 141.1, 142.5, 159.3, 185.2. The other spectral properties were identical to those previously reported.\textsuperscript{27}

**5-Methyl-5H-indeno[1,2-b]indol-10-one (45).** The reaction mixture was chromatographed using 2:1 hexanes/ethyl acetate to afford 12.2 mg (21 %) of the indicated compound as a red solid: mp 217-218 °C (lit.\textsuperscript{26} mp 216-218 °C). The spectral properties were identical to those previously reported.\textsuperscript{26}

**2,3-Diphenyl-1-indenone (49).** The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 57.2 mg (81 %) of the indicated compound as a red solid: mp 152-153 °C. This compound was identified by comparing the \textsuperscript{1}H NMR and \textsuperscript{13}C NMR spectra and melting point with an authentic sample obtained from Aldrich Chemical Co., Inc.

**2,3-Diphenyl-1-indenone (49) and triphenylethene (50).** These two compounds were obtained from the cyclocarbonylation of compound 51. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 43.0 mg (61 %) of the indenone
as a red solid, mp 152-153 °C; in addition, 15.4 mg (24 %) of compound 50 were isolated from the reaction mixture as a white solid, mp 68-69 °C. Compound 50 was identified by comparing the 'H NMR and 13C NMR spectra and melting point with an authentic sample obtained from Aldrich Chemical Co., Inc.

**Indeno[5,6]dibenz[b,f]oxepin-14-one (53).** The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 58.9 mg (80 %) of the indicated compound as a red solid: mp 162-164 °C; 'H NMR (CDCl₃) δ 7.22-7.47 (m, 8H), 7.49-7.55 (m, 1H), 7.60-7.63 (m, 1H), 7.75 (dd, J = 7.8, 1.5 Hz, 1H), 7.90-7.93 (m, 1H); 13C NMR (CDCl₃) δ 121.3, 121.9, 122.7, 123.7, 125.4, 125.4, 125.6, 126.8, 127.7, 129.5, 129.7, 130.0, 130.7, 131.9, 133.1, 133.7, 143.4, 153.2, 157.9, 158.8, 195.3; IR (CH₂Cl₂) 3076, 1707 cm⁻¹; HRMS m/z 296.0842 (calcd for C₂₁H₁₂O₂, 296.0837).

**1,2,3,4-Tetrahydrofluoren-9-one (59).** The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 15.7 mg (34 %) of the indicated compound 59 as a yellow oil with spectral properties identical to those previously reported.³¹

**6-H-Isoidolo[2,1a]indole (65).** The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 58.9 mg (70 %) of the indicated compound as a white solid: mp 226-228 °C (lit.³⁷ mp 209-211 °C) with spectral properties identical to those previously reported.³⁷

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and PPh₃.

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CHAPTER 2. NOVEL 1,4-PALLADIUM MIGRATION IN ORGANOPALLADIUM INTERMEDIATES DERIVED FROM o-HALOBIARYLS

Based on a communication published in the *Journal of the American Chemical Society* and a paper to be published in the *Journal of the American Chemical Society*

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Abstract

A novel 1,4-palladium migration between the o- and o’-positions of biaryls has been observed in organopalladium intermediates derived from o-halobiaryls. The organopalladium intermediates generated by this palladium migration have been trapped by way of a Heck reaction with ethyl acrylate and a Suzuki cross-coupling with arylboronic acids. The ratios of Heck and Suzuki products indicate that palladium has a tendency to migrate from a more electron-poor to a more electron-rich position in the biaryl.

Introduction

The extraordinary C-C bond forming ability of palladium places it among the most versatile and useful metals in organic synthesis. Organopalladium intermediates are often prepared by oxidative addition of an organic halide or triflate to Pd(0) and subsequent C-C bond formation normally occurs at the position originally occupied by the halogen or triflate.
Among the most important Pd-catalyzed C-C bond forming reactions is the Heck reaction for which there are numerous applications in the literature,\textsuperscript{1} including a few employing o-bromobiphenyls.\textsuperscript{2}

To our surprise, upon studying the palladium-catalyzed olefination of unsymmetrical o-halobiphenyls with ethyl acrylate, we obtained, under certain modified reaction conditions, the expected o-olefinated biphenyl (2) along with the o'-olefinated biphenyl (3) (Scheme 1).\textsuperscript{3}

Scheme 1

\[
\begin{align*}
\text{Y} & \quad \text{Y} \\
\text{1} & \quad \text{1,4-Pd shift} \\
\text{Pd(0)} & \quad \text{Pd(0)} \\
\text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{2} & \quad \text{3}
\end{align*}
\]

The observed mixture of Heck products points to the existence of arylpalladium intermediates in which the metal moiety is located in each of the two different ortho positions of the unsymmetrical biphenyl. This through-space relocation of the metal moiety between the ortho positions of biaryls amounts to an overall 1,4-palladium shift. The novel palladium migration observed in our o-halobiaryl systems has also been simultaneously reported by Gallagher, et al., who studied the Heck reaction of pyridine-containing biaryls.\textsuperscript{4} However, the results reported by Gallagher suggested that palladium migration occurred only in minor amounts in such biaryls, and that electron-withdrawing nitro groups were critical to migration. Furthermore, Larock, et al. have previously proposed a vinylic to aryl palladium migration to account for the formation of 9-benzylidene-9H-fluorene from diphenylacetylene.
and iodobenzene (Scheme 2). We now wish to report the full details of this novel palladium aryl to aryl migration chemistry.

Scheme 2

\[
\text{Phi} + \text{Ph} \xrightarrow{\text{cat. Pd, base}} \text{Ph} \begin{array}{c} \text{Pdl} \\ \text{Ph} \end{array} \xrightarrow{\text{H}} \text{Ph} \begin{array}{c} \text{Pdl} \\ \text{Ph} \end{array} \rightarrow \text{Ph} \begin{array}{c} \text{H} \\ \text{Ph} \end{array} 62\%
\]

Results and Discussion

In order to obtain a clear picture of how various reaction variables affect the palladium biaryl migration, we have studied the behavior of 2-iodo-4′-methylbiphenyl (1a) and ethyl acrylate under various reaction conditions (Table 1). We have found that under the classical reaction conditions described by Jeffrey, the expected ethyl E-3-(4′-methylbiphen-2-yl)acrylate (2a) was obtained exclusively in a quantitative yield (Table 1, entry 1). By simply diluting the reaction mixture 4-fold, we began to observe small amounts of the migration product ethyl E-3-(4-methylbiphen-2-yl)acrylate (3a) (entry 2), and 23% of 3a was obtained under the more dilute conditions obtained by reducing the number of equivalents of ethyl acrylate from 4 to 1 (entry 3). We have obtained almost equal amounts of the direct olefination product 2a and the rearranged product 3a when using CsO₂CCMe₃ (CsPiv) as the base (entry 4). Furthermore, under these conditions, the n-Bu₄NCl (TBAC) additive was unnecessary to achieve virtually the same results (entry 5). The use of phosphine ligands, such as 1,1-bis(diphenylphosphino)methane (dppm) and PPh₃, in the reaction further changed the isomer distribution to 50:50 (entries 6 and 7). The solubility of
the base in the reaction mixture seems to play a critical role in determining the isomer distribution. Thus, under identical conditions CsPiv, CsOAc, and NaOAc, which are listed in decreasing order of apparent solubility in DMF, gave decreasing amounts of isomer 3a (entries 6, 8 and 9). To further illustrate this phenomenon, we have run the reaction under our standard migration conditions, but used a less polar solvent toluene in which the CsPiv base has a much lower solubility than in DMF, and we obtained only 25% of 3a (entry 10 versus entry 6). The use of Et₃N as a base completely inhibited the migration process. Using Et₃N instead of CsPiv

Table 1. Pd-Catalyzed reaction of 2-iodo-4′-methylbiphenyl (1a) and ethyl acrylate (EA).a

<table>
<thead>
<tr>
<th>entry</th>
<th>equiv EA</th>
<th>conditions</th>
<th>time (d)</th>
<th>mol ratio 2a:3a</th>
<th>% yield</th>
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<td>1</td>
<td>4</td>
<td>TBAC, NaHCO₃c</td>
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<td>100:0</td>
<td>100</td>
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<td>4</td>
<td>TBAC, NaHCO₃</td>
<td>1.0</td>
<td>95:5</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>TBAC, NaHCO₃</td>
<td>1.0</td>
<td>77:23</td>
<td>92</td>
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<tr>
<td>4</td>
<td>1</td>
<td>TBAC, CsPiv</td>
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<td>55:45</td>
<td>89</td>
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<tr>
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<td>1</td>
<td>CsPiv</td>
<td>1.5</td>
<td>54:46</td>
<td>93</td>
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<td>6</td>
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<td>50:50</td>
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<td>87</td>
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<td>8</td>
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<td>5% dppm, CsOAc</td>
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<td>90</td>
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<td>5% dppm, Et₃N</td>
<td>1.0</td>
<td>100:0</td>
<td>90</td>
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</table>

aThe reaction was run using 0.25 mmol of the iodobiaryl, ethyl acrylate (EA), 2 equiv of an appropriate base, and 1 equiv of n-Bu₄NCl (TBAC) where indicated in 4 ml of DMF at 100 °C unless otherwise indicated. bThe mole ratio was determined by ¹H NMR spectroscopic analysis. cOne mL of DMF as solvent. dFour mL of toluene as solvent.
and conditions identical to those of entry 6, we obtained isomer 2a exclusively in a 90% yield (entry 11). It is important to note at this point that by manipulating the reaction conditions, we can switch the palladium migration "on" or "off" in this biphenyl system. Thus, our optimal migration conditions for activating palladium migration are those described in entry 6 of Table 1 (conditions A), and the conditions to prevent this process are those described in entry 1. Furthermore, it turned out that ethyl acrylate was superior to other olefins as a Heck trap. For instance, the reaction of 1a with either methyl vinyl ketone or styrene under conditions A favoring migration gave complex mixtures and no desired Heck products were isolated.

To investigate whether palladium migration will also occur with less reactive o-bromobiphenyls, we examined the Heck reaction of 2-bromo-4'-methylbiphenyl (1a') and ethyl acrylate under various reaction conditions (Table 2). We first carried out the reaction of 1a' under migration conditions A, but failed to observe any significant amount of Heck products after 3 days (entry 1, Table 2). In attempting to promote the reaction, we increased the temperature from 100 °C to 110 °C, but TLC analysis of the reaction mixture indicated that 1a' had failed to react (entry 2). We then resorted to the use of highly active palladium catalyst systems employing a combination of 5 mol % Pd(OAc)₂ and 10 mol % of a hindered, electron-rich phosphine ligand, such as 2-(di-r-butylphosphino)biphenyl or 2-(dicyclohexylphosphino)biphenyl. Unfortunately, the results were unfruitful (entries 3 and 4). Similarly, the use of air-stable and highly active Pd(di-r-butylphosphinous acid)₂Cl₂ as catalyst failed to promote the Heck reaction of 1a' (entry 5). It is somewhat surprising that the palladium catalysts described in entries 3-5 failed to promote the Heck reaction of 2-
bromo-4'-methylbiphenyl with ethyl acrylate, especially since these catalysts have been reported to activate aryl bromides, as well as aryl chlorides, towards Negishi, Suzuki, and amination reactions. \(^7\) Fortunately, we were able to circumvent the poor reactivity of 2-bromo-4'-methylbiphenyl by simply carrying the reaction out under conditions A, but we replaced the DMF solvent with wet DMF (5 % \(\text{H}_2\text{O}\) by volume) as the reaction solvent. Thus, compound 1a' produced a 50:50 mixture of 2a and 3a in a 49 % yield along with 45 %

**Table 2.** Pd-Catalyzed reaction of 2-bromo-4'-methylbiphenyl (1a') and ethyl acrylate.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>conditions</th>
<th>mol ratio 2a:3a(^b)</th>
<th>% yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 % dppm, 2.0 CsPiv, DMF (4 mL), 100 °C, 3 d</td>
<td>-</td>
<td>trace</td>
</tr>
<tr>
<td>2</td>
<td>5 % dppm, 2.0 CsPiv, DMF (4 mL), 110 °C, 2 d</td>
<td>-</td>
<td>trace</td>
</tr>
<tr>
<td>3</td>
<td>10 % 2-(di-r-butylphosphino)biphenyl, 2.0 CsPiv, DMF (4 mL), 100 °C, 2 d</td>
<td>-</td>
<td>trace</td>
</tr>
<tr>
<td>4</td>
<td>10 % 2-(dicyclohexylphosphino)biphenyl, 2.0 CsPiv, DMF (4 mL), 100 °C, 2 d</td>
<td>-</td>
<td>trace</td>
</tr>
<tr>
<td>5</td>
<td>5 % Pd(di-r-butylphosphinous acid)(_2)Cl(_2), 2.0 CsPiv, DMF (4 mL), 100 °C, 2 d</td>
<td>-</td>
<td>trace</td>
</tr>
<tr>
<td>6</td>
<td>5 % dppm, 2.0 CsPiv, DMF (3.8 mL), (\text{H}_2\text{O}) (0.2 mL) 100 °C, 1 d</td>
<td>49 (45)(^d)</td>
<td>50:50</td>
</tr>
<tr>
<td>7(^e)</td>
<td>5 % dppm, 2.0 CsPiv, DMF (3.8 mL), (\text{H}_2\text{O}) (0.2 mL), 100 °C, 1 d</td>
<td>85</td>
<td>50:50</td>
</tr>
</tbody>
</table>

\(^a\)The reaction was run using 0.25 mmol of the bromobiphenyl. \(^b\)The mole ratio was determined by \(^1\)H NMR spectroscopic analysis. \(^c\)The Pd(OAc)\(_2\) catalyst was omitted. \(^d\)The yield in parentheses corresponds to the amount of isolated 4-methylbiphenyl. \(^e\)Compound 1a was used in place of 1a'.
of 4-methylbiphenyl\textsuperscript{9}, which corresponds to the product arising from C-Br reduction to a C-H bond (entry 6). We were also pleased to find that 2-iodo-4'-methylbiphenyl and ethyl acrylate reacted under the reaction conditions described in entry 6 of Table 2 to produce a 50:50 mixture of 2a and 3a in an 85 % yield (entry 7), verifying that 1a and 1a' generate identical mixtures of 2a and 3a. Thus far, two sets of migration reaction conditions have been developed, namely conditions A, which are described in entry 6 of Table 1, and conditions B, which are described in entry 6 of Table 2.

An obvious question to answer is whether under our standard reaction conditions 2-iodo-4-methylbiphenyl (4a) and ethyl acrylate would generate the same distribution of isomers 2a and 3a as previously obtained from 1a and ethyl acrylate. Indeed, substrate 4a generated a 49:51 mixture of isomers 2a and 3a in an 86 % yield under our optimized migration conditions A (entry 6, Table 3). This interesting result seems to indicate that under our reaction conditions, the arylpalladium intermediates generated from either 1a or 4a undergo apparent equilibration prior to olefin-trapping to generate essentially identical mixtures of 2a and 3a (compare entries 5 and 6 of Table 3). Once again, we can suppress the Pd migration by carrying the reaction out under the conditions described by Jeffrey (Table 4). Thus, 2-iodo-4-methylbiphenyl (4a) produced 3a exclusively in a 93 % yield under the Jeffrey conditions (entry 6, Table 4).

In order to examine a possible correlation between electronic effects in the o-halobiphenyls and the ratio of Heck products they produce, we studied the reaction of various p-substituted o-halobiphenyls with ethyl acrylate under our standard migration conditions
Table 3. Heck reaction of $p$-substituted $o$-halobiphenyls with ethyl acrylate under Pd-migration conditions.\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>Y</th>
<th>X</th>
<th>time (d)</th>
<th>% yield</th>
<th>mol ratio 2:3\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>Me</td>
<td>I</td>
<td>1.5</td>
<td>88</td>
<td>50:50</td>
</tr>
<tr>
<td>2</td>
<td>4a</td>
<td>Me</td>
<td>I</td>
<td>1.5</td>
<td>86</td>
<td>49:51</td>
</tr>
<tr>
<td>3</td>
<td>1b</td>
<td>NMe\textsubscript{2}</td>
<td>I</td>
<td>1</td>
<td>90</td>
<td>55:45</td>
</tr>
<tr>
<td>4</td>
<td>4b</td>
<td>NMe\textsubscript{2}</td>
<td>I</td>
<td>1.5</td>
<td>93</td>
<td>49:51</td>
</tr>
<tr>
<td>5</td>
<td>1c</td>
<td>OMe</td>
<td>I</td>
<td>2</td>
<td>93</td>
<td>52:48</td>
</tr>
<tr>
<td>6</td>
<td>4c</td>
<td>OMe</td>
<td>I</td>
<td>2</td>
<td>92</td>
<td>48:52</td>
</tr>
<tr>
<td>7</td>
<td>1d</td>
<td>CO\textsubscript{2}Et</td>
<td>Br</td>
<td>1\textsuperscript{c}</td>
<td>45 (45)\textsuperscript{d}</td>
<td>47:53</td>
</tr>
<tr>
<td>8</td>
<td>4d</td>
<td>CO\textsubscript{2}Et</td>
<td>I</td>
<td>1\textsuperscript{c}</td>
<td>83</td>
<td>42:58</td>
</tr>
<tr>
<td>9</td>
<td>1e</td>
<td>NO\textsubscript{2}</td>
<td>I</td>
<td>2.5\textsuperscript{c}</td>
<td>46 (40)\textsuperscript{d}</td>
<td>39:61</td>
</tr>
<tr>
<td>10</td>
<td>4e</td>
<td>NO\textsubscript{2}</td>
<td>I</td>
<td>2.5\textsuperscript{c}</td>
<td>37 (50)\textsuperscript{d}</td>
<td>33:67</td>
</tr>
</tbody>
</table>

\textsuperscript{a}The reaction was run using 0.25 mmol of the halobiphenyl. \textsuperscript{b}The mole ratio was determined by $^1$H NMR spectroscopic analysis. \textsuperscript{c}Wet DMF was used as the reaction solvent: 3.8 mL of DMF plus 0.2 mL of H\textsubscript{2}O (conditions B). \textsuperscript{d}The yield in parentheses indicates the amount of isolated product in which C-X was reduced to C-H.

(Table 3). First of all, we used strong electron-donating dimethylamino-substituted biphenyls. For instance, the reaction of 4'-dimethylamino-2-iodobiphenyl (1b) with ethyl acrylate under migration conditions A produced a 55:45 mixture of isomers 2b and 3b respectively in a 90 % yield (entry 3, Table 3). Similarly, the reaction of 4-dimethylamino-2-iodobiphenyl (4b) and ethyl acrylate produced a 49:51 mixture of 2b and 3b respectively in a 93 % yield (entry 4). Notice that the Heck product ratios obtained from 1b and 4b differ by approximately 6 mol %, indicating that the migration kinetics for the arylpalladium intermediates derived from these dimethylamino-substituted biphenyls is apparently somewhat slower than the kinetics of their
methyl-substituted counterparts. Nevertheless, for practical purposes we can assume that the arylpalladium intermediates generated from 1b and 4b pretty much equilibrate prior to olefin-trapping by ethyl acrylate. Furthermore, we calculated the average ratio of 2b and 3b to be 52:48, indicating only a very slight preference for the formation of isomer 2b. In addition, we suppressed the palladium migration by carrying out the reaction of 1b and 4b under Jeffrey’s reaction conditions (Table 4). Thus, 1b produced 2b exclusively in an 80 % yield, while 4b produced 3b exclusively in a 100 % yield (entries 3 and 4 of Table 4).

Table 4. Heck reaction of p-substituted o-halobiphenyls with ethyl acrylate under Jeffrey’s conditions.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>Y</th>
<th>X</th>
<th>time (d)</th>
<th>% yield</th>
<th>mol ratio 2:3(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>Me</td>
<td>I</td>
<td>1.0</td>
<td>100</td>
<td>100:0</td>
</tr>
<tr>
<td>2</td>
<td>4a</td>
<td>Me</td>
<td>I</td>
<td>1.0</td>
<td>93</td>
<td>0:100</td>
</tr>
<tr>
<td>3</td>
<td>1b</td>
<td>NMe(_2)</td>
<td>I</td>
<td>1.0</td>
<td>80</td>
<td>100:0</td>
</tr>
<tr>
<td>4</td>
<td>4b</td>
<td>NMe(_2)</td>
<td>I</td>
<td>1.0</td>
<td>100</td>
<td>0:100</td>
</tr>
<tr>
<td>5</td>
<td>1c</td>
<td>OMe</td>
<td>I</td>
<td>2.0</td>
<td>100</td>
<td>100:0</td>
</tr>
<tr>
<td>6</td>
<td>4c</td>
<td>OMe</td>
<td>I</td>
<td>2.0</td>
<td>99</td>
<td>0:100</td>
</tr>
<tr>
<td>7</td>
<td>1d</td>
<td>CO(_2)Et</td>
<td>Br</td>
<td>2.0(^c)</td>
<td>77 + 11</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>4d</td>
<td>CO(_2)Et</td>
<td>I</td>
<td>1.0</td>
<td>99</td>
<td>0:100</td>
</tr>
<tr>
<td>9</td>
<td>1e</td>
<td>NO(_2)</td>
<td>I</td>
<td>1.0(^d)</td>
<td>85</td>
<td>100:0</td>
</tr>
<tr>
<td>10</td>
<td>4e</td>
<td>NO(_2)</td>
<td>I</td>
<td>1.0(^d)</td>
<td>89</td>
<td>0:100</td>
</tr>
</tbody>
</table>

\(^a\)The reaction was run using 0.25 mmol of the halobiphenyl. \(^b\)The mole ratio was determined by \(^1\)H NMR spectroscopic analysis. \(^c\)Ten mol % of 2-(di-t-butylphosphino)biphenyl was used as the ligand. \(^d\)2.0 Equiv of Et\(_3\)N were used as the base.
We continued our investigation by examining the reaction of methoxy-substituted biphenyls 1c and 4c under our standard palladium migration conditions A. Thus, compound 1c produced a 52:48 mixture of isomers 2c and 3c respectively in a 93 % yield (entry 5, Table 3), while compound 4c produced a 48:52 mixture of 2c and 3c respectively in a 92 % yield (entry 6, Table 3). These results validate the idea that our migration reaction conditions promote the near equilibration of arylpalladium intermediates derived from methoxy-substituted biphenyls 1b and 4b, and in this case the ratio of Heck products differs by only approximately 4 mol %. Similar to our results with other biphenyls bearing electron-donating substituents, the 50:50 average ratio of Heck products 2c and 3c indicates no preference for the formation of either one of these two isomers. At this point, we conclude that p-substituted biphenyls bearing electron-donating groups, such as Me, MeO, and Me₂N, produce nearly 50:50 mixtures of Heck products. To finalize our examination of the methoxy-substituted biphenyls 1c and 4c, we carried out the Heck reaction under Jeffrey’s conditions (Table 4). Thus, 1b produced 2b in a quantitative yield (entry 5), while 4a gave 3b exclusively in a 99% yield (entry 6).

Next, we switched our attention to the Heck reactions of biphenyls bearing electron-withdrawing substituents. To begin with, we considered the Heck reaction of biphenyls 1d and 4d bearing a CO₂Et group. Although the Pd-catalyzed reactions of 1d and 4d with ethyl acrylate were unsuccessful under migration conditions A, the reaction proceeded smoothly under conditions B. Thus, 1d produced a 47:53 mixture of 2d and 3d in a 45 % yield, along with ethyl 4-phenylbenzoate in 45 % yield, while 4d produced a 42:58 mixture of 2d and 3d in an 83 % yield. Again, we found that the Heck product ratios produced by 1d and 4d
differed by approximately 5 mol %, indicating near equilibration of the corresponding arylpalladium intermediates. Furthermore, the average ratio of 2d and 3d turned out to be 44:56, which indicates that there is a slight tendency for these halobiphenyls to form isomer 3d. Furthermore, the reaction of 1d with ethyl acrylate under Jeffrey's conditions was unsuccessful, but the addition of 2-(dicyclohexylphosphino)biphenyl as a ligand produced 2d in a 77 % yield along with an 11 % yield of isomer 3d (entry 7, Table 4). Thus, under these conditions, some migration appears to be taking place. Similarly, under Jeffrey's reaction conditions, compound 4d produced the expected isomer 3d exclusively in a 99 % yield (entry 8, Table 4).

Finally, the Heck reactions of strong electron-withdrawing nitro-substituted biphenyls 1e and 4e have displayed a trend similar to that observed previously with the ester-substituted biphenyls. For instance, using aqueous DMF (conditions B), 1e generated a 39:61 mixture of 2e and 3e respectively in a 46 % yield, plus a 40 % yield of reduction product (entry 9, Table 3). Under the same conditions, aryl iodide 4e produced a 33:67 mixture of 2e and 3e respectively in a 37 % yield, plus a 50 % yield of the reduction product (entry 11). The average ratio of 2e and 3e is 36:64, which clearly indicates a preference for the formation of isomer 3e arising from the arylpalladium intermediate having the metal moiety located on the nitro-substituted phenyl ring of the biphenyl. It is worth mentioning that under the migration conditions B the Heck reaction of biphenyls 1e and 4e was sluggish. Thus, after the prolonged heating required to complete these reactions, we isolated considerable amounts of 4-nitrobiphenyl (40 % and 50 % yields respectively from 1e and 4e) as a side product arising from reduction of the C-I bond to a C-H bond. On the other hand, aryl iodides 1e and 4e
smoothly underwent the Heck reaction under Jeffrey's conditions using Et$_3$N as the base to produce 2e in an 85 % yield and 3e in an 89 % yield respectively (entries 9 and 10, Table 4). It is worth noting that the use of Et$_3$N as a base for the Heck reaction of 1e and 4e was necessary to eliminate small amounts of migration products.

We propose a possible mechanism (Scheme 3) for the palladium migration in organopalladium intermediates derived from o-halobiaryls which involves oxidative addition of the aryl halide to Pd(0) to generate intermediate i, which can either (a) undergo oxidative addition of a neighboring C-H bond to produce a hydridopallada(IV)cycle (ii), followed by reductive elimination of CH to generate iii or i, or (b) electrophilic palladation to generate intermediate iv, followed by either protonolysis of a C-Pd bond to generate iii or i or oxidative addition to HX to generate ii. In regard to the mechanism, we would like to point out that not all ligands on palladium are shown for simplicity. We believe that the intermediacy of iv is highly unlikely for two main reasons. First of all, it is improbable that intermediate iv could react with HX under the basic reaction conditions we employed. Second of all, Catellani and Chiusoli have demonstrated that pallada(II)cycles, analogous to intermediate iv, easily undergo oxidative addition to aryl and alkyl halides to generate palladium(IV) intermediates, which after a series of rearrangements lead to unique polycyclic compounds. Thus, the presence of intermediate iv in our reaction would lead to the formation of signature compounds, which we were unable to observe under our reaction conditions. As a result, we favor the reversible interconversion between i and iii via hydridopallada(IV)cycle ii. It is also important to realize that palladium migration involves intramolecular C-H activation.
In order to rationalize the Heck product distributions in terms of electronic effects, we must consider the possible factors influencing these ratios. To begin with, we must consider the reactivity of the corresponding arylpalladium intermediates towards the olefin trap. To illustrate, the more reactive intermediate should be trapped faster by the olefin, giving rise to mixtures enriched with that isomer. However, since we were not able to find any such reactivity data in the literature, we have no way of predicting how electronic effects might influence the reactivities of such arylpalladium intermediates. Thus, for the time being, we can simplify our discussion by assuming that the reactivities of arylpalladium intermediates generated by palladium migration are fairly similar, and that the ratio of Heck products will not be significantly affected by such reactivities. With this argument in mind, the critical factor determining the ratio of Heck products is the actual distribution of the arylpalladium intermediates generated by palladium migration. Thus, this distribution must be determined.
by the electronic preference of the palladium within the biphenyl. Since the palladium species involved in the intramolecular C-H activation required for palladium migration is most likely electrophilic in nature, we speculate that palladium, as any other electrophile, will prefer the more electron-rich position of the biphenyl. HF/6-31G(d) calculations using the GAMESS suite of programs show that biphenyls with electron-donating substituents, such as Me and OMe, have relatively similar Mulliken electron densities between the 2 and 2' positions (see Figure 1). These calculations are consistent with the near 50:50 mol ratio of Heck products 2a and 2c to 3a and 3c obtained with iodobiphenyls substituted with Me and OMe groups under our palladium migration conditions (entries 1, 2, 5 and 6; Table 3). On the other hand, the Me₂N- substituted biphenyl has a relatively larger concentration of charge on the 2' position. Thus, this biphenyl should favor palladium migration to the more electron-rich 2 position. Indeed, we obtained Heck products slightly enriched with isomer 2b (entries 3 and 4). In contrast, substituted biphenyls bearing electron-withdrawing groups, such as CO₂Et.
and NO$_2$, have greater electron density in the 2 position of the substituted phenyl moiety of the biphenyl. Thus, it is not surprising that we have obtained Heck reaction mixtures enriched with isomers 3d and 3e (entries 7-10, Table 3), which indicates a tendency for palladium to migrate to the more electron-rich position of these biphenyls. As a result, we conclude that electron density calculations can be used in a qualitative fashion to predict the preference of palladium within these biphenyls. Furthermore, these results are consistent with the intermediacy of an electrophilic palladium species.

At this time, we are unable to find any obvious correlation between our results and those reported by Gallagher.$^4$ Gallagher has observed that electron-withdrawing nitro groups are critical to migration in his systems. However, it is impossible to compare his experimental data with ours, since equilibration of the corresponding palladium intermediates was apparently never established in his reactions. Therefore, in his system we cannot deduce whether the nitro group is promoting migration directly or indirectly by simply retarding the Heck reaction and allowing enough time for the palladium migration to take place.

We have continued to investigate the electronic effects of other unsymmetrical o-halobiaryls and found a more marked effect on the Heck product distribution in the reaction of 2-iodo-3-phenylbenzofuran (5a) and ethyl acrylate, which under our standard migration conditions A gives exclusively ethyl E-3-(3-phenylbenzofuran-2-yl)acrylate (6a) in an 85% yield (entry 1, Table 5). This unexpected result showing no apparent 1,4-Pd shift suggested that palladium has a strong preference for the 2-position of the benzofuran moiety. To test this hypothesis 3-(2-iodophenyl)benzofuran (8a) was allowed to react with ethyl acrylate under our standard migration conditions A. Acrylate 6a was produced in a 78% yield,
alongside only ~5 % of isomer 7a (entry 2), indicating a strong preference for palladium to migrate from the phenyl to the benzofuran ring. These results are consistent with the idea of an electrophilic palladium preferring the more reactive 2-position of the benzofuran moiety. However, keep in mind that very different reactivities of the two arylpalladium intermediates could be favoring the formation of 6a. Once again, compound 7a was prepared in a 75 % yield from 8a by carrying out the Heck reaction with ethyl acrylate under Jeffrey's reaction conditions (entry 3, Table 5).

Table 5. Heck reaction of o-halobiaryls with ethyl acrylate.

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>Y</th>
<th>conditions</th>
<th>% yield</th>
<th>mol ratio 6:7&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>O</td>
<td>A, 1.0 d</td>
<td>85</td>
<td>100:0</td>
</tr>
<tr>
<td>2</td>
<td>8a</td>
<td>O</td>
<td>A, 1.0 d</td>
<td>83</td>
<td>94:6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 % Pd(OAc)&lt;sub&gt;2&lt;/sub&gt;, 4.0 ethyl acrylate,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>8a</td>
<td>O</td>
<td>1.0 n-Bu&lt;sub&gt;4&lt;/sub&gt;NCl, 2.0 NaHCO&lt;sub&gt;3&lt;/sub&gt;, DMF (1.0 mL), 80 °C, 1.0 d</td>
<td>75</td>
<td>0:100</td>
</tr>
<tr>
<td>4</td>
<td>5b</td>
<td>NMe</td>
<td>A, 1.0 d</td>
<td>94</td>
<td>100:0</td>
</tr>
<tr>
<td>5</td>
<td>8b</td>
<td>NMe</td>
<td>A, 1.0 d</td>
<td>90</td>
<td>85:15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 % Pd(OAc)&lt;sub&gt;2&lt;/sub&gt;, 4.0 ethyl acrylate,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>8b</td>
<td>NMe</td>
<td>1.0 n-Bu&lt;sub&gt;4&lt;/sub&gt;NCl, 2.0 NaHCO&lt;sub&gt;3&lt;/sub&gt;, DMF (1.0 mL), 80 °C, 1.0 d</td>
<td>85</td>
<td>100:0</td>
</tr>
</tbody>
</table>

<sup>a</sup>The product ratio was determined by <sup>1</sup>H NMR spectroscopic analysis.

Similarly, we have studied the Heck reaction of indole-containing biaryls (Table 5). As expected, the Pd-catalyzed reaction of 2-iodo-1-methyl-3-phenyllindole (5b) and ethyl
acrylate under migration conditions A, produced ethyl E-3-(1-methyl-3-phenylindol-2-yl)acrylate (6b) exclusively in a 94% yield (entry 4). Clearly this result supports the idea that palladium prefers to reside on the 2 position of the indole, rather than the phenyl moiety of the biaryl. On the other hand, the Heck reaction of 3-(2-iodophenyl)-1-methylindole (8b), under migration conditions A, produced an 85:15 mixture of 6b and 7b in a 90% yield (entry 5). Although this latter result indicates a tendency for palladium to migrate to the indole ring, the arylpalladium intermediates formed were far from having reached equilibrium. We believe that the 15 mol% of retained product is a result of slow palladium migration kinetics, which might be due to unfavorable steric interactions imposed on the palladium when migrating to the relatively hindered 2 position of the 1-methylindole (Figure 2). Therefore, we postulate that steric hindrance might be a significant factor in this palladium migration chemistry disfavoring sterically congested arylpalladium intermediates.

Figure 2. Unfavorable steric interactions in 1-methyl-3-phenylindol-2-ylpalladium iodide.

In order to study the effect of steric hindrance on the palladium migration, we have prepared 2-iodo-3',5'-dimethylbiphenyl (9). We chose this dimethyl-substituted biphenyl for two main reasons. First of all, methyl substituents are not likely to chelate palladium. Second of all, based on previous observations with biphenyls 1a and 4a, methyl groups
should be essentially electronically neutral in the palladium migration. We began by carrying out the reaction of 9 under Jeffrey’s conditions to obtain the expected compound 10 exclusively in a 97 % yield (eq 1). Similarly, compound 9 also reacted with ethyl acrylate under our standard migration conditions A to generate compound 10 exclusively in a 94 % yield (eq 1). This result clearly indicates that the steric effect of the methyl substituents completely inhibited palladium migration to the dimethyl-substituted phenyl ring of the biphenyl.

![Chemical reaction diagram](image)

There is no reason to believe that these migrations should be restricted to a single 1,4-Pd shift. In fact, we have established a double 1,4-Pd shift in organopalladium intermediates generated from 2-iodo-3-methoxybiphenyl (12) (Scheme 4). Hypothetically, the palladium-catalyzed reaction involving compound 12 should give rise to three different arylpalladium intermediates 16-18 after a series of 1,4-Pd shifts, which should produce three different Heck products 13-15. Indeed, the reaction of 12 with ethyl acrylate under our standard migration conditions A produced a mixture of compounds 13, 14 and 15 (53:38:9 respectively) in an overall 97 % yield (Scheme 4). The presence of the key intermediate 18, generated after a minimum of two 1,4-Pd shifts between the 2-, 2′-, and 6-positions of the biphenyl, explains the formation of isomer 15. Interestingly, the reaction of 2-iodo-3′-methoxybiphenyl (19)
and ethyl acrylate under our standard migration conditions A, produced a mixture of compounds 13, 14 and 15 (25:62:13 respectively) in an 87 % overall yield (eq 2). The wide discrepancy in the Heck product distribution obtained from the reaction of 12 versus 19, indicates that palladium is unable to achieve equilibrium between the three different positions of the biphenyl prior to olefin trapping. This is not an unexpected result, since equilibration of the palladium moiety in this biphenyl requires a more kinetically demanding double 1,4-Pd shift between the three distinct positions of the biphenyl prior to ethyl acrylate trapping. Finally, another factor adding to the complexity of this biphenyl system involves the
possibility of intramolecular oxygen chelation in the arylpalladium intermediate 16 (Figure 3).

![Figure 3. Intramolecular chelation by oxygen.](image)

Another interesting example of palladium migration involves the use of 2-iodo-2'-methylbiphenyl (20) in the Heck reaction (eq 3). Notice that in this biphenyl, there is only one vacant position for palladium migration on the methyl-substituted phenyl ring versus two vacant positions on the other ring. Therefore, statistically speaking, we expect to obtain a 2:1 (67:33) mixture of isomers 21 and 22. To our satisfaction, the reaction of compound 20 with ethyl acrylate under migration conditions A produced a nearly theoretical 65:35 mixture of 21 and 22 in a 91 % yield. Furthermore, the reaction of compound 20 with ethyl acrylate under Jeffrey's conditions produced 21 exclusively in a 92 % yield.

![Equation 3](image)

After exploring the Heck reaction, we proceeded to examine the Suzuki-Miyaura cross-coupling of the same o-halobiaryls with arylboronic acids. First of all, we studied the coupling of 2-iodo-4'-methylbiphenyl (1a) with arylboronic acids under a variety of reaction
conditions (Table 6). For instance, the palladium-catalyzed coupling of 1a with 4-(methoxycarbonyl)phenylboronic acid under conditions described by Wright, et al. produced methyl 4-(4'-methylbiphenyl-2-yl)benzoate (23a) exclusively in a 62% yield (entry 1). Clearly under these conditions, the coupling reaction proceeds without any palladium migration. We then carried out the coupling reaction of 1a with 4-(methoxycarbonyl)phenylboronic acid under our standard migration conditions A, but after 3 d only trace amounts of the Suzuki-Miyaura product 23a could be identified by TLC analysis of the reaction mixture (entry 2). In order to improve the yield, we carried out this reaction with the more electron-rich 4-methoxyphenylboronic acid and obtained a 57:43 mixture of 2-(4-methoxyphenyl)-4'-methylbiphenyl (23b) and 2-(4-methoxyphenyl)-4-methylbiphenyl (24b) in a 33% yield, indicating that palladium migration had indeed occurred under these conditions. Even though we had obtained a low yield of Suzuki-Miyaura products under migration conditions A, we were encouraged by this positive result. We also suspected that the yield of this reaction could be improved by using water as an additive. Therefore, we proceeded to carry out the coupling reaction of 1a with 4-methoxyphenylboronic acid under migration conditions B, which employ 5% H2O by volume in DMF as the reaction solvent and we obtained a 66:34 mixture of isomers 23b and 24b in a substantially higher 77% overall yield. It should be pointed out that the addition of water to the reaction mixture improved the overall yield of the Suzuki reaction, but it lowered the amount of migration product 24b (compared entries 3 and 4). Furthermore, the Suzuki coupling of 1a with the electron-deficient 4-(methoxycarbonylphenyl)boronic acid under migration conditions B,
Table 6. Suzuki-Miyaura cross-coupling of 2-iodo-4'-methylbiphenyl (1a) with arylboronic acids.

![Chemical structures](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>reaction conditions</th>
<th>Ar/equiv</th>
<th>% yield</th>
<th>ratio (23:24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10 % PPh₃, 2.2 CsF, DME (1.0 mL), 90 °C, 8 h</td>
<td>p-MeO₂CC₆H₄/1.2</td>
<td>62</td>
<td>100:0</td>
</tr>
<tr>
<td>2</td>
<td>5 % dpmm, 2 CsPiv, DMF (4.0 mL), 100 °C, 72 h</td>
<td>p-MeO₂CC₆H₄/1.0</td>
<td>trace</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>5 % dpmm, 2 CsPiv, DMF (4.0 mL), 100 °C, 72 h</td>
<td>p-MeOC₆H₄/1.0</td>
<td>33</td>
<td>57:43</td>
</tr>
<tr>
<td>4</td>
<td>5 % dpmm, 2 CsPiv, DMF (3.8 mL), 44 H₂O (0.2 mL) 100 °C, 8 h</td>
<td>p-MeOC₆H₄/1.0</td>
<td>77</td>
<td>66:34</td>
</tr>
<tr>
<td>5</td>
<td>5 % dpmm, 2 CsPiv, DMF (3.8 mL), 44 H₂O (0.2 mL) 100 °C, 8 h</td>
<td>C₆H₆/1.0</td>
<td>complex mixture</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>5 % dpmm, 2 CsPiv, DMF (3.8 mL), 44 H₂O (0.2 mL) 100 °C, 8 h</td>
<td>C₆H₆BF₃K/1.0</td>
<td>complex mixture</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>5 % dpmm, 2 CsPiv, DMF (3.8 mL), 44 H₂O (0.2 mL) 100 °C, 8 h</td>
<td>p-MeO₂CC₆H₄/1.0</td>
<td>61</td>
<td>60:40</td>
</tr>
<tr>
<td>8</td>
<td>5 % dpmm, 2 CsPiv, DMF (4.0 mL), 20 H₂O, 100 °C, 8 h</td>
<td>p-MeO₂CC₆H₄/1.0</td>
<td>55</td>
<td>57:43</td>
</tr>
<tr>
<td>9</td>
<td>5 % dpmm, 2 CsPiv, 2 Me₂CCO₂H, DMF (4.0 mL), 20 H₂O, 100 °C, 24 h (buffered)</td>
<td>p-MeO₂CC₆H₄/1.0</td>
<td>57</td>
<td>50:50</td>
</tr>
<tr>
<td>10</td>
<td>5 % dpmm, 2 CsPiv, 2 Me₂CCO₂H, DMF (4.0 mL), 100 °C, 24 h (buffered)</td>
<td>p-MeO₂CC₆H₄/1.0</td>
<td>trace</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>5 % dpmm, 2 CsPiv, 2 Me₂CCO₂H, DMF (4.0 mL), 20 H₂O, 100 °C, 24 h (buffered)</td>
<td>p-MeOC₆H₄/1.0</td>
<td>38</td>
<td>52:48</td>
</tr>
<tr>
<td>12</td>
<td>5 % dpmm, 2 CsPiv, 2 Me₂CCO₂H, DMF (4.0 mL), 20 H₂O, 100 °C, 24 h (buffered)</td>
<td>p-MeO₂CC₆H₄/1.4</td>
<td>71</td>
<td>51:49</td>
</tr>
</tbody>
</table>

*The reaction was run using 0.25 mmol of the aryl iodide. *bThe mole ratio was determined by ¹H NMR spectroscopic analysis.
produced a 60:40 mixture of 23a and 24a in a 61% yield (entry 7). Obviously, the use of 4-(methoxycarbonyl)phenylboronic acid in place of 4-methoxyphenylboronic acid improved the amount of migration product, presumably due to the lower reactivity of the electron-deficient arylboronic acid.

At this stage, we looked more closely at the possible role of water in the Suzuki-Miyaura coupling reaction and realized that, in the presence of base, water may serve as a source of hydroxide ions. In turn, hydroxide ions probably activate the arylboronic acid by generating a more reactive arylboronate species (Scheme 5). So our new strategy aimed to control the relatively fast arylpalladium trapping kinetics by arylboronic acids by controlling the concentration of hydroxide ions in the reaction mixture and thus reducing the concentration of the more reactive boronate anion. The first step was to carry out the coupling of 1a with 4-(methoxycarbonyl)phenylboronic acid under conditions B, but we also reduced the amount of water from 44 equiv (corresponding to conditions B) to 20 equiv. Under these conditions, the coupling reaction produced a 57:43 mixture of 23a and 24a in a 55% overall yield (entry 8), indicating only a slight improvement in the isomer ratio (compare this with a 60:40 ratio previously obtained using conditions B). At this point, we decided to buffer the reaction mixture by using a combination of 2 equiv of CsPiv plus 2 equiv of pivalic acid. To our satisfaction, the coupling of 1a and 4-(methoxycarbonyl)phenylboronic acid under these buffered conditions produced a 50:50
mixture of 23a and 24a in a 57 % overall yield (entry 9). Naturally, we carried out the same reaction in the absence of water and observed only trace amounts of Suzuki-Miyaura products after 1 d of reaction (entry 10).

Now that we had apparently developed a set of optimal migration conditions for the Suzuki-Miyaura reaction, we proceeded to examine the use of the more electron-rich 4-methoxyphenylboronic acid as the coupling agent. As expected, the Suzuki-Miyaura coupling of 1a with this arylboronic acid produced a 52:48 mixture of isomers 23b and 24b in a disappointingly low 38 % overall yield. This experiment confirmed the idea that the more electron-rich 4-methoxyphenylboronic acid trapped the arylpalladium intermediates somewhat faster than the electron-poor 4-(methoxycarbonyl)phenylboronic acid, thus producing the observed ratio of isomers, which is slightly enriched with the direct coupling product 23b. On the other hand, the overall low yields obtained in the Suzuki-Miyaura reaction under our buffered conditions (entries 9 and 11) might be due to a side reaction involving protonation of the corresponding arylboronic acids by pivalic acid (eq 4). Thus, in

\[
\text{Me}_3\text{CCO}_2\text{H} + \text{ArB(OH)}_2 \rightarrow \text{Me}_3\text{CCO}_2\text{B(OH)}_2 + \text{Ar-H} \quad (4)
\]

an attempt to improve the reaction yield, we carried out the Suzuki cross-coupling of 1a with 1.4 equiv of 4-(methoxycarbonyl)phenylboronic acid as opposed to the usual 1.0 equiv (entry 12). Using this protocol, we obtained a 51:49 mixture of 23a and 24a in a 71 % overall yield. As a result, we chose this latter set of reaction conditions, described in entry 12 of Table 6, as our standard migration conditions (conditions C) for the Suzuki-Miyaura cross-coupling of o-halobiaryls with arylboronic acids. Equally significant is the fact that we can
suppress the palladium migration in the Suzuki-Miyaura reaction by simply employing the conditions described in entry 1 of Table 6.

As discussed previously, there are two possible factors determining the ratio of Heck products from the corresponding o-halobiaryls, namely the distribution of arylpalladium intermediates and/or their relative reactivities towards ethyl acrylate. Naturally, the same argument applies to the Suzuki-Miyaura reaction. Recall that we have previously assumed that the reactivities of the arylpalladium intermediates generated via palladium migration are similar, and differing reactivities does not significantly affect the ratio of Heck products. If such an assumption were true, there should be very little difference between the ratios of Heck versus Suzuki-Miyaura products, since the determining factor for such product ratios is a pre-established distribution of the arylpalladium intermediates independent of their reactivities. On the other hand, if the reactivity of the arylpalladium intermediates is playing a significant role in determining the ratio of the reaction products, we should expect a significant difference between the ratios of Heck and Suzuki-Miyaura products. With this argument in mind, it is important to point out that under our migration conditions, aryl iodide 1a produced nearly identical mixtures of Heck and Suzuki-Miyaura products. This is a very significant finding since this similarity supports our hypothesis that a pre-established distribution of arylpalladium intermediates determines these ratios. In order to further test this hypothesis, we have carried out the Suzuki-Miyaura cross-coupling of 2-iodo-3-phenylbenzofuran (5a) with 4-(methoxycarbonyl)-phenylboronic acid under our standard migration conditions C and obtained 2-(4-methoxycarbonylphenyl)-3-phenylbenzofuran (25) exclusively in a 79 % yield (entry 1, Table 7). Similarly, the reaction of 3-(2-iodophenyl)-
benzofuran (8a) with 4-(methoxycarbonyl)phenylboronic acid under our standard migration conditions C produced compound 25 in a 78 % overall yield, along with only a small amount (< 5 %) of the direct coupling product 26 (entry 2). In addition, the Suzuki-Miyaura reaction of 8a under Wright's conditions produced the expected compound 26 in a 78 % yield, along with compound 25 in a 7 % yield. Clearly, both the Heck and Suzuki-Miyaura experiments with the benzofuran-containing biaryls 5a and 8a give very similar results indicating a tendency for palladium to migrate from the phenyl to the benzofuran moiety of the biaryl (see Tables 5 and 7). Furthermore, the similarities in Heck and Suzuki-Miyaura product ratios obtained under our migration conditions support the hypothesis that a pre-established distribution of arylpalladium intermediates rather than their relative reactivities determines such product ratios.

Table 7. Suzuki-Miyaura cross-coupling of benzofuran-containing biaryls.³

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>reaction conditions</th>
<th>% yield 25 + 26</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>C, 1.0 d</td>
<td>79 + 0</td>
</tr>
<tr>
<td>2</td>
<td>8a</td>
<td>C, 1.0 d</td>
<td>78 + &lt; 5</td>
</tr>
<tr>
<td>3</td>
<td>8a</td>
<td>5 % Pd(OAc)₂, 10 % PPh₃, 2.2 CsF, 1.2 p-MeO₂CC₆H₄B(OH)₂, DME (1.0 mL), 90 °C, 6 h</td>
<td>7 + 75</td>
</tr>
</tbody>
</table>

³The reaction was run using 0.25 mmol of the corresponding aryl iodide.
To further explore the scope of this Pd migration process, we have carried out the palladium-catalyzed reaction of diphenylacetylene and aryl iodide 12 in the hope that the arylpalladium intermediates generated by a 1,4-Pd shift could be trapped by way of alkyne insertion-annulation chemistry described earlier by Larock et al.\(^{18}\) First, the reaction was carried out under the previously described annulation conditions employing 1.2 equiv of the acetylene, 5 mol % Pd(OAc)\(_2\), 1 equiv of LiCl and 2 equiv of NaOAc in DMF at 100 °C for 2 d. As expected, we obtained 1-methoxy-9,10-diphenylphenanthrene (27) in a 90 % yield (eq 5). We then switched “on” the palladium migration by allowing 12 to react with 1.2 equiv of diphenylacetylene under our standard Pd migration conditions A to obtain a 51:49 mixture of phenanthrenes 27 and 28 respectively in an 87 % overall yield (Scheme 6). The mechanism for the formation of phenanthrenes 27 and 28 is described in Scheme 6. Notice that there are multiple paths for the formation of isomer 28 (as well as 27). It is important to note that in these alkyne reactions the formation of product 28 cannot arise directly from the intermediacy of a simple bridged pallada(II)cycle,\(^{19}\) but instead its formation requires complete migration of the palladium moiety from the methoxy-bearing ring to the other aromatic ring. Similarly, aryl iodide 19 reacted with diphenylacetylene under our standard migration conditions A to generate a 40:60 mixture of phenanthrenes 27 and 28 respectively.
in a 78% overall yield (Scheme 7), indicating that the arylpalladium intermediates derived from 12 and 19 have not reached equilibrium under these conditions. These interesting

Scheme 6

\[
\begin{align*}
\text{OMe} & \quad \text{OMe} \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

12 + 1.2 \xrightarrow{5 \% \text{Pd(OAc)}_2} 5 \% \text{CH}_2(\text{PPh}_2)_2 \\
2 \text{CsO}_2 \text{CCMe}_3 \\
\text{DMF (4 mL)} \\
100^\circ \text{C}, 1 \text{ d} \\
87\% (51:49)

\[
\begin{align*}
\text{OMe} & \quad \text{OMe} \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

27 + 28

Scheme 7

\[
\begin{align*}
\text{OMe} & \quad \text{OMe} \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

19 + 1.2 \xrightarrow{5 \% \text{Pd(OAc)}_2} 5 \% \text{CH}_2(\text{PPh}_2)_2 \\
2 \text{CsO}_2 \text{CCMe}_3 \\
\text{DMF (4 mL)} \\
100^\circ \text{C}, 1 \text{ d} \\
78\% (40:60)
migration results suggest that there is the exciting possibility of trapping arylpalladium intermediates generated by 1,4-Pd shifts by many other synthetically useful palladium methodologies.

**Conclusion**

In conclusion, we have been able to establish a 1,4-palladium migration in organopalladium intermediates derived from o-halobiaryls. These arylpalladium intermediates have been generated under relatively mild reaction conditions compatible with the Heck, Suzuki and alkyne annulation reactions. We have developed standard migration conditions, which allow arylpalladium intermediates to approach equilibrium prior to the trapping step. The palladium migration can be activated or suppressed at will by simple manipulation of the reaction conditions. The nearly identical ratio of isomers obtained from the Heck and Suzuki reactions seem to indicate that there is a direct correlation between these ratios and the distribution of arylpalladium intermediates generated by palladium migration.

**Experimental**

**General procedures.** All $^1$H and $^{13}$C spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic KMnO$_4$ solution [3 g of KMnO$_4$ + 20 g of K$_2$CO$_3$ + 5 mL of NaOH (5 %) + 300 mL of H$_2$O]. All melting points are
uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV.

**Reagents.** All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of THF, DME, DMF, diethyl ether, ethyl acetate and hexanes were purchased from Fisher Scientific Co. Tetra-n-butylammonium chloride (TBAC) was purchased from Lancaster Synthesis, Inc. 3-Bromoanisole, 1-bromo-2-iodobenzene, diphenylacetylene and ethyl acrylate were purchased from Aldrich Chemical Co., Inc. Cesium pivalate was prepared according to the procedure of Larock and Campo.\(^{20}\)

Compounds 1a, 1b, 5b, 8a, 13 and 10 have been previously reported\(^{20}\) (see chapter 1 of this thesis).

**Synthesis of the o-halobiaryls**

**2-Bromo-4'-methylbiphenyl (1a').** A mixture of 2-iodo-4'-methylbiphenyl (1a) (0.147 g, 0.5 mmol), CuBr (1.435 g, 5.0 mmol), and KBr (0.595 g, 5.0 mmol) in DMF (12 mL) was stirred at 145 °C under Ar for 1 d. The reaction mixture was diluted with diethyl ether (80 mL) and filtered. The filtrate was washed with brine (50 mL), and the organic layer was dried (Na\(_2\)SO\(_4\)), filtered, and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using hexanes to obtain 0.105 g (85%) of the indicated compound as a clear oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.41 (s, 3H), 7.16-7.20 (m, 1H), 7.23-7.25 (m, 2H), 7.30-7.34 (m, 4H), 7.64-7.66 (m, 1H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 21.3, 122.8, 127.4, 128.6, 128.8, 129.3, 131.4, 133.1, 137.4, 138.3, 142.6. The other spectral properties were identical to those previously reported.\(^{21}\)
**2-Iodo-4-methylbiphenyl (4a).** This compound was prepared by the procedure of Hellwinkel: 22

\[
\begin{align*}
\text{\( ^1H \) NMR (CDCl}_3 \text{)} & \delta 2.35 (s, 3H), 7.18-7.19 (m, 2H), 7.30-7.41 (m, 5H), 7.79-7.80 (m, 1H); \\
\text{\( ^{13}C \) NMR (CDCl}_3 \text{)} & \delta 20.7, 98.7, 127.7, 128.1, 129.2, 129.6, 129.9, 139.1, 140.2, 144.0, 144.3; \\
\text{IR (CH}_2\text{Cl}_2 \text{)} & 3024, 2920, 1603, 1473 \text{ cm}^{-1}; \\
\text{HRMS } m/z & 293.9910 \text{ (calcd for } C_{13}H_{11}I, 293.9906). \\
\end{align*}
\]

**N,N-Dimethyl-4-(2-iodophenyl)aniline (1b).** Compound 1b was prepared in two steps from compound 1e. To a solution of 1e (0.389 g, 1.19 mmol), FeCl\(_3\)·6H\(_2\)O (5.0 mg, 0.018 mmol), and activated charcoal (2.4 mg) in methanol (10 mL) under reflux was added N\(_2\)H\(_4\)·1H\(_2\)O (0.115 g, 3.03 mmol) dropwise over 10 min. The mixture was refluxed for an additional 14 h and then allowed to cool to room temperature. The reaction mixture was diluted with diethyl ether (50 mL) and the organic layer was washed with water (50 mL). The organic layer was dried (Na\(_2\)SO\(_4\)), filtered, and the solvent evaporated under reduced pressure to obtain a yellow oil [presumed to be 4-(2-iodophenyl)aniline], which without further purification or characterization was dissolved in acetonitrile (8 mL). To this acetonitrile solution was added 37 % aq formaldehyde (0.96 mL) and NaBH\(_3\)CN (0.230 g, 3.66 mmol). The resulting reaction mixture was stirred at room temperature while glacial acetic acid (0.12 mL) was added dropwise over 10 min. After the addition, the reaction mixture was stirred for 40 min, then another portion of glacial acetic acid (0.12 mL) was added at once and stirring continued for an additional 30 min. The reaction mixture was diluted with diethyl ether (50 mL) and washed with 5 % aq NaOH. The organic layer was dried (Na\(_2\)SO\(_4\)), filtered, and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 9:1 hexanes/ethyl acetate to afford
36.9 mg (96 %) of the indicated compound 1b as a colorless oil: 'H NMR (CDCl₃) δ 3.00 (s, 6H), 6.75-6.77 (m, 2H), 6.94-6.98 (m, 1H), 7.23-7.26 (m, 2H), 7.29-7.36 (m, 2H), 7.93 (d, J = 8.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 40.5, 99.6, 111.5, 128.1, 128.2, 130.1, 130.3, 132.4, 139.5, 146.8, 149.9; IR (CH₂Cl₂) 2917, 2849, 1612, 1525, 1461, 1351 cm⁻¹; HRMS m/z 323.0176 (calcd for C₁₄H₁₄N, 323.0171).

N,N-Dimethyl-3-iodo-4-phenylaniline (4b). Compound 4b was prepared in two steps from 2-iodo-4-nitrobiphenyl (4e) by a procedure similar to that used for 1d. The reaction mixture was purified by chromatography on a silica gel column using 9:1 hexanes/ethyl acetate to afford 38.1 mg (98 %) of the indicated compound (4b) as a yellow solid: mp 76-77 °C; 'H NMR (CDCl₃) δ 2.96 (s, 6H), 6.75 (dd, J = 8.4, 2.8 Hz, 1H), 7.14 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 2.8 Hz, 1H), 7.33-7.38 (m, 5H); ¹³C NMR (CDCl₃) δ 40.5, 99.5, 112.3, 122.9, 127.0, 127.8, 129.8, 130.1, 134.4, 144.3, 150.4; IR (CH₂Cl₂) 2917, 2849, 1598, 1486, 1511, 1442 cm⁻¹; HRMS m/z 323.0176 (calcd for C₁₄H₁₄N, 323.0171).

2-Iodo-4-methoxybiphenyl (4c). This compound was prepared by the Sandmeyer reaction of diazotized 5-methoxy-2-phenylaniline:²³ 'H NMR (CDCl₃) δ 3.60-3.79 (br s, 2H), 3.79 (s, 3H), 6.32 (d, J = 2.4 Hz, 1H), 6.41 (dd, J = 8.4, 2.4 Hz, 1H), 7.05 (d, J = 8.8 Hz, 1H), 7.29-7.33 (m, 1H), 7.39-7.42 (m, 4H); ¹³C NMR (CDCl₃) δ 55.3, 101.2, 104.4, 120.9, 126.9, 128.8, 129.3, 131.4, 139.4, 144.6, 160.1. To a solution of 5-methoxy-2-phenylaniline (0.66 g, 3.3 mmol) in a mixture of H₂O (9 ml), H₂SO₄ (0.8 ml), and DME (20 ml) at 0 °C was added slowly with stirring NaN₃O₂ (0.33 g, 4.8 mmol) and the resulting solution stirred for an additional 30 min at 0 °C. The resulting mixture was added slowly to a solution of NaI (3 g, 20 mmol) in H₂O (7 ml) and the mixture was stirred vigorously for an additional 15 min.
The I₂ present was destroyed by adding 10% aq Na₂S₂O₃ (20 mL) and the reaction mixture was subsequently extracted with diethyl ether (100 ml). The organic layer was dried (Na₂SO₄) and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 20:1 hexanes/ethyl acetate to afford 0.635 g (62%) of the desired compound 4c as a yellow solid, which was recrystallized from methanol: mp 83-84 °C; ¹H NMR (CDCl₃) δ 3.83 (s, 3 H), 6.94 (dd, J = 8.4, 2.4 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 7.31-7.33 (m, 2H), 7.36-7.41 (m, 3 H), 7.48 (d, J = 2.4 Hz, 1H); ¹³C NMR (CDCl₃) δ 55.6, 98.5, 114.3, 124.5, 127.4, 127.9, 129.6, 130.3, 139.2, 143.9, 158.9; IR (CH₂Cl₂) 3051, 2966, 1554, 1592, 1475 cm⁻¹; HRMS m/z 309.9859 (calcd for C₁₃H₁₀O₂, 309.9855).

**Ethyl 4-(2-bromophenyl)benzoate (1d).** Compound 1d was prepared by a selective Suzuki-Miyaura cross-coupling reaction as follows. 2-Bromophenylboronic acid (0.462 g, 2.3 mmol), ethyl 4-iodobenzoate (0.552 g, 2.0 mmol), CsF (0.668 g, 4.4 mmol), Pd(OAc)₂ (0.022 g, 5 mol %), and PPh₃ (0.052 g, 10 mol %) in DME (10 mL) were stirred under Ar at 90 °C for 7 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (30 mL). The organic layer was dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 9:1 hexanes/ethyl acetate to afford 0.493 g (81%) of the desired compound 1d as a yellow oil: ¹H NMR (CDCl₃) δ 1.42 (t, J = 7.2 Hz, 3H), 4.41 (q, J = 7.2 Hz, 2H), 7.21-7.26 (m, 1H), 7.31-7.33 (m, 1H), 7.36-7.40 (m, 1H), 7.48-7.50 (m, 2H), 7.68 (dd, J = 8.0, 1.2 Hz, 1H), 8.10-8.12 (m, 2H); ¹³C NMR (CDCl₃) δ 14.4, 61.1, 122.3, 127.5, 129.3, 129.5, 129.7, 131.1, 133.3, 141.7, 145.5, 166.5 (one sp² carbon missing due to overlap); IR (CH₂Cl₂) 2980, 1715, 1611, 1466, 1275 cm⁻¹; HRMS m/z 304.0104 (calcd for C₁₅H₁₃BrO₂, 304.0099).
Ethyl 3-iodo-4-phenylbenzoate (4d). Compound 4d was prepared from ethyl 4-iodo-3-nitrobenzoate. First, we carried out a Suzuki-Miyaura cross-coupling of ethyl 2-iodo-3-nitrobenzoate and NaBPh₄ as follows. NaBPh₄ (1.69 g, 4.94 mmol), ethyl 4-iodo-3-nitrobenzoate (1.38 g, 4.3 mmol), LiCl (0.182 g, 4.3 mmol), Pd(OAc)₂ (48.0 mg, 5 mol %), and PPh₃ (0.113 g, 10 mol %) in DMF (10 mL) were stirred under Ar at 70 °C for 2 d. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (50 mL). The organic layer was dried (MgSO₄), filtered, and the solvent removed under reduced pressure to obtain a yellow oil (presumed to be ethyl 3-nitro-4-phenylbenzoate), which without further purification was dissolved in 50 mL of a mixture of DME/EtOH/AcOH (50:40:10 % by volume respectively). To this solution was added SnCl₂ (5.71 g, 30.1 mmol) and the resulting mixture was stirred at 60 °C under Ar for 16 h. The reaction mixture was diluted with diethyl ether (100 mL) and washed with 10 % aq Na₂CO₃ (100 mL). The organic layer was dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column using 3:1 hexanes/ethyl acetate to obtain ~0.93 g (90 %) of ethyl 3-amino-4-phenylbenzoate as a yellow oil, which quickly decomposed as a neat liquid (no spectral data was obtained for this compound due to its instability). Ethyl 3-amino-4-phenylbenzoate was diazotized and iodinated by the following procedure. To a solution of ethyl 3-amino-4-phenylbenzoate (~0.93 g, 3.86 mmol) in DME (10 mL) was added water (8 mL) containing H₂SO₄ (0.7 mL). This reaction mixture was stirred at 0 °C while NaN₃ (0.386 g, 5.60 mmol) in H₂O (2 mL) was added dropwise over 30 min. After the addition, the mixture was stirred for an additional 20 min at 0 °C, then this mixture was added to NaI (3.0 g, 20.0 mmol) in H₂O (7 mL). Any I₂ formed was
destroyed by adding 10% aq Na$_2$S$_2$O$_3$ (10 mL) and the mixture was extracted twice with diethyl ether (50 mL x 2). The organic layers were combined, dried (Na$_2$SO$_4$), filtered, and the solvent evaporated under reduced pressure. The residue was purified by column chromatography on a silica gel column using 7:1 hexanes/ethyl acetate to obtain 1.06 g (78 %) of the title compound 4d as a white solid: mp 76-77 °C; $^1$H NMR (CDCl$_3$) $\delta$ 1.41 (t, $J$ = 7.2 Hz, 3H), 4.40 (q, $J$ = 7.2 Hz, 2H), 7.33-7.37 (m, 3H), 7.41-7.45 (m, 3H), 8.04 (dd, $J$ = 8.0, 1.6 Hz, 1H), 8.61 (d, $J$ = 1.6 Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.4, 61.4, 98.1, 128.2, 128.2, 129.0, 129.2, 129.9, 130.8, 140.6, 143.4, 150.9, 165.0; IR (CH$_2$Cl$_2$) 2973, 2818, 1722, 1276, 1378 cm$^{-1}$; HRMS m/z 351.9966 (calcd for C$_{15}$H$_{13}$I$_2$O$_2$, 351.9960); Anal. C, 51.14, H, 3.34 (calcd for C$_{15}$H$_{13}$I$_2$O$_2$: C, 51.16; H, 3.72)

2-Iodo-4'-nitrobiphenyl (4e). Compound 4e was prepared in two steps from 2-iodo-4-nitroaniline. First of all, 2-iodo-4-nitroaniline was diazotized by the following procedure. To a solution of 2-iodo-4-nitroaniline (1.09 g, 4.13 mmol), and 48-50 % aq HBF$_4$ (3.0 g) in methanol (20 mL) was added NaN$_2$ (0.342 g, 4.96 mmol) in H$_2$O (0.5 mL) at room temperature. The reaction mixture was stirred for 30 min, and then the reaction mixture was concentrated to 10 mL by passing a stream of Ar over it. At this point, a yellow solid had precipitated out of solution, and further crystallization was induced by cooling the mixture to -20 °C. The solid was filtered and washed repeatedly with diethyl ether. Recrystallization from methanol/diethyl ether afforded 0.673 g (49 %) of 4-nitro-2-iodophenyldiazonium tetrafluoroborate as a yellow solid. 4-Nitro-2-iodophenyldiazonium tetrafluoroborate (82.7
mg, 0.25 mmol) was dissolved in dry DMSO (2.0 mL), then diluted with dry benzene (8.0 mL). The reaction mixture was stirred at 80 °C for 2 h under Ar. The reaction mixture was diluted with diethyl ether (20 mL) and washed with brine (30 mL). The organic layer was dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 12:1 hexanes/ethyl acetate to obtain 35.8 mg (44 %) of the indicated compound 4e as a yellow solid: mp 91-92 °C; ¹H NMR (CDCl₃) δ 7.33-7.35 (m, 2H), 7.45-7.48 (m, 4H), 8.25 (dd, J = 8.4, 2.4 Hz, 1H), 8.80 (d, J = 2.4 Hz, 1H); ¹³C NMR (CDCl₃) δ 97.9, 123.1, 128.4, 128.8, 130.2, 134.5, 142.3, 147.0, 153.1 (one sp² carbon missing due to overlap); IR (CH₂Cl₂) 2918, 2850, 1523, 1349 cm⁻¹; HRMS m/z 324.9606 (calcd for C₁₂H₈INO₂, 324.9600); Anal. C, 44.29, H, 2.29; N, 4.11 (calcd for C₁₂H₈INO₂: C, 44.33; H, 2.48; N, 4.34).

2-Iodo-3-phenylbenzofuran (5a). This iodobiaryl was prepared from 3-phenyl-2-(triisopropylsilyl)benzofuran (29)²⁷ using an iodination procedure from the literature.²⁸ To a solution of 29 (0.329 g, 0.938 mmol) in CH₂Cl₂ (2 mL) was added ICl (0.162 g, 1.0 mmol) in CH₂Cl₂ (3 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min, then the excess ICl was destroyed by adding 10 % aq Na₂S₂O₃ (10 mL) and diluted with 50 ml of Et₂O. The organic layer was dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The remaining oil was purified by column chromatography using 30:1 hexanes/ethyl acetate to afford 0.267 g (89 %) of the desired compound 5a as a colorless oil: ¹H NMR (CDCl₃) δ 7.19-7.28 (m, 2H), 7.38-7.43 (m, 1 H), 7.46-7.61 (m, 6H); ¹³C NMR (CDCl₃) δ 97.2, 111.2, 119.4, 123.4, 124.7, 128.0, 128.1, 128.9, 129.2, 131.7, 158.4;
3-(2-Iodophenyl)-1-methylindoIe (8b). Compound 8b was prepared in two steps from 2-(2-iodophenyl)acetaldehyde. A solution of 2-(2-iodophenyl)acetaldehyde (0.216 g, 0.88 mmol), phenylhydrazine (0.105 g, 0.97 mmol), and methanesulfonic acid (17 mg, 0.18 mmol) in absolute ethanol (5.0 mL) was stirred at room temperature for 40 min under Ar. Then methanesulfonic acid (0.152 g, 1.58 mmol) was added and the mixture was stirred at 85 °C for 1.5 d under Ar. The reaction mixture was diluted with diethyl ether (50 mL) and washed with satd aq NH₄Cl (30 mL). The organic layer was dried (Na₂SO₄), filtered, and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using hexanes/ethyl acetate 3:1 to afford 11.5 mg (41 %) of 3-(2-iodophenyl)indole as a brown oil: 1H NMR (CDCl₃) δ 6.99 (m, 1H), 7.13-7.17 (m, 1H), 7.21-7.25 (m, 1H), 7.32-7.47 (m, 4H), 7.53 (d, J = 8.0 Hz, 1H), 8.00 (dd, J = 8.0, 0.8 Hz, 1H), 8.18 (br s, 1H); 13C NMR (CDCl₃) δ 100.9, 111.4, 120.2, 122.5, 123.7, 126.6, 128.1, 128.4, 131.5, 135.7, 139.9, 140.0 (two sp² carbons missing due to overlap). To a suspension of NaH (0.031 g, 1.3 mmol) in DMF (2.0 mL) at 0 °C was added 3-(2-iodophenyl)indoIe (0.319 g, 1.0 mmol) in DMF (3.0 mL) and the mixture was stirred at room temperature for 30 min. At this point, MeI (1.42 g, 10.0 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 14 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried (MgSO₄), and the solvent removed under reduced pressure. The residue was purified by column
chromatography using 5:1 hexanes/ethyl acetate to afford 0.320 g (96 %) of the desired 3-(2-iodophenyl)-1-methylindole (8b) as a clear oil: \( ^1\text{H} \text{NMR (CDCl}_3 \) \( \delta \) 3.84 (s, 3H), 6.97-7.01 (m, 1H), 7.12-7.16 (m, 1H), 7.22-7.28 (m, 2H), 7.35-7.40 (m, 2H), 7.45 (dd, \( J = 7.6, 1.6 \text{ Hz, 1H} \)), 7.53 (d, \( J = 8.0 \text{ Hz, 1H} \)), 7.99 (dd, \( J = 7.6, 0.8 \text{ Hz, 1H} \)); \(^{13}\text{C} \text{NMR (CDCl}_3 \) \( \delta \) 33.1, 100.8, 109.5, 118.5, 119.7, 120.3, 122.0, 127.0, 128.1, 128.2, 128.4, 131.5, 136.6, 139.9, 140.1; IR (CH\(_2\)Cl\(_2\)) 3050, 2922, 1547, 1478, 1459, 1376 cm\(^{-1}\); HRMS \text{m/z 333.0024 (calcd for C\(_{15}\)H\(_{12}\)IN, 333.0014).}

**2-Iodo-3',5'-dimethylbiphenyl (9).** 2-Iodo-3',5'-dimethylbiphenyl (9) was prepared by a procedure reported by Hart.\(^{30}\) A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 3,5-dimethylphenylmagnesium bromide [prepared from 1-bromo-3,5-dimethylbenzene (1.85 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I\(_2\) (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I\(_2\) was destroyed by adding 10% aq NaHSO\(_3\) (35 mL) and the organic layer was separated and rewashed with brine (20 mL). Finally, the organic layer was dried (MgSO\(_4\)), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using hexanes to afford 0.836 g (54 %) of the desired compound 9 as a clear oil: \( ^1\text{H} \text{NMR (CDCl}_3 \) \( \delta \) 2.36 (s, 6H), 6.95-7.02 (m, 4H), 7.33-7.82 (m, 1H), 7.92-7.94 (m, 1H); \(^{13}\text{C} \text{NMR (CDCl}_3 \) \( \delta \) 21.6, 98.9, 127.3, 128.3, 128.8, 129.4, 130.3, 137.6, 139.6, 144.3, 147.1; IR (CH\(_2\)Cl\(_2\)) 2917, 2849, 1602, 1461, 1015 cm\(^{-1}\); HRMS \text{m/z 308.0070 (calcd for C\(_{14}\)H\(_{13}\)I, 308.0062).}
**2-Iodo-3'-methoxybiphenyl (19).** Compound 19 was prepared by a procedure reported by Hart.\(^3\) A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 3-methoxyphenylmagnesium bromide [prepared from 3-bromoanisole (1.87 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I\(_2\) (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I\(_2\) was destroyed by adding 10% aq NaHSO\(_3\) (35 mL) and the organic layer was separated and rewashed with brine (20 mL). Finally, the organic layer was dried (MgSO\(_4\)), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using 30:1 hexanes/ethyl acetate to afford 0.620 g (40 %) of the desired compound 19 as a clear oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 3.84 (s, 3H), 6.88-6.95 (m, 3H), 7.01-7.05 (m, 1H), 7.29-7.38 (m, 3H), 7.95 (dd, \(J = 8.0, 1.2\) Hz, 1H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 55.4, 98.5, 113.4, 115.0, 121.8, 128.1, 128.9, 129.1, 130.1, 139.6, 145.5, 146.5, 159.1; HRMS m/z 309.9859 (calcd for C\(_{13}\)H\(_{11}\)IO, 309.9855).

**2-Iodo-2'-methylbiphenyl (20).** Compound 20 was prepared by a procedure reported by Hart.\(^3\) A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 2-methylphenylmagnesium bromide [prepared from 2-bromotoluene (1.71 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I\(_2\) (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I\(_2\) was destroyed by adding 10% aq NaHSO\(_3\) (35 mL) and the organic layer was separated and rewashed with brine (20 mL). Finally, the organic
layer was dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using hexanes to afford 0.97 g (66\%) of the desired compound 20 as a clear oil: \(^1\)H NMR (CDCl₃) \(\delta\) 2.07 (s, 3H), 7.01-7.07 (m, 2H), 7.20-7.31 (m, 4H), 7.36-7.40 (m, 1H), 7.92-7.94 (m, 1H); \(^{13}\)C NMR (CDCl₃) \(\delta\) 20.1, 100.1, 125.6, 128.0, 128.1, 128.7, 129.2, 129.7, 135.7, 138.9, 144.4, 146.8; IR (CH₂Cl₂) 3056, 3018, 2921, 1461, 1428 cm\(^{-1}\); HRMS \(m/\zeta\) 293.9910 (calcd for C\(_{14}\)H\(_{13}\)I, 293.9906).

**Heck reactions**

The following procedures are representative of the palladium-catalyzed Heck reactions with ethyl acrylate.

**Migration reaction conditions A:** The appropriate aryl halide (0.25 mmol), Pd(OAc)₂ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol), Cs₂CCMe₃ (CsPiv) (0.117 g, 0.5 mmol) and ethyl acrylate (0.025 g, 0.25 mmol) in DMF (4.0 ml) under Ar at 100 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

**Migration reaction conditions B:** The appropriate aryl halide (0.25 mmol), Pd(OAc)₂ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol), Cs₂CCMe₃ (CsPiv) (0.117 g, 0.5 mmol) and ethyl acrylate (0.025 g, 0.25 mmol) in wet DMF (5 % H₂O by volume) (4.0 mL) under Ar at 100 °C were stirred for the specified length
of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO$_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

**Jeffrey's reaction conditions:** The appropriate aryl iodide (0.25 mmol), Pd(OAc)$_2$ (2.8 mg, 0.0125 mmol), $n$-Bu$_4$NCl (0.0694 g, 0.25 mmol), NaHCO$_3$ (0.042 g, 0.5 mmol) and ethyl acrylate (0.10 g, 1.0 mmol) in DMF (1 ml) under Ar at 100 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO$_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

**Ethyl E-3-(4'-methylbiphen-2-yl)acrylate (2a).** 2-Iodo-4'-methylbiphenyl (1a) (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 day. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 66.6 mg (100 %) of the indicated compound as a clear oil: $^1$H NMR (CDCl$_3$) δ 1.28 (t, $J$ = 7.2 Hz, 3H), 2.41 (s, 3H), 4.21 (q, $J$ = 7.2 Hz, 2H), 6.39 (d, $J$ = 16.0 Hz, 1H), 7.18-7.26 (m, 4H), 7.34-7.42 (m, 3H), 7.67-7.70 (m, 1H), 7.75 (d, $J$ = 16.0 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.4, 21.2, 60.4, 119.0, 126.8, 127.5, 129.1, 129.8, 129.9, 130.6, 132.7, 137.0, 137.4, 143.0, 144.0, 167.0; IR (CH$_2$Cl$_2$) 3024, 2977, 1712, 1631 cm$^{-1}$; HRMS m/z 266.1312 (calcd for C$_{16}$H$_{18}$O$_2$, 266.1307).
Ethyl E-3-(4'-methylbiphen-2-yl)acrylate (3a). Compound 4a (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 61.9 mg (93 %) of the indicated compound as a clear oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.28 (t, \(J = 7.2\) Hz, 3H), 2.42 (s, 3H), 4.20 (q, \(J = 7.2\) Hz, 2H), 6.39 (d, \(J = 16.0\) Hz, 1H), 7.25-7.31 (m, 4H), 7.36-7.44 (m, 3H), 7.51-7.51 (m, 1H), 7.72 (d, \(J = 16.0\) Hz, 1H); \(^1^3\)C NMR (CDCl\(_3\)) \(\delta\) 14.3, 21.2, 60.4, 119.0, 127.3, 127.4, 128.3, 130.0, 130.8, 132.5, 137.4, 139.9, 140.3, 143.9, 167.0; IR (CH\(_2\)Cl\(_2\)) 3026, 2980, 1633, 1711 cm\(^{-1}\); HRMS \(m/z\) 266.1312 (calcd for C\(_{18}\)H\(_{18}\)O\(_2\), 266.1307).

Ethyl E-3-(4'-methylbiphen-2-yl)acrylate (2a) and ethyl E-3-(4-methylbiphen-2-yl)acrylate (3a). Compound 1a (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1.5 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 58.6 mg (88 %) of the indicated compounds as a clear oil in a 50:50 ratio. Similarly, compound 4a (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1.5 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 57.3 mg (86 %) of the indicated compounds as a clear oil in a 49:51 ratio.

Ethyl E-3-(4'-dimethylaminobiphen-2-yl)acrylate (2b). N,N-Dimethyl-4-(2-iodophenyl)aniline (1b) (80.8 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 day. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 59.0 mg (80 %) of the indicated compound as a yellow solid: mp 117-118 °C; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.30 (t, \(J = 7.0\) Hz, 3H), 3.01 (s, 6H), 4.22 (q, \(J = 7.2\) Hz, 2H), 6.39 (d, \(J = 15.6\) Hz, 1H), 6.78-6.80 (m, 2H), 7.20-7.22 (m, 2H), 7.31-7.40 (m, 3H),
7.66 (d, J = 7.2 Hz, 1H), 7.84 (d, J = 16.0 Hz, 1H); ^13^C NMR (CDCl$_3$) δ 14.4, 40.6, 60.3, 112.2, 118.5, 126.7, 126.9, 127.7, 129.8, 130.4, 130.7, 132.6, 143.2, 144.7, 150.0, 167.2; IR (CH$_2$Cl$_2$) 2975, 2926, 2857, 1715, 1612, 1631, 1526 cm$^{-1}$; HRMS m/z 295.1580 (calcd for C$_{19}$H$_{21}$NO$_2$, 295.1572); Anal. C, 77.05, H, 7.29; N, 4.57 (calcd for C$_{19}$H$_{21}$NO$_2$: C, 77.26; H, 7.17; N, 4.77).

**Ethyl E-3-(4-dimethylaminobiphen-2-yl)acrylate (3b).** N,N-Dimethyl-3-iodo-4-phenylaniline (4b) (80.8 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 73.8 mg (100 %) of the indicated compound as a yellow oil: ^1^H NMR (CDCl$_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 3.01 (s, 6H), 4.21 (q, J = 7.2 Hz, 2H), 6.39 (d, J = 15.6 Hz, 1H), 6.85 (dd, J = 8.8, 2.8 Hz, 1H), 6.97 (d, J = 2.8 Hz, 1H), 7.24-7.34 (m, 4H), 7.38-7.42 (m, 2H), 7.77 (d, J = 16.0 Hz, 1H); ^13^C NMR (CDCl$_3$) δ 14.4, 40.6, 60.4, 109.8, 114.7, 118.7, 126.8, 128.2, 130.0, 131.3, 131.6, 133.1, 140.2, 145.1, 149.8, 167.1; IR (CH$_2$Cl$_2$) 2975, 2920, 1711, 1632, 1605, 1174 cm$^{-1}$; HRMS m/z 295.1577 (calcd for C$_{19}$H$_{21}$NO$_2$, 295.1572).

**Ethyl E-3-(4’-dimethylaminobiphen-2-yl)acrylate (2b) and ethyl E-3-(4-dimethylaminobiphen-2-yl)acrylate (3b).** Compound 1b (80.8 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 66.4 mg (90 %) of the indicated compounds as a clear oil in a 55:45 ratio. Similarly, compound 4b (80.8 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using
5:1 hexanes/ethyl acetate to afford 68.6 mg (93 %) of the indicated compounds as a clear oil in a 49:51 ratio.

**Ethyl E-3-(4'-methoxybiphen-2-yl)acrylate (2c).** 2-Iodo-4'-methoxybiphenyl (1c) (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 70.6 mg (100 %) of the indicated compound as a white solid: mp 67-68 °C; ¹H NMR (CDCl₃) δ 1.29 (t, J = 7.2 Hz, 3H), 3.86 (s, 3H), 4.21 (q, J = 7.2 Hz, 2H), 6.40 (d, J = 16.0 Hz, 1H), 6.96-6.98 (m, 2H), 7.23-7.25 (m, 2H), 7.34-7.36 (m, 2H), 7.34-7.41 (m, 1H), 7.67-7.69 (m, 1H), 7.75 (d, J = 16.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.4, 55.4, 60.4, 113.8, 119.0, 126.9, 127.3, 129.9, 130.6, 131.0, 132.3, 132.7, 142.6, 144.1, 159.2, 167.0; IR (CH₂Cl₂) 3060, 2979, 1710, 1631, 1516 cm⁻¹; HRMS m/z 282.1259 (calcd for C₁₈H₁₄O₃, 282.1256).

**Ethyl E-3-(4'-methoxybiphen-2-yl)acrylate (3c).** Compound 4c (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 69.9 mg (99 %) of the indicated compound as a clear oil: ¹H NMR (CDCl₃) δ 1.28 (t, J = 7.2 Hz, 3H), 3.87 (s, 3H), 4.20 (q, J = 7.2 Hz, 2H), 6.38 (d, J = 15.6 Hz, 1H), 7.00 (dd, J = 5.6, 2.8 Hz, 1H), 7.19 (d, J = 2.8 Hz, 1H), 7.27-7.31 (m, 3H), 7.35-7.42 (m, 3H), 7.71 (d, J = 16.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.5, 55.7, 60.6, 111.4, 116.4, 119.6, 127.4, 128.5, 130.1, 131.9, 133.8, 136.1, 139.9, 144.0, 159.2, 167.0; IR (CH₂Cl₂) 2980, 2935, 1711, 1633, 1481 cm⁻¹; HRMS m/z 282.1259 (calcd for C₁₈H₁₄O₃, 282.1256).
Ethyl \( E-3-(4'-\text{methoxybiphen-2-yl})\)acrylate (2c) and ethyl \( E-3-(4'-\text{methoxybiphen-2-yl})\)acrylate (3c). Compound 1c (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 65.6 mg (93%) of the indicated compounds as a clear oil in a 52:48 ratio. Similarly, compound 4c (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 64.9 mg (92%) of the indicated compounds as a clear oil in a 48:52 ratio.

Ethyl \( E-3-(4'-\text{ethoxycarbonylbiphen-2-yl})\)acrylate (2d). Ethyl 4-(2-bromophenyl)benzoate (1d) (76.2 mg, 0.25 mmol) was allowed to react for 2 d under Jeffrey's reaction conditions with ethyl acrylate plus added 2-(di-\( t \)-butylphosphino)biphenyl (7.46 mg, 10 mol%). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 62.4 mg (77%) of the indicated compound (2d) as a clear oil: \(^1\)H NMR (CDCl\(_3\)) \( \delta \) 1.28 (t, \( J = 7.0 \) Hz, 3H), 1.42 (t, \( J = 7.2 \) Hz, 3H), 4.21 (q, \( J = 7.2 \) Hz, 2H), 4.42 (q, \( J = 7.2 \) Hz, 2H), 6.41 (d, \( J = 15.6 \) Hz, 1H), 7.36-7.46 (m, 5H), 7.66 (d, \( J = 16.0 \) Hz, 1H), 7.70-7.72 (m, 1H), 8.11-8.13 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \) 14.3, 14.4, 60.5, 61.1, 119.8, 127.0, 128.3, 129.6, 129.7, 129.9, 130.0, 130.4, 132.7, 141.8, 143.2, 144.5, 166.4, 166.7; IR (CH\(_2\)Cl\(_2\)) 2880, 2933, 1713, 1633 cm\(^{-1}\); HRMS \( m/z \) 324.1368 (calcd for C\(_{20}\)H\(_{19}\)O\(_4\), 324.1362). In addition, we also obtained 8.9 mg (11%) of compound 3d as a clear oil.

Ethyl \( E-3-(4'-\text{ethoxycarbonylbiphen-2-yl})\)acrylate (3d). Ethyl 3-iodo-4-phenylbenzoate (4d) (76.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1
hexanes/ethyl acetate to afford 80.2 mg (99 %) of the indicated compound (3d) as a clear oil:

$^1$H NMR (CDCl$_3$) $\delta$ 1.30 (t, $J = 7.2$ Hz, 3H), 1.43 (t, $J = 7.0$ Hz, 3H), 4.22 (q, $J = 7.2$ Hz, 2H), 4.42 (q, $J = 7.2$ Hz, 2H), 6.52 (d, $J = 16.0$ Hz, 1H), 7.32-7.33 (m, 2H), 7.42-7.48 (m, 4H), 7.72 (d, $J = 16.0$ Hz, 1H), 8.08-8.10 (m, 1H), 8.38 (s, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.3, 14.4, 60.6, 61.3, 120.4, 128.2, 128.5, 129.7, 129.9, 130.5, 130.7, 132.9, 139.0, 142.8, 146.9, 166.0, 166.7 (one sp$^2$ carbon missing due to overlap); IR (CH$_2$Cl$_2$) 2980, 1717, 1636, 1285, 1245 cm$^{-1}$; HRMS m/z 324.1368 (calcd for C$_{20}$H$_{20}$O$_4$, 324.1362).

Ethyl E-3-(4'-ethoxycarbonylbiphen-2-yl)acrylate (2d) and ethyl E-3-(4'-ethoxycarbonylbiphen-2-yl)acrylate (3d). Compound 1d (76.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions B for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 36.4 mg (45 %) of the indicated compounds as a clear oil in a 47:53 ratio. In addition, we obtained 26.0 mg (46 %) of ethyl 4-phenylbenzoate as a white solid with spectral properties identical to those previously described in the literature. Similarly, compound 4d (76.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions B for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 67.2 mg (83 %) of the indicated compounds as a clear oil in a 42:58 ratio.

Ethyl E-3-(4'-nitrobiphen-2-yl)acrylate (2e). Compound 1e (81.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions, but Et$_3$N (50.5 mg, 0.5 mmol) was used in place of NaHCO$_3$ as the base. After 1 d, the reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 63.1 mg (85 %) of the indicated compound 3e as a yellow oil: $^1$H NMR (CDCl$_3$) $\delta$ 1.29 (t, $J = 7.0$ Hz, 3H), 4.22 (q, $J = 7.2$
Hz, 2H), 6.43 (d, J = 16.0 Hz, 1H), 7.36-7.38 (m, 1H), 7.46-7.51 (m, 4H), 7.60 (d, J = 15.6 Hz, 1H), 7.72-7.74 (m, 1H), 8.29-8.32 (m, 2H); $^{13}$C NMR (CDCl$_3$) δ 14.3, 60.7, 120.5, 123.6, 127.3, 129.0, 130.1, 130.3, 130.7, 132.7, 140.3, 142.4, 146.7, 147.3, 166.6; IR (CH$_2$Cl$_2$) 2917, 1710, 1517, 1348, 1314, 1179 cm$^{-1}$; HRMS m/z 297.1010 (calcd for C$_{17}$H$_{15}$NO$_4$, 297.1001).

**Ethyl E-3-(4-nitrobiphen-2-yl)acrylate (3e).** Compound 4e (81.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions, but Et$_3$N (50.5 mg, 0.5 mmol) was used in place of NaHCO$_3$ as the base. After 1 d, the reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 66.1 mg (89 %) of the indicated compound 3e as a yellow solid: mp = 118-119 °C, $^1$H NMR (CDCl$_3$) δ 1.31 (t, J = 7.2 Hz, 3H), 4.24 (t, J = 7.2 Hz, 2H), 6.55 (d, J = 15.9 Hz, 1H), 7.31-7.34 (m, 2H), 7.46-7.56 (m, 4H), 7.69 (d, J = 15.9 Hz, 1H), 8.26 (dd, J = 8.4, 2.4 Hz, 1H), 8.55 (d, J = 2.4 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.5, 61.0, 122.2, 122.2, 124.2, 128.9, 129.1, 129.7, 131.8, 134.4, 138.1, 141.6, 147.5, 148.8, 166.3; IR (CH$_2$Cl$_2$) 2974, 2917, 2849, 1719, 1523, 1347, 1179, 1118 cm$^{-1}$; HRMS m/z 297.1010 (calcd for C$_{17}$H$_{15}$NO$_4$, 297.1001); Anal. C, 68.41; H, 4.84; N, 4.51 (calcd for C$_{17}$H$_{15}$NO$_4$: C, 68.68; H, 5.09; N, 4.71).

**Ethyl E-3-(4'-nitrobiphen-2-yl)acrylate (2e) and ethyl E-3-(4-nitrobiphen-2-yl)acrylate (3e).** Compound 1e (81.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions B for 2.5 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 34.2 mg (46 %) of the indicated compounds as a yellow oil in a 39:61 ratio. In addition, we obtained 19.9 mg (40 %) of 4-nitrobiphenyl as a yellow solid with spectral properties identical to those previously
reported. Similarly, compound 4e (81.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions B for 2.5 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 27.5 mg (37%) of the indicated compounds as a yellow oil in a 33:67 ratio. In addition, we obtained 24.9 mg (50%) of 4-nitrobiphenyl as a yellow solid with spectral properties identical to those previously reported.

**Ethyl E-3-(3-phenylbenzofuran-2-yl)acrylate (6a).** Compound 5a (80.0 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 62.1 mg (85%) of the indicated compound as a white solid: mp 84-85 °C, $^1$H NMR (CDCl$_3$) δ 1.32 (t, $J = 7.2$ Hz, 3H), 4.25 (q, $J = 7.2$ Hz, 2H), 6.68 (d, $J = 15.6$ Hz, 1H), 7.25-7.29 (m, 1H), 7.40-7.54 (m, 7H), 7.63-7.68 (m, 2H); $^{13}$C NMR (CDCl$_3$) δ 14.4, 60.7, 111.6, 119.4, 121.0, 123.5, 125.7, 127.0, 128.4, 129.2, 129.6, 130.3, 131.2, 148.3, 155.0, 167.0; IR (CH$_2$Cl$_2$) 3062, 2979, 1709, 1628, 1450 cm$^{-1}$; HRMS m/z 292.1104 (calcd for C$_{19}$H$_{16}$O$_3$, 292.1099). Similarly, compound 8a (80.0 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 57.0 mg (78%) of the indicated compound as a yellow solid: mp 82-84 °C.

**Ethyl E-3-[2-(benzofuran-3-yl)phenyl]acrylate (7a).** Compound 8a (80.0 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions at 80 °C for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 54.8 mg (75%) of the indicated compound as a clear oil: $^1$H NMR (CDCl$_3$) δ 1.24 (t, $J = 7.0$
Hz, 3H), 4.18 (q, J = 7.2 Hz, 2H), 6.44 (d, J = 16.0 Hz, 1H), 7.24-7.28 (m, 1H), 7.33-7.58 (m, 6H), 7.60 (s, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.86 (d, J = 15.6 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.3, 60.5, 111.8, 119.8, 119.8, 120.5, 123.2, 124.9, 127.1, 127.6, 128.2, 130.1, 130.7, 132.2, 133.7, 143.1, 143.5, 155.3, 166.8; IR (CH$_2$Cl$_2$) 3060, 2979, 1711, 1633, 1452 cm$^{-1}$; HRMS m/z 292.1104 (calcd for C$_{19}$H$_{16}$O$_3$, 292.1099).

**Ethyl E-3-(1-methyl-3-phenylindol-2-yl)acrylate (6b).** Compound 5b (83.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 71.2 mg (94%) of the indicated compound 6b as a yellow oil: $^1$H NMR (CDCl$_3$) δ 1.29 (t, J = 7.2 Hz, 3H), 3.90 (s, 3H), 4.22 (q, J = 7.2 Hz, 2H), 6.23 (d, J = 16.4 Hz, 1H), 7.12-7.14 (m, 1H), 7.33-7.39 (m, 3H), 7.45-7.48 (m, 4H), 7.62 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 16.4 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.4, 31.7, 60.6, 109.7, 118.7, 120.6, 122.7, 124.6, 127.0, 127.9, 128.8, 130.4, 131.1, 133.3, 134.2, 139.1, 167.2; IR (CH$_2$Cl$_2$) 3057, 2975, 2927, 1708, 1625, 1369, 1289, 1180 cm$^{-1}$; HRMS m/z 305.1420 (calcd for C$_{20}$H$_{19}$NO$_2$, 305.1416).

**Ethyl E-3-(2-(1-methylindol-3-yl)phenyl)acrylate (7b).** Compound 8b (83.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey’s reaction conditions at 75 °C for 2 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 64.4 mg (85%) of the indicated compound as a white solid: mp 130-131 °C; $^1$H NMR (CDCl$_3$) δ 1.26 (t, J = 7.2 Hz, 3H), 3.85 (s, 3H), 4.19 (q, J = 7.2 Hz, 2H), 6.43 (d, J = 16.0 Hz, 1H), 7.01 (s, 1H), 7.14-7.18 (m, 1H), 7.27-7.39 (m, 3H), 7.42-7.46 (m, 1H), 7.60-7.64 (m, 2H), 7.73 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 16.0 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.4, 33.0,
60.3, 109.5, 113.9, 118.5, 120.0, 120.1, 122.2, 126.6, 127.0, 127.4, 129.4, 129.9, 131.0, 133.2, 136.0, 137.0, 144.6, 167.2; IR (CH$_2$Cl$_2$) 2918, 2848, 1712, 1631, 1314 cm$^{-1}$; HRMS m/z 305.1420 (calcd for C$_{20}$H$_{19}$NO$_2$, 305.1416); Anal. C, 78.36; H, 6.28; N, 4.45 (calcd for C$_{20}$H$_{19}$NO$_2$: C, 78.66; H, 6.27; N, 4.59).

**Ethyl E-3-(3',5'-dimethylbiphen-2-yl)acrylate (10).** Compound 9 (77.0 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 69.0 mg (97 %) of the indicated compound 10 as a clear oil: $^1$H NMR (CDCl$_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 2.36 (s, 6H), 4.20 (q, J = 7.2 Hz, 2H), 6.38 (d, J = 16.0 Hz, 1H), 6.92 (s, 2H), 7.02 (s, 1H), 7.33-7.41 (m, 3H), 7.67-7.69 (m, 1H), 7.75 (d, J = 15.6 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.4, 21.4, 60.3, 118.9, 126.6, 127.5, 127.8, 129.2, 129.8, 130.5, 132.6, 137.8, 139.9, 143.3, 143.9, 167.0; IR (CH$_2$Cl$_2$) 2918, 2976, 1712, 1632, 1313 cm$^{-1}$; HRMS m/z 280.1468 (calcd for C$_{19}$H$_{20}$O$_2$, 280.1463).

**Ethyl E-3-(3-methoxybiphen-2-yl)acrylate (13).** Compound 12 (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 55.1 mg (78 %) of the indicated compound 13 as a clear oil: $^1$H NMR (CDCl$_3$) δ 1.25 (t, J = 7.2 Hz, 3H), 3.94 (s, 3H), 4.16 (q, J = 7.2 Hz, 2H), 6.61 (d, J = 16.4 Hz, 1H), 6.94-6.96 (m, 2H), 7.28-7.41 (m, 6H), 7.63 (d, J = 16.4 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.3, 55.7, 60.2, 110.0, 121.5, 122.4, 123.0, 127.5, 128.2, 129.9, 130.0, 139.8, 140.6, 145.5, 159.3, 168.0; IR (CH$_2$Cl$_2$) 3054, 2985, 2926, 1705, 1265, cm$^{-1}$; HRMS 282.1256 m/z (calcd for C$_{18}$H$_{18}$O$_3$, 282.1256).
Ethyl \( E-3-(3'-\text{methoxybiphen-2-yl})\)acrylate (14). Compound 19 (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 60.0 mg (85 %) of the indicated compound as a clear oil: \(^1H\) NMR (CDCl\(_3\)) \( \delta \) 1.28 (t, \( J = 7.2 \) Hz, 3H), 3.83 (s, 3H), 4.21 (q, \( J = 7.2 \) Hz, 2H), 6.39 (d, \( J = 16.0 \) Hz, 1H), 6.85-6.95 (m, 3H), 7.32-7.43 (m, 4H), 7.68-7.70 (m, 1H), 7.75 (d, \( J = 16.0 \) Hz, 1H); \(^{13}C\) NMR (CDCl\(_3\)) \( \delta \) 14.3, 55.4, 60.4, 113.4, 115.4, 119.2, 122.4, 126.8, 127.8, 129.3, 129.8, 130.4, 132.7, 141.3, 142.8, 143.8, 159.4, 166.9; IR (CH\(_2\)Cl\(_2\)) 3061, 2980, 1711, 1632, 1314, 1177, cm\(^{-1}\); HRMS \( m/z \) (calcd for C\(_{18}\)H\(_{18}\)O\(_3\), 282.1256).

Ethyl \( E-3-(5'-\text{methoxybiphen-2-yl})\)acrylate (15). An authentic sample of compound 15 was prepared in two steps from 2-iodo-4-methoxybenzaldehyde\(^3\) \([\text{mp} \ 113-114^\circC]\); \(^1H\) NMR (CDCl\(_3\)) \( \delta \) 3.88 (s, 3H), 6.99 (dd, \( J = 8.8, 2.4 \) Hz, 1H), 7.44 (d, \( J = 2.0 \) Hz, 1H), 7.85 (d, \( J = 8.8 \) Hz, 1H), 9.93 (s, 1H); \(^{13}C\) NMR (CDCl\(_3\)) \( \delta \) 55.9, 102.4, 114.9, 125.4, 128.6, 131.6, 164.4, 194.5] in the following matter. 2-Iodo-4-methoxybenzaldehyde (0.262 g, 1.0 mmol), Pd(OAc)\(_2\) (11.2 mg, 0.05 mmol), PPh\(_3\) (26.2 mg, 0.1 mmol), CsF (0.334 g, 2.2 mmol) and phenylboronic acid (0.146 g, 1.2 mmol) in DME (5 ml) under Ar at 90 °C were stirred for 3 h. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO\(_4\)), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column using 7:1 hexanes/ethyl acetate to afford 21.0 mg (99 %) of 2-phenyl-4-methoxybenzaldehyde as a clear oil: \(^1H\) NMR (CDCl\(_3\)) \( \delta \) 3.91 (s, 3H), 6.88 (d, \( J = 2.4 \) Hz,
1H), 6.99-7.02 (m, 1H), 7.38-7.47 (m, 5H), 8.03 (d, J = 8.8 Hz, 1H), 9.84 (d, J = 0.4 Hz, 1H);

\(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 55.7, 114.0, 115.2, 127.4, 128.3, 128.4, 129.9, 130.0, 137.9, 148.6, 163.6, 191.1. 2-Phenyl-4-methoxybenzaldehyde (53.0 mg, 0.25 mmol) and (carboethoxymethylene)triphenylphosphorane (0.1305 g, 0.375 mmol) in CH\(_2\)Cl\(_2\) (5 ml) were stirred at 60 °C under argon for 15 h. The reaction mixture was allowed to cool to room temperature and the solvent evaporated under reduced pressure. The resulting yellow oil was purified by column chromatography on a silica gel column using 1:9 ethyl acetate/hexanes to afford 43.7 mg (62 %) of the desired compound 15 as a clear oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.27 (t, \(J = 7.2\) Hz, 3H), 3.85 (s, 3H), 4.18 (q, \(J = 7.2\) Hz, 2H), 6.29 (d, \(J = 15.9\) Hz, 1H), 6.87 (d, \(J = 2.7\) Hz, 1H), 6.92-6.95 (m, 1H), 7.29-7.33 (m, 2H), 7.39-7.44 (m, 3H), 7.64-7.69 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 14.5, 55.7, 60.4, 114.2, 115.4, 117.0, 125.6, 127.9, 128.5, 128.5, 129.9, 140.1, 143.4, 145.1, 160.9, 167.4; IR (CH\(_2\)Cl\(_2\)) 3056, 2978, 2937, 1709, 1630, 1484 cm\(^{-1}\); HRMS m/z (calcd for C\(_{18}\)H\(_{18}\)O\(_3\), 282.1256).

**Ethyl E-3-(3-methoxybiphen-2-yl)acrylate (13), ethyl E-3-(3'-methoxybiphen-2-yl)acrylate (14), and ethyl E-3-(5-methoxybiphen-2-yl)acrylate (15).** Compound 12 (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 68.5 mg (97 %) of the indicated compounds as a clear oil in a 53:38:9 ratio. Similarly, compound 19 (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 61.3 mg (87 %) of the indicated compounds as a clear oil in a 25:62:13 ratio.
**Ethyl E-3-(2'-methylbiphen-2-yl)acrylate (21).** Compound 21 (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 61.2 mg (92 %) of the indicated compound 21 as a yellow oil: $^1$H NMR (CDCl$_3$) $\delta$ 1.24 (t, $J$ = 7.2 Hz, 3H), 2.03 (s, 3H), 4.16 (q, $J$ = 7.2 Hz, 2H), 6.33 (d, $J$ = 16.0 Hz, 1H), 7.10 (d, $J$ = 7.2 Hz, 1H), 7.20-7.29 (m, 4H), 7.37-7.44 (m, 3H), 7.70-7.72 (m, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.3, 20.1, 60.4, 119.0, 125.7, 126.2, 127.7, 128.0, 129.8, 129.9, 130.1, 130.5, 133.0, 136.1, 139.6, 142.9, 143.0, 166.9; IR (CH$_2$Cl$_2$) 3061, 2978, 2920, 1713, 1633, 1177 cm$^{-1}$; HRMS m/z 266.1312 (calcd for C$_{18}$H$_{18}$O$_2$, 266.1307).

**Ethyl E-3-(2'-methylbiphen-2-yl)acrylate (21) and ethyl E-3-(6-methylbiphen-2-yl)acrylate (22).** Compound 20 (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 60.5 mg (91 %) of the indicated compounds as a yellow oil in a 65:35 ratio. Minor isomer 22: $^1$H NMR (CDCl$_3$) $\delta$ 2.08 (s, 3H), 6.27 (d, $J$ = 16.0 Hz, 1H), 7.54-7.56 (m, 1H) as characteristic peaks; $^{13}$C NMR (CDCl$_3$) $\delta$ 20.9, 60.3, 118.8, 123.8, 127.4, 127.5, 128.5, 129.7, 131.5, 133.4, 137.0, 138.9, 142.8, 143.9, 143.9 as characteristic peaks; HRMS m/z 266.1312 (calcd for C$_{18}$H$_{18}$O$_2$, 266.1307).

**1-Methoxy-9,10-diphenylphenanthrene (27).** 2-Iodo-3-methoxybiphenyl (12) (77.5 mg, 0.25 mmol), Pd(OAc)$_2$ (2.8 mg, 0.0125 mmol), LiCl (0.0105 g, 0.25 mmol), NaOAc (0.0175 g, 0.5 mmol) and diphenylacetylene (0.0534 g, 0.30 mmol) in DMF (4 ml) under Ar at 100 °C were stirred for 2 d. The reaction mixture was then cooled to room temperature,
diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was
reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO₄),
filtered, and the solvent removed under reduced pressure. The residue was chromatographed
using 25:1 hexanes/ethyl acetate to afford 81.1 mg (90 %) of the indicated compound 27 as a
white solid: mp 188-189 °C; 'H NMR (CDCl₃) δ 3.34 (s, 3H), 6.96-7.20 (m, 11H), 7.43-7.45
(m, 2H), 7.58-7.63 (m, 2H), 8.46 (d, J = 8.1 Hz, 1H), 8.77 (d, J = 8.4 Hz, 1H); ¹³C NMR
(CDCl₃) δ 55.9, 109.3, 115.5, 122.6, 123.1, 124.8, 126.2, 126.2, 126.4, 126.8, 126.9, 127.4,
127.8, 129.5, 129.7, 131.3, 132.1, 132.2, 135.1, 138.2, 139.8, 144.1, 157.9; IR (CH₂Cl₂)
3026, 1576, 1462 cm⁻¹; HRMS m/z 360.1521 (calcd for C₂₇H₂₀O, 360.1514).

3-Methoxy-9,10-diphenylphenanthrene (28). Compound 12 (77.5 mg, 0.25 mmol),
Pd(OAc)₂ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg,
0.0125 mmol), CsPiv (0.117 g, 0.5 mmol) and diphenylacetylene (0.0534 g, 0.30 mmol) in
DMF (4 ml) under Ar at 100 °C were stirred for 2 d. The reaction mixture was then cooled to
room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The
aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were
combined, dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The
residue was chromatographed using 25:1 hexanes/ethyl acetate to afford 40.0 mg (44 %) of
compound 27, alongside 38.4 mg (43 %) of compound 28 as a white solid: mp 184-186 °C;
¹H NMR (CDCl₃) δ 4.03 (s, 3H), 7.11-7.25 (m, 11H), 7.47-7.49 (m, 2H), 7.54-7.56 (m, 1H),
7.61-7.65 (m, 1H), 8.17 (d, J = 2.4 Hz, 1H), 8.72 (d, J = 8.4 Hz, 1H); ¹³C NMR (CDCl₃) δ
55.6, 104.0, 116.5, 122.6, 126.0, 126.4, 126.5, 126.6, 126.8, 127.6, 127.9, 129.4, 129.5,
131.1, 131.3, 131.5, 132.4, 135.0, 137.1, 139.7, 139.8, 158.3 (missing one sp² carbon due to
overlap); IR (CH₂Cl₂) 3056, 3022, 1576, 1460 cm⁻¹; HRMS m/z 360.1521 (calcd for C₂₇H₂₀O₂, 360.1514).

Suzuki-Miyaura reactions

The following procedures are representative of the Suzuki-Miyaura cross-coupling reactions of o-iodobiaryls with arylboronic acids.

**Migration reaction conditions C:** The appropriate aryl iodide (0.25 mmol), Pd(OAc)₂ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol), Cs₂CCMe₃ (CsPiv) (0.117 g, 0.5 mmol), Me₃CCO₂H (0.051 g, 0.5 mmol), H₂O (0.09 g, 5.0 mmol) and the corresponding arylboronic acid (0.35 mmol) in DMF (4.0 ml) under Ar at 100 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

**Wright's reaction conditions:** The appropriate aryl iodide (0.25 mmol), Pd(OAc)₂ (2.8 mg, 5 mol %), PPh₃ (6.56 mg, 10 mol %), CsF (0.084 g, 0.55 mmol), and the corresponding arylboronic acid (0.30 mmol) in DME (1.0 ml) under Ar at 90 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.
Methyl 4-(4'-methylbiphen-2-yl)benzoate (23a). Compound 1a and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under Wright's conditions for 8 h. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 46.6 mg (62 %) of the indicated compound 23a as a clear oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta 2.3 \text{ (s, 3H), 3.89 (s, 3H), 6.97-7.04 (m, 4H), 7.20-7.23 (m, 2H), 7.40-7.44 (m, 4H), 7.87-7.90 (m, 2H);}

\(^1^3\)C NMR (CDCl\(_3\)) \(\delta 21.3, 52.3, 127.6, 128.3, 129.0, 129.4, 129.9, 130.1, 130.6, 131.0, 136.6, 138.3, 139.7, 140.9, 146.9, 167.4;\) IR (CH\(_2\)Cl\(_2\)) 2918, 3023, 1724, 1277 cm\(^{-1}\); HRMS \(m/z\) 302.1313 (calcd for C\(_{21}\)H\(_{18}\)O\(_2\), 302.1307).

Methyl 4-(4'-methylbiphen-2-yl)benzoate (23a) and methyl 4-(4-methylbiphen-2-yl)benzoate (24a). Compound 1a and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under our standard migration conditions C for 1 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 59.7 mg (71 % corrected yield) of the indicated compounds as a clear oil in a 51:49 ratio. Minor isomer 24a: \(^1\)H NMR (CDCl\(_3\)) \(\delta 2.44 \text{ (s, 3H), 3.88 (s, 3H) as characteristic peaks; HRMS} \(m/z\) 302.1313 (calcd for C\(_{21}\)H\(_{18}\)O\(_2\), 302.1307). In addition, this sample was contaminated with what is presumed to be 4,4'-bis(dimethoxycarbonylbiphenyl (21 mol %): \(^1\)H NMR (CDCl\(_3\)) \(\delta 3.92 \text{ (s, 3H), as a characteristic peak.}

4-(4'-Methylbiphen-2-yl)anisole (23b) and 4-(4-methylbiphen-2-yl)anisole (24b). Compound 1a and 4-methoxyphenylboronic acid (38.0 mg, 0.25 mmol) were allowed to react under our standard migration conditions C for 1 d. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 26.2 mg (38 %) of the indicated compounds as a clear oil in 52:48 ratio. Major isomer 23b: \(^1\)H NMR (CDCl\(_3\)) \(\delta 2.31 \text{ (s, 3H),}
3.77 (s, 3H) as characteristic peaks; HRMS m/z 274.1353 (calcd for C_{20}H_{18}O, 274.1358).

Minor isomer 24b: $^1$H NMR (CDCl$_3$) δ 2.42 (s, 3H), 3.76 (s, 3H) as characteristic peaks; HRMS m/z 274.1353 (calcd for C$_{20}$H$_{18}$O, 274.1358).

**Methyl 4-(3-phenylbenzofuran-2-yl)benzoate (25).** Compound 5a and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under our standard migration conditions for 1 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 64.9 mg (79 %) of the indicated 25 compound as a white solid: mp 122-123 °C; $^1$H NMR (CDCl$_3$) δ 3.90 (s, 3H), 7.23-7.27 (m, 1H), 7.34-7.38 (m, 1H), 7.43-7.51 (m, 6H), 7.56-7.58 (m, 1H), 7.71-7.73 (m, 2H), 7.96-7.98 (m, 2H); $^{13}$C NMR (CDCl$_3$) δ 52.2, 111.3, 119.6, 120.4, 123.2, 125.5, 126.6, 128.1, 129.2, 129.4, 129.7, 130.1, 132.4, 134.9, 149.3, 154.2, 166.7 (one sp$^2$ carbon missing due to overlap); IR (CH$_2$Cl$_2$) 2917, 2849, 1727, 1609, 1453, 1278, 1118 cm$^{-1}$; HRMS m/z 328.1104 (calcd for C$_{22}$H$_{16}$O$_3$, 328.1099); Anal. C, 80.12; H, 4.81; N (calcd for C$_{22}$H$_{16}$O$_3$: C, 80.47; H, 4.91). In addition, compound 8a and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under our standard migration conditions C for 1 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 63.9 mg (78 %) of the indicated compound as a white solid.

**Methyl 4-[2-(benzofuran-3-yl)phenyl]benzoate (26).** Compound 8a and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under Wright's conditions for 6 h. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 61.5 mg (75 %) of the indicated compound 26 as a clear oil: $^1$H NMR (CDCl$_3$) δ 3.87 (s, 3H), 7.11-7.14 (m, 1H), 7.21-7.27 (m, 2H), 7.30-7.34 (m, 3H), 7.42-7.49 (m, 4H), 7.58-7.60 (m, 1H), 7.87-7.89 (m, 2H); $^{13}$C NMR (CDCl$_3$) δ 52.3, 111.7, 120.6, 121.2, 123.0, 124.6, 127.4,
128.3, 128.4, 128.8, 129.5, 129.6, 130.1, 130.8, 131.1, 140.7, 143.1, 146.4, 155.3, 167.2; IR (CH\textsubscript{2}Cl\textsubscript{2}) 2850, 2973, 1723, 1609, 1452, 1279 cm\textsuperscript{-1}; HRMS m/z 328.1104 (calcd for C\textsubscript{22}H\textsubscript{16}O\textsubscript{3}, 328.1099). In addition, we isolated 6.0 mg (7%) of compound 25 from this reaction mixture.

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**References**


(9) The spectral properties of this compound were identical to those previously reported, see: Bregbreiter, D. E.; Osburn, P. L.; Wilson, A.; Sink, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 9058.

(10) The spectral properties of this compound were identical to those previously reported, see: Rottlaender, M.; Knochel, P.; *J. Org. Chem.* **1998**, *63*, 203.

(11) The spectral properties of this compound were identical to those previously reported, see: Wallow, T. I.; Novak, B. M. *J. Org. Chem.* **1994**, *59*, 5034.


(15) For examples of electrophilic aromatic substitutions involving 3-phenylbenzofuran, see:


CHAPTER 3. SEQUENTIAL 1,4-PALLADIUM MIGRATION FOLLOWED BY INTRAMOLECULAR ARYLATION: SYNTHESIS OF FUSED POLYCYCLES

Based on a communication to be submitted to the Journal of the American Chemical Society and a paper to be submitted to the Journal of the American Chemical Society

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Abstract

The synthesis of various fused carbocycles and heterocycles has been accomplished by the Pd-catalyzed intramolecular C-H activation of o-halobiaryls. This methodology makes use of a 1,4-palladium migration to generate key organopalladium intermediates, which undergo intramolecular arylation producing complex polycyclic compounds containing fused benzofuran, quinoline, oxepine, indole, phenanthrene, and naphthalene rings. This methodology offers a unique approach to the preparation of complex systems, which would be difficult to access by other known methodologies.

Introduction

The ability of palladium to activate C-H bonds has been used extensively in organic synthesis. In recent years, palladium-catalyzed C-H activation has received considerable attention due to the wide variety of reactions this metal will catalyze. For instance, catalytic amounts of Pd salts have been used to activate the addition of C-H bonds of electron-rich
arenes to alkenes and alkynes, as well as to undergo other transformations, such as carbonylation. We have previously reported the synthesis of 9-benzylidene-9H-fluorenes by Pd-catalyzed intramolecular C-H activation involving the rearrangement of organopalladium intermediates derived from aryl halides and internal alkynes. Similarly, intramolecular C-H activation in organopalladium intermediates derived from o-halobiaryls leads to a 1,4-palladium migration (Scheme 1). We have already shown that such intermediates can be trapped by Heck, Suzuki and alkyne annulation reactions. We have recently explored the synthetic potential of this aryl-aryl migration process, and now wish to report a novel synthesis of fused polycycles using this novel rearrangement. Our strategy involves the use of palladium C-H activation to catalyze a 1,4-palladium migration within biaryls generating key arylpalladium intermediates, which subsequently undergo C-C bond formation by intramolecular arylation producing fused polycycles (Scheme 2). This process represents a very powerful new tool for the preparation of complex molecules, which might be difficult to prepare by any other present methodology.

Scheme 1
**Scheme 2**

\[
\begin{align*}
\text{R}^2 & \quad \text{Y} = \text{O, CH}_2, \text{etc.} \\
\text{R}^2 & \quad \text{base} \\
\text{R}^1 & \quad \text{cat. Pd(0)} \\
\text{1,4-Pd shift} & \\
\text{HI} & \\
\end{align*}
\]

**Results and Discussion**

In order to obtain an optimum set of reaction conditions for migration, we have reinvestigated the palladium-catalyzed transformation of 1-iodo-1,2,2-triphenylethene (1) to 9-benzylidene-9\textit{H}-fluorene (2) as our model system\(^3\) (Table 1). While this system may not be the most obvious for a study of aryl to aryl Pd migrations, we had previously accumulated substantial data on this system. To begin with, we carried out this reaction using our previously reported conditions\(^3\) and obtained a 73% yield of the desired compound 2, along with a 15% yield of triphenylethene (3) (entry 1). The first variable to be examined was the ligand on palladium. We examined phosphines other than PPh\(_3\). Entries 2 and 3 indicate that P(\text{o-tolyl})\(_3\) and CH\(_2\)(PPh\(_2\))\(_2\) (dppm) are superior to PPh\(_3\) in affording higher yields of the fluorene 2. However, the reactions with all of these phosphine ligands required 3 d to reach completion. In order to shorten this relatively lengthy reaction time, we eliminated n-Bu\(_4\)NCl (TBAC) and found that the reaction was complete after only 1 d (entry 4). Unfortunately,
this led to a much lower yield of the desired compound 2 (47 %), and the yield of reduced product 3 increased to 47 %. In order to investigate whether DMF was the hydride source for the reduction of 1 to 3, we carried out this reaction using other solvents.

Table 1. Palladium-catalyzed transformation of 1-iodo-1,2,2-triphenylethene (1) to 9-benzylidenefluorene (2).

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<tr>
<th>entry</th>
<th>ligand (mol %)</th>
<th>base</th>
<th>chloride source</th>
<th>solvent</th>
<th>time (d)</th>
<th>% yield 1</th>
<th>% yield 2</th>
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<td>NaOAc</td>
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<td>DMF</td>
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<td>P(o-tolyl)₃ (10)</td>
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⁹The reaction was run using 0.25 mmol of 1-iodo-1,2,2-triphenylethene (1), 5 mol % of Pd(OAc)₂ and 4 mL of solvent at 100 °C. TBAC = n-Bu₄NCl. Dppm = 1,1-bis(diphenylphosphino)methane. ¹One equiv of NaI was added. ²Twenty four percent of 1 was recovered. ³Dppe = 1,2-bis(diphenylphosphino)ethane.
such as DMA, NMP, and DMSO (entries 5-7). DMSO gave none of the desired fluorene 2 or any reduction product 3. The amount of reduction was more or less the same in the other solvents. Thus, we continued our investigation using DMF as the reaction solvent.

We also examined the effect of various bases on the yield of 3, including organic bases, such as pyridine and diisopropylethylamine (entries 8 and 9). These bases were ineffective in promoting the reaction and TLC analysis of the reaction mixtures indicated only the presence of starting vinylic halide 1. The use of Na$_2$CO$_3$ as the base provided 2 in a 70 % yield, but we also obtained a 26 % yield of reduced product 3. The base NaHCO$_3$ provided a 65 % yield of 2 and a 23 % yield of 3. We believe that the solubility of these bases in the reaction mixture may be playing a critical role in determining the outcome. Thus, once again we used Na$_2$CO$_3$ as the base, but this time we added 1 equiv of NaI, which is completely soluble in DMF, as an additive to promote a sodium common ion effect intended to make Na$_2$CO$_3$ less soluble in the reaction mixture. Indeed, this experiment revealed that under such reaction conditions only reduced product 3 was produced in a 47 % yield. None of the desired product 2 was observed (compare entries 10 and 12). Although there may be a number of other effects going on under these reaction conditions, it seemed logical to assume that the yield of the reaction would improve by using more soluble inorganic bases. Thus, the use of Cs$_2$CO$_3$, which presumably has better solubility than other alkali carbonates in DMF, provided a slightly higher 74 % yield of compound 2, along with a 22 % yield of reduced product 3. Similarly, the use of very soluble CsOAc as base provided a 90 % yield of the desired product 2, along with 4 % of the reduced product 3 after 2 d (entry 14). We subsequently found that cesium pivalate (CsO$_2$CCMe$_3$), unlike any other
previously studied base, was completely soluble in DMF at 100 °C. In this case, we obtained an impressive 96 % yield of the desired compound 2, along with only a small amount of the reduced product 3 (4 %) after only 1 d (entry 15). Clearly, cesium pivalate is far superior as a base in this reaction, and its high solubility in DMF seems to explain this phenomena. To illustrate, we carried out the reaction of 1 under conditions identical to those described in entry 15, but we used DMA instead of DMF as the solvent, in which cesium pivalate is not completely soluble. Under these conditions, we obtained a relatively low 59 % yield of the desired compound 2, along with a 17 % yield of reduced product 3 (entry 16). Twenty four percent of the starting vinylic iodide 1 was also obtained. Finally, to test whether dppe was indeed critical to this reaction, we carried out the transformation using another chelating phosphine ligand, namely 1,2-bis(diphenylphosphino)ethane (dppe), and we obtained a 90 % yield of 2, along with a 10 % yield of the reduced product 3 (entry 17). As a result, our optimal set of reaction conditions for this transformation are those listed in entry 15 of Table 1. Notice that the newly developed conditions catalyze the transformation of 1 to 2 in high yield and much shorter reaction time than our earlier reported procedure.³ The most critical element to achieve these positive results was the use of the highly soluble cesium pivalate base. Surprisingly, the use of n-Bu₄NOAc as the base, which is also completely soluble in DMF under reaction conditions identical to those described in entry 15, failed to promote this reaction, affording only trace amounts of the desired product 2 after 1 d. As a result, not only the solubility, but also the exact nature of the base, appears critical in determining the reaction yield. It is interesting to note that the work of Buchwald, Hartwig and Fu has demonstrated that steric congestion imposed on palladium by bulky, electron-rich ligands
facilitate both the oxidative addition and reductive elimination steps involving palladium, and
give rise to more effective catalyst systems. However, nothing is apparently known about
the effects of using a sterically hindered base, such as pivalate, in palladium chemistry, and
whether or not it may give similar results to those obtained using bulky ligands.

With an apparently “optimal” set of reaction conditions at our disposal, we proceeded
to study the sequential Pd-catalyzed migration/arylation of various 3'-substituted 2-
iodobiphenyls (Table 2). We began by allowing 3'-benzyl-2-iodobiphenyl (4) to react under
our standard reaction conditions at 100 °C, but after 2 d this substrate failed to react.
However, by simply increasing the reaction temperature to 110 °C, we were able to obtain the
desired compound 5 in a 40 % yield (entry 1). The disappointingly low yield obtained with
this substrate might be explained by the poor reactivity of the benzyl moiety as an
intramolecular trap. To test this idea, we carried out the reaction with the more electron-rich
2-iodo-3'-phenoxybiphenyl (6) and obtained the desired 4-phenyldibenzo[1,4]furan (7) in an
impressive 89 % yield (entry 2). Clearly, these results indicate that the electron-rich oxygen-
substituted phenyl ring was superior as an arylating agent. Our finding that electron-rich
arenes are superior to electron-neutral arene traps is consistent with literature reports
indicating that the ease of C-H activation by palladium parallels electrophilic aromatic
substitution. Similarly, we were able to selectively obtain 3-chloro-5-phenyldibenzo[1,4]furan
(9) in an 82 % yield from 3-(p-chlorophenoxy)-2-iodobiphenyl (8) under our standard
conditions while leaving the chloro functionality intact (entry 3).

Motivated by the ease of preparation of the following starting materials and by the
knowledge that electron-rich arenes are apparently superior as intramolecular traps for our
<table>
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<th>time (d)</th>
<th>% yield</th>
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<td>2</td>
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<td><img src="image6" alt="" /></td>
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<td>82</td>
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<td>1&lt;sup&gt;e&lt;/sup&gt;</td>
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<td>9</td>
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<td><img src="image2" alt="Structure" /> $X$</td>
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<td><img src="image4" alt="Structure" /> $X$</td>
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<td>71 (22)</td>
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<td><img src="image14" alt="Structure" /> $X$</td>
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<td>0 (80)</td>
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<td><img src="image16" alt="Structure" /> $X$</td>
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Table 2. (continued)

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<td><img src="image2" alt="image" /></td>
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<tr>
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<td><img src="image4" alt="image" /></td>
<td>2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup>The reaction was carried under the previously described standard conditions employing 0.25 mmol of the o-halobenzyl, 5 mol % Pd(OAc)<sub>2</sub>, 5 mol % dppm, and 2 equivs of CsO<sub>2</sub>CMe<sub>3</sub> in DMF (4 mL) at 100 °C unless otherwise noted.  
<sup>b</sup>The yield in parentheses corresponds to GC yield of product in which the C-I bond has been reduced to a C-H.  
<sup>c</sup>The reaction temperature was increased to 110 °C.  
<sup>d</sup>The reaction temperature was increased to 120 °C.

aryl-palladium intermediates, we synthesized the indole derivatives 10 and 12. To our great satisfaction, compound 10 smoothly underwent the desired reaction producing the relatively strained isoindoloindole 11 in a 70 % yield (entry 4). Surprisingly, compound 12 produced the strained and sterically congested 2-methyl isoindoloindole 13 in a 71 % yield. We next examined the possibility of using an intramolecular arylation to form six-membered rings. Unfortunately, 3-(2-iodophenyl)benzyl phenyl ether (14) failed to react under our standard reaction conditions. Even at 110 °C, the reaction was sluggish, so the temperature was increased to 120 °C, in which case the reaction was complete after 2 d. Unfortunately, a 60:40 inseparable mixture of the desired compound 15 and reduced product 16 was obtained in a 75 % overall yield. Clearly, the formation of a six-membered ring is not as favorable as
five-membered ring formation (compare entries 2 and 6). This might be due to the 
intermediacy of an unfavorable seven-membered ring palladacycle (Figure 1).

Figure 1. Unfavorable seven-membered ring palladacycle intermediates.

We proceeded to investigate the sequential migration/arylation reaction of more 
complex polyaromatic compounds. In theory, 2-iodo-1-phenylnaphthalene (17) should 
afford fluoranthene (18) using our methodology. Mechanistically, the palladium must first 
undergo a 1,4-palladium migration from the 2-position of the naphthalene to the o-position of 
the phenyl substituent, followed by arylation at the 8-position of the naphthalene (Scheme 3). 
Although the reaction did not proceed at 100 °C, at 110 °C, compound 17 produced the

Scheme 3
desired compound 18 in an 81 % yield. Similarly, 2-bromo-1-phenynaphthalene (19) produced the desired fluoranthene (18) in a 70 % yield, indicating that this aryl bromide also undergoes the desired transformation, but in a somewhat lower yield and a longer reaction time.

Another interesting example of this migration involves the rearrangement of easily prepared 9-iodo-10-phenylphenanthrenes to benz[e]acephenanthrylene. In this case, the palladium migrates from the 9 position of the phenanthrene to the ortho position of the phenyl substituent, followed by cyclization onto the 8 position of the phenanthrene. Indeed, the reaction of 9-iodo-10-phenylphenanthrene (20) under our standard reaction conditions at 110 °C produced the desired benz[e]acephenanthrylene (21) in a 78 % yield (entry 9). We proceeded to investigate electronic effects in this phenanthrene reaction by looking at different substituents on the phenyl moiety. As expected, the use of an electron-donating methoxy group in compound 22 gave a good yield (71 %) of the corresponding benz[e]acephenanthrylene 23 (entry 10). However, the introduction of an electron-withdrawing CO₂Et group in the para position of the phenyl substituent was detrimental to the reaction, producing compound 25 in only a 50 % yield. We have also studied the regioselectivity of the migration by using a 3-methyl-substituted phenyl moiety in the 10-position of the 9-iodophenanthrene (entry 12). Compound 26 has two available positions for palladium migration, the more sterically-congested neighboring 2 position or the remote 6 position of the phenyl ring. The palladium-catalyzed cyclization of compound 26 generated compound 27 exclusively in a 56 % yield. This result indicates that palladium migration occurs exclusively onto the less sterically-congested 6 position of the phenyl moiety and that
the presence of a methyl group apparently completely inhibited migration to the more hindered 2 position. This result is in complete agreement with our previous observation that the Heck reaction of 2-iodo-3',5'-dimethylbiphenyl (40) with ethyl acrylate under our standard migration conditions afforded exclusively ester 41 and failed to produce any of the migration product 42 (eq 1). Furthermore, the less statistically favorable palladium migration to only the distal 6 position of the phenyl moiety might help explain the relatively low yield obtained for this transformation.

We next tried to prepare the more strained fused thiophene 29 from phenanthrene 28. Unfortunately, this reaction led to a very complex mixture, which produced none of the desired compound 29. Besides the unfavorable ring strain associated with the final product 29, intramolecular sulfur chelation of the intermediate 10-thiophen-1-ylphenanthren-9-ylpalladium iodide might be inhibiting the palladium migration step (Figure 2).

![Figure 2. Intramolecular palladium chelation by sulfur.](image)

In addition, the relatively electron-rich benzo[e]phenanthrene 30 also underwent the migration/arylation reaction, producing the highly conjugated hexacyclic compound 31 in a
65 % yield (entry 14). Unfortunately, compound 32 failed to generate the desired hexacycle 33 under our reaction conditions at 110 °C (entry 15). Only reduction product was isolated in 80 % yield. This example once again indicates that intramolecular annulation to form a six membered ring is rather unfavorable.

Having studied the palladium-catalyzed transformation of a variety of polycyclic aromatic halides, we switched our attention to heterocyclic aromatic compounds. To begin with, we carried out the reaction of 3-iodo-4-phenylquinoline (34) under our standard reaction conditions at 100 °C, but after 2 d this substrate failed to react. Fortunately, by simply increasing the reaction temperature to 110 °C, we obtained the desired indeno[1,2,3-de]quinoline (35) in a 54 % yield. Again the modest yield obtained with this electron-deficient substrate is consistent with our previous observations that electron-deficient substrates do not perform as well as more electron-rich substrates (compare entries 7 and 16). We also allowed 2-iodo-1-methyl-3-phenylindole (36) to react under our standard reaction conditions at 110 °C, but failed to obtain the desired tricyclic compound 37 (entry 17). A similar negative result was obtained with 2-iodo-3-phenylbenzofuran (38) (entry 18). The poor results obtained with substrates 36 and 38 can be explained in terms of the unfavorable ring strain of the corresponding products 37 and 39. In addition, we have previously established, using Heck trapping experiments, that palladium prefers to reside on the benzofuran and indole moieties in these substrates (Scheme 4).
Scheme 4

Table 3. Palladium-catalyzed migration and annulation of vinylic iodides.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>time (d)</th>
<th>% yield(^b)</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>Ph-(\text{I}))</td>
<td>Ph-H</td>
<td>1</td>
<td>96 (4)</td>
</tr>
<tr>
<td>2</td>
<td>Ph-(\text{I}))</td>
<td>Ph-H</td>
<td>2</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>Ph-(\text{I}))</td>
<td>Ph-H</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Ph-(\text{I}))</td>
<td>Ph-H</td>
<td>5</td>
<td>0 (12)</td>
</tr>
</tbody>
</table>

\(^a\)The reaction was carried under the previously described standard Pd migration conditions employing 0.25 mmol of the vinylic iodide, 5 mol % of Pd(OAc)\(_2\), 5 mol % of dppm, 2 equiv of CsO\(_2\)CCMe\(_3\) in DMF (4 mL) at 100 °C, unless otherwise noted. \(^b\)The yield in parentheses corresponds to the product in which the C-I has been reduced to a C-H bond. \(^c\)The reaction temperature was increased to 110 °C.
While our efforts had been focused on synthesizing polycyclic compounds in which the key 1,4-palladium shift occurs from an aryl to another aryl position, we wanted to establish that our methodology could also make use of a vinylic to aryl palladium migration to generate the key intermediate for the intramolecular arylation step. We have already shown one example of such a transformation in converting compound 1 to 2 (entry 1, Table 3). Another illustration of this process involves the use of 9-iodo-10-phenyl dibenz[b,f]oxepine (43). The reaction of this relatively electron-rich substrate produced the desired pentacyclic compound 44 in an 80% yield (entry 2). On the other hand, treating the electron-deficient 3-iodo-4-phenylisocoumarin (45) under our standard reaction conditions gave a complex mixture, and we failed to isolate any of the desired compound 46 (entry 3). This disappointing result was not unexpected, since our experience with compound 45 has indicated that palladium easily catalyzes its decomposition. Our last attempt to generate polycycles from vinylic iodides involved the use of isoquinolone 47. This substrate suffers the disadvantage that the intramolecular arylation step requires the formation of a six-membered ring. As expected, the reaction of substrate 47 under our standard reaction conditions at 110 °C failed to produce the desired pentacyclic product 48 and after 5 d of reaction time, we were only able to isolate the reduction product N-phenyl-3-phenylisoquinolone \(^\text{10}\) in a 12% yield as a side product (entry 4).

We have also examined the possibility of preparing polycycles using annulation reactions other than the usual intramolecular arylation. The first set of experiments involved the use of intramolecular alkyne annulation reactions (entries 1 and 2, Table 4; Scheme 5). We have previously established that the corresponding intermolecular version of this alkyne
The annulation methodology works well under our migration conditions. Therefore, it was surprising to find that the reaction of either compound 49 or 51 gave complex reaction mixtures and that none of the desired tetracyclic compounds 50 or 52 could be isolated. It is conceivable that intermolecular side reactions might be giving rise to dimers, trimers and other oligomers, which would account for the complexity of these reaction mixtures.

**Scheme 5**

We also tested whether an intramolecular version of the Heck reaction could be used to trap key arylpalladium intermediates generated via palladium migration. Therefore, we prepared two biphenyl derivatives having a strategically positioned C-C double bond. Biphenyl 53 was designed to produce the cyclic compound 54 by intramolecular Heck reaction with the allyl ether moiety (entry 3). Unfortunately, the reaction of compound 53 produced a very complex reaction mixture, and we failed to isolate the desired compound 54. Biphenyl 55 was designed to trap the corresponding palladium intermediate by
intramolecular annulation onto the methallyl amine moiety generating a stable alkylpalladium intermediate lacking β-hydrogens. In turn, this alkylpalladium intermediate

Table 4. Attempted palladium-catalyzed intramolecular alkyne and alkene annulations of 3'-substituted 2-iodobiphenyls.\(^a\)

<table>
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<tr>
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<th>substrate</th>
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<th>time (d)</th>
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\(^a\)The reaction was carried out under the previously described standard reaction conditions employing 0.25 mmol of the aryl iodide, 5 mol % of Pd(OAc)\(_2\), 5 mol % of dppm, 2 equiv of CsO\(_2\)CCMe\(_3\) in DMF (4 mL) at 100 °C.

might be expected to undergo a second cyclization onto the neighboring phenyl ring via C-H activation to render the tetracyclic compound 56 (entry 4, Table 4; Scheme 6).

Unfortunately, as previously observed with other substrates, compound 55 produced a very complex reaction mixture, and we failed to isolate the desired tetracycle 56. At this point, we conclude that intramolecular Heck and alkyne annulation reactions are ineffective for the
synthesis of complex polycycles using our present methodology. These negative results can most likely be attributed to unwanted intermolecular side reactions.

**Scheme 6**

We have continued to investigate the generality of our methodology for the synthesis of polycycles. Particularly, we were interested in exploiting other types of palladium migration. To elaborate, we have previously studied systems in which a 1,4-palladium shift between aryl and aryl positions or vinylic and aryl positions has been used to generated key palladium intermediates, which in turn undergo subsequent cyclization rendering the desired polycycles. We now report catalytic alkyl to aryl 1,4-palladium migration to prepare polycycles. This type of migration has been previously observed as a side reaction using stoichiometric amounts of palladium acetate and neophylmercuric acetate (Scheme 7).\(^{11}\)

In order to accomplish this goal, we have used 2-iodobenzyl methallyl ether (57) as a precursor to generate a stable alkylpalladium intermediate. A stepwise examination of our experimental design reveals that the Pd-catalyzed annulation of 2-iodobenzyl methallyl ether
Scheme 7

should generate a stable alkylpalladium intermediate lacking β-hydrogens (Scheme 8). In turn, this intermediate might undergo the key alkyl to aryl palladium migration generating an arylpalladium, which is subsequently trapped by way of an intramolecular Heck reaction with ethyl acrylate. Thus, the reaction of compound 57 with ethyl acrylate under our standard conditions led to the formation of polycyclic compound 58 in a 56% yield (Scheme 8). Clearly, under our palladium-catalyzed reaction conditions the desired alkyl to aryl migration had occurred, indicating the potential of our methodology for generating polyfunctional cyclic compounds from relatively simple starting materials.

Scheme 8
A second example of a reaction involving an alkyl to aryl palladium migration to generate a functionalized polycycle was obtained during the reaction of 3-iodo-1-p-tosylindole (59) with norbornene under our standard Pd migration reaction conditions (Scheme 9). The first step of this reaction involves the cis addition of an indol-3-ylpalladium iodide to norbornene, generating a stable alkylpalladium intermediate lacking cis β-hydrogens properly aligned for β-hydride elimination. This intermediate in turn undergoes a 1,4-alkyl to aryl palladium shift to the 2-position of the indole, followed by intramolecular annulation onto the p-toluenesulfonyl moiety. The overall transformation produced a 75% yield of the desired polycycle 60. The possibility of using this process to prepare other carbocycles and heterocycles is currently being investigated in our research group.

Scheme 9

To further extend the scope of our methodology, we have explored other possible palladium migrations. Next, we describe experiments aimed towards establishing an aryl to
carbonyl palladium migration. First of all, we looked at an aryl to acyl palladium migration using \( N-(2\text{-iodophenyl})\text{formamide} \) (61). Thus, the reaction of 61 under our standard migration reaction conditions in the presence of 10 equiv of \( n\)-butanol as a trapping agent for the anticipated acylpalladium intermediate produced the desired carbamate 62 in a 15 % yield along with the surprising pivalanilide (63) product in a 15 % yield. Scheme 9 shows a possible mechanism for the formation of these compounds from the key acylpalladium intermediate generated after the desired palladium migration. It is worth noting that by carrying out this reaction in the presence of 50 equiv of \( n\)-BuOH, we obtained the desired carbamate 62 exclusively in a 27 % yield, thus inhibiting the formation of pivalanilide (63). Similarly, if this reaction is carried out in the absence of \( n\)-BuOH, we obtained pivalanilide (63) exclusively in a 26 % yield.\(^{13}\)

**Scheme 9**

\[
\text{H}_n\text{BuOH} \quad \text{H} \quad 5\% \text{Pd(OAc)}_2 \quad 5\% \text{CH}_2(\text{PPh}_2)_2 \quad 2 \text{CsO}_2\text{CCMe}_3 \quad n\text{-BuOH} \quad \text{DMF (4 mL)} \quad 100 \ ^\circ\text{C}, 1 \text{ d}
\]

\[
\text{H} \quad \text{rrV} \quad f\text{-Bu} \quad \text{C}O \quad \text{CT} \quad N \quad x: \quad 0 \quad 2 \quad \text{CCMe}_3 \quad \text{Me}_3\text{CO}_2
\]

\[
\text{O} \quad n\text{-Bu} \quad \text{H} \quad \text{H}
\]

\[
\text{O} \quad n\text{-Bu} \quad \text{H} \quad \text{H}
\]
Similarly, the reaction of benzylidene(2-iodophenyl)amine (64) under our migration conditions in the presence of 10 equiv of water produced the desired benzanilide (65) in a 56% yield (Scheme 11). The formation of benzanilide suggests that a palladium migration from an aryl to an imidoyl position has taken place, generating a Pd species which upon hydrolysis and subsequent tautomerization leads to the benzanilide product.\textsuperscript{14}

Scheme 11

![Scheme 11 diagram]

Finally, we have explored the possibility of using an aryl to allyl palladium migration to prepare functionalized alkenes, as well as heterocycles. Scheme 12 illustrates a possible mechanism for the reaction of iodobenzene with 1-phenyl-1-propyne under our standard reaction conditions. Notice that the sterically-controlled, regioselective addition of phenylpalladium iodide to 1-phenyl-1-propyne should generate a vinylic palladium intermediate, which might undergo the expected 1,4-vinylic to aryl palladium migration to produce an arylpalladium intermediate. We anticipated that this arylpalladium intermediate might undergo a second migration to the methyl position, producing a π-allylpalladium species, which should react with the nucleophilic pivalate base, generating the desired
pivalate ester 66. Indeed, this reaction produced the indicated pivalate ester 66 in a 25% yield as a 50:50 mixture of

Scheme 12

\[
\begin{align*}
\text{Ph} & + \text{PhI} \\
\text{Me} & \text{Pd(OAc)}_2 \\
\text{DMF (4 mL)} & 100 \, ^\circ \text{C}, 1 \, \text{d} \\
25 \% \, (50:50) & \\
\end{align*}
\]

\[\text{H}_3\text{C} \quad \text{H}_3\text{C} \]

\[\text{Ph} \quad \text{H} \quad \text{Ph} \]

\[\text{Me}_3\text{CCO}_2 \quad \text{Me}_3\text{CCO}_2^{-} \]

\[\text{E and Z isomers. Having established the possibility of generating allylpalladium intermediates from aryl iodides and alkynes, we thought it should be feasible to trap such intermediates in an intramolecular fashion to generate heterocycles. Unfortunately, the reaction of iodobenzene with 2-methylpent-3-yn-2-ol failed to produce the desired cyclic ether 67 (Scheme 13). The potential of this type of annulation is currently being investigated in our research group.}

Conclusions

In conclusion, we have developed novel methodology for the synthesis of complex fused polycycles employing two sequential Pd-catalyzed intramolecular processes involving C-H activation. This methodology exploits relatively general aryl to aryl, vinylic to aryl, and alkyl to aryl 1,4-palladium migrations combined with intramolecular arylation to prepare a wide variety of carbocycles and heterocycles. The chemistry developed here works best with
Scheme 13

Scheme 13 illustrates the reaction scheme involving electron-rich aromatics, which is in agreement with the idea that these palladium-catalyzed C-H activation reactions parallel electrophilic aromatic substitution.

**Experimental**

**General procedures.** All $^1$H and $^{13}$C spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic KMnO$_4$ solution [3 g of KMnO$_4$ + 20 g of K$_2$CO$_3$ + 5 mL of NaOH (5 %) + 300 mL of H$_2$O]. All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV.

**Reagents.** All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of THF, DME, DMF, benzene, diethyl ether, ethyl acetate and
hexanes were purchased from Fisher Scientific Co. \(n\)-Bu\(_4\)NCl (TBAC) was purchased from Lancaster Synthesis, Inc. AgClO\(_4\), Cu(OAc)\(_2\), 3,4-dihydro-1-phenynaphthalene and Et\(_3\)N were purchased from Aldrich Chemical Co., Inc. Cesium pivalate was prepared according to the procedure of Larock and Campo.\(^{15}\) Compounds 1, 2, 19, 20, 36, 38, 40, 41, 43, and 59 have been previously reported\(^{15}\) (see Chapter 1 of this thesis).

**Synthesis of the organic halides**

3'-Benzyl-2-iodobiphenyl (4). This biphenyl was prepared from 3'-bromomethyl-2-iodobiphenyl (68)\(^{15}\) by following a procedure from the literature.\(^{16}\) To a suspension of AgClO\(_4\) (0.28 g, 1.4 mmol) in benzene (4.0 mL) was added 68 (0.261 g, 0.7 mmol) in benzene (4.0 mL) and the resulting mixture stirred overnight at room temperature in the dark. The reaction mixture was diluted with diethyl ether (50 mL), filtered and washed with brine (25 mL). The organic layer was dried (Na\(_2\)SO\(_4\)), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 50:1 hexanes/ethyl acetate to afford 0.187 g (72 \%) of the indicated compound 4 as a colorless oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 4.03 (s, 3H), 6.97-7.01 (m, 1H), 7.15-7.34 (m, 11H), 7.92 (dd, \(J = 8.0, 1.0\) Hz, 1H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 42.0, 98.8, 126.2, 127.1, 128.2, 128.2, 128.3, 128.6, 128.8, 129.1, 130.1, 130.2, 139.6, 140.8, 141.0, 144.3, 146.6; IR (CH\(_2\)Cl\(_2\)) 3056, 3025, 2917, 1601, 1583, 1494, 1461 cm\(^{-1}\); HRMS m/z 370.0224 (calcd for C\(_{19}\)H\(_{15}\)I, 370.0218).

2-Iodo-3'-methoxybiphenyl (69). Compound 69 was prepared by a procedure reported by Hart.\(^{17}\) A solution of 2-bromioiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 3-methoxyphenylmagnesium bromide [prepared from 3-bromoanisole (1.87 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and
the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I₂ (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I₂ was destroyed by adding 10% aq NaHSO₃ (35 mL) and the organic layer was separated and rewashed with brine (20 mL). Finally, the organic layer was dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using 30:1 hexanes/ethyl acetate to afford 0.620 g (40 %) of the desired compound 69 as a clear oil: ¹H NMR (CDCl₃) δ 3.84 (s, 3H), 6.88-6.95 (m, 3H), 7.01-7.05 (m, 1H), 7.29-7.38 (m, 3H), 7.95 (dd, J = 8.0, 1.2 Hz, 1H); ¹³C NMR (CDCl₃) δ 55.4, 98.5, 113.4, 115.0, 121.8, 128.1, 128.9, 129.1, 130.1, 139.6, 145.5, 146.5, 159.1; HRMS m/z 309.9859 (calcd for C₁₃H₁₁IO, 309.9855).

2-Iodo-3'-phenoxybiphenyl (6). This biphenyl was prepared in two steps from 2-iodo-3-methoxybiphenyl (69). To a solution of 69 (0.97 g, 3.14 mmol) in CH₂Cl₂ (20 mL) at -78 °C was added 1.0 M BBr₃ in CH₂Cl₂ (4.1 mL, 4.1 mmol). The resulting solution was allowed to warm to room temperature and stirred for 2 h. The mixture was worked up with ice (15 g) and extracted with diethyl ether (75 mL). The organic layer was dried (Na₂SO₄), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 3:1 hexanes/ethyl acetate to afford 0.91 g (98 %) of 3-(2-iodophenyl)phenol (70) as a clear oil: ¹H NMR (CDCl₃) δ 5.04 (br s, 1H), 6.80-6.81 (m, 1H), 6.85-6.90 (m, 2H), 7.00-7.05 (m, 1H), 7.25-7.31 (m, 2H), 7.37 (td, J = 7.6, 0.8 Hz, 1H), 7.94 (dd, J = 8.0, 0.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 98.4, 114.7, 116.4, 122.0, 128.1, 128.9, 129.3, 130.0, 139.5, 145.8, 146.2, 155.0. Compound 70 was phenylated by a procedure found in the literature.¹⁸ A suspension of 70 (0.222 g, 0.75 mmol), phenylboronic
acid (0.183 g, 1.5 mmol), Cu(OAc)$_2$ (0.163 g, 0.90 mmol), Et$_3$N (0.38 g, 3.75 mmol), 5
Angstrom molecular sieves (0.2 g) in CH$_2$Cl$_2$ (6.0 mL) was stirred under O$_2$ (1 atm) for 2 d at
room temperature. The reaction mixture was diluted with diethyl ether (50 mL), filtered, and
the solvent evaporated under reduced pressure. The residue was purified by chromatography
on a silica gel column using 15:1 hexanes/ethyl acetate to afford 0.129 g (46 %) of the
indicated compound 6 as a clear oil: $^1$H NMR (CDCl$_3$) $\delta$ 7.00-7.12 (m, 7H), 7.25-7.40 (m,
5H), 7.92 (dd, $J = 8.0, 1.2$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 98.4, 118.2, 119.1, 119.8, 123.4,
124.2, 128.2, 129.0, 129.4, 129.8, 130.0, 139.6, 145.9, 146.0, 156.8, 157.1; IR (CH$_2$Cl$_2$)
3058, 1578, 1488, 1460, 1222, cm$^{-1}$; HRMS m/z 372.0020 (calcd for C$_{18}$H$_{13}$I0, 372.0011).

2-Iodo-3'-(p-chlorophenoxy)biphenyl (8). This biphenyl was prepared by a
procedure similar to that used for compound 6. A suspension of 70 (0.222 g, 0.75 mmol), p-
chlorophenylboronic acid (0.235 g, 1.5 mmol), Cu(OAc)$_2$ (0.163 g, 0.90 mmol), Et$_3$N (0.38 g,
3.75 mmol), 5 Angstrom molecular sieves (0.2 g) in CH$_2$Cl$_2$ (6.0 mL) was stirred under O$_2$ (1
atm) for 2 d at room temperature. The reaction mixture was diluted with diethyl ether (50
mL), filtered, and the solvent evaporated under reduced pressure. The residue was purified
by chromatography on a silica gel column using 30:1 hexanes/ethyl acetate to afford 79.5 mg
(26 %) of the indicated compound 6 as a clear oil: $^1$H NMR (CDCl$_3$) $\delta$ 6.96-7.09 (m, 6H),
7.27-7.41 (m, 5H), 7.93 (d, $J = 8.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 98.4, 118.2, 119.9, 120.3,
124.6, 128.2, 128.4, 129.1, 129.6, 129.8, 130.0, 139.6, 145.8, 146.0, 155.8, 156.4; IR
(CH$_2$Cl$_2$) 3057, 1576, 1484, 1460, 1228 cm$^{-1}$; HRMS m/z 405.9632 (calcd for C$_{18}$H$_{12}$IClO,
405.9621).
1-[3-(2-Iodophenyl)benzyl]indole (10). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added 1H-indole (0.117 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point 3'-bromomethyl-2-iodobiphenyl (68) (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at 50 °C for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried (MgSO₄), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 12:1 hexanes/ethyl acetate to afford 0.335 g (88 %) of the desired compound 10 as a clear oil: ¹H NMR (CDCl₃) δ 5.34 (s, 2H), 6.54 (d, J = 2.8 Hz, 1H), 6.98 (td, J = 7.6, 1.6 Hz, 1H), 7.09-7.23 (m, 7H), 7.30-7.34 (m, 3H), 7.64 (d, J = 7.6 Hz, 1H), 7.90 (dd, J = 8.0, 0.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 50.1, 98.6, 101.9, 109.9, 119.6, 121.1, 121.8, 126.2, 128.0, 128.2, 128.4, 128.6, 128.6, 128.9, 129.0, 130.1, 136.4, 137.4, 139.6, 144.6, 146.1; IR (CH₂Cl₂) 3052, 2972, 2922, 2863, 1462, 1437, 1316 cm⁻¹; HRMS m/z 409.0334 (calcd for C₂₁H₁₆IN, 409.0328).

1-[3-(2-Iodophenyl)benzyl]-3-methylindole (12). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added 3-methyl-1H-indole (0.131 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point 3'-bromomethyl-2-iodobiphenyl (68) (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at 50 °C for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried (MgSO₄), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 12:1 hexanes/ethyl acetate to afford 0.335 g (88 %) of the desired compound 12 as a clear oil: ¹H NMR (CDCl₃) δ 5.34 (s, 2H), 6.54 (d, J = 2.8 Hz, 1H), 6.98 (td, J = 7.6, 1.6 Hz, 1H), 7.09-7.23 (m, 7H), 7.30-7.34 (m, 3H), 7.64 (d, J = 7.6 Hz, 1H), 7.90 (dd, J = 8.0, 0.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 50.1, 98.6, 101.9, 109.9, 119.6, 121.1, 121.8, 126.2, 128.0, 128.2, 128.4, 128.6, 128.6, 128.9, 129.0, 130.1, 136.4, 137.4, 139.6, 144.6, 146.1; IR (CH₂Cl₂) 3052, 2972, 2922, 2863, 1462, 1437, 1316 cm⁻¹; HRMS m/z 409.0334 (calcd for C₂₁H₁₆IN, 409.0328).
using 12:1 hexanes/ethyl acetate to afford 0.362 g (92 %) of the desired compound 12 as a clear oil: $^1\text{H NMR (CDCl}_3$ $\delta$ 2.33 (d, J = 0.8 Hz, 3H), 5.29 (s, 2H), 6.92-6.92 (m, 1H), 6.97-6.99 (m, 1H), 7.10-7.24 (m, 6H), 7.27-7.34 (m, 3H), 7.56-7.58 (m, 1H), 7.90-7.92 (m, 1H); $^{13}\text{C NMR (CDCl}_3$ $\delta$ 10.1, 50.1, 98.8, 109.9, 111.2, 119.1, 119.3, 121.9, 126.2, 126.4, 128.2, 128.4, 128.7, 128.7, 129.2, 129.3, 130.3, 136.9, 137.9, 139.8, 144.7, 146.4; IR (CH$_2$C$_2$Cl) 3053, 2914, 1611, 1465, 1330, 1012 cm$^{-1}$; HRMS m/z 423.0491 (calcd for C$_{22}$H$_{18}$IN, 423.0484).

3-(2-Iodophenyl)benzyl phenyl ether (14). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added phenol (0.094 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point, 3'-bromomethyl-2-iodobiphenyl (68) (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried (MgSO$_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 12:1 hexanes/ethyl acetate to afford 0.359 g (100 %) of the desired compound 14 as a clear oil: $^1\text{H NMR (CDCl}_3$ $\delta$ 5.13 (s, 2H), 6.96-7.04 (m, 4H), 7.26-7.33 (m, 4H), 7.39-7.46 (m, 4H), 7.94-7.96 (m, 1H); $^{13}\text{C NMR (CDCl}_3$ $\delta$ 69.9, 98.6, 115.0, 121.1, 126.8, 128.3, 128.4, 128.5, 129.0, 129.0, 129.6, 130.2, 137.0, 139.6, 144.5, 146.4, 158.8; IR (CH$_2$C$_2$Cl) 3056, 2919, 1598, 1494, 1238 cm$^{-1}$; HRMS m/z 386.0172 (calcd for C$_{19}$H$_{15}$IO, 386.0168).

2-Iodo-1-phenynaphthalene (17). To a solution of 3,4-dihydro-1-phenynaphthalene (1.30 g, 6.3 mmol) and I$_2$ (2.24 g, mmol) in anhydrous CH$_3$CN (15 mL)
was added dropwise AgOTf (1.75 g, 6.8 mmol) in anhydrous CH$_3$CN (20 mL). The resulting mixture was stirred at room temperature in the dark for 1 h. The reaction was diluted with diethyl ether (70 mL) and washed with satd aq Na$_2$S$_2$O$_3$ (25 mL). The organic layer was dried (Na$_2$SO$_4$), filtered and the solvent removed under reduced pressure. The residue was dissolved in benzene (25 mL). To this solution was added DDQ (2.86 g, 12.6 mmol) and the reaction heated at 65 °C for 2 d. The resulting mixture is filtered and washed with 10 % aq Na$_2$CO$_3$ (25 mL). The organic layer was filtered, dried (Na$_2$SO$_4$) and the solvent removed under reduced pressure. The residue was purified using chromatography on a silica gel column using 50:1 hexanes/ethyl acetate to afford 1.47 g (70 %) of the indicated compound 17 as a clear oil:  $^1$H NMR (CDCl$_3$) $\delta$ 7.22-7.26 (m, 2H), 7.32-7.34 (m, 1H), 7.38-7.56 (m, 6H), 7.80-7.83 (m, 1H), 7.95 (d, $J = 8.7$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 98.7, 126.5, 127.0, 127.4, 128.1, 128.1, 128.7, 129.3, 130.2, 133.1, 133.6, 135.8, 143.5, 144.7; IR (CH$_2$Cl$_2$) 3053, 1577, 1502, 1442, 1382, 1306 cm$^{-1}$; HRMS m/z 329.9910 (calcd for C$_{16}$H$_n$I, 329.9906).

General procedure for synthesis of the phenanthrenes

The following procedure was used to prepare phenanthrenes 22, 24, 26, 28, 30 and chrysene 32. To a solution of 2-(arylethynyl)biphenyl (0.30 mmol) in CH$_2$Cl$_2$ (3 mL) under N$_2$ was added ICl (1.2 equiv) in CH$_2$Cl$_2$ (0.5 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 1 h unless otherwise indicated. The reaction mixture was then diluted with diethyl ether (50 mL), washed with 25 mL of satd aq Na$_2$S$_2$O$_3$, dried (MgSO$_4$), and filtered. The solvent was evaporated under reduced pressure and the product was purified by chromatography on a silica gel column.
General procedure for preparation of the 2-(arylethynyl)biphenyls. To a solution of the corresponding aryl iodide (1.0 mmol) and the terminal alkyne (1.2 mmol, 1.2 equiv) in Et$_3$N (4.0 mL) were added PdCl$_2$(PPh$_3$)$_2$ (1.4 mg, 2 mol %) and CuI (2.0 mg, 1 mol %). The resulting mixture was then heated under an N$_2$ atmosphere at 55 °C for 3 h. The mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding product.

2-[(4-Methoxyphenyl)ethynyl]biphenyl (71). 2-Ethynylbiphenyl$^{19}$ and 4-iodoanisole were employed. Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.21 g (74 %) of the product as a clear liquid: $^1$H NMR (CDCl$_3$) δ 3.80 (s, 3H), 6.84 (dd, $J = 2.4, 6.9$ Hz, 2H), 7.30 (dd, $J = 2.1, 6.9$ Hz, 2H), 7.34-7.50 (m, 6H), 7.64-7.73 (m, 3H); $^{13}$C NMR (CDCl$_3$) δ 55.5, 88.4, 92.5, 114.2, 115.9, 122.2, 127.3, 127.6, 128.1, 128.4, 129.6, 129.7, 132.9, 133.1, 140.9, 143.9, 159.8.

2-[(3-Methylphenyl)ethynyl]biphenyl (72). 2-Ethynylbiphenyl$^{19}$ and 3-iodotoluene were employed. Purification by flash chromatography (40:1 hexane/EtOAc) afforded 0.26 g (95 %) of the product as a clear liquid: $^1$H NMR (CDCl$_3$) δ 2.34 (s, 3H), 7.12-7.22 (m, 4H), 7.33-7.53 (m, 6H), 7.67-7.74 (m, 3H); $^{13}$C NMR (CDCl$_3$) δ 21.5, 89.3, 92.7, 122.0, 123.5, 127.3, 127.7, 128.2, 128.4, 128.7, 128.7, 129.3, 129.7, 129.7, 132.2, 133.1, 138.2, 140.9, 144.1.

Ethyl 4-(biphen-2-ylethynyl)benzoate (73). 2-Ethynylbiphenyl$^{19}$ and ethyl 4-iodobenzoate were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.27 g (84 %) of the product as a white solid: mp 58-60 °C; $^1$H NMR (CDCl$_3$) δ
1.38 (t, J = 6.9 Hz, 3H), 4.36 (q, J = 7.2 Hz, 2H), 7.32-7.48 (m, 8H), 7.64-7.66 (m, 3H), 7.96 (d, J = 8.4 Hz, 2H); 13C NMR (CDCl₃) δ 14.6, 61.3, 91.7, 92.6, 121.3, 127.4, 127.9, 128.2, 128.3, 129.3, 129.63, 129.64, 129.8, 129.9, 131.4, 133.2, 140.6, 144.5, 166.3.

2-(Biphen-2-ylethynyl)thiophene (74). 2-Ethynylbiphenyl²⁹ and 2-iodothiophene were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.22 g (85 %) of the product as a light yellow liquid: ¹H NMR (CDCl₃) δ 6.98-7.00 (m, 1H), 7.15-7.17 (m, 1H), 7.25-7.27 (m, 1H), 7.37-7.55 (m, 6H), 7.66-7.75 (m, 3H); ¹³C NMR (CDCl₃) δ 85.9, 93.5, 121.6, 123.8, 127.3, 127.4, 127.5, 127.8, 128.3, 129.0, 129.6, 129.8, 131.8, 132.8, 140.7, 144.0.

2-[2-(Phenylethynyl)phenyl]naphthalene (75). 2-(2-Iodophenyl)naphthalene¹⁷ and phenylacetylene were employed. Purification by flash chromatography (40:1 hexane/EtOAc) afforded 0.29 g (96 %) of the product as a light yellow liquid: ¹H NMR (CDCl₃) δ 7.24-7.58 (m, 10H), 7.70-7.72 (m, 1H), 7.86-7.97 (m, 4H), 8.17 (s, 1H); ¹³C NMR (CDCl₃) δ 89.7, 92.7, 122.0, 123.6, 126.2, 126.3, 127.4, 127.5, 127.9, 128.0, 128.3, 128.4, 128.5, 128.9, 130.0, 131.6, 132.9, 133.3, 133.5, 138.3, 144.0 (one sp² carbon missing due to overlap).

2-[(4-Methoxyphenyl)ethynyl]-1-phenylnaphthalene (76). 2-Iodo-1-phenylnaphthalene and 4-ethynylanisole²⁰ were employed. Purification by flash chromatography (20:1 hexane/EtOAc) afforded 0.27 g (82 %) of the product as a clear oil: ¹H NMR (CDCl₃) δ 3.81 (s, 3H), 6.82 (dd, J = 6.9, 2.1 Hz, 2H), 7.17 (d, J = 6.9, 2.1 Hz, 2H), 7.43-7.60 (m, 7H), 7.68-7.72 (m, 2H), 7.83-7.94 (m, 2H); ¹³C NMR (CDCl₃) δ 55.4, 88.9, 93.5, 114, 115.7, 120.7, 126.4, 126.6, 126.8, 127.6, 127.6, 128.1, 128.2, 128.4, 130.9, 132.4, 133.0, 133.1, 139.3, 142.8, 159.7.
9-Iodo-10-(4-methoxyphenyl)phenanthrene (22). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.122 g (99 %) of the product as a white solid: mp 170-171 °C; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 3.94 (s, 3H), 7.09 (dd, \(J = 2.1, 6.6\) Hz, 2H), 7.21 (dd, \(J = 2.1, 6.6\) Hz, 2H), 7.40-7.49 (m, 2H), 7.64-7.72 (m, 3H), 8.45-8.49 (m, 1H), 8.67-8.78 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 55.6, 107.7, 114.0, 122.8, 122.9, 127.2, 127.3, 127.7, 128.3, 129.0, 130.5, 130.8, 131.3, 132.7, 132.9, 135.0, 138.2, 145.3, 159.4; IR (neat) 3066, 3024, 2834, 1610 cm\(^{-1}\); HRMS \(m/z\) 410.0172 (calcd for C\(_{21}\)H\(_{15}\)IO, 410.0168).

Ethyl 4-(10-iodophenanthren-9-yl)benzoate (24). The reaction mixture was stirred at room temperature for 1 h. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.136 g (100 %) of the product as a white solid: mp 152-153 °C; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.46 (t, \(J = 7.2\) Hz, 3H), 4.47 (q, \(J = 7.2\) Hz, 2H), 7.30-7.45 (m, 4H), 7.66-7.75 (m, 3H), 8.26 (dd, \(J = 1.8, 6.6\) Hz, 2H), 8.45-8.49 (m, 1H), 8.68-8.78 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 14.6, 61.4, 106.0, 122.9, 123.0, 127.4, 127.5, 128.0, 128.4, 128.5, 130.1, 130.3, 130.4, 130.5, 130.8, 132.1, 132.5, 134.9, 144.6, 150.0, 166.7; IR (CH\(_2\)Cl\(_2\)) 3069, 2979, 1714 cm\(^{-1}\); HRMS \(m/z\) 452.0278 (calcd for C\(_{23}\)H\(_{17}\)IO\(_2\), 452.0273).

9-Iodo-10-(3-methylphenyl)phenanthrene (26). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.117 g (99 %) of the product as a white solid: mp 134-135 °C; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.44 (s, 3H), 7.07-7.09 (m, 2H), 7.30-7.32 (m, 1H), 7.41-7.45 (m, 3H), 7.63-7.70 (m, 3H), 8.45-8.48 (m, 1H), 8.67-8.73 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 21.7, 106.5, 122.6, 122.7, 127.1, 127.1, 127.5, 128.1, 128.4, 128.5, 128.8, 130.3, 130.6, 130.6, 132.5, 132.5, 134.7, 138.1, 145.4, 145.5 (one sp\(^2\) carbon missing due to
overlap); IR \((\text{CH}_2\text{Cl}_2)\) 3067, 2971, 2921, 1602, 1563 cm\(^{-1}\); HRMS \(m/z\) 394.0226 (calcd for \(\text{C}_{21}\text{H}_{15}\text{I}\), 394.0219).

**9-Iodo-10-(thiophen-2-yl)phenanthrene (28).** Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.111 g (96 \%) of the product as a white solid: \(\text{mp} \ 140-142 \degree \text{C}\); \(^1\text{H} \text{NMR} \ (\text{CDCl}_3) \delta 7.06-7.08 \ (m, 1\text{H}), 7.23-7.26 \ (m, 1\text{H}), 7.45-7.76 \ (m, 6\text{H}), 8.44-8.49 \ (m, 1\text{H}), 8.66-8.75 \ (m, 2\text{H}); ^{13}\text{C} \text{NMR} \ (\text{CDCl}_3) \delta 110.5, 122.7, 122.9, 126.5, 127.2, 127.5, 128.2, 128.4, 128.7, 128.8, 130.3, 131.1, 132.6, 133.2, 135.3, 138.4, 146.5; IR \ (\text{neat}) 2925, 1464, 1216 cm\(^{-1}\); HRMS \(m/z\) 385.9631 (calcd for \(\text{C}_{18}\text{H}_{14}\text{I}\), 385.9626).

**6-Iodo-5-(4-methoxyphenyl)benzo[c]phenanthrene (30).** Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.138 g (97 \%) of the product as a white solid: \(\text{mp} \ 186-187 \degree \text{C}\); \(^1\text{H} \text{NMR} \ (\text{CDCl}_3) \delta 3.94 \ (s, 3\text{H}), 7.08-7.12 \ (m, 2\text{H}), 7.23-7.26 \ (m, 2\text{H}), 7.42-7.47 \ (m, 1\text{H}), 7.57-7.69 \ (m, 4\text{H}), 7.94 \ (d, J = 9.0 \text{ Hz}, 1\text{H}), 8.04-8.06 \ (m, 1\text{H}), 8.42 \ (d, J = 9.0 \text{ Hz}, 1\text{H}), 9.01-9.04 \ (m, 2\text{H}); ^{13}\text{C} \text{NMR} \ (\text{CDCl}_3) \delta 55.6, 107.3, 114.1, 126.4, 126.6, 126.7, 126.8, 128.4, 128.6, 128.8, 129.0, 129.7, 130.2, 131.3, 131.5, 132.4, 133.8, 133.8, 138.0, 145.0, 159.4; IR \ (\text{neat}) 2950, 1606, 1506 cm\(^{-1}\); HRMS \(m/z\) 460.0330 (calcd for \(\text{C}_{25}\text{H}_{17}\text{I}\), 460.0324).

**6-Iodo-5-phenylchrysene (32).** Purification by flash chromatography (40:1 hexane/EtOAc) afforded 98 mg (76 \%) of the product as a yellow solid: \(\text{mp} \ 168-169 \degree \text{C}\); \(^1\text{H} \text{NMR} \ (\text{CDCl}_3) \delta 7.07 \ (t, J = 6.9 \text{ Hz}, 1\text{H}), 7.33-7.57 \ (m, 7\text{H}), 7.71-7.76 \ (m, 2\text{H}), 8.89 \ (d, J = 6.5 \text{ Hz}, 1\text{H}), 8.04 \ (d, J = 7.6 \text{ Hz}, 1\text{H}), 8.56-8.60 \ (m, 1\text{H}), 8.78 \ (d, J = 7.0 \text{ Hz}, 2\text{H}); ^{13}\text{C} \text{NMR} \ (\text{CDCl}_3) \delta 111.5, 121.3, 123.7, 125.4, 126.1, 127.7, 128.2, 128.4, 128.6, 128.9, 129.0, 129.2,
3-Iodo-4-phenylquinoline (34). To a solution of N-phenylmethanesulfonyamide (0.513 g, 3.0 mmol), PPh₃ (1.18 g, 4.5 mmol) and 3-phenylpropargyl alcohol (0.594 g, 4.5 mmol) in anhydrous THF (30 mL) at 0 °C was added DEAD (0.784 g, 4.5 mmol). The resulting solution was stirred at 0 °C for 1 h and an additional 3 h at room temperature. The mixture was washed with brine (30 mL) and the organic layer was dried (Na₂SO₄), filtered, and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 3:1 hexanes/ethyl acetate to obtain 0.534 g (63 %) of N-methanesulfonyl-N-(3-phenyl-2-propyn-1-yl)aniline as a white solid: mp 76-77 °C; \(^1\)H NMR (CDCl₃) δ 3.08 (s, 3H), 4.67 (s, 2H), 7.34-7.46 (m, 8H), 7.62-7.66 (m, 2H); \(^13\)C NMR (CDCl₃) δ 39.2, 42.3, 84.4, 86.3, 122.3, 127.7, 128.4, 128.7, 129.1, 129.7, 131.9, 140.5. To a solution of N-methanesulfonyl-N-(3-phenyl-2-propyn-1-yl)aniline (71.2 mg, 0.25 mmol) in CH₂Cl₂ (3.0 mL) at -78 °C was added ICl (48.7 mg, 0.3 mmol) in CH₂Cl₂ (0.5 mL) and the resulting solution stirred at this temperature for 1 h. The reaction mixture was washed with satd aq Na₂S₂O₅ (20 mL) and the organic layer dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to obtain 82.2 mg (80 %) of 3-iodo-1-methanesulfonyl-4-phenyl-1,2-dihydroquinoline as a white solid: mp 173-175 °C; \(^1\)H NMR (CDCl₃) δ 2.89 (s, 3H), 4.82 (s, 2H), 6.80 (dd, \(J = 7.8, 1.2\) Hz, 1H), 7.11-7.16 (m, 3H), 7.30-7.33 (m, 1H), 7.44-7.48 (m, 3H), 7.62 (dd, \(J = 8.1, 0.9\) Hz, 1H); \(^13\)C NMR (CDCl₃) δ 38.6, 56.7, 92.0, 126.9, 127.2, 127.2, 128.6, 128.8, 129.0, 129.2, 130.7, 134.5, 140.3, 143.9. A
solution of 3-iodo-1-methanesulfonyl-4-phenyl-1,2-dihydroquinoline (0.103 g, 0.25 mmol) and NaOH (0.10 g, 2.5 mmol) in EtOH (10 mL) was stirred at 50 °C under O_2 (1 atm) for 12 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to afford 76.1 mg (92 %) of the desired compound 34 as a white solid: mp 131-132 °C; ^1H NMR (CDCl_3) δ 7.25-7.28 (m, 2H), 7.42-7.48 (m, 2H), 7.52-7.55 (m, 3H), 7.69-7.74 (m, 1H), 8.12 (d, J = 8.8 Hz, 1H), 9.24 (s, 1H); ^13C NMR (CDCl_3) δ 96.4, 126.8, 127.4, 128.7, 129.0, 129.1, 129.5, 129.8, 140.4, 147.2, 152.4, 156.6 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3061, 2918, 1566, 1501, 1485 cm\(^{-1}\); HRMS m/z 330.9864 (calcd for C_{15}H_{10}IN, 330.9858).

3-Iodo-4-phenylisocoumarin (45). A solution of 4-phenyl-3-(trimethylsilyl)isocoumarin\(^{22}\) (0.435 g, 1.48 mmol), I\(_2\) (1.13 g, 4.45 mmol), and AgOTf (0.76 g, 2.96 mmol) in CH_3CN (20 mL) was heated at 55 °C for 5 d. The reaction mixture was diluted with diethyl ether (100 mL), and washed with satd aq Na_2S_2O_3 (30 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure to obtain 0.498 g (97 %) of the indicated compound 45 as a yellow solid. Recrystallization from hexanes/ethyl acetate afforded the indicated compound 45 as a yellow solid: mp 170-171 °C, ^1H NMR (CDCl_3) δ 6.97 (d, J = 8.0 Hz, 1H), 7.26-7.28 (m, 2H), 7.50-7.56 (m, 4H), 7.59-7.63 (m, 1H), 8.31 (dd, J = 8.0, 0.8 Hz, 1H); ^13C NMR (CDCl_3) δ 107.9, 119.6, 125.6, 127.4, 128.7, 128.9, 129.1, 129.9, 130.5, 135.2, 137.0, 137.3, 161.2; IR (CH_2Cl_2) 1736.0 cm\(^{-1}\); HRMS m/z 347.9652 (calcd for C_{15}H_{10}O_2, 347.9647).
4-Iodo-2,3-diphenyl-2H-isquinolin-1-one (47). To a solution of N-phenyl-2-(phenylethynyl)benzamide\(^2\) (74.2 mg, 0.25 mmol) in CH\(_2\)Cl\(_2\) (3.0 mL) at room temperature was added ICl (48.7 mg, 0.3 mmol) in CH\(_2\)Cl\(_2\) (0.5 mL) and the resulting solution stirred at this temperature for 1 h. The reaction mixture was washed with satd aq Na\(_2\)S\(_2\)O\(_3\) (20 mL) and the organic layer dried (Na\(_2\)SO\(_4\)), filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to obtain 42.3 mg (40 %) of the indicated compound 47 as a yellow solid: mp 129-130 °C; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.08-7.11 (m, 1H), 7.20-7.30 (m, 3H), 7.33-7.38 (m, 4H), 7.57-7.64 (m, 3H), 7.67-7.72 (m, 1H), 8.03-8.06 (m, 1H), 8.84-8.87 (m, 1H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 75.2, 124.1, 125.1, 125.4, 128.1, 128.7, 128.7, 130.5, 130.9, 132.0, 132.7, 135.7, 140.6, 145.0, 147.8, 152.1; IR (CH\(_2\)Cl\(_2\)) 2916, 2849, 1642, 1586, 1488, 1445 cm\(^{-1}\); HRMS m/z 423.0131 (calcd for C\(_{18}\)H\(_9\)IO\(_2\), 423.0120).

3-(2-Iodophenyl)benzyl but-2-ynoate (49). To a solution of 3'-bromomethyl-2-iodobiphenyl (68)\(^5\) (0.186 g, 0.5 mmol) and 2-butylnoic acid (58.8 mg, 0.7 mmol) in DMF (2.5 mL) was added diisopropylethylamine (84.0 mg, 0.65 mmol) and the resulting solution was stirred at 50 °C for 1 d. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (Na\(_2\)SO\(_4\)), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 7:1 hexanes/ethyl acetate to afford 0.153 g (82 %) of the indicated compound 49 as a colorless oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.99 (s, 3H), 5.24 (s, 2H), 7.01-7.07 (m, 1H), 7.28-7.44 (m, 6H), 7.95 (dd, \(J = 8.1, 1.2\) Hz, 1H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 3.9, 67.3, 72.4, 86.3, 98.5, 127.7, 128.3, 128.4, 129.0, 129.4, 129.6, 130.2, 134.8, 139.6, 144.5, 146.1, 153.6;
IR (neat) 3054, 2957, 2241, 1709, 1254 cm⁻¹; HRMS m/z 375.9967 (calcd for C₁₇H₁₃IO₂, 375.9960).

3-(2-Iodophenyl)benzyl 3-phenylprop-2-ynoate (51). To a solution of 3'-bromomethyl-2-iodobiphenyl (68)¹⁵ (0.186 g, 0.5 mmol), 3-phenylpropynoic acid (0.102 g, 0.7 mmol) in DMF (2.5 mL) was added diisopropylethylamine (84.0 mg, 0.65 mmol) and the resulting solution stirred at 50 °C for 1 d. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (Na₂SO₄), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 7:1 hexanes/ethyl acetate to afford 0.197 g (90 %) of the indicated compound 5₁ as a colorless oil: ¹H NMR (CDCl₃) δ 5.32 (s, 2H), 7.04 (td, J = 7.8, 1.6 Hz, 1H), 7.30-7.46 (m, 9H), 7.57-7.59 (m, 2H), 7.96 (dd, J = 8.0, 0.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 67.6, 80.6, 87.0, 98.6, 119.6, 127.9, 128.3, 128.4, 128.7, 129.1, 129.5, 129.7, 130.2, 130.8, 133.1, 134.8, 139.7, 144.5, 146.0, 154.0; IR (neat) 3056, 2220, 1709, 1489 cm⁻¹; HRMS m/z 438.0122 (calcd for C₂₂H₁₅IO₂, 438.0117).

3-(2-Iodophenyl)benzyl allyl ether (53). To a solution of sodium allyl alkoxide [prepared by dissolving metallic Na (0.10 g, 4.35 mmol) in allyl alcohol (5 mL)] in allyl alcohol was added 3'-bromomethyl-2-iodobiphenyl (68)¹⁵ (0.347 g, 0.93 mmol) and the resulting solution was stirred at 55 °C for 5 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (Na₂SO₄), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 20:1 hexanes/ethyl acetate to afford 0.293 g (90 %) of the indicated compound 5 as a colorless oil: ¹H NMR (CDCl₃) δ 4.07 (dt, J = 5.7, 1.5...
Hz, 1H), 4.58 (s, 2H), 5.19-5.23 (m, 1H), 5.29-5.36 (m, 1H), 5.92-5.98 (m, 1H), 6.99-7.05 (m, 1H), 7.25-7.41 (m, 6H), 7.93-7.96 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 71.3, 72.0, 98.6, 117.3, 127.0, 128.1, 128.2, 128.6, 128.7, 128.9, 130.1, 134.8, 138.1, 139.5, 144.3, 146.5; IR (neat) 3058, 2850, 1461, 1418, 1012 cm$^{-1}$; HRMS m/z 350.0171 (calcd for C$_{16}$H$_{15}$IO$_3$, 350.0168).

$N$-[3-(2-Iodophenyl)benzyl]-N-methallylmethanesulfonamide (55). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added $N$-methallylmethanesulfonamide [prepared from methallylamine and methanesulfonyl chloride: $^1$H NMR (CDCl$_3$) δ 1.79 (d, $J = 0.3$ Hz, 3H), 2.97, (s, 3H), 3.69 (m, 2H), 4.64 (br s, 1H), 4.93-4.95 (m, 1H), 4.99-5.00 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 20.2, 41.1, 49.1, 113.0, 141.1] (0.149 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point 3'-bromomethyl-2-iodobiphenyl (68)$^{15}$ (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (50 mL) and washed with brine (60 mL). The combined, dried (MgSO$_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 2:1 hexanes/ethyl acetate to afford 0.353 g (86 %) of the desired compound 55 as a clear oil: $^1$H NMR (CDCl$_3$) δ 1.75 (s, 3H), 2.82 (t, $J = 3.4$ Hz, 3H), 3.82 (s, 2H), 4.44 (s, 2H), 4.98-5.00 (m, 2H), 7.03 (t, $J = 4.0$ Hz, 1H), 7.26-7.28 (m, 3H), 7.38-7.42 (m, 3H), 7.95 (dd, $J = 8.0$, 1.2 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 20.1, 40.3, 49.9, 52.6, 98.6, 115.0, 128.3, 128.3, 128.5, 129.0, 129.1, 129.7, 130.0, 135.5, 139.5, 139.9, 144.7, 146.2; IR (CH$_2$Cl$_2$) 3051, 2919, 1329, 1148, 1012 cm$^{-1}$; HRMS m/z 441.0267 (calcd for C$_{19}$H$_{20}$IN$_2$O$_2$S, 441.0260).
2-Iodobenzyl methallyl ether (57). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added 2-iodobenzyl alcohol (0.234 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point, methallyl chloride (0.122 g, 1.35 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried (MgSO₄), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 20:1 hexanes/ethyl acetate to afford 0.27 g (94 %) of the desired compound 57 as a clear oil: 'H NMR (CDCl₃) δ 1.80 (s, 3H), 4.02 (s, 2H), 4.47 (s, 2H), 4.95 (s, 1H), 5.05 (s, 1H), 6.96-7.00 (m, 1H), 7.33-7.37 (m, 1H), 7.46-7.48 (m, 1H), 7.81-7.83 (m, 1H); ¹³C NMR (CDCl₃) δ 19.8, 74.9, 75.9, 97.8, 112.7, 128.4, 128.9, 129.3, 139.3, 140.9, 142.2; HRMS m/z 288.0018 (calcd for C₁₁H₁₃IO₂, 288.0011).

N-(2-Iodophenyl)formamide (61). Compound 61 was prepared according to the procedure of Fukuyama et al.²⁴

Benzylidene(2-iodophenyl)amine (64). Compound 64 was prepared according to the procedure of Larock et al.²⁵

Representative procedure for the palladium-catalyzed migration reactions. The appropriate aryl iodide (0.25 mmol), Pd(OAc)₂ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol) and Cs₂CO₂CMe₃ (CsPiv) (0.117 g, 0.5 mmol) in DMF (4 ml) under Ar at 100 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl
ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried (MgSO₄), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

**9-Benzylimidenefluorene (2).** Compound 1 (95.6 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 61.0 mg (96%) of the indicated compound 2 as a yellow solid with melting point and spectral properties identical to those previously reported.³

**1,1,2-Triphenylethene (3).** Compound 3 was obtained as a side product from compound 1. This compound was characterized by comparing the melting point and ¹H and ¹³C NMR spectra with an authentic sample obtained from Aldrich Chemical Co., Inc.

**1-Phenyl-9H-fluorene (5).** Compound 4 (92.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 3 d. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 24.2 mg (40%) of the indicated compound 5 as a colorless oil: ¹H NMR (CDCl₃) δ 3.95 (s, 2H), 6.94 (d, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 7.19-7.22 (m, 2H), 7.33 (t, J = 7.6 Hz, 1H), 7.45-7.55 (m, 7H); ¹³C NMR (CDCl₃) δ 37.0, 122.9, 124.0, 124.8, 126.3, 126.4, 127.5, 128.5, 128.8, 129.2, 137.9, 138.7, 141.3, 141.6, 143.7, 143.9 (one sp² carbon missing due to overlap); IR (CH₂Cl₂) 3056, 3025, 1454, 1417, 1478 cm⁻¹; HRMS m/z 242.1101 (calcd for C₁₉H₁₄, 242.1096).

**1-Phenyldibenzofuran (7).** Compound 6 (93.0 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed
using 30:1 hexanes/ethyl acetate to afford 54.4 mg (89 %) of the indicated compound 7 as a white solid: mp 62-63 °C (lit\textsuperscript{26} mp 63-64 °C); \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \textdelta 7.10-7.14 (m, 1H), 7.24-7.26 (m, 1H), 7.37-7.42 (m, 1H), 7.46-7.64 (m, 9H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \textdelta 110.5, 111.6, 121.8, 122.3, 122.5, 123.9, 124.0, 127.1, 127.1, 127.9, 128.6, 129.0, 138.0, 140.0, 156.4, 156.5. The other spectral properties were identical to those previously reported.\textsuperscript{26}

**7-Chloro-1-phenyldibenzofuran (9).** Compound 8 (0.101 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 57.1 mg (82 %) of the indicated compound 9 as a colorless oil: \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \textdelta 7.25 (dd, \textit{J} = 6.8, 1.2 Hz, 1H), 7.34 (dd, \textit{J} = 8.4, 2.4 Hz, 1H), 7.45-7.60 (m, 9H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \textdelta 110.7, 112.5, 121.0, 122.1, 124.3, 125.3, 127.1, 127.7, 127.8, 128.3, 128.8, 128.9, 138.2, 139.4, 154.7, 157.1; IR (CH\textsubscript{2}Cl\textsubscript{2}) 3061, 3032, 1444, 1400, 1199, 1243 cm\textsuperscript{-1}; HRMS \textit{m/z} 278.0501 (calcd for C\textsubscript{18}H\textsubscript{11}ClO, 278.0498).

**10-Phenyl-6H-isoindolo[2,1-a]indole (11).** Compound 10 (0.102 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 49.2 mg (70 %) of the indicated compound 11 as a white solid: mp 139-140 °C; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \textdelta 5.08 (s, 2H), 6.16 (s, 1H), 7.03-7.07 (m, 1H), 7.14-7.18 (m, 1H), 7.32-7.54 (m, 8H), 7.64-7.66 (m, 2H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \textdelta 48.2, 94.3, 109.1, 119.7, 121.7, 122.4, 127.3, 128.0, 128.5, 128.8, 129.3, 131.0, 132.4, 133.7, 137.0, 139.9, 142.5, 143.2 (one sp\textsuperscript{2} carbon missing due to overlap); IR (CH\textsubscript{2}Cl\textsubscript{2}) 3053, 2916, 2850, 1471, 1551, 1446 cm\textsuperscript{-1}; HRMS \textit{m/z} 281.1210 (calcd for C\textsubscript{21}H\textsubscript{15}N, 281.1204).
2-Methyl-10-phenyl-6H-isoindolo[2,1-a]indole (13). Compound 12 (0.106 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 52.4 mg (71 %) of the indicated compound 13 as a white solid: mp 143-145 °C (decomposes); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.41 (s, 3H), 5.06 (s, 2H), 7.03-7.07 (m, 1H), 7.16-7.20 (m, 1H), 7.23-7.31 (m, 3H), 7.40-7.50 (m, 7H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 9.5, 48.1, 104.2, 109.0, 119.1, 120.0, 122.0, 122.4, 126.5, 127.9, 128.7, 129.9, 130.2, 132.6, 133.8, 134.0, 137.0, 140.0, 142.6, 142.8; IR (CH\(_2\)C\(_2\)) 3048, 2976, 2853, 1469, 2976, 2853, 1469, 1411 cm\(^{-1}\); HRMS \(m/z\) 295.1369 (calcd for C\(_{22}\)H\(_{17}\)N, 295.1361).

10-Phenyl-6H-benzo[c]chromene (15) and phenyl 3-phenylbenzyl ether (16). Compound 14 (96.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 120 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 47.8 mg (75 %) of a 60:40 inseparable mixture of compounds 15 and 16 respectively. Major isomer 15: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.02 (s, 2H) as a characteristic peak; HRMS \(m/z\) 258.1050 (calcd for C\(_{19}\)H\(_{14}\)O, 258.1045). Minor isomer 16: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.11 (s, 2H) as a characteristic peak; HRMS \(m/z\) 260.1206 (calcd for C\(_{19}\)H\(_{16}\)O, 260.1201). Mixture: \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 69.9, 70.2, 115.1, 117.6, 121.3, 121.3, 123.6, 124.1, 126.6, 126.7, 127.1, 127.4, 127.4, 127.5, 127.5, 127.7, 128.4, 128.9, 128.9, 128.9, 129.1, 129.1, 129.3, 129.4, 129.4, 129.8, 132.0, 135.5, 137.8, 139.3, 141.2, 141.9, 142.5, 156.6, 159.0; IR (neat) 3058, 3029, 1599, 1495, 1453, 1243 cm\(^{-1}\).

Fluoranthene (18). Compound 17 (82.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 1 d. The reaction mixture was
chromatographed using 50:1 hexanes/ethyl acetate to afford 41.0 mg (81%) of the indicated compound 13 as a white solid: mp 107-108 °C (lit\textsuperscript{27} mp 106-108 °C). The other spectral properties were identical to those previously reported.\textsuperscript{28}

**Benzo[e]acephenanthrylene (21).** Compound 20\textsuperscript{15} (95.0 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 49.2 mg (78%) of the indicated compound 21 as a white solid: mp 166-167 °C (lit\textsuperscript{29} mp 165-166 °C). The other spectral properties were identical to those previously reported.\textsuperscript{30}

**5-Methoxybenzo[e]acephenanthrylene (23).** Compound 22 (0.103 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 50.1 mg (71%) of the indicated compound 23 as a white solid: mp 188-189 °C (lit\textsuperscript{30} mp 189-190 °C). The other spectral properties were identical to those previously reported.\textsuperscript{30}

**Ethyl benzo[e]acephenanthrylene-5-carboxylate (25).** Compound 24 (0.113 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 40.5 mg (50%) of the indicated compound 25 as a white solid: mp 153-154 °C; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 1.46 (t, \(J = 7.2\) Hz, 3H), 4.45 (q, \(J = 7.2\) Hz, 2H), 7.63-7.65 (m, 1H), 7.68-7.70 (m, 1H), 7.74-7.78 (m, 1H), 7.98-8.04 (m, 3H), 8.09 (dd, \(J = 7.6, 1.6\) Hz, 1H), 8.24 (s, 1H), 8.45 (d, \(J = 8.0\) Hz, 1H), 8.54 (d, \(J = 0.8\) Hz, 1H), 8.64 (d, \(J = 8.0\) Hz, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 14.5, 61.2, 120.1, 121.5, 122.1, 122.5, 123.2, 123.3, 127.0, 127.6, 127.7, 128.5, 129.0, 129.9, 130.6,
6-Methylbenzo[e]acephenanthrylene (27). Compound 26 (98.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 37.2 mg (56 %) of the indicated compound 27 as a white solid: mp 149-151 °C; ¹H NMR (CDCl₃) δ 2.50 (s, 3H), 7.22 (d, J = 7.6 Hz, 1H), 7.59-7.80 (m, 5H), 7.91 (d, J = 7.2 Hz, 1H), 8.01-8.02 (m, 1H), 8.17 (s, 1H), 8.40 (d, J = 8.0 Hz, 1H), 8.63 (d, J = 8.4 Hz, 1H); ¹³C NMR (CDCl₃) δ 21.9, 119.2, 121.2, 121.3, 122.8, 123.2, 126.8, 127.0, 127.6, 128.3, 129.0, 130.2, 130.8, 132.4, 134.1, 135.3, 137.2, 137.5, 138.2, 138.9; IR (CH₂Cl₂) 2979, 1710, 1240, 1290 cm⁻¹; HRMS m/z 324.1157 (calcd for C₂₂H₁₆O₂, 324.1150).

10-Methoxydibenzo[e,f]acephenanthrylene (31). Compound 30 (0.115 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 54.0 mg (65 %) of the indicated compound 31 as a white solid: mp 178-179 °C; ¹H NMR (CDCl₃) δ 3.95 (s, 3H), 6.93 (dd, J = 8.1, 2.4 Hz, 1H), 7.46 (d, J = 2.1 Hz, 1H), 7.60-7.66 (m, 1H), 7.70-8.03 (m, 7H), 8.11 (s, 1H), 8.98 (d, J = 8.4 Hz, 1H), 9.19 (d, J = 8.7 Hz, 1H); ¹³C NMR (CDCl₃) δ 55.9, 107.4, 113.4, 119.6, 121.0, 122.8, 122.8, 126.0, 126.8, 127.3, 127.5, 127.8, 128.3, 128.4, 128.6, 128.7, 129.0, 131.5, 131.5, 133.8, 133.8, 136.1, 137.4, 142.6, 160.6; IR (CH₂Cl₂) 2921, 2849, 1608, 1461, 1285, 1213 cm⁻¹; HRMS m/z 332.1209 (calcd for C₂₅H₁₆O, 332.1201).
**Indeno[1,2,3-de]quinoline (35).** Compound 34 (82.8 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2.5 d. The reaction mixture was chromatographed using 3:2 hexanes/ethyl acetate to afford 27.4 mg (54 %) of the indicated compound 35 as a white solid: mp 100-101 °C (lit\(^3\) mp 102-103 °C); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.35-7.51 (m, 2H), 7.72-7.77 (m, 2H), 7.84-7.91 (m, 3H), 7.99 (d, \(J = 8.4\) Hz, 1H), 9.07 (d, \(J = 4.2\) Hz, 1H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 114.4, 121.0, 122.2, 123.7, 128.2, 128.4, 130.4, 131.7, 135.4, 138.2, 140.5, 145.1, 145.7, 152.9. The other spectral properties were identical to those previously reported.\(^3\)

**Benzo[\(\beta\)]fluoreno[1,9-b,c]oxepine (44).** Compound 43 (99.1 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 18:1 hexanes/ethyl acetate to afford 53.6 mg (80 %) of the indicated compound 44 as a white solid: mp 106-107 °C; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 6.69 (dd, \(J = 7.6, 0.8\) Hz, 1H), 6.83 (s, 1H), 6.93-6.95 (m, 1H), 6.97-6.99 (m, 1H), 7.05-7.07 (m, 1H), 7.16-7.30 (m, 5H), 7.58-7.59 (m, 1H), 7.62-7.64 (m, 1H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 115.4, 117.2, 120.4, 120.6, 122.3, 124.8, 126.0, 127.2, 128.3, 128.7, 129.1, 131.3, 131.4, 132.4, 137.1, 137.6, 139.9, 141.0, 154.8, 155.6; IR (CH\(_2\)Cl\(_2\)) 3050, 1580, 1238, 1450, 1426 cm\(^{-1}\); HRMS m/z 268.0892 (calcd for C\(_{20}\)H\(_{12}\)O, 268.0888).

**Ethyl E-3-(4,4-dimethylisochroman-5-yl)acrylate (58).** Compound 57 (72.0 mg, 0.25 mmol) and ethyl acrylate (32.5 mg, 0.325 mmol) were allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 36.4 mg (56 %) of the indicated compound 58 as a clear oil: \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.35 (t, \(J = 7.2\) Hz, 3H), 1.38 (s, 6H), 3.54 (s, 2H), 4.28 (q, \(J = 7.2\) Hz,
2H), 4.80 (s, 2H), 6.19 (d, J = 15.6 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 8.30 (d, J = 15.6 Hz, 1H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 14.5, 26.5, 34.0, 60.7, 69.6, 78.9, 119.8, 126.1, 126.3, 127.5, 134.9, 135.0, 141.5, 145.7, 167.0; IR (CH\(_2\)Cl\(_2\)) 3056.1, 2962.9, 2844.3, 1711.3, 1632.3, 1446.0 cm\(^{-1}\); HRMS \(m/z\) 260.1416 (calcd for C\(_{16}\)H\(_{20}\)O\(_3\), 260.1412).

**8-Methyl-1H-indole[1,2-b]benzo[d]isothiazole-10-(endo-norbornan-2-yl)-5,5-dioxide (60).** Compound 59\(^{15}\) (99.3 mg, 0.25 mmol) and norbornene (25.9 mg, 0.275 mmol) were allowed to react under our standard reaction conditions for 1 d. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (Na\(_2\)SO\(_4\)), filtered and the solvent removed under reduced pressure to afford 68.0 mg (75 %) of the indicated compound 60 as a yellow solid, which is easily recrystallized from CHCl\(_3\)/hexanes: mp 255-256 °C; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.42-1.49 (m, 3H), 1.71-1.75 (m, 2H), 1.89-1.94 (m, 2H), 2.07-2.08 (m, 1H), 2.51 (br s, 4H), 2.65 (br s, 1H), 3.28-3.31 (m, 1H), 7.18-7.23 (m, 1H), 7.26-7.28 (m, 1H), 7.31-7.36 (m, 1H), 7.60 (s, 1H), 7.68-7.72 (m, 1H), 7.83 (d, J = 8.4 Hz, 1H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 22.3, 29.4, 30.7, 36.5, 37.8, 37.9, 41.1, 42.7, 112.0, 122.6, 122.8, 123.0, 123.2, 123.5, 125.5, 128.7, 129.2, 132.2, 133.0, 135.5, 145.0 (one sp\(^2\) carbon missing due to overlap); IR (neat) 2952, 2866, 1597, 1326, 1179 cm\(^{-1}\); HRMS \(m/z\) 363.1300 (calcd for C\(_{22}\)H\(_{21}\)N\(_2\)SO\(_2\)), 363.1293).

**N-Phenylcarbamic acid butyl ester (62).** Compound 61 (61.8 mg, 0.25 mmol) and n-BuOH (0.925 g, 12.5 mmol) were allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford
13.0 mg (27 %) of the indicated compound 62 as a yellow oil with spectral properties identical to those previously reported.\textsuperscript{33}

**Pivalanilide (63).** Compound 61 (61.8 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 11.4 mg (26 %) of the indicated compound 63 as a white solid: mp 130-132 °C (lit\textsuperscript{34} mp 133-134 °C). All the spectral properties were identical to those previously reported.\textsuperscript{35}

**Benzanilide (65).** Compound 64\textsuperscript{25} (76.8 mg, 0.25 mmol) and H\textsubscript{2}O (45.0 mg, 2.5 mmol) were allowed to react under our standard reaction conditions for 2 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 27.6 mg (56 %) of the indicated compound 65 as a white solid: mp 163-164 °C. This compound was characterized by comparing the melting point and \textsuperscript{1}H and \textsuperscript{13}C NMR spectra with an authentic sample obtained from Aldrich Chemical Co., Inc.

**E-2,3-Diphenylprop-2-en-1-yl pivalate (66a) and Z-2,3-diphenylprop-2-en-1-yl pivalate (66b).** Iodobenzene (51.0 mg, 0.25 mmol) and 1-phenyl-1-propyne (34.8 mg, 0.30 mmol) were allowed to react under our standard reaction conditions at 100 °C for 21 h. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 18.7 mg (25 %) of the indicated compounds 66a and 66b as an inseparable 50:50 mixture: \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 1.11 (s, 9H), 1.13 (s, 9H), 4.91 (br s, 2H), 5.12 (br s, 2H), 6.67 (s, 1H), 6.67 (s, 1H), 6.98-7.47 (m, 20H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 27.2, 27.3, 62.2, 69.2, 126.7, 127.3, 127.7, 127.8, 128.2, 128.6, 128.7, 128.8, 129.0, 129.1, 129.1, 129.5, 133.0; IR (CH\textsubscript{2}Cl\textsubscript{2}) 3058, 2971, 2926, 2869, 1729, 1479, 1446 cm\textsuperscript{-1}; HRMS \(m/z\) 294.1623 (calcd for C\textsubscript{20}H\textsubscript{22}O\textsubscript{2}, 294.1620).
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References


(8) Tuanli Yao, Marino A. Campo and Richard C. Larock, work in progress.

(9) For full details, see Chapter 2 of this dissertation.

(10) The spectral properties of this compound were identical to those previously reported, see: Hellwinkel, D.; Goeke, K. *Synthesis*, **1995**, 1135.


GENERAL CONCLUSIONS

In this dissertation, the scope and limitations of several palladium-catalyzed processes have been presented. In particular, the palladium-catalyzed intramolecular C-H activation of o-halobiaryls has been exploited for the synthesis of a wide variety of polycycles and heterocycles.

Chapter 1 describes the synthesis of various carbocyclic and heterocyclic ketones by the palladium-catalyzed cyclocarbonylation of o-halobiaryls. This methodology works well for electron-rich, as well as electron-poor, o-halobiaryls. This reaction proceeds with good regioselectivity favoring the less sterically-congested isomer.

Chapter 2 describes Heck, Suzuki and alkyne annulation reactions with o-halobiaryls. These reactions have revealed that arylpalladium intermediates undergo a facile 1,4-palladium shift. After studying various reaction variables, we have learned that this palladium migration can be activated or suppressed at will by simply choosing the appropriate set of reaction conditions. These experiments consistently point to the intermediacy of an electrophilic palladium species.

Chapter 3 describes novel methodology involving the sequential transformation of o-halobiaryls to fused polycycles. This methodology works best for electron-rich arenes, which is in agreement with the idea that C-H activation by palladium parallels electrophilic aromatic substitution. We have been able to exploit a wide range of palladium migrations to generate the key organopalladium intermediates required for these cyclizations.
APPENDIX A. CHAPTER 1 $^1$H AND $^{13}$C NMR SPECTRA
2-ido-5-methylphenyl
9-iodo-10-phenylphenanthrene
2-adode-3-phenyl-1H-indole
3-halo-2-phenyl-1-(4-toluene)sulfonylindole
APPENDIX B. CHAPTER 2 $^1$H AND $^{13}$C NMR SPECTRA
$\text{N,N-dimethyl-4-(2-iодофенил)амина}$
Ethyl 4-(2-bromophenyl)benzoate

![Diagram of the chemical structure of ethyl 4-(2-bromophenyl)benzoate]

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
ethyl 3,4,5-tris(4-fluorophenyl)benzoate
232

[Diagram with chemical shifts and a structural formula of 2-iodo-3-methoxyphenyl]
ethyl 5,4-nonylphenyl-2-ylacrylate
ethyl E3,4'-dimethylamnobiphenyl-2'-ylacrylate

- 167.173
- 149.989
- 144.666
- 143.208
- 132.567
- 130.740
- 130.446
- 129.806
- 127.719
- 126.941
- 126.699
- 118.534
- 112.215

- 77.383
- 77.066
- 76.748

- 60.326

- 40.559

- 14.380
ethyl E3-4-dimethylaminobutyl-2-vinylate
ethyl 3-(4-ethoxycarbonyl)biphen-2-yl)acrylate
ethyl E-3-(4-ethoxycarbonylbiphen-2-yl)acrylate
ethyl 5-14-dinitrophenyl-2-pyrydylate

- 1.000
- 0.988
- 0.974
- 4.123
- 2.037

8.552
8.544
8.275
8.267
8.247
8.239
7.713
7.660
7.563
7.535
7.499
7.493
7.488
7.479
7.474
7.464
7.344
7.336
7.329
7.325
7.318
7.312
6.580
6.527

4.271
4.247
4.223
4.199

1.658
1.330
1.306
1.282
ethyl E-3-[2-(benzofuran-3-yl)phenyl]acrylate
ethy1 E3-(3-phenyl-1-methylindole-2-carboxylic acid
ethyl E-4(3,5-dimethylphenyl)-2-propenoate

\[
\begin{align*}
21.391 & 60.369 & 77.465 & 109.260 \\
118.832 & 121.463 & 129.831 & 137.781 \\
143.931 & 148.462 & 166.956 & 173.807
\end{align*}
\]
ethyl E-3'-methylphen-2'-ylacrylate
ethyl E-3-(2'-methylbiphen-2-yl)acrylate and ethyl E-3-(6-methylbiphen-2-yl)acrylate
ethyl E3-(3-methoxyphenyl)-2-ylacrylate
3-methoxy-9,10-diphenylphenanthrene
methyl 4-(4'-methylbiphen-2-yl)benzoate and methyl 4-(4-methylbiphen-2-yl)benzoate
methyl 4-(3-phenylbenzofuran-2-yl)benzoate
methyl 4-[2-(benzofuran-3-yl)phenyl]benzoate
APPENDIX C. CHAPTER 3 $^1$H AND $^{13}$C NMR SPECTRA
2-methoxy-3-phenylphenyl
3.312
3.225
2.089
2.136
2.153
1.000
2.127
3.940
0.009
8.473
8.470
8.462
7.721
7.714
7.701
7.695
7.689
7.681
7.675
7.667
7.661
7.646
7.640
7.462
7.455
7.452
7.434
7.430
7.260
7.231
7.224
7.209
7.202
7.106
7.099
7.084
7.077
0.009
9-iodo-10-(3-methylphenyl)phenanthrene

[Chemical structure image]

ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160

21.660
- 146.485
- 138.364
- 135.304
- 133.240
- 132.599
- 131.142
- 130.314
- 128.819
- 128.748
- 128.382
- 128.271
- 127.522
- 127.218
- 126.466
- 122.916
- 122.742
- 110.531

- 77.675
- 77.252
- 76.828

9-halo-10-thiophen-2-ylphenanthrene
2-iodobenzyl methallyl ether
10-phenyl-6H-benzo[cl]chrysene and 3-phenylbenzyl phenyl ether
10-phenyl-6H-benzo[c]chromene and 3-phenylbenzyl phenyl ether
3.100

10-methoxydibenzol(o)naphtanaphthalene

0.951
0.921

1.005
7.176
0.980
0.931

0.942

7.945
7.902
7.898
7.854
7.826
7.806
7.783
7.778
7.758
7.754
7.735
7.730
7.725
7.707
7.702
7.657
7.653
7.634
7.630
7.627
7.607
7.604
7.459
7.452
7.260
6.944
6.937
6.917
6.909

3.949

1.453

0.027
ethyl E-3-(4,4-dimethylisochroman-5-yl)acrylate
ethyl E-3-(4,4-dimethylisochroman-5-yl)acrylate
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