Abstract: Certain disclosed embodiments of the present invention concern a method for making biaryl compounds by combining a diene with a dienophile under reaction conditions that facilitate a Diels-Alder reaction. Certain embodiments are particularly directed to making a tetra-ortho-substituted biaryl compounds. The disclosed method may involve using novel dienes, dienophiles, or both. Similarly, certain of the biaryl compounds are novel compounds too. Additional disclosed embodiments concern a method for making useful compounds by first making a Diels-Alder adduct. The Diels-Alder adduct is then further modified or coupled to other compounds. The method can be used to make carbazoles, such as Siamenol. Disclosed biaryl compounds are useful for a number of applications, such as pharmacophores and organocatalysts.
METHOD FOR MAKING BIARYL COMPOUNDS,
COMPOUNDS MADE BY THE METHOD, AND
METHOD FOR THEIR USE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 60/934,588 filed on June 13, 2007, and U.S. Provisional Application No. 61/028,820, filed February 14, 2008. The entire disclosures of these prior provisional applications are considered to be part of the disclosure of the following application and are hereby incorporated by reference.

FIELD

The present disclosure concerns embodiments of a method for making biaryl compounds, compounds made by the method, and embodiments of methods for using such compounds.

ACKNOWLEDGMENT OF GOVERNMENT SUPPORT

The present invention was developed, at least in part, using funds provided by the National Science Foundation (CHE-0549884). The United States government may have rights in this invention.

BACKGROUND

Numerous biaryl compounds are known, and they have utility for a variety of applications, including pharmacophores for potential medicinal treatments and ligands in metal catalysis. As a result, synthesis of highly substituted biaryl compounds, particularly structures containing four ortho-substituents, via the aryl-aryl sigma bond has generated considerable synthetic attention. This task has long been considered one of the premier challenges for constructing complex polyaromatic systems.

While synthetic methods are known for constructing selected biaryls, innovative strategies are still needed to broaden their accessibility. Effective methods for the synthesis of biaryl linkages have progressed dramatically in recent
years, primarily due to the use of palladium-mediated strategies such as the Kharasch, Negishi, Stille, and Suzuki reactions. Iron-catalyzed couplings, as well as other metal catalyzed reactions using manganese, nickel or copper, are of equal and more recent importance. While prior approaches provide valuable options, limitations in their effectiveness have been observed. For example, while successful cases do exist, tetra-ortho substituted biaryls are difficult to construct, due to the added degree of difficulty in coupling two bis-ortho-substituted aryl precursors. Documented reports of the significant cost of the necessary coupling partners (e.g. aryl halide or boronic acid) for traditional metal-mediated approaches to highly functionalized biaryls have made alternate strategies more attractive. A corollary to the high cost of select coupling components is that the aryl halides and/or aryl metallo species are not always readily available, as access to the proper substitution pattern has proven difficult to control.

5 SUMMARY

No general approach to making biaryl compounds has been reported using a Diels-Alder cycloaddition strategy. As a result, the present disclosure concerns embodiments of a Diels-Alder method for making biaryl compounds generally, and particularly biaryls, such as tri- and tetra-or/zo-substituted biaryls, that are difficult or impossible to make using metal-mediated coupling reactions. The Diels-Alder approach to Biaryls (DAB) allows making biaryl compounds possessing four different atoms at the four ortho positions, which has not been previously accomplished. Certain embodiments concern cycloaddition of di-substituted alkynes with oxygenated, cyclic and acyclic dienes to yield (after aromatization) the required tetra-or/zo-substituted biaryls. Substituents on the alkyne were able to activate the dienophile via their resonance-based, electron withdrawing character. Additional embodiments allow construction of tetra-or/ho-substituted biaryl compounds using alkynes possessing just one resonance-based, electron withdrawing group.

One added advantage to disclosed embodiments of the present invention is that the Diels-Alder approach allows the incorporation of functional group combinations (e.g. halogenated biaryls) that would not be readily accessible using traditional metal-mediated aryl-aryl couplings. In addition, the proper choice of
substituents on the diene and dienophile allows combining the benefits of Diels-Alder cycloadditions with the power of subsequent metal-mediated couplings using the Diels-Alder adducts to produce polyaryl compounds.

Certain disclosed embodiments of the present invention concern a method for making a biaryl compound comprising providing a diene and providing a dienophile having a formula:

\[
\begin{array}{c}
R_1 \\
R_2 \\
R_3 \\
R_4 \\
R_5 \\
R_6
\end{array}
\]

where \( R_1 \) and \( R_3 \) are independently selected from halide, hydrogen or nitrogen-containing moieties, \( R_2 \) is selected from aliphatic, substituted aliphatic, aryl, substituted aryl, boron or boron-containing moieties, carbonyl bearing moieties, halogen, hydrogen, phosphorus-containing moieties, tin or tin-containing moieties, sulfur or sulfur-containing moieties, silicon or silicon-containing moieties, and \( R_4 - R_6 \) independently are selected from aliphatic, substituted aliphatic, aryl, substituted aryl, carbonyl-containing moieties, cyclic, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, or hydrogen. The biaryl compound is then made by combining the diene with the dienophile under reaction conditions that facilitate a Diels-Alder reaction between the diene and the dienophile.

Certain embodiments are particularly concerned making a tetra-ortho-substituted biaryl compound. One disclosed embodiment comprises reacting a diene with a dienophile under reaction conditions that promote a Diels-Alder reaction. The tetra-\( \text{ort} / \text{ro} \)-substituted biaryl compound produced by the reaction typically has a formula:
where \( R_3, R_4, R_8 \) and \( R_9 \) are different, \( R_3 \) is a nitrogen-containing moiety, \( R_9 \) is carbon, a halide or hydrogen, and remaining \( R_i-R_2, R_4-R_8 \) and \( R_{io} \) groups are selected from alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties (such as aldehydes, amides, carboxylic acids, esters, ketones and thioesters), cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties [e.g. nitrile (RCN), nitro (NO_2) and nitroso (RNO)] phosphorus-containing moieties [such as phosphines (\( R_3P \), where \( R_3 \) generally, but not necessarily, is other than hydrogen, and the \( R_3 \) functional groups can be the same or different) and phosphine oxides (\( OPR_3 \), again where the \( R \) groups can be the same or different)], silicon, silicon-containing moieties, including particularly silyl ethers, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, or combinations thereof.

The disclosed method may involve using novel dienes, dienophiles, or both. For example, certain disclosed embodiments used novel dienophiles having a formula
where R_i is a nitrogen-containing moiety [e.g. nitrile (RCN), nitro (NO_2) and nitroso (RNO)], R_2 and R_4-R_6 independently are alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties (such as aldehydes, amides, carboxylic acids, esters, ketones and thioesters), cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroary1, substituted heteroary1, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties [e.g. nitrile (RCN), nitro (NO_2) and nitroso (RNO)] phosphorus-containing moieties [such as phosphines (R_3P, where R_3 generally, but not necessarily, is other than hydrogen, and the R_3 functional groups can be the same or different) and phosphine oxides (OPR_3, again where the R groups can be the same or different)], silicon, silicon-containing moieties, including particularly silyl ethers, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, or combinations thereof, and R_3 is halide or hydrogen, excluding compounds where (a) R_i is nitro, R_2 is n-pentyl, and R_3 is bromide, and (b) R_1 is nitro, R_2 is carboxylic acid or methyl ester, and R_3 is chloride or bromide.

Similarly, certain biaryl compounds are novel compounds too. For example, novel unsymmetrical, tetra-ø-ø-substituted biaryl compounds disclosed herein have a formula:
where $R_3, R_4, R_8$ and $R_9$ are different, $R_3$ is a nitrogen-containing moiety, $R_9$ is carbon, a halide or hydrogen, and remaining $R_1$-$R_2, R_4$-$R_8$ and $R_{10}$ groups are selected from alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties (such as aldehydes, amides, carboxylic acids, esters, ketones and thioesters), cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties [e.g. nitrile (RCN), nitro (NO$_2$) and nitroso (RNO)] phosphorus-containing moieties [such as phosphines ($R_3$P, where $R_3$ generally, but not necessarily, is other than hydrogen, and the $R_3$ functional groups can be the same or different) and phosphine oxides (OPR$_3$, again where the R groups can be the same or different)], silicon, silicon-containing moieties, including particularly silyl ethers, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, or combinations thereof.

Additional disclosed embodiments concern a method for making useful compounds by first making a biaryl compound by combining a diene with a dienophile under reaction conditions that facilitate a Diels-Alder reaction between the diene and the dienophile to form a Diels-Alder adduct. The Diels-Alder adduct may be further modified or coupled to other compounds. Certain embodiments of the diene have a formula:
With reference to the general formula, $R_i-R_6$ independently are selected from aliphatic; substituted aliphatic; alkoxy; amino; amine; substituted amine; aryl; substituted aryl; arylalkyl; carbonyl-bearing groups, including acids (-$CO_2H$), aldehydes ($RCO$), amides (e.g. $R_2NCO$), but also including without limitation acyl oxazolidinones, such as Evans' oxazolidinones, and sulfonamides, such as Oppolzer' sultams), esters ($RCO_2$-), ketones ($RCOR$-) and thiesters ($RCSO$-), where $R$ for these carbonyl bearing groups is aliphatic, including particularly alkyl, and even more particularly lower alkyl, substituted aliphatic, aryl, substituted aryl, and arylalkyl; halogens; hydrogen; nitriles; phosphorous, such as phosphine and phosphine oxide; silyl; silyl ether; sulfide; sulfones; or sulfoxide. $R_i$ and $R_6$ also can be a carbon atom or a heteroatom, such as nitrogen, to form cyclic or heterocyclic compounds having 5 or more atoms in a ring. $R_7$ and $R_8$ typically are carbon atoms, but also may be heteroatoms, particularly nitrogen, such as in diazines, where $R_1$ and $R_6$ or $R_7$ and $R_8$ are nitrogen atoms, triazines, where 3 of $R_i$, $R_6$, $R_7$ or $R_8$ are nitrogen atoms, or tetrazines where $R_i$, $R_6$, $R_7$ and $R_8$ are nitrogen atoms. A person of ordinary skill in the art will appreciate that these $R$ groups often have pairs of electrons, such as with oxygen-, nitrogen-, phosphorous- and sulfur-based substituents, and further that such $R$ groups often are electron withdrawing groups.

And certain embodiments of the method use a dienophile having a formula:
where \( R_1 \) and \( R_3 \) are independently selected from aliphatic, such as alkyl, hydrogen, halide, and nitrogen-containing moieties, \( R_2 \) is selected from aliphatic, substituted aliphatic, aryl, substituted aryl, boron, boron-containing moieties, carbonyl-containing moieties, cyclic, heteroaryl, heterocyclic, hydrogen, halogen, phosphorus-containing moieties, sulfur, sulfur-containing moieties, silicon, silicon-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, and \( R_4 \text{-} R_6 \) independently are selected from hydrogen, halide, aliphatic, substituted aliphatic, aryl, substituted aryl, carbonyl bearing moieties, cyclic, heteroaryl, and substituted heteroaryl. The Diels-Alder adduct subsequently can be modified, such as by functional group transformation on the biaryl compound, coupling the biaryl compound with an aliphatic or aryl compound using a metal-mediated coupling reaction, such as Suzuki, Stille, Negishi coupling, Sonagashira coupling, Heck coupling, or combinations thereof.

The method can be used to make carbazoles. For example, the biaryl compound may have a formula:

\[
\begin{align*}
R_1 - R_2, R_4 - R_5 \text{ and } R_7, \text{ and } R_9 - R_{10} \text{ independently are alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes,}
\end{align*}
\]
aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties (such as aldehydes, amides, carboxylic acids, esters, ketones and thioesters), cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties [e.g. nitrile (RCN), nitro (NO₂) and nitroso (RNO)] phosphorus-containing moieties [such as phosphines (R₃P, where R₃ generally, but not necessarily, is other than hydrogen, and the R₃ functional groups can be the same or different) and phosphine oxides (OPR₃, again where the R groups can be the same or different)], silicon, silicon-containing moieties, including particularly silyl ethers, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, or combinations thereof. More typically, R₁-R₂, R₄-R₅ and R₇, and R₉-R₁₀ are aliphatic, substituted aliphatic, halogen or hydrogen. R₆ and R₈ typically are independently hydrogen, alcohol, protected alcohol, or aliphatic. Carbazoles can be made from such biaryl compounds having a formula:

\[
\begin{align*}
&\text{A particular example of useful carbazole made by the method is Siamenol.} \\
&\text{Siamenol was made, more particularly, by first forming a biaryl compound by a} \\
&\text{Diels-Alder reaction, forming a Claisen precursor and subsequently performing a} \\
&\text{Claisen rearrangement. Siamenol was then formed by a Cadogan cyclization.} \\
&\text{Biaryl compounds are useful for a number of applications, such as ligands} \\
&\text{for transition metal reactions, organocatalysts and pharmacophores. One disclosed} \\
&\text{embodiment of a method for using biaryl compounds as ligands for transition metal} \\
&\text{reactions comprises providing an organic biaryl compound made by a Diels-Alder}
\end{align*}
\]
reaction, and then using the biaryl compound as a ligand for a transition metal in a reaction comprising the transition metal. Similarly, one disclosed embodiment of a method for using biaryl compounds comprises providing an organic biaryl compound made by a Diels-Alder reaction, and then performing an organocatalytic reaction comprises providing an organic biaryl compound made by a Diels-Alder reaction, and then using the biaryl compound as an organic catalyst. One example of such a catalyst is a dialkylamino phosphine having a formula:

\[
\begin{align*}
&\text{With reference to this general formula, } R_1-R_i_0 \text{ typically independently are alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, aroylalkyl, substituted aroylalkyl, boron, boron-containing moieties, carbonyl-containing moieties (such as aldehydes, amides, carboxylic acids, esters, ketones and thioesters), cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties [e.g. nitrile (RCN), nitro (NO_2) and nitroso (RNO)] phosphorus-containing moieties [such as phosphines (R_3P, where R_3 generally, but not necessarily, is other than hydrogen, and the R_3 functional groups can be the same or different) and phoshine oxides (OPR_3, again where the R groups can be the same or different)], silicon, silicon-containing moieties, including particularly silyl ethers, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, or combinations thereof. } R_{13}-R_{16} \text{ most typically are selected from hydrogen and aliphatic, particularly alkyl, and even more typically lower alkyl.}
\end{align*}
\]
More typically, working embodiments of compounds useful as catalysts had the following formula

```
    R_{10} R_{1}    
    |      |    
    R_{9}  R_{13}R_{14}    
    |      |    
    R_{8}O  PR_{15}R_{16}    
    |      |    
    R_{7} R_{5}    
    |      |    
    R_{6} OR_{6}    
```

Where $R_i-R_2$, $R_5$, $R_7$, $R_9$, and $R_{10}$ independently are aliphatic, aryl or hydrogen, $R_6$ and $R_8$ independently are hydrogen, alcohol protecting group, aliphatic or aryl, and $R_{13}-R_{16}$ independently are lower alkyl. The dialkylamino phosphine catalysts may be used, for example, as a ligand in palladium-mediated processes.

Disclosed embodiments of the present invention also concern a method for treating a subject. The method comprises providing a compound having a formula

```
    R_{8} R_{1}    
    |      |    
    R_{7}  NH    
    |      |    
    R_{6} R_{3}    
    |      |    
    R_{5} R_{4}    
```

where $R_i-R_8$ are independently selected from hydrogen, halogen, hydroxyl, aliphatic, substituted aliphatic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and the like. A therapeutically effective amount of the compound is administered to a subject to, for example, treat HIV or a cellular proliferation disease, such as cancer. A person of ordinary skill in the art will appreciate that the therapeutically effective amount will depend on various factors, including the particular compound, the effectiveness and toxicity thereof, the nature of the disease
or ailment being treated, etc., but for certain embodiments the effective amount is a concentration ranging from about 0.005 \( \mu g/mL \) to at least about 5 \( \mu g/mL \).

The foregoing and other objects, features, and advantages of the invention will become more apparent from the following detailed description, which proceeds with reference to the accompanying figures.

**BRIEF DESCRIPTION OF THE DRAWINGS**

FIG. 1 is an ORTEP representation of the crystal structure obtained to confirm the absolute stereochemistry for one embodiment of a biaryl compound (biaryl 14-(a/?) made according to a disclosed embodiment of the present invention.

FIG. 2 is an ORTEP representation of the crystal structure for one embodiment of a biaryl compound (biaryl 14) made according to a disclosed embodiment of the present invention.

FIG. 3 is an ORTEP representation of the crystal structure for one embodiment of a biaryl compound (biaryl 5b) made according to a disclosed embodiment of the present invention.

FIG. 4 is an ORTEP representation of the crystal structure for one embodiment of a biaryl compound (biaryl 34) made according to a disclosed embodiment of the present invention.

FIG. 5 is an ORTEP representation of the crystal structure for one embodiment of a biaryl compound (biaryl 49) made according to a disclosed embodiment of the present invention.

FIG. 6 is an ORTEP representation of the crystal structure of lactam ent-52 made according to a disclosed embodiment of the present invention.

**DETAILED DESCRIPTION**

1. **Terms and Introduction**

The following term definitions are provided to aid the reader, and should not be considered to provide a definition different from that known by a person of ordinary skill in the art. And, unless otherwise noted, technical terms are used according to conventional usage.
As used herein, the singular terms "a," "an," and "the" include plural referents unless context clearly indicates otherwise. Similarly, the word "or" is intended to include "and" unless the context clearly indicates otherwise. Also, as used herein, the term "comprises" means "includes." Hence "comprising A or B" means including A, B, or A and B. It is further to be understood that all nucleotide sizes or amino acid sizes, and all molecular weight or molecular mass values, given for nucleic acids or polypeptides or other compounds are approximate, and are provided for description.

**Aldehyde:** Is a carbonyl-bearing functional group having a formula

![Aldehyde](image)

where the line drawn through the bond indicates that the functional group can be attached to any other moiety, but that such moiety simply is not indicated.

**Aliphatic:** A substantially hydrocarbon-based compound, or a radical thereof (e.g., C₆H₁₃, for a hexane radical), including alkanes, alkenes and alkynes, and further including straight- and branched-chain arrangements, and all stereo and position isomers as well.

**Analog, Derivative or Mimetic:** An analog is a molecule that differs in chemical structure from a parent compound, for example a homolog (differing by an increment in the chemical structure, such as a difference in the length of an alkyl chain), a molecular fragment, a structure that differs by one or more functional groups, a change in ionization. Structural analogs are often found using quantitative structure activity relationships (QSAR), with techniques such as those disclosed in Remington *The Science and Practice of Pharmacology*, 19th Edition (1995), chapter 28. A derivative is a biologically active molecule derived from the base structure. A mimic is a molecule that mimics the activity of another molecule, such as a biologically active molecule. Biologically active molecules can include chemical structures that mimic the biological activities of a compound.

**Animal:** Living multi-cellular vertebrate organisms, a category that includes, for example, mammals and birds. The term mammal includes both human and non-human mammals. Similarly, the term "subject" includes both human and veterinary subjects, for example, humans, non-human primates, dogs, cats, horses, and cows.
Aryl: A substantially hydrocarbon-based aromatic compound, or a radical thereof (e.g. \( \text{C}_6\text{H}_5 \)) as a substituent bonded to another group, particularly other organic groups, having a ring structure as exemplified by benzene, naphthalene, phenanthrene, anthracene, etc.

Arylalkyl: A compound, or a radical thereof (\( \text{C}_7\text{H}_7 \) for toluene) as a substituent bonded to another group, particularly other organic groups, containing both aliphatic and aromatic structures.

Carboxylic Acid: Refers to a carbonyl-bearing functional group having a formula

\[
\text{HO-C=O}
\]

Cyclic: Designates a substantially hydrocarbon, closed-ring compound, or a radical thereof. Cyclic compounds or substituents also can include one or more sites of unsaturation, but does not include aromatic compounds. One example of such a cyclic compound is cyclopentadienone.

Diels-Alder Reaction: An organic cycloaddition chemical reaction between a conjugated diene and a dienophile, such as an alkene, a substituted alkene, an alkyne or a substituted alkyne.

Diene: A diene, for purposes of the present invention, is any compound that can participate in a Diels-Alder reaction having at least two double bonds in conjugation, i.e. in a 1-3 arrangement. Suitable dienes can be aliphatic, acyclic or cyclic.

Dienophile: An alkene, substituted alkene or other two-\( \pi \)-electron systems that reacts with a diene in a Diels-Alder reaction.

Ester: A carbonyl-bearing substituent having a formula

\[
\text{R-O-C=O}
\]

where R is virtually any group, including aliphatic, substituted aliphatic, aryl, arylalkyl, heteroaryl, etc.
**Heteroaryl:** Refers to an aromatic, closed-ring compound, or radical thereof as a substituent bonded to another group, particularly other organic groups, where at least one atom in the ring structure is other than carbon, and typically is oxygen, sulfur and/or nitrogen.

**Heterocyclic:** Refers to a closed-ring compound, or radical thereof as a substituent bonded to another group, particularly other organic groups, where at least one atom in the ring structure is other than carbon, and typically is oxygen, sulfur and/or nitrogen.

**Ketone:** A carbonyl-bearing substituent having a formula

![Ketone Structure](image)

where R is virtually any group, including aliphatic, substituted aliphatic, aryl, arylalkyl, heteroaryl, etc.

**Lower:** Refers to organic compounds having 10 or fewer carbon atoms in a chain, including all branched and stereochemical variations, particularly including methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, and decyl.

**Mammal:** This term includes both human and non-human mammals. Similarly, the term "subject" includes both human and veterinary subjects.

**Neoplasia and Tumor:** The process of abnormal and uncontrolled growth of cells. Neoplasia is one example of a proliferative disorder.

The product of neoplasia is a neoplasm (a tumor), which is an abnormal growth of tissue that results from excessive cell division. A tumor that does not metastasize is referred to as "benign." A tumor that invades the surrounding tissue and/or can metastasize is referred to as "malignant." Examples of hematological tumors include leukemias, including acute leukemias (such as acute lymphocytic leukemia, acute myelocytic leukemia, acute myelogenous leukemia and myeloblasts, promyelocyte, myelomonocytic, monocytic and erythroleukemia), chronic leukemias (such as chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, and chronic lymphocytic leukemia), polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma (indolent and high grade forms), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukemia and myelodysplasia.
Examples of solid tumors, such as sarcomas and carcinomas, include fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, and other sarcomas, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, lymphoid malignancy, pancreatic cancer, breast cancer, lung cancers, ovarian cancer, prostate cancer, hepatocellular carcinoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, medullary thyroid carcinoma, papillary thyroid carcinoma, pheochromocytomas sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, Wilms' tumor, cervical cancer, testicular tumor, seminoma, bladder carcinoma, and CNS tumors (such as a glioma, astrocytoma, medulloblastoma, cranioopharygioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma and retinoblastoma).

**Substituted:** A fundamental compound, such as an aryl or aliphatic compound, or a radical thereof, having coupled thereto, typically in place of a hydrogen atom, a second substituent. For example, substituted aryl compounds or substituents may have an aliphatic group coupled to the closed ring of the aryl base, such as with toluene. Again solely by way of example and without limitation, a long-chain hydrocarbon may have a substituent bonded thereto, such as an aryl group, a cyclic group, a heteroaryl group or a heterocyclic group.

**Therapeutically Effective Amount:** A quantity of a specified agent sufficient to achieve a desired effect in a subject being treated with that agent. For example, this may be the amount of a conjugate useful in increasing resistance to, preventing, ameliorating, and/or treating infection and disease. Ideally, a therapeutically effective amount of an agent is an amount sufficient to increase resistance to, prevent, ameliorate, and/or treat infection and without causing a substantial cytotoxic effect in the subject. The effective amount of an agent useful for increasing resistance to, preventing, ameliorating, and/or treating infection and disease in a subject will be dependent on the subject being treated, the severity of the affliction, and the manner of administration of the therapeutic composition.

**Vaccine:** A vaccine is a pharmaceutical composition that elicits a prophylactic or therapeutic immune response in a subject. In some cases, the immune response is a protective response. Typically, a vaccine elicits an antigen-specific immune response to an antigen of a pathogen, for example, a bacterial or viral pathogen, or to a cellular constituent correlated with a pathological condition. A vaccine may include a polynucleotide, a peptide
or polypeptide, a polysaccharide, a virus, a bacteria, a cell or one or more cellular constituents. In some cases, the virus, bacteria or cell may be inactivated or attenuated to prevent or reduce the likelihood of infection, while maintaining the immunogenicity of the vaccine constituent.

Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. In case of conflict, the present specification, including explanations of terms, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety, unless the context clearly indicates otherwise.

II. Dienes and Dienophiles

The present invention provides dienes and dienophiles useful for making biaryl compounds. Each of these is discussed below in further detail.

A. Dienes Generally

Dienes suitable for practicing disclosed embodiments of the present invention can be substantially non-substituted, i.e. having only hydrogen atoms connected to carbon atoms in the diene. Alternatively, and more typically, dienes also can be substituted with functionality other than hydrogen atoms. Selecting suitable dienes can include considering, amongst other things, functional groups desired in an end product, functional groups that can be transformed into desired functionality after the Diels-Alder reaction, functional groups that facilitate the Diels-Alder reaction, etc., and for various combination of these reasons.

Certain embodiments of the present invention have used dienes having the following formula:
With reference to the general formula, $R_i-R_6$ independently are selected from aliphatic; substituted aliphatic; alkoxy; amino; amine; substituted amine; aryl; substituted aryl; arylalkyl; carbonyl-bearing groups, including acids (-CO$_2$H), aldehydes (RCO-), amides (e.g. $R_2$NCO), but also including without limitation acyl oxazolidinones, such as Evans' oxazolidinones, and sulfonamides, such as Oppolzer'sultams), esters (RCO$_2$-), ketones (RCOR-) and thioesters (RCSO-), where $R$ for these carbonyl bearing groups is aliphatic, including particularly alkyl, and even more particularly lower alkyl, substituted aliphatic, aryl, substituted aryl, and arylalkyl; halogens; hydrogen; nitriles; phosphorous, such as phosphate and phosphine oxide; silyl; silyl ether; sulfide; sulfones; or sulfoxide. $R_i$ and $R_6$ also can be a carbon atom or a heteroatom, such as nitrogen, to form cyclic or heterocyclic compounds having 5 or more atoms in a ring. $R_7$ and $R_8$ typically are carbon atoms, but also may be heteroatoms, particularly nitrogen, such as in diazines, where $R_i$ and $R_6$ or $R_7$ and $R_8$ are nitrogen atoms, triazines, where 3 of $R_i$, $R_6$, $R_7$ or $R_8$ are nitrogen atoms, or tetrazines where $R_i$, $R_6$, $R_7$ and $R_8$ are nitrogen atoms. A person of ordinary skill in the art will appreciate that these $R$ groups often have pairs of electrons, such as with oxygen-, nitrogen-, phosphorus- and sulfur-based substituents, and further that such $R$ groups often are electron withdrawing groups.

B. **Acyclic Dienes**

Certain embodiments of the present invention concern acyclic dienes, such as dienes having a formula:
With reference to the acyclic compounds, Ri-R6 independently are as stated above, except that Ri and R6 are not carbon or heteroatoms in a cyclic structure. Particular acyclic dienes, are well known or commercially available, such as Brassard's diene and commercially available TBS Danishefsky's diene.

A variety of silyl ethers, particularly alkyl silyl ethers, including trimethylsilyl (TMS) and tert-butyl dimethyl silyl (TBS), can be used.

**C. Cyclic Dienes**

Cyclic dienes also are useful for making biaryl compounds according to the present disclosure, particularly alkoxy substituted dienes, silyl ether substituted dienes, and dienes having both alkoxy and silyl ether groups, as shown by the following general formulas, where dashed line bonds indicates that a group is optional at that position.

\[
\begin{align*}
R_1 & \quad R_2 \\
R_3 & \quad R_4 \\
R_5 & \quad R_6
\end{align*}
\]
Substitution patterns for these disubstituted dienes can be other than 1-3 substitutions. For example, the substituents can be at the one and four positions, as indicated below.

Working embodiments have used the following exemplary cyclohexadienes.
Cyclic dienes having the following formula also have been used in working embodiments.

Particular embodiments include:

With reference to this general formula, \( R_1-R_4 \) typically are selected from hydrogen, aliphatic, particularly lower alkyl, such as methyl and ethyl, aryl, and arylalkyl, such as benzyl.

Dienes having heteroatoms other than those depicted so far also have been used. For example, nitrogen-containing dienes having the following formula can be used to practice the present invention.

Particular embodiments include:


D. Electron-Withdrawing Groups on Dienes

Electron withdrawing groups can be functional groups associated with dienes. Exemplarily electron withdrawing groups include nitriles (-CN) and carbonyl-bearing substituents. A general formula for cyclic dienes having carbonyl-bearing substituents is provided below.

![Image of general formula for cyclic dienes with carbonyl-bearing substituents]

This general formula indicates that the carbonyl-bearing substituent can be at either position 1 or 2. Other substitution patterns also may be possible for such cyclic dienes having carbonyl-bearing substituents, such as 1-3 and 1-4 substitution patterns, but these compounds may be difficult to make and/or may not be sufficiently stable for further use. The carbonyl-bearing substituent can be, for example, an aldehyde, an amide, ketone, carboxylic acid, ester, phosphine oxides, sulfones, thioesters, or combinations thereof. Sulfur analogs thereof, including thiocarbonyls (-C=S), also can be used. One particular example of a carbonyl-based diene is 1-carbomethoxy-cyclohexadiene, indicated as compound 11 in Scheme 4.

![Image of 1-carbomethoxy-cyclohexadiene]

This diene undergoes [4+2] cycloadditions with electron rich dienophiles such as ynamines in an inverse electron demand Diels-Alder process.

Chiral carbonyl-based dienes also can be used to practice disclosed embodiments of the present invention. Exemplary chiral dienes include Evans' oxazolidinones.
Evans'-type oxazolidinones

\[ X = O, S \]
\[ R = \text{alkyl, aryl, benzyl, allyl etc} \]
\[ R' = \text{alkyl, aryl, benzyl, allyl etc} \]

and sulfonamides, such as Oppolzer' sultams.

Oppolzer sultam-based dienes

Carbonyl-based dienes, particularly esters, also have been used in working embodiments. Exemplary carbonyl-based dienes include the methyl ester dienes shown below.

A person of ordinary skill in the art will appreciate that cyclic structures having both fewer and greater numbers of atoms than 6 also are useful for performing Diels-Alder reactions that produce biaryl compounds.

Certain embodiments of disclosed dienes can be made regioselectively. For example, dienol ethers can be formed regioselectively from enones using the Kharasch reagent. See, for example, Kraft and Holton, "The Kharasch Reagent. Regioselective Generation of Dienol Ethers from Enones," *J. Am. Chem. Soc.*, 106, pp. 7619-7621 (1984).

**E. Chiral Dienes**

Chiral dienes also can be used in disclosed embodiments of the present invention. One such chiral diene is provided below.
Chiral dienes also can be used to make biaryl compounds, as discussed in further detail below.

III. General Description of Dienophiles

The present invention can be practiced using a dienophile selected to provide desired structure and functionality in a Diels-Alder adduct. Particular embodiments of the present invention are directed to aryl alkyne dienophiles, such as propargyl substituted dienophiles. Aryl alkyne dienophiles typically have a formula

```
R1 - R5
/   \
R2  R6
```

With reference to this general formula, R1-R6 generally can be selected from alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties, including ketones, carboxylic acids and esters, cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, phosphorus-containing moieties, silicon, silicon-containing moieties, including particularly silyl ethers, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, or combinations thereof. More typically, R1 generally is a nitrogen-containing moiety, such as nitro or nitroso. R2 and R4-R6 can be any of various
functionalities, and typically independently are alcohols, substituted alcohols, aliphatic, substituted aliphatic, aryl, substituted aryl, arylalkyl, carbonyl-containing moieties (e.g., aldehydes, amides, carboxylic acids, esters, ketones, nitriles, thioesters), phosphorus-containing moieties (e.g., phosphine oxide, phosphines), halide, heteroaliphatic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties. R₃ most typically, but not necessarily, is halide, such as fluoride, chloride or bromide.

With reference to these working embodiments, note that the halide bond is not coupled to a particular atom on the aryl ring. This is to indicate that the halide can be at any such position. It also is possible that more than 1 halide atom, including two different halides, can be present on suitable dienophiles.

![Chemical Structures](image)

Embodiments of exemplary halide-substituted dienophiles are provided herein, such as the following chlorinated series of dienophiles that have been used in working embodiments.

![Chemical Structures](image)

A person of ordinary skill in the art will appreciate that suitable compounds can be made where the nitro group is some other nitrogen-containing group, such as a nitroso group.

Dienophiles based on propargyl alcohol have been used in working embodiments, including dienophiles having a formula
With reference to this general formula, \( R_1 \) and \( R_2 \) independently are aliphatic, typically lower alkyl (e.g. methyl, ethyl, propyl, butyl, pentyl), substituted aliphatic aryl (e.g. phenyl), substituted aryl (e.g. halophenyl), or hydrogen, the nitrogen-containing group typically is nitro or nitroso, and \( X \) is halide.

Alkynylnyl stannanes also are suitable dienophiles. A general formula for certain embodiments of alkynylnyl stannanes is provided below.

Particular examples of alkynylnyl stannanes include the exemplary compounds provided below, where the halide most typically is chlorine or bromine, and the nitrogen group most typically is nitro.

Alkynylnyl halides also are suitable dienophiles. A general formula for certain embodiments of alkynylnyl halides is provided below.
With reference to this general formula, \( R_1 \) and \( R_2 \) are selected from aliphatic, such as lower alkyl, halide, hydrogen, and nitrogen-bearing substituents, such as nitro. Exemplary alkynyl halide dienophiles are provided below.

Dienophiles having phosphorus-containing moieties or carbonyl-containing moieties also have been made. Phosphorus-containing compounds typically had the following formula where halide most typically is chloride or bromide.

Compounds having two or more halogen atoms also are useful dienophiles. "Phosphorus group" most typically refers to phosphine oxides. Working embodiments of dienophiles are exemplified by the following compounds.
With reference to this general formula, R and R' independently are aliphatic, typically lower alkyl, such as methyl, ethyl, propyl, butyl and pentyl, substituted aliphatic, aryl, such as phenyl; and substituted aryl. Parentheses around the bromine atom in this general formula mean that the position can be occupied by a halide generally, but most typically the halide was bromide or chloride.

Carbonyl-containing dienophiles are exemplified by compounds having a formula:

Where working embodiments had R selected from CO₂Me, CO₂Et, CO₂CH₂CCl₃, C(O)-r-Bu, C(O)Ph, C(O)-P-Cl-C₆H₄, C(O)NMe₂, C(O)NPh₂, C(O)-N-morpholinyl, CO₂-menthyl and

Non-halogenated alkynes also can be used to practice disclosed embodiments of the present invention. For example, certain working embodiments used the non-halogenated alkyne provided below.
IV. Biaryl Compounds

The method disclosed herein is particularly suitable for making biaryl compounds. Certain of the biaryl compounds that can be made by the disclosed embodiments are novel compounds, or can be converted into novel compounds by transforming the biaryl compounds initially synthesized by a Diels-Alder reaction.

A. Biaryl Compounds

Biaryl compounds generally can be made according to disclosed embodiments of the present invention. These biaryl compounds typically have a formula:

\[ \text{Formula} \]

and can be substituted with virtually any additional functionality. Solely by way of example and without limitation, \(R_i-R_i\) typically independently are alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties (such as aldehydes,
amides, carboxylic acids, esters, ketones and thioesters), cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties [e.g. nitrile (RCN), nitro (NO₂) and nitroso (RNO)] phosphorus-containing moieties [such as phosphines (R₃P, where R₃ generally, but not necessarily, is other than hydrogen, and the R₃ functional groups can be the same or different) and phosphine oxides (OPRᵢ, again where the R groups can be the same or different)], silicon, silicon-containing moieties, including particularly silyl ethers, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, or combinations thereof. Aliphatic substituents often are alkyl, and even more typically lower (i.e. 10 or fewer carbon atoms) alkyl groups. Halides typically, but not necessarily are chloride and bromide, and compounds having plural halogens also are within the scope of the present invention.

B. Unsymmetric tetra-ortho-Substituted Biaryl Compounds

Certain novel biaryl compounds that can be made according to disclosed embodiments of the present invention are unsymmetrical, tetra-ortho-substituted biaryl compounds. Such compounds generally can be represented by the same formula provided above, i.e.

![Diagram]

But, for tetra-ortho substituted biaryl compounds, R₃, R₄, R₈ and R₉ are different. For particular compounds, at least one substituent, typically R₃, is a nitrogen-containing moiety. And at least one OfRᵢ-R₂ and R₉-Rᵢ₀ often is, or are, carbon-bearing substituent, such as aliphatic, halide or hydrogen. If a halide is present, most typically at least R₉ is a halide. The remaining groups can be virtually any

- 30 -
functionality. By way of example, the remaining $R_pR_2$, $R_4-R_8$ and $R_{i0}$ groups typically are alcohols, boron, boron-containing moieties, carbonyl-containing groups (such as aldehydes, amides, ketones, carboxylic acids, esters, nitriles and thioesters) aliphatic (including lower alkyl, such as methyl and ethyl), substituted aliphatic, aryl (including benzyl), alkyl aryl, cyclic, halide, heteroaliphatic, heteroaryl, heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing groups, phosphorus-containing groups, silicon, silicon-containing moieties (including silyl ethers), sulfur, sulfur-containing moieties, tin, tin-containing moieties, or combinations thereof. Aliphatic substituents often are alkyl, and even more typically lower (i.e. 10 or fewer carbon atoms) alkyl groups. A particular embodiment, solely by way of example, of a tetra-$\alpha$-$\alpha$-substituted biaryl compound according to the present example, and the aryl compound from which the tetra-or $t$/$z$-substituted biaryl compound may be made, is provided below.

![Diagram](attachment:diagram.png)

Solely by way of example, $R_i$ often is aliphatic, such as lower alkyl, substituted aliphatic, such as alkoxy, or halogen, $R_2$ is aliphatic, such as alkyl or allyl, substituted aliphatic, such as alkoxy, aryl or aryl alkyl, such as benzyl, or silyl ether, and $R_3$ is aliphatic-$\alpha$, such as alkyl or aryl, substituted aliphatic, such as alkoxy, aryl or aryl alkyl, such as benzyl, hydrogen or silyl ether.

C. **Tetra-$\alpha$-$\alpha$-Substituted Biaryl Compounds from Chiral Dienes**

Chiral dienes also can be used to make biaryl compounds according to the present invention. This embodiment of the present invention is exemplified below in Scheme 1.
D. **Substituted Biaryl Compounds using Non-Halogenated Alkynes**

Working embodiments have used non-halogenated alkynes to produce phosphorus-containing compounds, as indicated below in Scheme 2.

With reference to Scheme 2, non-halogenated alkyne 2 is converted to phosphorus-containing derivative 4. Dienophile 4 is then reacted with diene 6 under conditions that promote a Diels-Alder reaction to produce biaryl compound 8. The nitro group of biaryl compound 8 is then reduced to form amine derivative 14. The dimethyl amine phosphine oxide derivative 12 is then formed, which can be converted to the corresponding phosphine by reaction with Ti(Oi-Pr)₄·PMHS at elevated temperature.

E. **Substituted Biaryl Compounds using Chiral Dienes and Non-Halogenated Alkynes**

Chiral dienes can be reacted with non-halogenated aryl alkynes to produce compounds within the present invention as well. This is illustrated below in Scheme 3.
With reference to Scheme 3, non-halogenated aryl alkyne dienophile 2 is reacted with chiral diene 4 or 6 to produce substituted biaryl compound 8. The nitro group of biaryl compound 8 is then reduced to form amine derivative 10. The dimethyl amine phosphine oxide derivative 12 is then formed, which can be converted to the corresponding phosphine by reaction with Ti(CwPr)$_4$, PMHS at elevated temperature.

**F. Biaryl Compounds using Carbonyl-Based Dienes**

Scheme 4 below illustrates using electron-deficient dienes, such as carbonyl-based dienes, for cycloadditions. With reference to Scheme 4, diene 11 was reacted with chloro alkyne 13. The diene 11 can be prepared in two steps from methyl 4-bromocrotonate. Alkyne 13 can be prepared in one step from the commercially available 2-chloro-6-nitrobenzaldehyde. Heating a mixture of the two reagents 11 and 13 at 140°C in xylenes for 6 hours resulted in the consumption of starting materials and the formation of two products as a 1.3:1 mixture (14:15) based on crude $^1$H NMR analysis. The compounds proved quite challenging to separate by...
standard chromatographic techniques on small scale; however, this mixture could be purified via recrystallization from diethyl ether/petroleum ether. On large scale (> 2 g), reasonable separation could be achieved via careful silica gel chromatography using a CH₂Cl₂/hexanes gradient. The structure of compound 15 was unambiguously established by X-ray crystallographic analysis. No other regioisomers of either biaryl 14 or bicycle 15 were isolated from the reaction. This selectivity speaks once again to the powerful directing ability of the ortho-nitrophenyl moiety.

Electron rich dienes such as 1-methoxy-1,3-cyclohexadiene (5) react cleanly with alkyne 13 to provide solely biaryl 16 in excellent yield (82%).

The reactivity of other alkynes with the diene 11 also has been explored. In the case of the analogous 2-bromo series (compound 18), a similar reactivity pattern was found to the chloro alkyne 13. Non-halogenated alkene 21 was also screened. Purification of the products 22 and 23 from this reaction has proven quite challenging. Fortunately, treatment of the mixture with Zn/AcOH affected reduction of the nitro moiety with in situ cyclization to form the known lactam 24.

The performance of the acetylenic ester 25 in the cycloaddition process with diene 11 also was explored; however, a complex mixture of products was observed.
V. Additional Transformations to or with Biaryl Compounds

Following synthesis of biaryl compounds according to disclosed embodiments of the present invention, such biaryl compounds can be used as starting materials for additional coupling reactions, functional group transformations, etc. A person of ordinary skill in the art will appreciate that the scope of such additional transformations is substantially unlimited. The following provides a partial list of general reactions that can be used to transform biaryl compounds.
A. Metal-Mediated Coupling Reactions

One of the primary reactions contemplated for biaryl compounds made according to the present invention is to couple an additional aliphatic, such as alkyl, or aryl compound, such as phenyl or substituted phenyl, to the biaryl compound as originally synthesized. While this coupling reaction may be accomplished in a number of ways, a primary approach is to use metal-mediated coupling reactions, and even more typically to use palladium-mediated coupling. The palladium-mediated reaction also can be done using a number of named reactions, including Stille, Negishi, Suzuki, Sonogashira, or Heck couplings.

In general, the Stille reaction couples an organo-tin compound with an sp\(^3\)-hybridized organic halide catalyzed by palladium.

\[
\text{R-Sn}(R)\_3 + \text{R}^1-\text{X} \rightarrow \text{R-R'} + \text{X-Sn}(R)\_3
\]

X typically is a halide, but also can be a pseudo-halide, such as a triflate, e.g. RO-CF\(_3\)SO\(_3\)\(^-\) or ROTf. The Stille reaction was discovered in 1977 by John K. Stille and coworkers and usually is performed under inert atmosphere using dehydrated and degassed solvent. This is because atmospheric oxygen oxidizes the palladium catalyst and promotes homo coupling of organic stannyl compounds. The organic tin compound typically is a trimethylstannyl or tributylstannyl compound.

The Negishi coupling is a cross coupling reaction using an organo zinc compound, an organic halide, and a metal catalyst, such as nickel or palladium, most typically palladium, that creates a new carbon-carbon covalent bond.

\[
\text{R-X} + \text{R}^1-\text{Zn}-\text{X} \rightarrow \text{R-R'}
\]

X is a halide, most typically chloride, bromide, or iodide, although acetoxy and triflates also can be used.

The Suzuki reaction (many publications refer to this reaction as the Miyaura-Suzuki reaction) is a reaction between an aryl, vinyl or alkyl boronic acid (or boroxine or K\(^+\)RBF\(_3\)\(^-\) salt) with an aryl, vinyl or alkyl halide (or enol triflate or enol phosphonate) catalyzed by a palladium (0) complex.

\[
\text{R-BY}_2 + \text{R}^1-\text{X} \rightarrow \text{R-R'}
\]
The Suzuki reaction also works with pseudohalides, such as triflates, instead of halides, and also with boron-esters instead of boronic acids. The palladium catalyst is usually 4-coordinate, and usually involves phosphine supporting groups.


\[
\begin{align*}
\text{H} & \equiv \text{R} & \text{R-X} & \rightarrow & \text{R} & \equiv \text{R}' \\
\text{Pd, Cu, base} & & & & & \\
\end{align*}
\]

With reference to this general scheme, X typically is Cl, Br, I, -OTf, and R typically is aryl or aliphatic.

The Heck reaction involves reacting an unsaturated halide or triflate with an alkene in the presence of a strong base and a palladium catalyst to form a substituted alkene. See, for example, Littke and Fu, "A versatile Catalyst for Heck Reaction of Aryl Chlorides and Aryl Bromides under Mild Conditions," *J. Am. Chem. Soc*, 123, pp. 6989-700 (2001). The Heck reaction is indicated by the general scheme presented below.

\[
\begin{align*}
\text{R-X} & & \text{R'} & \rightarrow & \text{R} & \equiv \text{R}' \\
\text{Pd, Base} & & & & & \\
\end{align*}
\]

The reaction typically is performed in the presence of an organopalladium catalyst. Suitable catalysts include *tetra*-kis(triphenylphosphine)palladium(0), palladium halide, or palladium (II) acetate. Suitable bases include, but are not limited to, alkyl amines, potassium carbonate or sodium acetate. The halide typically is a halide or triflate, most typically an aryl, benzyl or vinyl compound. The alkene typically includes at least one proton, and may be electron deficient, such as with acrylate esters or acrylonitriles.
B. Functional Group Transformations

1. Amines/Substituted Amines

Many Diels-Alder adducts that can be made according to disclosed embodiments of the present invention include functional groups that can be transformed into a different functional group. For example, many disclosed compounds include a nitrogen-containing group, such as a nitro or nitroso group, that can be converted into an amine, e.g., transforming an NO₂ group into an NH₂ group. One method for forming an amine is a reduction reaction using Zn/AcOH. Substituted amines, i.e. where one or more of the hydrogen atoms is substituted with another atom, such as an aliphatic group, and typically an alkyl group, also are desirable compounds that can be made by reductive animation. Reductive amination can be accomplished, for example, using a sodium cyanoborohydride (NaBH₃CN) reducing agent.

2. Phosphines

Many of the compounds that can be made by disclosed embodiments of the present invention are phosphine oxides. Phosphines also are desirable compounds. Working embodiments have produced phosphines from phosphine oxides using Ti(Oi-Pr)₄/PMHS.

3. Carbyonls/Carbonylation

Many compounds that can be made by disclosed embodiments of the present invention include hydroxyl groups, or protected hydroxyl groups. Hydroxyl groups can be converted into a variety of different functional groups, such as carbonyls, by oxidation. Many oxidation reagents are known to persons of ordinary skill in the art. Different oxidation reagents can be selected for a particular purpose, such as to form an aldehyde, a ketone, or a carboxylic acid, or any equivalent or derivative thereof, such as an ester.

Carbonylation reactions can be used to convert halides, particularly aryl halides, into corresponding carbonyl-containing compounds, such as aryl esters (Ar-CO₂Ar).
4. **Carbonylative Stille Coupling**

The Stille coupling reaction can be done in combination with a carbonylation reaction. This is useful for producing compounds such as benzophenones \([\text{Ar-C(O)-Ar}]\) and aryl vinyl ketones \([\text{Ar-C(O)-CR=CR}i]\).

5. **Transmetallation of Aryl Halides**

Aryl halides can be converted to aryl metal compounds. Lithiation can be accomplished, for example, using an alkyl lithium, such as butyl lithium, in an ether solvent, such as tetrahydrofuran or diethyl ether. The reaction generally is conducted at reduced temperatures, such as at or about \(-78^\circ\text{C}\). Other transmetallation reactions include exchanging halogens for magnesium and zinc. One example of a transmetallation reaction is Grignard reagent formation, such as by using Mg, Et\(_2\)O or THF (additive such as BrCH\(_2\)CH\(_2\)Br, ICH\(_2\)CH\(_2\)I, I\(_2\), or HgCl\(_2\) can be added to accelerate the Grignard reagent formation). Other conditions include: iPrMgCl, LiCl, THF or i-Pr\(_2\)Mg•LiCl, THF/dioxane. For zinc metallation, suitable conditions include: Zn, THF or Et\(_2\)O, or initial formation of an organolithium (n-BuLi or t-BuLi, THF or Et\(_2\)O) then addition of ZnBr\(_2\) or ZnCl\(_2\) to transmetallate to zinc.

C. **Aromatic Substitution**

The biaryl compounds provide aromatic rings that can be substituted with other groups, such as by electrophilic or nucleophilic aromatic substitution. Nucleophilic aromatic substitution is a substitution reaction in organic chemistry in which a nucleophile displaces a good leaving group, such as a halide on an aromatic ring. There are at least 5 nucleophilic substitution mechanisms encountered with aromatic systems, three of the most important of which are illustrated below:
\[ S_{\text{NAT}} \text{(addition-elimination) mechanism} \]

\[ \text{SNl mechanism, typically with diazonium salts} \]

\[ \text{Benzyne mechanism} \]

Electron withdrawing groups, such as nitro functional groups positioned ortho or para to the halide leaving group, activate the ring towards nucleophilic attack.

Nucleophilic aromatic substitution is not limited to arenes. In fact, the reaction takes place more readily with heteroarenes. For example, pyridines are especially reactive when substituted in the ortho or para position because then the negative charge is effectively delocalized at the nitrogen position.
D. Aromatization

The initially formed Diels-Alder adduct can be aromatic or non-aromatic. For non-aromatic adducts, it may be desirable to form the aromatic analog of the initial Diels-Alder adduct. Any suitable method can be used for aromatizing the initially formed Diels-Alder adduct. Suitable bases include 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), tetra-n-butylammonium fluoride (TBAF), trialkyl amines, such as triethyl amine and diisopropylethylamine (Hunig's base) and potassium carbonate (K$_2$CO$_3$). Aromatization also may be accomplished using an acid, such as ammonium chloride (NH$_4$Cl), pyridinium-p-toluene sulfonate (PPTS), p-toluene sulfonic acid (p-TsOH), and trimethylamine hydrochloride (Me$_3$NHCl). However, after screening a range of acids and bases, DABCO appeared to provide optimum results for aromatization of the compounds tested to date.

E. Deprotection

Protecting and deprotecting functional groups are standard synthetic steps used in organic synthesis, and are applicable to disclosed embodiments of the present invention. For example, many of the initial Diels-Alder reagents are silyl ethers that can be converted into alcohols by treating the silyl ether with a fluoride, such as tetrabutylammonium fluoride (TBAF). TBAF also is the preferred reagent for desilylation, elimination and aromatization with the TBS-variant of Danishefsky's diene.

Hydroxyl groups also can be protected using other protecting groups, such as benzyl ethers. Benzyl ethers can be removed using hydrogen and a catalyst.

Other protecting groups, methods for their synthesis, and methods for their removal are disclosed in Green et al.'s Protective Groups in Organic Synthesis, which is incorporated herein by reference.

F. Cyclization

The biaryl compounds, having other functional groups attached thereto, also can be used to form heterocycles from the initially formed biaryl compound. This class of transformations is exemplified herein by the Cadogan cyclization, which can be used
to form carbazoles, such as Siamenol. The Cadogan cyclization is illustrated below.

The illustrated carbazole 1 is the major compound formed. The solvent used for the reaction typically was a trialkyl or triphenyl phosphine (or an alkyl phosphite, such as triethyl phosphite). The reaction requires elevated temperatures, with working methods using temperatures ranging from about 100 °C to about 180 °C.

The Cadogan cyclization also can be performed using an azide variant, as illustrated below. This cyclization occurs at relatively low temperatures, and is a currently preferred method for making the illustrated carbazoles.

VI. Working Embodiment Syntheses

A. Alkyne Dienophiles

Alkynes provide one example of dienophiles useful for practicing disclosed embodiments of the present invention. With reference to Scheme 5, certain alkynes can be made as follows. Inexpensive 6-chloro-2-nitro-toluene (compound 1, Scheme 5) and 4-chloro-2-nitro-toluene (2) can be converted to the corresponding benzaldehyde derivatives 4 and 5 using an oxidative protocol developed by Pfizer. Aldehyde 4 also is commercially available from the Sigma-Aldrich Corporation.
Subsequent alkyne formation using the Ohira-Bestmann reagent 6 yielded alkynes 7 and 8 in good yield. Alkynes also can be formed using other protocols. For example, the Corey-Fuchs protocol (Step 1: PPh3, CBr4; Step 2: LDA, THF) can be used to generate the alkyne. BuLi, TMSCHN also have been used to generate the alkyne from an aldehyde in one step.

For 3-chloro-2-nitro and 5-chloro-2-nitro substitution patterns, the preferred starting materials were the commercially available acids 9 and 10. A two-step protocol was used to make aldehydes 11 and 12. Alkynes 13 and 14 were made using diazophosphonate 6. Aldehyde 12 also is commercially available, but the purity of this compound is less than optimal.

Scheme 5
Exemplary Synthesis of Acetylenic Dienophiles

The synthesis of useful exemplary propargylic 3° alcohols, such as those of Table 1, from such alkynes is illustrated in Scheme 6. Starting from the known
alkyne 1 (available in one step from the commercially available 6-chloro-2-nitrobenzaldehyde), deprotonation using LDA, THF, -78 °C, followed by the addition of the electrophile, -78°C to room temperature, generated the propargylic alcohols in moderate to good yield (52-78%). Both acyclic and cyclic ketones with either alkyl or aromatic substituents were tolerated in this transformation. Attempts to form the 2° alcohol derived from trapping the lithiated acetylene with benzaldehyde led to extensive decomposition - possibly due to Oppenhauer-type hydride transfer by the resultant propargylic 2° alkoxide.

Table 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Electrophile</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Acetone</td>
<td>71% (R = Me)</td>
</tr>
<tr>
<td>B</td>
<td>3-Pentanone</td>
<td>63% (R = Et)</td>
</tr>
<tr>
<td>C</td>
<td>Cyclobutanone</td>
<td>60% (R = (CH₃)₃)</td>
</tr>
<tr>
<td>D</td>
<td>Cyclopentanone</td>
<td>52% (R = CH₃)₆</td>
</tr>
<tr>
<td>E</td>
<td>Cyclohexanone</td>
<td>68% (R = CH₂)₆</td>
</tr>
<tr>
<td>F</td>
<td>Benzophenone</td>
<td>77% (R = Ph)</td>
</tr>
<tr>
<td>G</td>
<td>4,4'-Dimethylbenzophenone</td>
<td>78% (R = p-Me-C₆H₄)</td>
</tr>
<tr>
<td>H</td>
<td>4,4'-Dichlorobenzophenone</td>
<td>69% (R = p-Cl-C₆H₄)</td>
</tr>
<tr>
<td>I</td>
<td>9-Fluorenone</td>
<td>77%</td>
</tr>
</tbody>
</table>

Another embodiment of a method for making alkyne dienophiles is illustrated below in Scheme 7.
With reference to Scheme 7, toluene 2 is commercially available. Compound 2 is heated in the presence of a dimethylacetal formed from DMF to form an iminium ion and evolve methoxide. The evolved methoxide deprotonates...
the methyl group of compound 2. This deprotonated compound then reacts with the iminium ion to form a carbon-carbon bond. Methanol is then eliminated to form an enamine. The enamine then reacts with sodium periodate to form aldehyde 4.

Aldehyde 6 is converted to geminal dichloride 8 by a Wittig reaction. A Corey-Fuchs reaction involves reacting triphenyl phosphine with carbon tetrachloride to form an ylide in situ. The ylide reacts with aldehyde 6 to form compound 8. Treatment of base to ge/n-dichloride 8 eliminates chloride to form chloroacetylene 10.

Alternatively, compound 12 can be used as a starting material. Deprotonation using LDA, followed by treatment with an electrophile MeI afforded compounds 14. Electrophiles other than methyl iodide can be used, as indicated by the synthesis of compounds 16.

The formation of biaryl compound 18 in Scheme 7 provides another alkylation example. The addition of DMPU facilitates the alkylation reaction during the formation of compound 16.

Yet another alternative route to making suitable alkyne dienophiles is illustrated below in Scheme 8.

**Scheme 8**

With reference to Scheme 8, the conversion of toluene 2 to aldehyde 4 involves forming the dimethylacetal of DMF, which then thermally ionizes to make an iminium ion and releases a methoxy group. The released methoxy deprotonates the methyl group ortho to the nitro group to make the corresponding anion, which reacts with the iminium ion and eliminates methanol to make an enamine. Upon aqueous
workup, the enamine is hydrolyzed to form aldehyde 4. The aldehyde is then converted to compounds with suitable leaving groups, such as -OSO₂R or -OP(O)(OR)₂, to form a compounds 6 or 8. Treating enol triflates 6 or 8 with a base eliminates the leaving group to form acetylene 10.

**B. Diels-Alder Cycloaddition Reactions**

With reference to Scheme 9, alkynes 7, 8 and 13 performed well in the Diels-Alder cycloaddition reaction with dienes 15, 19 and 23. In each case, the resultant phenol was protected as its benzyl ether and the yields were reported over two steps. Using Brassard's diene, TBAF initially was used for aromatizing the initially formed Diels-Alder adduct. Under these conditions, low yields (30-50%) were routinely observed - despite the clean formation of the Diels-Alder adduct. After screening a range of acids and bases, DABCO gave the optimum results for aromatization - providing significant yield improvements over the original protocol. One possible explanation is deprotonation of one of the methylene protons in the lower ring, inducing selective elimination of the methoxy moiety. An alternate mechanism would involve the attack of the silyl ether by methoxide and subsequent collapse to the biaryls 16-18. The methoxide is likely formed from thermal decomposition of the excess Brassard diene during the Diels-Alder reaction.

In contrast, TBAF is the preferred reagent for desilylation, elimination and aromatization with the TBS-variant of Danishefsky's diene 19. Cyclohexadienes possessing two oxygen substituents (e.g. diene 23) also were effective for synthesis of biaryl adducts - proceeding through an initial Diels-Alder cycloaddition to generate the [2.2.2] bicyclic adduct followed by ethylene extrusion to reveal the aromatic product.
Diels-Alder Reactions with Oxygenated Dienes.

Exemplary 3-chloro series Diels-Alder reactions are illustrated in Scheme 10. Reaction of the Brassard diene 15 with the (3-chloro-2-nitroaryl)-alkyne 14 did cleanly yield a small amount of the expected aromatized product 30 after benzylation. In addition to this product, an interesting enol ether product 29 was also observed. One possible mechanism would involve an initial formation of [2+2] cycloaddition adduct 27 followed by ring opening.
In order to access the desired substitution pattern in compound 30, previously unknown diene 31 was an effective substitute for Brassard's diene. Diene 31 could be readily prepared from 1,3-cyclohexanedione in two steps. The Diels-Alder reaction was also performed with diene 19 to give the halogenated biaryl 32 in a reasonable yield. Finally, use of the diene 23 gave the corresponding biaryl 33 after benzylation.

Scheme 10

Diels-Alder Reactions of the meta-Chloro Arenes with Oxygenated Dienes
Treating propargyl alcohols with the commercially available 1-methoxy-1,3-cyclohexadiene in xylenes at 145 °C cleanly generated exemplary tetra- or tri-substituted biaryls. The yields for this transformation were good-to-excellent (55-80%). The significant steric requirement for the construction of the tel\(\alpha\)-ortho-substituted biaryl with a 3° alcohol moiety is nicely addressed through this DAB strategy. The regiochemistry from the Diels-Alder process was confirmed for each product by HMBC analysis. Without limiting the present invention to a theory of operation, these reactions are believed to proceed through a bicyclic intermediate followed by the extrusion of ethylene to generate the biaryl. If the reaction is conducted initially at a lower temperature (e.g. 100 °C, 25 hours), the intermediate bicycle can be observed. One possible explanation for the facile nature of these transformations could be an internal hydrogen-bond activation between the propargylic alcohol and either the nitro or chloro moieties. Support for this working hypothesis can be found in the inability of the TMS silylated alcohol (TMSCl, imidazole, cat. DMAP, CH\(_2\)Cl\(_2\), 65%, 88% borm) version of 2f to undergo the same cycloaddition (130-150 °C over 43 hours).

**Table 2**

Diels-Alder Construction of Biaryls
A range of cyclic dienes did successfully undergo the Diels-Alder reaction and gave rise to highly functionalized biaryls. With reference to Scheme 11, an ortho-amino functionality was incorporated via the previously unknown diene 6 (synthesized from 1,3-cyclohexandione in 3 steps) in reasonable yield. Di-oxygenated dienes 8 and 10 also cleanly yielded their requisite biaryl products 9 and 11 in excellent yields (95% and 72% respectively).
Diene Scope for Working Embodiments in Diels-Alder Construction of Biaryls

1. Enantiomerically Enriched Biaryls

One important attribute of highly substituted biaryls is the restricted rotation around the sigma aryl-aryl linkage. Consequently, enantiomerically enriched biaryls have proven useful as chiral ligands in a range of enantioselective pathways.

Certain disclosed embodiments of the present invention provide an efficient protocol for obtaining commercially important, enantiomerically enriched biaryls (Scheme 12). For example, after reduction of biaryl 2g with zinc in acetic acid (94%), the resultant aniline moiety was treated with commercially available (-)-menthyl chloroformate 13. After standard column chromatography, the diastereomeric carbamates were dissolved in hexanes. A single diastereomer 14-(aR) was crystallized from the mother liquor in excellent yield and diastereoselectivity (45%, > 20:1 dr). Confirmation of the absolute stereochemistry was obtained by X-ray crystallographic analysis of biaryl 14-(aR) (FIG. 1). Concentration of the mother liquor and a second recrystallization from hexanes revealed that the remaining material consisted of the alternate diastereomer 14(aS) - again in excellent yield and diastereoselectivity (44%, > 20:1 dr).
Resolution of Atropic Isomers via Derivatization and Crystallization

Cleavage of the carbamate was possible under basic conditions (Scheme 13).

Treating diastereomer 14-(a/f) with KOH in hot α-butanol/triethyleneglycol provided a 79% yield of the amino alcohol 15-(a/f). Confirmation that no racemization had occurred under the reaction conditions was achieved by reacylation of 15-(a/f) with the (-)-menthyl chloroformate (13) to provide 14-(a/f) as a single diastereomer (86%). Attempted cleavage of the diastereomeric carbamates 14-(a/S) gave the desired product 15-(a/s) in only modest yield (32%). A second product 16 was competitively produced under the reaction conditions (57%). Extended reaction time led to exclusive formation of this dibenzo[b,d]pyran 16 in 92% yield. This product 16 is presumably formed via nucleophilic aromatic substitution by the 3º alcohol on the aryl chloride. This compound is formed as the racemate. The added strain induced by the dibenzopyran ring system presumably lowered the activation energy for racemization of the atropic diastereomers. Fortunately, this side-product can be suppressed by protecting the 3º alcohol as its THP ether followed by saponification and acidic workup [56% yield from 14-(a/S)].

Again, conversion back to its menthyl carbamate 14-(a/S) confirmed no racemization had occurred under the reaction process (83%, > 20: 1 dr).
Thus, disclosed embodiments of the present invention allow efficient synthesis of tri- and tetra-or t/z-o-substituted biaryl compounds using propargyl 3° alcohols as dienophiles. A range of substituents are tolerated for the 3° alcohols. Cyclic dienes facilitate effective cycloaddition. Facile resolution of the Diels-Alder adduct 12 provided a rapid synthesis of enantiomerically enriched biaryls 14 and 15.

Another embodiment of this approach is illustrated below in Scheme 14.

Scheme 14 again illustrates that axially chiral biaryl compounds can be derivatized using chiral ligands to form diastereomeric compounds that then can be separated using separation techniques known in the art, such as chromatography and/or
crystallization. After separation, the chiral ligand can be removed to provide single enantiomers of axially chiral biaryl compounds.

2. Axially Chiral Amino Acids

The ability to produce axially chiral biaryl compound also allows for the production of axially chiral amino acid peptide mimetics. One working embodiment of this approach is illustrated below in Scheme 15.

![Scheme 15](image-url)

With reference to Scheme 15, ester biaryl compound 7.22 can be hydrolyzed to the corresponding acid 8.6. The acid is then acylated with (S)-Bn-oxazolidinone to form compounds 8.7-(aR) and 8.7-(aS). This reaction involves forming a mixed
anhydride using pivalic acid chloride, and then (S)-Bn-oxazolidinone reacts to form 8.7-(aR) and 8.7-(aS). These diastereomers can be resolved, such as chromatographically. A person of ordinary skill in the art will appreciate that this general approach to forming diastereomers can be applied using compounds other than (S)-Bn-oxazolidinone, such that various chiral amides and esters can be used in the same manner to resolve enantiomers. Once resolved, the enantiomers can be reacted in a palladium coupling reaction to replace the chlorine, or other halogen, with a desired R group. This is exemplified in Scheme 15 by replacing the chlorine of compound 8.7-(aR) with a methyl group to form compound 8.8-(aR). Various coupling partners can be used to incorporate the different groups available in the 20 amino acids most commonly found in peptides, as well as other amino acids that are not so commonly used. These R groups can be incorporated via Suzuki couplings, as well as Stille, Negishi, Heck and other types of metal-mediated cross couplings. Compound 8.8-(aR) is then hydrolyzed to form the corresponding axially chiral acid 8.9-(aR). Compound 8.9 has a carboxylic acid side chain, which can be coupled with a nucleophile, such as an amine group of an amino acid. This reaction is exemplified by reacting compound 8.9 with the methyl ester derivative of phenyl alanine to form compound 8.10. Hence, such compounds are useful for forming peptide mimetics. The nitro group of compound 8.10 also can be reduced to form an amine, providing another reactive functional group for further derivatizing such compounds, such as to form an amide bond by reaction with a carboxylic acid, such as an amino acid.

Compound 8.8-(aR) includes a methyl group as a side chain, as would appear for an alanine-type amino acid. However, any side chain found on an amino acid, particularly naturally occurring amino acids, can be coupled to the biaryl compound to form useful peptide mimetics. Such side chain R groups for amino acids include hydrogen, lower alkyl groups, such as methyl, isopropyl, isobutyl, sec-butyl, aryl groups, such as benzyl, indolomethylene, substituted aryl compounds, such as 4-hydroxybenzyl, imidizolomethylene, substituted alkyl groups, such as 2-hydroxyethyl, hydroxymethyl, sulfides, such as ethyl methyl sulfide, mercaptomethyl, amines, such as 4-amino-butyl, and primary and secondary amines, such as with the proline side chain, 3-propyl-guanidino, carboxylated substituents,
such as carboxymethyl, carboxyethyl, and amides, such as 1-ethyl-amido and 1-methyl-amido.

Scheme 15 also includes an alternative route to forming compounds 8.7. Silyl ether diene 12 undergoes a (2+2) cycloaddition reaction with acetylene 14 to form diastereomeric phenols 16 and 18, which should be separable, such as by chromatography. If not, phenols 16 and 18 can be converted into compounds 20 and 22, which are known to be separable according to Scheme 15.

C. Synthesis of Phosphorus-Containing Dienophiles

With reference to Scheme 16, an exemplary dienophile subunit can be constructed quickly from a commercially available toluene derivative 1. Treating 1 with \( \mathcal{N}_2\mathcal{N}\)-dimethylformamide dimethyl acetal at 135 °C followed by addition to a cooled (0 °C) solution of NaIO\(_4\) in aqueous DMF yielded the aldehyde 2. This approach is based on a protocol developed by researchers at Pfizer; however, use of their exact conditions led to formation of a significant amount of by-products. Cooling the enamine solution to 0 °C and rapid addition to a vigorously stirred solution of NaIO\(_4\) at 0 °C completely suppressed the formation of these impurities. Reacting aldehyde 2 with the Ohira-Bestmann reagent 3 provided the desired alkyne 4. Subsequent lithiation with LDA (1 equivalent) followed by the addition of the requisite electrophiles (0.8 equiv) generated the dienophiles 5-7 in high yields (>80%).

![Scheme 16](image_url)

**Scheme 16**

**Synthesis of Exemplary Phosphorus-Containing Dienophiles. Conditions: a)** \((\text{MeO})_2\text{CH(NMe}_2\text{)}\), DMF, 135°C then NaIO\(_4\), DMF, H\(_2\)O, 0°C, 67%; **b)** 3, K\(_2\)CO\(_3\), MeOH, 85%; **c)** LDA, ClP(O)R\(_2\) (0.8 equiv.).
D. Diels-Alder Reactions Using Phosphorus-Containing Dienophiles

With reference to Scheme 17, Diels-Alder cycloaddition of the dienophiles 5-7 with the Brassard diene 8 followed by in situ aromatization using Et$_3$N yielded the target tetra-ortfzo-substituted biaryls. TBAF treatment initially was used to induce silyl deprotection and aromatization; however, the yields were inconsistent and lower than with the Et$_3$N workup. This approach provides access to aryl- and alkyl-substituted phosphine oxides as well as phosphonates. Due to the highly crystalline nature of the tetra-ortfzo-substituted phenolic biaryls, protection of the phenol as its benzyl ether improved solubility for subsequent transformations. X-ray crystallographic analysis of biaryl 14 shows the perpendicular orientation of the biaryl linkage.

Scheme 17

Synthesis of Biaryls via Diels-Alder Cycloaddition. **Conditions:** a) PhMe, 80°C, 16 h then Et$_3$N, O/C; b) BnBr, NaH, DMF, THF, O/C - r.t, yields reported over 2 steps.

Diels-Alder cycloadditions with the acetylenic phosphonates are not limited to the Brassard diene (Scheme 18). Treating dienophiles 5-7 with the commercially available TBS Danishefsky’s diene 15 followed by in situ desilylation and aromatization yielded the tri-substituted biaryls 16-18. As demonstrated previously, benzylation of the resultant phenol was performed to improve solubility for subsequent transformations and yields were reported over the two steps (61-69%).

Oxygenated cyclohexadienes are active dienes for this process. The commercially available 1-methoxy derivative 22 gave the corresponding tetra-substituted biaryls 23-25 in good yield (66-71%). Finally, using known 1,3-
dialkoxy substrate 26 efficiently provided the corresponding biaryls 30-32 in 67-88% yield after benzylation.

Scheme 18

Exploration of Diene Scope in Diels-Alder Cycloaddition. **Conditions**: a) PhMe, 80°C, 16 h then TBAF, 0°C; b) BnBr, NaH, DMF, THF, O°C - r.t., yields reported over 2 steps; c) neat, 155°C, 24 h; d) neat, 140°C, 17 h.

Metal-mediated couplings of the halide-containing biaryls could be accomplished in good yield (Scheme 19). As the **pen/a**-substituted biaryls 12-14 possessed the highest degree of orthogonal functionalization, this series was used to explore the coupling process. After screening several of the commercially available catalyst systems developed for sterically challenging palladium couplings (including Buchwald’s ligands, P(C₆H₅)i₃/Pd₂dba₃, Pd(dppf)Cl₂ and Pd(OAc)₂/dppp), Fu’s Pd(P-η-Bu₃)₂ catalyst proved the most effective in generating the coupled adducts 33-35. Boroxine-based Suzuki couplings with a range of palladium-based catalysts
(as listed above) are also likely to be effective in this transformation. For both Suzuki and Stille couplings, high catalyst loading (20 mol%) and excess boronic acid or stannane (3 equivalents) were used to drive the reaction to completion. In contrast, the Negishi-style organozinc couplings proceeded in good yield with more reasonable catalyst loading (10 mol%) and lower amounts of the organozinc species (1.5 equivalents). Nickel-catalyzed couplings are not effective on substrates such as 12-14 due to the NO₂ functionality.

![Scheme 19](image)

Negishi Coupling of Biaryls. **Conditions:** a) (/-Bu₃P)₂Pd (10 mol%), PhZnCl (1.5 equiv.), NMP / THF, 80°C, 16 h.

Given the efficiency of the Negishi couplings with tetra-ortho-/meta-substituted biaryls 12-14 and phenylzinc chloride, a range of organozinc species was explored to gauge the potential utility for metal-mediated couplings (Scheme 20). As shown in Table 3, these palladium-couplings proved successful with a variety of substituents on the organozinc moiety. Both electron donating and electron withdrawing groups are tolerated. Surprisingly, the more sterically hindered examples performed better in the coupling process. And the pentafluorophenylzinc species cleanly coupled with bromide 14 to yield the pentafluorophenyl product 36f (Entry f).

![Scheme 20](image)

Selected Examples of Negishi Couplings with Biaryl 14. **Conditions:** a) (/-Bu₃P)₂Pd (10 mol%), RZnCl (1.5 equiv.), NMP / THF, 80°C, 16 h.
Table 3
Selected Examples of Negishi Couplings with Biaryl 14

<table>
<thead>
<tr>
<th>Entry</th>
<th>RZnCl[a]</th>
<th>% Yield of 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4-methoxyphenylzinc chloride</td>
<td>59%</td>
</tr>
<tr>
<td>B</td>
<td>3-methoxyphenylzinc chloride</td>
<td>58%</td>
</tr>
<tr>
<td>C</td>
<td>2-methoxyphenylzinc chloride</td>
<td>0%</td>
</tr>
<tr>
<td>D</td>
<td>2-methylphenylzinc chloride</td>
<td>61%</td>
</tr>
<tr>
<td>E</td>
<td>2,6-dimethylphenylzinc chloride[b]</td>
<td>66%</td>
</tr>
<tr>
<td>F</td>
<td>pentafluorophenylzinc chloride</td>
<td>57%</td>
</tr>
</tbody>
</table>

[a] Organozinc species was formed by addition of the in situ generated organomagnesium species to a 1 M THF solution of anhydrous zinc chloride. [b] Extended reaction time (48 h) was employed for this coupling.

The reduction of selected biaryls was also studied (Scheme 21). The nitro arene 36e can be cleanly converted to the corresponding amine 37 via reduction with Zn/AcOH. After screening a broad range of conditions for converting the phosphine oxide 37 into its corresponding phosphine 38, this process could be accomplished using Ti(Oi-Pr)₄/PMHS in reasonable yield. Reductive amination generated the dimethylamino phosphine 39. Attempted removal of the benzyl moiety using hydrogenation conditions (e.g. Pd/C or PtO₂, H₂) gave problematic results. Fortunately, benzyl ether 37 could be cleanly removed accomplished using BCl₃.
Reduction of Selected Biaryls. **Conditions:**

a) Zn, HOAc, 5 h, 85%;
b) Ti(OZ-Pr)$_4$, PMHS, THF, 80°C, 48 h, 61%;
c) NaBH$_3$CN, paraformaldehyde, MeCN, AcOH, 80%;
d) BCl$_3$, CH$_2$Cl$_2$, 0°C, 3 h, 70%. PMHS = poly(methylhydroxsiloxane).

In order to illustrate a particular utility for the synthesized materials as reaction catalysts, palladium-mediated couplings using amino phosphine 39 as a ligand (Scheme 22) were investigated. The structure of this catalyst is based on the pioneering work of Buchwald and co-workers. Preliminary screening of 39 indicates that a highly active catalyst is generated for Suzuki couplings, as demonstrated by the synthesis of the sterically challenging tri-or tetra-substituted biaryl 43. A control experiment (in the absence of phosphine) with boronic acid 41 and bromide 42 [5 mol% Pd(OAc)$_2$, K$_3$PO$_4$, PhMe, 100°C, 20 h] gave only a minor amount (18%) of the desired coupled material 43. Using PPh$_3$ as the ligand also gave inferior results.
Utility of Synthesized Biaryl in Suzuki Coupling. **Conditions:** a) \( \text{Pd(OAc)}_2 \) (5 mol%), \( \text{K}_3\text{PO}_4 \), PhMe, 100°C, \( 20 \) h.

**E. Phosphorus-Containing Biaryl Chloro Series**

Certain disclosed embodiments used started from the alkyne 1, Scheme 23, available in one step from the commercially available 2-chloro-6-nitro-benzaldehyde using the Ohira-Bestmann reagent (\( \text{K}_2\text{CO}_3 \), MeOH, 96%). Lithium diisopropylamide (LDA) followed by addition of 0.8 equiv. of the requisite phosphorus electrophile \([\text{Ph}_2\text{P(O)Cl}} \text{ or (EtO)}_2\text{P(O)Cl}\] gave excellent yields of the di-substituted acetylenes 2a and 2b. Alternate bases (\( \text{«-BuLi, NaH, KHMDS, LiHMDS, TBAF, /-PrMgCl} \)) led to only trace amounts of the desired product. It is not certain at this time why LDA is uniquely capable in the deprotonation of these terminal alkynes.

Brassard diene 3 was well-suited for this transformation, and the Diels-Alder process proceeded quite cleanly via the intermediate 4. This intermediate was not isolated (as it proved quite unstable) and \emph{in situ} cleavage of the silyl ether 4 to induce aromatization was accomplished with TBAF to yield the biaryls 5a and 5b in good yield (60-84%). Conclusive structural assignment of biaryl 5b was obtained via X-ray crystallographic analysis.

**Scheme 23**

Synthesis of First-Generation Phosphorus-Containing Biaryls
F. Palladium-Mediated Couplings of Aryl Halides

Palladium-coupling of certain exemplary aryl chlorides is illustrated in Scheme 24. Phenolic biaryls 5a and 5b were insoluble in most organic solvents; therefore, the phenolic moiety was protected as its benzyl ether 6, in order to improve solubility. Despite considerable efforts with a wide range of catalyst systems [e.g. Fu's catalyst (/-Bu₃P)₂Pd, Pd₂dba/(c-C₆H₄I)₃P, Pd₂dba/P(ø-tol)₃, Buchwald ligands / Pd(OAc)₂], no C-Cl insertion on biaryl 6 was achieved. Suzuki, Stille and Negishi couplings have been done previously using Fu's catalyst. See, for example, Littke, A. F.; Dai, C.; Fu, G. C. "Versatile Catalysts for the Suzuki Cross-Coupling of Arylboronic Acids with Aryl and Vinyl Halides and Triflates under Mild Conditions." *J. Am. Chem. Soc.* 2000, 122(17), 4020-4028.; Littke, A. F.; Schwarz, L.; Fu, G. C. "Pd/P(t-Bu)₃: A Mild and General Catalyst for Stille Reactions of Aryl Chlorides and Aryl Bromides," *J Am. Chem. Soc.* 2002, 124(22), 6343-6348; Dai, C., Fu, G. C. "The First General Method for Palladium-Catalyzed Negishi Cross-Coupling of Aryl and Vinyl Chlorides: Use of Commercially Available Pd(P(t-Bu))₂ as a Catalyst," *J Am. Chem. Soc.* 2001, 123(12), 2719-2724. Two possible explanations can be offered for this reduced reactivity: the increased steric requirement of the additional øt/zo-substituent or the disruptive coordinating ability of the phosphine-oxide.

\[
\begin{align*}
5a & \xrightarrow{\text{BnBr, NaH, DMF, 98\%}} 5b \\
6 & \xrightarrow{\text{Ph₃P}} 7
\end{align*}
\]

**Scheme 24**

Attempted Palladium-Coupling of Chlorinated Phosphorus-Containing Biaryls

However, boroxine-based couplings are more effective. Moreover, Buchwald S-phosphine ligand systems and Ph₂X-phosphine ligands work well with boroxines in Suzuki couplings.

G. Phosphorus-Containing Bromo Compounds

Based on the inability to couple the C-Cl bond, a more reactive halogen substituent was used. With reference to Scheme 25, bromo-acetylene 12 needed to
be synthesized. While the 2-bromo-6-nitro-benzaldehyde 10 is known, its preparation required a tedious 3-step protocol. Initial reaction conditions on the 2-bromo-6-nitro-toluene (8) did not cleanly generate the desired aldehyde 10. However, undesired impurities were completely suppressed by cooling the intermediate enamine 9 solution to 0°C and rapidly adding the solution to a vigorously stirred solution of NaIO₄ at 0°C. This one-pot protocol does not require isolating intermediate enamine 9 and has proven quite effective. Subsequent alkyn formation with the Ohira-Bestmann reagent 11 provided 12. Again, deprotonation with LDA followed by addition of the phosphorus electrophile (Ph₂P(O)Cl, (c-C₆H₄)₂P(O)Cl or (EtO)₂P(O)Cl gave the desired di-substituted alkynes 13a-c.

![Scheme 25](image)

**H. Synthesis of Brominated, Phosphorus-Containing Dienophiles**

The Diels-Alder reactions again proceeded well (Scheme 26) using various dienes, such as 15, 17 and 19, in addition to Brassard diene 3. The generality of this approach clearly demonstrates the unique power of the Diels-Alder reaction to construct even the most congested biaryl linkages. X-ray crystal structures of biaryls 14a and 14c were determined to further confirm the regiochemical outcome of the Diels-Alder process. Interestingly, Diels-Alder reaction of the mono-substituted alkyne 12 with Brassard diene 3 generates none of the expected biaryl adduct 22 - instead the enol ether 21 is formed in reasonable yield (41%). This product was not observed with the 2-chloro version but with the 3-chloro variant - demonstrating the unique role that the halogen plays in the Diels-Alder process.
Scheme 26
Synthesis of Second-Generation Phosphorus-Containing Biaryls
1. Metal Mediated Coupling using Biaryls

Penta-substituted exemplary biaryls 14a-c, Scheme 26, were selected for initial screening (Table 4) using a range of metal-mediated couplings, such as Suzuki, Stille and Negishi reactions- including Buchwald's ligands, P(c-C\textsubscript{6}H\textsubscript{11})\textsubscript{3}/Pd\textsubscript{2}dba\textsubscript{3}, Pd(dppf)Cl\textsubscript{2} and Pd(OAc)\textsubscript{2}/dppp. The (t-Bu\textsubscript{3}P)\textsubscript{2}Pd° system developed by the Fu laboratory gave positive results in the coupling processes.

1. Suzuki and Stille Couplings

With a viable route developed for the synthesis of the halogenated biaryl compounds, their utility in Suzuki couplings was explored (Scheme 27). For the majority of the biaryl compounds, an optimized protocol for working embodiments used \textit{in situ} generation of the presumed Pd[P(C-C\textsubscript{6}H\textsubscript{11})\textsubscript{3}]\textsubscript{2} catalyst from Pd\textsubscript{2}(dba)\textsubscript{3} and P(C-C\textsubscript{6}Hn)\textsubscript{3}. The yields on these transformations were generally high (>80%) with only modest catalyst loading (5 mol% Pd). For the more challenging 3-chloro-2-nitroaryl series 30, incomplete conversion to the desired poly-aryl product 37 was observed with this catalyst system - even at high catalyst loading (20 mol%). Fortunately, use of the commercially available (t-Bu\textsubscript{3}P)\textsubscript{2}Pd catalyst, developed by the Fu laboratory, allowed the reaction to proceed to completion using reasonable catalyst loading (5 mol%). The 3-chloro-2-nitroaryl substitution pattern found in 30 is among the most challenging systems for accomplishing effective palladium couplings - due to the perpendicular orientation of the nitro moiety and the difficulty of insertion into carbon-chloride bonds.
Scheme 27
Suzuki Couplings with Phenylboronic acid

^Extended reaction time (48 h) was employed for this coupling.

A range of substitution patterns on the boronic acid also was studied to investigate the scope of this approach (Table 4). For this purpose, only the most challenging substrates, biaryls 16 and 30 were screened. With aryl chloride 16, electron rich boronic acid coupled smoothly under the normal Pd$_2$(dba)$_3$/P(c-C$_6$H$_{11}$)$_3$ conditions with good-to-excellent yields. For embodiments tried to date, electron deficient boronic acids, such as 4-cyanophenyl boronic acid, did not perform as well as desired using the Pd$_2$(dba)$_3$/P(c-C$_6$H$_{11}$)$_3$ conditions, with typical conversion rates being about 40%. Using the more active (/-Bu$_3$P)$_2$Pd system allowed this transformation to proceed cleanly to completion. The pentafluorophenyl boronic acid appears to be one limitation to this protocol (Entry 6). In addition, the 7-trifluoromethylphenyl boronic acid and the o-trifluoromethylphenyl boronic acid both proved capricious as significant amounts of dehalogenated product was observed along with incomplete conversion (Entries 7 and 9). The m-trifluoromethylphenyl boronic acid was effective in the coupling process (Entry 8). In the 3-chloro series 30, electron-rich boronic acids coupled well. Electron-deficient boronic acids coupled with reasonable efficiencies; however, using pentafluorophenyl boronic acid again gave none of the desired product (Entry 15). Using alternative coupling conditions, such as Buchwald ligands or PEPPSI®
(Pyridine-Enhanced-Precatalyst-Preparation-Stabilization and Initiation, using the catalyst indicated below), were equally unsuccessful.

\[
\begin{align*}
&\text{Cl-Pd-Cl} \\
&\text{Cl}
\end{align*}
\]

Table 4

<table>
<thead>
<tr>
<th>Suzuki Couplings with Arylboronic Acids</th>
</tr>
</thead>
</table>
| \[
\begin{align*}
&\text{Ar} \\
&\text{NO}_2 \\
&\text{OMe} \\
\text{BnO} \\
\text{Ar}
\end{align*}
\] |

**Conditions:**

- a. Pd$_2$(dba)$_3$ (2.5 mol%), P(C$_6$H$_{11}$)$_3$ (10 mol%), dioxane, Cs$_2$CO$_3$, 80°C 24 h;
- b. (--Bu$_3$P)$_2$Pd (5 mol%), KF, NMP, 80°C, 24 h.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Halide</th>
<th>Ar</th>
<th>Conditions</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>4-OMe-C₆H₄</td>
<td>a</td>
<td>90% (38)</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>3-OMe-C₆H₄</td>
<td>a</td>
<td>91% (39)</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>2-OMe-C₆H₄</td>
<td>a</td>
<td>80% (40)</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>2-Me-C₆H₄</td>
<td>a</td>
<td>89% (41)</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>4-CN-C₆H₄</td>
<td>b</td>
<td>80% (42)</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
<td>C₆F₅</td>
<td>b</td>
<td>0% (43)</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>4-CF₃-C₆H₄</td>
<td>b†</td>
<td>N/A (44)</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>3-CF₃-C₆H₄</td>
<td>b†</td>
<td>77% (45)</td>
</tr>
<tr>
<td>9</td>
<td>16</td>
<td>2-CF₃-C₆H₄</td>
<td>b†</td>
<td>N/A (46)</td>
</tr>
<tr>
<td>10</td>
<td>30</td>
<td>4-OMe-C₆H₄</td>
<td>b†</td>
<td>86% (47)</td>
</tr>
<tr>
<td>11</td>
<td>30</td>
<td>3-OMe-C₆H₄</td>
<td>b†</td>
<td>64% (48)</td>
</tr>
<tr>
<td>12</td>
<td>30</td>
<td>2-OMe-C₆H₄</td>
<td>b†</td>
<td>44% (49)</td>
</tr>
<tr>
<td>13</td>
<td>30</td>
<td>2-Me-C₆H₄</td>
<td>b†</td>
<td>34% (50)</td>
</tr>
<tr>
<td>14</td>
<td>30</td>
<td>4-CN-C₆H₄</td>
<td>b†</td>
<td>61% (51)</td>
</tr>
<tr>
<td>15</td>
<td>30</td>
<td>C₆F₅</td>
<td>b†</td>
<td>0% (52)</td>
</tr>
<tr>
<td>16</td>
<td>30</td>
<td>4-CF₃-C₆H₄</td>
<td>b</td>
<td>60% (53)</td>
</tr>
<tr>
<td>17</td>
<td>30</td>
<td>3-CF₃-C₆H₄</td>
<td>b†</td>
<td>71% (54)</td>
</tr>
<tr>
<td>18</td>
<td>30</td>
<td>2-CF₃-C₆H₄</td>
<td>b†</td>
<td>22% (55)</td>
</tr>
</tbody>
</table>

† Extended reaction time (48 h) was employed for this coupling.

With reference to Table 5, below, efficient Suzuki and Stille couplings could be accomplished with the corresponding phenyl boronic acid (24) and the tributylphenyl stannane (25). These couplings, however, required high catalyst loading (20 mol%) and excess aryl-metallo species (3 equivalents) to proceed to completion. In addition, poor functional group tolerance with substituted aryl boronic acids or aryl stannane was observed - routinely resulting in incomplete reaction and low chemical yields. In contrast, organozinc species coupled quite efficiently with reduced catalyst loading (10 mol%) and phenylzinc chloride (26, 1.5 equivalents).
Table 5
Phenyl Suzuki, Stille and Negishi Couplings of Biaryls

<table>
<thead>
<tr>
<th>R</th>
<th>Suzuki(^b) % Yield</th>
<th>Stille(^c) % Yield</th>
<th>Negishi(^c) % Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph</td>
<td>61%</td>
<td>60%</td>
<td>59%</td>
</tr>
<tr>
<td>c-C(_6)H(_12)</td>
<td>72%</td>
<td>66%</td>
<td>62%</td>
</tr>
<tr>
<td>EtO</td>
<td>63%</td>
<td>60%</td>
<td>57%</td>
</tr>
</tbody>
</table>

(a) catalyst (20 mol%), 23 (3 equiv.), KF (9 equiv.), NMP, 100°C, 16 h; (b) catalyst (20 mol%), 24 (3 equiv.), CsF (9 equiv.), NMP, 60°C, 16 h; (c) catalyst (10 mol%), 25 (1.5 equiv.), NMP / THF, 80°C, 16 h.

2. Negishi Couplings

The Negishi conditions provided the largest opportunity for substrate scope variability (Table 6). Dicyclohexylphosphine oxide biaryl was selected for further exploration. Good tolerance for substitution on the aryl ring was observed with substitution in the ortho, meta or para positions. One exception to this observation is the failure of 2-methoxyphenyl zinc chloride to undergo successful coupling. The problem appears to be electronic in nature as additional steric substitution ortho to the organozinc species does not disrupt the palladium coupling (Entries d and e). In fact, the 2,6-dimethylphenyl zinc chloride proved the most efficient substrate for this coupling process. Electron-withdrawing substituents are tolerated (Entry f). The structures of compounds 28a, 28e and 28f were confirmed by single crystal X-ray diffraction methods.
J. Carbonyl-Containing Series

The scope of electron-withdrawing groups that can be tolerated on exemplary acetylenic dienophiles disclosed herein, including the possibility that the regiochemistry could be altered by the selection of alternate groups on the alkyne, also has been considered. The effects of carbonyl moieties and whether their added electron withdrawing ability might perturb the regiochemical outcome of the cycloaddition also have been considered. With reference to Table 7, exemplary compounds were made from alkyne 12. Treating acetylene 12 with LDA followed by the addition of the various chloroformates, carbamyl chlorides, and acid chlorides yielded the acetylenic carbonyl adducts 40a-k. Esters (Entries a-c), ketones (Entries d-f) and amides (Entries g-i) were constructed using this general approach. Menthol ester 40j and the benzyl oxazolidinone 40k also were prepared via analogous methods, and the yields were generally good to excellent.
Table 7
Synthesis of the Disubstituted, Carbonyl-Containing Alkynes.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Electrophile (Cl-E)</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>ClCO₂Me</td>
<td>92%</td>
</tr>
<tr>
<td>B</td>
<td>ClCO₂Et</td>
<td>91%</td>
</tr>
<tr>
<td>C</td>
<td>ClCO₂CH₂CCl₃</td>
<td>68%</td>
</tr>
<tr>
<td>D</td>
<td>ClC(Ο)-t-Bu</td>
<td>74%</td>
</tr>
<tr>
<td>E</td>
<td>ClC(Ο)Ph</td>
<td>67%</td>
</tr>
<tr>
<td>F</td>
<td>ClC(Ο)-p-Cl-C₆H₄</td>
<td>59%</td>
</tr>
<tr>
<td>F₂</td>
<td>ClC(Ο)-p-NO₂-C₆H₄</td>
<td>35%</td>
</tr>
<tr>
<td>G</td>
<td>ClC(Ο)NMe₂</td>
<td>65%</td>
</tr>
<tr>
<td>H</td>
<td>ClC(Ο)NPh₂</td>
<td>56%</td>
</tr>
<tr>
<td>I</td>
<td>ClC(Ο)-N-morpholoinyl</td>
<td>89%</td>
</tr>
<tr>
<td>J</td>
<td>(-)-ClCO₂-menthyl</td>
<td>63%</td>
</tr>
<tr>
<td>K</td>
<td></td>
<td>61%</td>
</tr>
</tbody>
</table>

This compound did not form a biaryl compound in cycloaddition reactions conducted to date.

K. Diels-Alder Reactions Using Carbonyl-Containing Reagents

With the dienophiles 40a-k in hand, Diels-Alder cycloadditions were explored (Table 8). Commercially available 1-methoxy-1,3-cyclohexadiene (17) was used for the cycloaddition process. Tetra-ortho-substituted biaryls 42 were formed in good-to-excellent yield (64-85%). In the vast majority of cases, a single regioisomer 42 was observed, potentially as a result of the directing ability of the ortho-nitro-phenyl substitution. This is true even in the presence of additional strong electron withdrawing groups. The regiochemistry of each biaryl product 42 was confirmed via HMBC 2D NMR. Further confirmation was obtained via x-ray crystallographic analysis of compound 42b. On certain aromatic ketone systems (Entry f), a minor amount (<10%) of the alternate regioisomer was observed. This Diels-Alder process is believed to work via initial cycloaddition to the [2.2.2]
bicyclic adduct 41 followed by extrusion of ethylene to provide aromatized biaryl 42.

Bicyclic intermediate 41 is produced if the reaction is conducted at lower temperatures (e.g. about 50°C, 16 hours). In the case of the ethyl ester 40b, the ratio between the two diastereomers is 1.5:1 as judged by $^1$H NMR. These diastereomers are the result of diene approach of the acetylene from the same side as the NO$_2$ group (endo approach) or the opposite side from the NO$_2$ group (exo approach). Subsequent heating at higher temperatures (130 °C, 16 hours) does induce ethylene extrusion to produce the desired biaryl 42 as a single regioisomer.

Table 8
Diels-Alder Reactions of Carbonyl-Containing Acetylenes with 1-Methoxy-1,3-cyclohexadiene

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>OMe</td>
<td>82%</td>
</tr>
<tr>
<td>b</td>
<td>OEt</td>
<td>85%</td>
</tr>
<tr>
<td>c</td>
<td>OCH$_2$CCl$_3$</td>
<td>64%</td>
</tr>
<tr>
<td>d</td>
<td>$t$-Bu</td>
<td>81%</td>
</tr>
<tr>
<td>e</td>
<td>Ph</td>
<td>71%</td>
</tr>
<tr>
<td>f</td>
<td>$p$-Cl-C$_6$H$_4$</td>
<td>64%</td>
</tr>
<tr>
<td>g</td>
<td>NMe$_2$</td>
<td>75%</td>
</tr>
<tr>
<td>h</td>
<td>NPh$_2$</td>
<td>72%</td>
</tr>
<tr>
<td>i</td>
<td>N-morpholinyl</td>
<td>83%</td>
</tr>
</tbody>
</table>

L. Diene Variations for Carbonyl-containing Dienophiles

The diene scope of certain disclosed embodiments was explored using the dienophile 40b (Scheme 28). In addition to the mono-oxygenated cyclic diene 43, 1,3-bisoxigenation is tolerated in the cycloaddition process (diene 19 and 46). Diene 46 was used to provide benzyloxy substitution at the ortho-phenolic position. Initially acyclic dienes, such as Brassard's diene, were used, but no cycloadduct was observed. Cyclic dienes undergo facile cycloaddition with these carbonyl-
containing dienophiles 40. One possible explanation is that the acyclic dienes (e.g. Brassard's diene 3) may undergo a stepwise or [2+2] addition to the acetylene followed by decomposition of the resultant intermediate. Support for this possibility can be seen in the fact that consumption of the dienophile is observed with diene 3.

Additionally, some of the carbonyl-containing dienophiles 40 have proven significantly more sensitive than the phosphorus-containing series. For example, esters 40a-c have been purified using Florisil® and the oxazolidinone 40k is purified using SiO₂ in the presence of 1% Et₃N in order to avoid decomposition.

M. Synthesis of Atropisomers

Disclosed embodiments of the Diels-Alder process can be used for rapid synthesis of enantiomerically pure atropic isomers (Scheme 29). Using menthol ester 40j generated a 1:1 mixture of diastereomeric atropisomers (78%), but the two compounds could not be separated. Fortunately, when the benzyl oxazolidine-containing dienophile 40k was reacted with the commercially available diene 17, chromatographically separable atropic diastereomers 49-(aS) and 49-(a/?) (1:1) were produced. The absolute configuration of the atropic center of chirality was assigned
via the X-ray crystal structure of 49-(aS) (FIG. 5). The atropic integrity is maintained even with prolonged heating. For example, no change was observed even after heating at 130 °C for 24 hours. Other oxazolidinones were screened, including the tert-butyl derived oxazolidinone and SuperQuat™ but led to similar results (1:1 ratio of diastereomers).

**Scheme 29**
Chiral Dienophiles in the Carbonyl-Containing Diels-Alder Reactions

**N. Stannane Dienophiles**

Stannane dienophiles also have been made. Highly θ-substituted biaryls can be made where two or more of the ortho substituents are available for subsequent functionalization. One disclosed embodiment of method for making such compounds uses of an alkynyl halide or organometallic species as the dienophile in the cycloaddition process. Unsymmetrical, programmable tetra- or penta- or hexa-substituted biaryls containing ortho-oxygen and ortho-nitrogen functionality utilizing di-substituted alkynyl stannanes as dienophiles as illustrated below.

The key Diels-Alder cycloadditions/cycloreversions to form the highly substituted biaryl templates are shown below in Table 9. The stannyl alkynes 1-4 were synthesized from their known corresponding 2-halo-6-nitrophenylacetylenes Bu₃SnOMe (neat, 130°C) or LDA, THF then Ph₃SnCl. The cycloaddition/cycloreversion sequence with chloro alkyne 1 proceeded in modest to good yields (48-75%) to provide the penta- or hexa-substituted biaryl products Ha-
d with complete orthogonal functionality between the five or six non-hydrogen substituents - four of which are ortho to the biaryl linkage. These biaryls ℓla-d are available in just 3 steps from commercially available reagents. While both alkyl and aryl groups are tolerated on the stannane, the alkyl groups consistently performed more efficiently in the biaryl formation. We attribute part of this superior reactivity to the relative robustness of the tributylacetylenic stannane as compared to the triphenylacetylenic stannane. Two oxygen substituents were required on the cyclic diene platform in order to facilitate reaction. Use of dienes such as 1-methoxy-1,3-cyclohexadiene, which had proven effective in previous DAB examples from our laboratory, gave none of the desired biaryl product. Dimethyl dienes 6 and 10 were employed in cases where the resulting product was difficult to purify from the diene by-products, particularly where oxidation of the dienes 5 and 8 to the corresponding benzene derivatives were competitive with cycloaddition.

Table 9

Synthesis of Biaryl Templates
The biaryl templates were then functionalized as indicated below in (Table 10). Biaryl lie was selected as the platform to exemplify the reactivity of these compounds. For ease of subsequent functionalization, the /αo-phenolic moiety was protected as its methyl ether in excellent yield. For a range of Stille-based couplings with aryltributylstannane, little to no coupling were observed with considerable amounts of protodestannylation. Consequently, the aryl stannane was converted into its corresponding iodide 12 in excellent yield. Optimum conditions for coupling the aryl iodide 12 employed the Pd$_2$(dba)$_3$/P(C$_6$H$_n$)$_3$ ligand system. The carbon-iodine bond was readily functionalized through Suzuki couplings (entries a-d), a Stille coupling (entry e) and a Heck coupling (entries f). The success of the Stille coupling (entry e) combined with the inability to couple the methylated derivative of stannane lie supports the working hypothesis that the more sterically hindered of the two possible coupling partners should be functionalized as the aryl halide for optimum performance.
Table 10

Exploration of Scope for Lower Ring.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Coupling Partner</th>
<th>R</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>(MeBO)₃ (80⁰C)</td>
<td>Me</td>
<td>92%</td>
</tr>
<tr>
<td>b</td>
<td>PhB(OH)₂ (80⁰C)</td>
<td>Ph</td>
<td>82%</td>
</tr>
<tr>
<td>c</td>
<td>4-MeO-C₆H₄B(OH)₂ (100⁰C)</td>
<td>4-OMe-C₆H₄</td>
<td>86%</td>
</tr>
<tr>
<td>d</td>
<td>2-Me-C₆H₄B(OH)₂ (100⁰C)</td>
<td>2-Me-C₆H₄</td>
<td>74%</td>
</tr>
<tr>
<td>e</td>
<td>PhSnBu₃ (45-80⁰C)⁺</td>
<td>Ph</td>
<td>63%</td>
</tr>
<tr>
<td>f</td>
<td>CH₂=CHCO₂Me (100⁰C)</td>
<td>E-CH=CH₂CO₂Me</td>
<td>73%</td>
</tr>
</tbody>
</table>

⁺ Alternate Conditions used: Pd(PPh₃)₄, CuI, CsF, DMF.

The chlorine substituent in the upper ring also can be modified. However, there are inherent challenges associated with coupling a highly substituted aryl chloride such as 13a based on previous experience with tetra-or/ho-substituted aryl chlorides in phosphorus-containing biaryls. As a methyl moiety is the least sterically demanding of the carbon-based nucleophiles, commercially available methyl boroxine was used as the coupling partner for the initial investigation. A wide range of coupling systems were used, including those developed by Fu [(/-Bu₃P)₂Pd] and Buchwald [Pd(OAc)₂, S-Phos]. Only poor or incomplete reaction was observed in all cases. The recently developed and commercially available PEPPSI™-IPr catalyst (15) by Organ and co-workers was then tried. Clean conversion to the Suzuki product 16a was observed in good yield (74%). When alternate boron-based nucleophiles, such as PhB(OH)₂, were tried no reaction was observed in good yield (74%).
observed even at high catalyst loading and with excess boronic acid. Phenyl boroxine 14b was then tried in the reaction protocol, which provided clean construction of the tetra-or \textit{ortho}-substituted biaryl 16b. Optimum conditions employed 3 equivalents of the boroxine 14 and powdered 4A molecular sieves in order to remove any adventitious water. These conditions have proven to be the most reactive that were found during in challenging C-C bond forming reactions. Additionally, reasonable functional group tolerance was observed using this reaction protocol. Electron donating substituents in the \textit{ortho}, \textit{meta} and \textit{para} position of the aryl boroxine are all tolerated. One limitation appears to be the 2,6-dimethylphenyl boroxine 14f. Successful coupling with electron deficient boroxine 14g was also observed in reasonable yield (50%).

\textbf{Table 11}

\textit{Exploration of Scope for Suzuki Reaction in Upper Ring.}

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Me</td>
<td>74%</td>
</tr>
<tr>
<td>b</td>
<td>Ph</td>
<td>83%</td>
</tr>
<tr>
<td>c</td>
<td>4-MeO-C\textsubscript{6}H\textsubscript{4}</td>
<td>70%</td>
</tr>
<tr>
<td>d</td>
<td>3-MeO-C\textsubscript{6}H\textsubscript{4}</td>
<td>75%</td>
</tr>
<tr>
<td>e</td>
<td>2-Me-C\textsubscript{6}H\textsubscript{4}</td>
<td>63%</td>
</tr>
<tr>
<td>f</td>
<td>2,6-Me-C\textsubscript{6}H\textsubscript{3}</td>
<td>0%</td>
</tr>
<tr>
<td>g</td>
<td>4-CF\textsubscript{3}-C\textsubscript{6}H\textsubscript{4}</td>
<td>50%</td>
</tr>
</tbody>
</table>
Orthogonal and/or tandem functionalization of these highly substituted biaryls could be readily accomplished (Scheme 30). Selective formation of the \( \sigma rt/z\sigma \)-anilino or \( ort\&o \)-phenolic functionalities were demonstrated using Zn/AcOH or BCl\(_3\) respectively. Tandem reduction using Pd/C, H\(_2\) revealed the anilino phenol \( rac\)-19 in excellent yield. This biaryl could be readily resolved using chiral HPLC separation (Daicel OD column). These axially chiral anilino phenols 19-(aR) and 19-(aS) are of considerable interest to the synthetic community as they closely resemble the 2-amino-2'-hydroxy-1,1'-binaphthyl (NOBIN) class of binaphthalene-based ligands. Interestingly, while NOBIN has been utilized in asymmetric catalysis - including in Carreira's asymmetric aldol methodology,'little variation of the binaphthalene core structure has been explored to date.

Further Functionalization of Tetra-\( ortho \)-Substituted Biaryl 16b

![Scheme 30](image)

O. Biaryl Compounds as Synthesis Catalysts

The dimethylamino phosphine 34 was screened for its potential utility as a ligand in palladium-mediated processes (Scheme 31). It serves as a highly active ligand for cross-coupling reactions. The synthesized ligand 34 appears to be critical to the success for these transformations as the experiment in the absence of phosphine with boronic acid 35 and bromide 36 [5 mol\% Pd(OAc)\(_2\), K\(_3\)PO\(_4\), PhMe, 100°C, 20 h] gave only a small amount (18\%) of the desired coupled material 37. The use of alternate phosphines (e.g. PPh\(_3\)) as a substitute ligand also gave inferior results. Phosphine 34 is the sole compound screened to date in this process and yet
it is already able to perform comparably with the Buchwald's $N,N$-dimethylamino biaryl system in side-by-side experiments.

\[
\begin{align*}
\text{Scheme 31} \\
\text{Utility of Ligand 34 in Cross Coupling Reactions}
\end{align*}
\]

With reference to Scheme 32, ligand 34 also can be utilized for carbon-nitrogen bond formation. For example, p-anisidine (40) was cleanly coupled to aryl iodides 41 and 43 to generate disubstituted anilines 42 and 44 in excellent yields. Very low ligand loading amounts (e.g. 2 mole percent) are needed to facilitate this transformation.

\[
\begin{align*}
\text{Scheme 32} \\
\text{P. Biaryl-Derived, Enantioenriched Amino Alcohols and Lactams}
\end{align*}
\]

Available axially chiral biaryl compounds produced via the Diels-Alder approach provide opportunities to convert these structures into compounds useful as potential organocatalysts. Despite the wealth of research that has been directed
toward organocatalysis, relatively little attention has been focused on using axial chirality for asymmetric organocatalytic induction.

With reference to Scheme 33, reduction of the oxazolidinone 49-(aS) with LiBH₄, MeOH at 0°C generated alcohol 50 in good yield. Using alternate reduction systems (e.g. LiAlH₄) led to complex mixtures. Reduction of both the nitro moiety and the carbonyl may be accomplished in a single step by simply conducting the same reduction at reflux to yield the anilino alcohol 51 in reasonable yield (64%).

Amino alcohol 51 represents one of the first reported examples of a potential organocatalyst possessing solely axial chirality - particularly with anilino-derived structures. Recent reports on the potential organocatalytic ability of anilines have been disclosed. The ability to further functionalize the aryl bromide (via palladium couplings) and the aniline (via reductive amination) makes compound 51 an ideal springboard for constructing new organocatalysts. Alternatively, reduction of the nitro moiety 49 with Zn/AcOH induced formation of the highly strained lactam 52 in modest yield. The structure of ent-52 (FIG. 6) was determined by single crystal X-ray diffraction methods.

Based on the X-ray structure, the bromide and methoxy moiety are oriented significantly out of the plane. The dihedral angle between the bromide and the methoxy group is about 35.3°. Interestingly, reduction of the nitro moiety with Zn in aqueous HOAc produced the dehalogenated lactam derivative 53.

![Scheme 33](image)

Scheme 33
Synthesis of Potential Organocatalysts
Disclosed embodiments allow synthesis of entire classes of biaryl compounds that would not be readily accessible from alternative methods. In fact, the successful construction of biaryl compounds possessing four different atoms (N, Cl/Br, O and P for the phosphorus series and N, Br, O and C for the carbonyl series) at the four ortho positions has not been accomplished by any other method. One intriguing feature of disclosed embodiments of the Diels-Alder process is the ability to construct sterically challenging functionality under quite mild conditions. In many cases, the cycloaddition sequence appears to work better on the more substituted systems. Additionally, the strong directing ability of the ortho-nitro moiety, even in the presence of ketones, esters and amides is noteworthy.

Disclosed embodiments also allow synthesis of a novel ligand system for Suzuki-couplings. The first generation ligand 34 has demonstrated early potential for facilitating challenging cross couplings. This example embodies the power of the DAB methodology, that is the ability to construct sterically demanding biaryl structures not accessible from traditional metal-mediated methods. This methodology provides an ideal complement to the powerful coupling technologies developed by Fu, Buchwald, Hartwig and others for the synthesis of complex biaryl structures. Combining these two technologies allows developing new ligand systems that may facilitate cross coupling processes not currently accessible from the existing ligand systems.

Carbonyl-containing biaryl series have been exploited for the synthesis of an axially chiral, biaryl anilino alcohol 51. Again, the highly substituted nature of 51 is uniquely accessible via the DAB protocol. Biaryl 51 should find application in both iminium-catalyzed processes as well as hydrogen-bonding catalysis.

Q. Functional Modification of Biaryl Compounds

Further functionalization of the biaryl moiety is possible (Scheme 34). The nitro group can be easily reduced using Zn in acetic acid (85%). Attempted hydrogenation of the nitro compound 28e to the amino compound 29 gave complex mixtures and low mass recovery [presumably due to irreversible binding of the resultant phosphine-oxide, amino alcohol (e.g. 32) to the metal surface].
A wide range of conditions was screened for the reduction of the phosphine oxide moiety. The most common set of conditions typically used for this transformation employs HSiCl$_3$ and Et$_3$N; however, these conditions provided none of the desired phosphine-only extensive decomposition was observed. Several aluminum-based reagents (e.g. LAH, AlH$_3$) also were screened, which again provided none of the desired product. Instead, a small amount of the $X_1$-ortho-substituted biaryl 31 was isolated with selective C-P bond cleavage. Fortunately, the desired reduction of the P-O bond could be accomplished using conditions developed by Lawrence and co-workers.

Protecting groups can be readily added or removed. For example, benzyl ethers could be readily cleaved with BCl$_3$ to provide corresponding alcohols, such as phenol 32, in good yield. Also, the anilino group present in compounds 29 and 30 could be reductively aminated using NaBH$_3$CN and paraformaldehyde to give the dimethylamino compounds 33 and 34. X-ray crystallographic analysis of the hydrochloride salt of the dimethylamino phosphine 34 is shown in FIG. 4. Also, attempted reduction of the phosphine oxide moiety in biaryl 33 (using the Lawrence conditions) gave low yield of the product 34 (38%) with significant amounts of recovered starting material.
A tandem reduction process to reveal both the phenol and aniline moieties is also possible via hydrogenation with Pd/C, as indicated below in Scheme 35.

\[ \text{Scheme 35} \]

Selective Functionalization

**R. Carbazole Synthesis**

Chlorinated carbazoles have been made using disclosed embodiments of the DAB methodology (Scheme 36). Carbazoles have garnered considerable synthetic attention due to the diverse array of biologically active, carbazole natural products and potential materials applications. Using the biaryls 20-22 and 32, Cadogan cyclization has been used to provide the C_5-C_8 halogenated carbazoles 61-64. These transformations proceeded cleanly with yields ranging between 65-87%. C_5-substituted carbazoles are of particular interest as they are difficult to construct via alternate methods.

\[ \text{Scheme 36} \]

Synthesis of Chlorinated Carbazoles
S. Siamenol Synthesis

Cadogan cyclization and the DAB methodology has been applied to the construction of the anti-HIV natural product siamenol (66) (Scheme 37). This carbazole 66 has displayed significant anti-HIV activity (EC50 = 2.6 µg/mL) in the XTT-tetrazolium assay. Biaryl template 70 provides an excellent intermediate for making 66, by selective introduction of the allyl group in the C₃ position. The selectivity for C₉₈ in the Cadogan cyclization has not been significantly explored (resulting in a C₃-allyl carbazole versus a C₁-allyl carbazole). In addition, there appears to be little documented evidence on the effect of free phenols in Cadogan cyclizations.

Scheme 37
Retrosynthetic Analysis of Siamenol

Starting from the previously described alkyne 13, Diels-Alder cycloaddition with the diene 71 followed by in situ TBAF treatment cleanly generated the phenol 70.

While the yields in the Diels-Alder process using the cyclohexadiene 71 and TBS-Danishefsky's diene were quite similar, the cyclic diene reaction proved easier to purify.

For the Suzuki coupling, standard conditions were used with the boroxine 72 to give the methylated adduct 73 (Scheme 38). Next, the phenol 73 was converted to its corresponding allyl ether. The Claisen rearrangement was accomplished by thermolysis of the allyl ether in dichlorobenzene (250 °C, sealed tube, 5 hours) to induce a [3,3]-sigmatropic rearrangement to provide 68 in 62% yield. Alternatively, treating the allyl ether with BCl₃ in CH₂Cl₂ led to rapid Claisen rearrangement at lower temperatures (25 °C) and in higher yield (85% yield of 68).
Scheme 38
Synthesis of the Cadogan Precursor

For carbazole synthesis using a Cadogan cyclization (Scheme 39) (PPh$_3$, o-DCB, 180 °C), the major product was the undesired Ci allylated product 75 (51%), along with 32% yield of the desired isomer 74 and 11% yield of the aniline 76. Under these conditions, it appears that the electronic preference for the construction of a Ci substituted carbazole overrides any steric bias. A Claisen rearrangement of the requisite allyl ether carbazole is known to result in the placement of the allyl group in the more sterically congested Ci position (e.g. compound 75). Using lower temperatures (of about 100°C) and a more nucleophile phosphine (Bu$_3$P) did provide an improved ratio of regioisomeric carbazoles (1:1.2, 74:75) but at a reduced yield (60% overall) and with an increased amount of the aniline by-product 76 (19%).

The next reaction concerned metathesis of 74 under the conditions reported by Grubbs and Stoltz. Unfortunately, treating 74 with 2nd Generation Grubbs catalyst in 2-methyl-2-butene gave only a trace of the desired natural product 66. Grubbs has demonstrated a successful example of metathesizing an ortho-allylated phenol; however, the phenolic moiety was protected as its TBS-ether.
First Generation Strategy Toward Siamenol

The successful construction of siamenol is shown in Scheme 40. Treatment of phenol 68 under the identical metathesis conditions [2nd Gen. Grubbs (20 mol%), 2-methyl-2-butene, CH₂Cl₂ rt, 18 h, 73% yield] cleanly provided the prenylated phenol 77. In order to explore if the electronic bias for C₁i substitution in the carbazole formation could be overridden at lower temperatures, the nitro moiety was reduced with Zn/HOAc followed by diazotization and azide displacement to give compound 78. Azides have been used to form carbazoles by treatment with a Lewis acid (usually BCl₃) at low temperatures. Treating azide 79 with BCl₃ in toluene at -10 °C did induce cyclization to form the carbazoles 66 and 67; however, the aniline by-product 78 was again observed. One possible explanation for the unwanted aniline formation was the presence of the phenolic O-H bond. To address this issue, the phenol 76 was first treated with MeLi (0.9 equiv.) followed by the addition of BCl₃ at -50 °C. Under these conditions, clean conversion to the separable carbazoles 66 and 67 (1:1.1 ratio) occurred in good overall yield (78%). Sodium hydride also could be used for cyclization with similar results. Carbazole 66 was identical in all respects with the previously reported data for siamenol.

Alternatively, treatment of nitro phenol 77 with PBu₃ at 100 °C did provide the carbazoles 66 and 67 (70% overall yield, 1:1.5 ratio (66:67) along with the aniline 78 (24%). Interestingly, addition of NaH to remove the phenolic O-H prior to treatment with PBu₃ completely suppressed carbazole formation.

Scheme 40
Total Synthesis of Siamenol

Synthesis of various Siamenol derivatives is indicated below in Schemes 41-43.

Scheme 41

With reference to Scheme 41, cyclohexyl diene silyl ether 2 undergoes cycloaddition with acetylene 4 to form biaryl phenol 6. Deprotonation of phenol 6 with sodium hydride, followed by coupling with allyl iodide forms compound 8. Compound 8 is then the starting material referred to in Scheme 43 as compound 2.
Scheme 42

Scheme 42 illustrates a working embodiment of a method for making starting compound 20 in Scheme 43.
With reference to Scheme 43 compound 2 undergoes a Lewis acid accelerated Claisen rearrangement to form compound 4. The hydroxyl group of
compound 4 is then protected by reacting with tert-butyl-dimethyl silyl chloride to form silyl ether 6. Once the oxygen is protected, compound 6 then undergoes a Cadogan cyclization to form compounds 8 and 10.

Scheme 43 also includes another embodiment of a method for forming siamenol analogues. Compound 12 includes an allyl group that is converted to the prenyl group of compound 14 by a Grubbs metathesis. Compound 14 then undergoes a Cadogan cyclization to form siamenol analogues 16 and 18.

Scheme 43 includes yet another embodiment of a method for forming siamenol analogues 24 and 26. This embodiment involves replacing a halogen, such as chlorine, with an R group, such as methyl. Accordingly, compound 20 is converted into its alkyl analog 22 using a Suzuki coupling and with the PEPPSI catalyst, potassium carbonate and methyl boroxine. A person of ordinary skill in the art will appreciate that analogues other than lower alkyl compounds can be made using the same approach, including aryl and heteroaryl compounds. Furthermore, Scheme 43 indicates replacing a single halogen with a lower alkyl group, particularly methyl. However, plural halogens can be replaced with plural different R groups too. And, where more than a single halogen is present, then one of the halogens can be replaced with an R group to form halogenated derivatives as well, particularly at the position occupied by the X group. Compound 22 then undergoes a Cadogan cyclization, followed by hydroxyl deprotection to remove the TBS protecting group, to form analogues 24 and 26.

**T. Siamenol Analogues**

Siamenol analogues made according to the present invention have biological activity. Particular siamenol analogues have been submitted for anti-HIV testing, and will be tested for anti-cancer activity. Siamenol analogues that have been submitted for anti-HIV screening are provided below in Table 12.
Selected Siamenol Analogues for Biological Evaluation

The analogs of Table 12 have been subjected to initial anti-HIV screening. Briefly, the compounds were dissolved in DMSO and then tested at 5, .5, .05 and .005 µg/mL. The no treatment HIV control had much fewer infected cells than
anticipated. For these preliminary tests, a statistical test was not performed since the one compound that was effective had zero infected cells. The results of this initial screening are provided below in Table 13.

Table 13
Initial Qualitative Results for HIV Screening

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toxic (More than 50% dead), surviving cells little infection</td>
</tr>
<tr>
<td>3</td>
<td>Toxic (More than 50% dead), surviving cells little infection</td>
</tr>
<tr>
<td>4</td>
<td>Toxic (More than 50% dead), surviving cells little infection</td>
</tr>
<tr>
<td>5</td>
<td>Toxic (More than 50% dead), surviving cells little infection</td>
</tr>
<tr>
<td>7</td>
<td>Highly Toxic (no surviving cells)</td>
</tr>
<tr>
<td>8</td>
<td>Very Toxic</td>
</tr>
<tr>
<td>12</td>
<td>Slightly Toxic, and Very Effective</td>
</tr>
<tr>
<td>15</td>
<td>Non-toxic, more infected cells than positive control</td>
</tr>
<tr>
<td>17</td>
<td>Very Toxic, likely less than 25% Survival</td>
</tr>
<tr>
<td>19</td>
<td>Very Toxic</td>
</tr>
<tr>
<td>21</td>
<td>Very Toxic</td>
</tr>
</tbody>
</table>

Additional analogs also shall be made based on the structures provided above and further on biological information obtained concerning such analogs. Exemplary additional analogs include the following.
VII. EXAMPLES

The following examples are provided to illustrate specific features of certain disclosed embodiments of the present invention. A person of ordinary skill in the art will appreciate that the scope of the present invention is not limited to those features exemplified by such examples.

**General.** Infrared spectra were recorded neat unless otherwise indicated and are reported in cm⁻¹. ¹H NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent. ¹³C NMR spectra were recorded in deuterated solvents and are reported in ppm relative to trimethylsilane and referenced internally to the residually protonated solvent.

Routine monitoring of reactions was performed using EM Science DC-Alufolien silica gel, aluminum-backed TLC plates. Flash chromatography was performed with the indicated eluents on EM Science Gedurian 230-400 mesh silica gel.

Air and/or moisture sensitive reactions were performed under usual inert atmosphere conditions. Reactions requiring anhydrous conditions were performed under a blanket of argon, in glassware dried in an oven at 120°C or by a bunsen
flame, then cooled under argon. Solvents and commercial reagents were purified in accord with Perrin and Armarego or used without further purification.

**Example 1**

This example provides detail concerning the synthesis of Acetylene 2a (Schemes 1-3): To a stirred solution of 1 (46.6 mg, 0.257 mmol) and THF (1.25 mL) was added LDA (0.257 mL, 0.257 mmol, 1.0 M in THF / Hexanes) at -78°C. After 5 min, freshly distilled acetone (44.8 mg, 56.6 µL, 0.771 mmol) was added. After 30 min at -78°C, the dark brown solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to give 2a (43.8 mg, 0.183 mmol, 71%) as a yellow oil.

IR (neat) 3407, 2984, 2232, 1532 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.89 (dd, J = 8.3, 1.1 Hz, IH), 7.69 (dd, J = 8.2, 1.2 Hz, IH), 7.39 (t, J = 8.2 Hz, IH), 2.27 (s, IH), 1.68 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 151.4, 138.7, 133.5, 128.5, 122.7, 117.9, 107.9, 74.4, 65.9, 30.9; HRMS (Cl+) calcd. for C₁₁H₁₀NO₃ClNa (M+Na) 262.0247, found 262.0241.

**Example 2**

This example provides detail concerning the synthesis of Acetylene 2b (Schemes 1-3): To a stirred solution of 1 (106 mg, 0.584 mmol) and THF (2.92 mL) was added LDA (0.584 mL, 0.584 mmol, 1.0 M in THF / Hexanes) at -78°C. After 5 min, 3-pentanone (151 mg, 185 µL, 1.75 mmol) was added. After 30 min at -78°C, the dark brown solution was allowed to warm to rt.
After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL),
diluted with EtOAc (15 mL), and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to give 2b (98.5 mg, 0.368 mmol, 63%) as a yellow oil. IR (neat) 3443, 2972, 2229, 1533 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.89 (dd, J = 8.2, 1.2 Hz, IH), 7.69 (dd, J = 8.1, 1.1 Hz, IH), 7.39 (t, J = 8.2 Hz, IH), 2.24 (bs, IH), 1.76-1.90 (m, 4H), 1.14 (t, J = 7.2 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 151.5, 138.8, 133.5, 128.5, 122.6, 118.0, 106.4, 76.6, 73.0, 34.2, 8.52; HRMS (EI+) calcd. for C₆H₄NO₃Cl (M+H) 267.0662, found 267.0659.

**Example 3**

![Diagram of reaction](attachment:image.png)

This example provides detail concerning the synthesis of Acetylene 2c (Schemes 1-3): To a stirred solution of 1 (108 mg, 0.594 mmol) and THF (2.97 mL) was added LDA Error! Bookmark not defined.- (0.594 mL, 0.594 mmol, 1.0 M in THF / Hexanes) at -78°C. After 5 min, cyclobutanone (125 mg, 150 µL, 1.78 mmol) was added. After 30 min at -78°C, the dark brown solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL),
diluted with EtOAc (15 mL), and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 2c (90.4 mg, 0.359 mmol, 60%) as a yellow oil. IR (neat) 3374, 2992, 2228, 1531 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.92 (dd, J = 8.2, 1.1 Hz, IH), 7.71 (dd, J = 8.0, 1.1 Hz, IH), 7.41 (t, J = 8.2 Hz, IH), 2.64 (bs, IH), 2.57-2.65 (m, 2H), 2.38-2.46 (m, 2H), 1.87-2.01 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 151.2, 138.6, 133.6, 128.5, 122.8, 118.0, 107.0, 75.7, 68.4, 38.4, 12.9; HRMS (EI+) calcd. for C₁₉H₁₈NO₃Cl (M+H) 251.0349, found 251.0347.
Example 4

This example provides detail concerning the synthesis of Acetylene 2d (Schemes 1-3): To a stirred solution of 1 (92.6 mg, 0.510 mmol) and THF (2.55 mL) was added LDA (0.510 mL, 0.510 mmol, 1.0 M in THF / Hexanes) at -78°C. After 5 min, cyclopentanone (129 mg, 1.53 mmol) was added. After 30 min at -78°C, the dark brown solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 2d (70.4 mg, 0.265 mmol, 52%) as a yellow oil. IR (neat) 3410, 2959, 2216, 1531 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.90 (dd, J = 8.3, 1.2 Hz, 1H), 7.69 (dd, J = 8.1, 1.1 Hz, IH), 7.38 (t, J = 8.2 Hz, IH), 2.03-2.19 (m, 5H), 1.81-1.96 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 151.3, 138.6, 133.5, 128.4, 122.7, 118.1, 107.5, 75.4, 75.1, 42.3, 23.6; HRMS (EI+) calcd. for C₁₃H₁₂NO₃Cl (M+H) 265.0506, found 265.0509.

Example 5

This example provides detail concerning the synthesis of Acetylene 2e (Schemes 1-3): To a stirred solution of 1 (89.3 mg, 0.492 mmol) and THF (2.46 mL) was added LDA (0.492 mL, 0.492 mmol, 1.0 M in THF / Hexanes) at -78°C. After 5 min, the dark brown solution was cannulated into a stirred solution of cyclohexanone (144 mg, 1.48 mmol) in THF (0.49 mL) at -78°C. After 30 min at -78°C, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL).
dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to give 2e (93.2 mg, 0.333 mmol, 68%) as a yellow oil. IR (neat) 3398, 2936, 2232, 1532 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.89 (dd, J = 8.3, 1.2 Hz, IH), 7.69 (dd, J = 8.1, 1.2 Hz, IH), 7.39 (t, J = 8.2 Hz, IH), 2.41 (s, IH), 2.08-2.12 (m, 2H), 1.61-1.82 (m, 8H), 1.26-1.30 (m, IH); ¹³C NMR (75 MHz, CDCl₃) δ 151.3, 138.7, 133.5, 128.4, 122.7, 118.1, 107.4, 76.3, 69.6, 39.6, 25.1, 23.2; HRMS (EI+) calcd. for C₁₄H₁₄NO₃Cl (M+H) 364.0740, found 364.0748.

Example 6

This example provides detail concerning the synthesis of Acetylene 2f (Schemes 1-3): To a stirred solution of 1 (2.05 g, 11.3 mmol) and THF (56.5 mL) was added LDA (11.3 mL, 11.3 mmol, 1.0 M in THF / Hexanes) at -78°C. After 10 min, the solution was transferred via cannulation into a stirred solution of benzophenone (3.09 g, 16.9 mmol) in THF (16.9 mL) at -78°C. After 30 min, the dark brown solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (100 mL), diluted with EtOAc (100 mL), and washed with H₂O (100 mL) and sat. aq. NaCl (100 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 25-75% CH₂Cl₂ / Hexanes to give 2f (3.16 g, 8.69 mmol, 77%) as a white crystalline solid. Mp 134-35°C; IR (neat) 3524, 3077, 2220, 1531 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.97 (dd, J = 8.2, 1.4 Hz, IH), 7.75-7.77 (m, 4H), 7.73 (dd, J = 8.2, 1.0 Hz, IH), 7.39-7.44 (m, 5H), 7.29-7.35 (m, 2H), 3.11 (s, IH); ¹³C NMR (100 MHz, CDCl₃) δ 151.0, 144.1, 139.1, 133.8, 128.9, 128.5, 128.0, 126.2, 122.9, 117.8, 105.7, 79.3, 75.3; HRMS (EI+) calcd. for C₂₁H₁₄NO₃Cl (M+H) 364.0740, found 364.0748.
Example 7

This example provides detail concerning the synthesis of Acetylene 2g (Schemes 1-3): To a stirred solution of 1 (57.2 mg, 0.315 mmol) and THF (1.58 mL) was added LDA (0.315 mL, 0.315 mmol, 1.0 M in THF / Hexanes) at -78°C. After 5 min, 4,4'-dimethylbenzophenone (199 mg, 0.945 mmol) was added. After 30 min at -78°C, the dark brown solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to give 2g (95.7 mg, 0.244 mmol, 78%) as a yellow oil. IR (neat) 3528, 2919, 2216, 1531 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.97 (dd, J = 8.3, 1.2 Hz, IH), 7.72 (dd, J = 8.1, 1.2 Hz, IH), 7.58-7.62 (m, 4H), 7.41 (t, J = 8.2 Hz, IH), 7.17-7.28 (m, 4H), 2.92 (s, IH), 2.36 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 151.0, 141.4, 139.0, 137.9, 133.7, 129.1, 128.7, 126.1, 122.9, 117.9, 106.1, 78.9, 75.0, 21.1; HRMS (ES⁺) calcd. for C₂₃H₁₈NO₃NaCl (M+Na) 414.0873, found 414.0869.

Example 8

This example provides detail concerning the synthesis of Acetylene 2h (Schemes 1-3): To a stirred solution of 1 (54.0 mg, 0.297 mmol) and THF (1.49 mL) was added LDA (0.297 mL, 0.297 mmol, 1.0 M in THF / Hexanes) at -78°C. After 5 min, 4,4'-dichlorobenzophenone (224 mg, 0.892 mmol)
was added. After 30 min at -78°C, the dark brown solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. \( \text{NH}_4\text{Cl} \) (15 mL), diluted with EtOAc (15 mL), and washed with \( \text{H}_2\text{O} \) (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO\(_4\)) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to give 2h (88.0 mg, 0.203 mmol, 69%) as a yellow oil. IR (neat) 3544, 2322, 1531, 1488 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.79 (dd, \( J = 8.2, 1.0\) Hz, IH), 7.75 (dd, \( J = 8.1, 1.1\) Hz, IH), 7.62-7.66 (m, 4H), 7.46 (t, \( J = 8.2\) Hz, IH), 7.34-7.38 (m, 4H), 3.27 (s, IH); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 150.9, 142.3, 139.1, 134.2, 133.9, 129.2, 128.7, 127.6, 123.1, 117.4, 104.3, 79.8, 74.4; HRMS (ES+) calcd. for \( \text{C}_{21}\text{H}_{12}\text{NO}_3\text{NaCl}_3 \) (M+Na) 453.9780, found 453.9766.

**Example 9**

\[
\begin{array}{c}
\text{Cl} & \text{Cl} & \text{NO}_2 \\
\text{1} & \rightarrow & \text{Cl} & \text{NO}_2 \\
& & \text{OH} & \\
& & \text{2} & \\
\end{array}
\]

This example provides detail concerning the synthesis of Acetylene 2i (Schemes 1-3): To a stirred solution of 1 (50.9 mg, 0.280 mmol) and THF (1.40 mL) was added LDA (0.280 mL, 0.280 mmol, 1.0 M in THF / Hexanes) at -78°C. After 5 min, 9-fluorenone (152 mg, 0.841 mmol) was added. After 30 min at -78°C, the dark brown solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. \( \text{NH}_4\text{Cl} \) (15 mL), diluted with EtOAc (15 mL), and washed with \( \text{H}_2\text{O} \) (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO\(_4\)) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-40% EtOAc / Hexanes to give 2i (78.2 mg, 0.216 mmol, 77%) as a yellow solid. Mp 52-53°C; IR (neat) 3516, 3061, 2224, 1529 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.85-7.90 (m, 3H), 7.63-7.67 (m, 3H), 7.39-7.47 (m, 4H), 7.34 (t, \( J = 8.2\) Hz, IH), 3.01 (s, IH); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 151.2, 146.1, 139.4, 139.3, 133.7, 130.0, 128.9, 128.7, 124.8, 122.8, 120.4, 117.7, 103.0, 75.3, 75.0; HRMS (ES+) calcd. for \( \text{C}_{21}\text{H}_{12}\text{NO}_3\text{NaCl}_3 \) (M+Na) 384.0403, found 384.0370.

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**Example 10**

![Diagram](image)

This example provides detail concerning the synthesis of Acetylene 17 (entry G, Schemes 2, TMS derivative): To a stirred solution of 2f (97.0 mg, 0.267 mmol) in DMF (0.27 mL) was added imidazole (54.5 mg, 0.801 mmol) and TMSCl (144 mg, 0.170 mL, 1.33 mmol) at r.t. After 2 h, the reaction was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL) and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20-50% CH₂Cl₂ / Hexanes to give recovered 2f (28.0 mg, 0.0769 mmol) and 17 (76.2 mg, 0.175 mmol, 65% / 88% borsm) as an oil. IR (neat) 2963, 2220, 1534, 1450 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.94 (dd, J = 8.2, 1.1 Hz, 1H), 7.72 (dd, J = 8.1, 1.1 Hz, IH), 7.66-7.71 (m, 4H), 7.44 (t, J = 8.2 Hz, IH), 7.34-7.38 (m, 4H), 7.25-7.31 (m, 2H), 0.15 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 151.4, 145.7, 139.3, 133.6, 128.8, 128.0, 127.5, 126.5, 122.7, 117.8, 105.8, 79.9, 76.5, 1.55; HRMS (CI⁺) calcd. for C₂₄H₂₂NO₃ClSi (M+H) 435.1058, found 435.1056.

**Example 11**

![Diagram](image)

This example provides detail concerning the synthesis of biaryl 4a (Table 2): To a pressure vessel containing 2a (32.5 mg, 0.136 mmol) and xylenes (0.27 mL) was added diene 3 (44.8 mg, 48.2 µL, 0.417 mmol) at r.t. The mixture was heated at 145°C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10-30% EtOAc / Hexanes to give 4a (35.3 mg, 0.1 10 mmol, 80%) as a yellow crystalline solid. Mp 139-40°C; IR (neat) 3561, 2923, 1529, 1425...
\( ^1H \) NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.85 (dd, \( J = 8.2, 1.2 \) Hz, IH), 7.68 (dd, \( J = 8.1, 1.3 \) Hz, IH), 7.39 (t, \( J = 8.1 \) Hz, IH), 7.38 (t, \( J = 8.1 \) Hz, IH), 7.02 (dd, \( J = 7.9, 0.9 \) Hz, IH), 6.87 (dd, \( J = 7.8, 0.8 \) Hz, IH), 3.67 (s, 3H), 1.67 (s, IH), 1.60 (s, 3H), 1.49 (s, 3H); \( ^{13}C \) NMR (75 MHz, CDCl\(_3\)) \( \delta \) 156.7, 150.4, 147.5, 136.1, 134.9, 133.1, 129.5, 127.8, 121.9, 121.2, 119.2, 109.1, 74.3, 56.2, 32.6, 31.4; HRMS (ES+) calcd. for \( C_{16}H_{16}NO_4NaCl \) (M+Na) 344.0666, found 344.0681.

**Example 12**

This example provides detail concerning the synthesis of biaryl 4b (Table 2): To a pressure vessel containing 2b (80.1 mg, 0.299 mmol) and xylenes (0.60 mL) was added diene 3 (98.9 mg, 106 \( \mu \)L, 0.897 mmol) at r.t. The mixture was heated at 145\( ^\circ \)C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 4b (60.1 mg, 0.172 mmol, 58\%) as a yellow crystalline solid. Mp 92-93\( ^\circ \)C; IR (neat) 3471, 2976, 1527, 1462 cm\(^{-1}\); \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.89 (dd, \( J = 8.2, 1.2 \) Hz, IH), 7.68 (dd, \( J = 8.0, 1.2 \) Hz, IH), 7.39 (t, \( J = 8.1 \) Hz, 2H), 6.88-6.92 (m, 2H), 3.71 (s, 3H), 1.91-2.00 (m, IH), 1.64-1.86 (m, 4H), 0.82 (t, \( J = 7.4 \) Hz, 6H); \( ^{13}C \) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 157.4, 150.4, 144.3, 135.9, 135.4, 133.2, 128.9, 127.6, 122.9, 122.2, 120.3, 108.9, 79.2, 56.2, 34.6, 33.6, 8.54, 7.56; HRMS (EI+) calcd. for \( C_{18}H_{20}NO_4Cl \) (M+H) 349.1081, found 349.1085.

**Example 13**

This example provides detail concerning the synthesis of biaryl 4c (Table 2): To a pressure vessel containing 2c (76.9 mg, 0.306 mmol) and xylenes (0.61 mL) was added diene 3 (98.9 mg, 106 \( \mu \)L, 0.897 mmol) at r.t. The mixture was heated at 145\( ^\circ \)C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 4c (60.1 mg, 0.172 mmol, 58\%) as a yellow crystalline solid. Mp 92-93\( ^\circ \)C; IR (neat) 3471, 2976, 1527, 1462 cm\(^{-1}\); \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.89 (dd, \( J = 8.2, 1.2 \) Hz, IH), 7.68 (dd, \( J = 8.0, 1.2 \) Hz, IH), 7.39 (t, \( J = 8.1 \) Hz, 2H), 6.88-6.92 (m, 2H), 3.71 (s, 3H), 1.91-2.00 (m, IH), 1.64-1.86 (m, 4H), 0.82 (t, \( J = 7.4 \) Hz, 6H); \( ^{13}C \) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 157.4, 150.4, 144.3, 135.9, 135.4, 133.2, 128.9, 127.6, 122.9, 122.2, 120.3, 108.9, 79.2, 56.2, 34.6, 33.6, 8.54, 7.56; HRMS (EI+) calcd. for \( C_{18}H_{20}NO_4Cl \) (M+H) 349.1081, found 349.1085.
mL) was added diene 3 (101 mg, 109 µL, 0.917 mmol) at r.t. The mixture was heated at 145°C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes to give 4c (68.6 mg, 0.205 mmol, 67%) as a yellow crystalline solid. Mp 116-170°C; IR (neat) 3420, 2935, 1530, 1470 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.05 (dd, J = 8.3, 1.2 Hz, IH), 7.72 (dd, J = 8.2, 1.2 Hz, IH), 7.48 (t, J = 8.0 Hz, IH), 7.44 (t, J = 8.0 Hz, IH), 6.98-7.01 (m, 2H), 3.78 (s, 3H), 2.59-2.67 (m, 1H), 2.23-2.30 (m, 1H), 2.07-2.18 (m, 1H), 1.92-1.99 (m, 2H), 1.63-1.71 (m, IH), 1.29-1.37 (m, IH); ¹³C NMR (100 MHz, CDCl₃) δ 157.2, 150.9, 143.2, 137.2, 133.5, 132.5, 129.8, 128.8, 122.9, 118.1, 110.3, 78.8, 56.2, 35.1, 34.4, 15.7; HRMS (EI+) calcd. for C₁₇H₁₆NO₄Cl (M+H) 333.0768, found 333.0774.

Example 14

This example provides detail concerning the synthesis of biaryl 4d (Table 2): To a pressure vessel containing 2d (48.0 mg, 0.181 mmol) and xylenes (0.36 mL) was added diene 3 (59.7 mg, 64.2 µL, 0.542 mmol) at r.t. The mixture was heated at 145°C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10-30% EtOAc / Hexanes to give 4d (34.5 mg, 0.0992 mmol, 55%) as a yellow crystalline solid. Mp 105-06°C; IR (neat) 3567, 2955, 1528, 1466 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.97 (dd, J = 8.2, 1.2 Hz, IH), 7.71 (dd, J = 8.0, 1.2 Hz, IH), 7.45 (t, J = 8.1 Hz, IH), 7.41 (t, J = 8.1 Hz, IH), 7.14 (dd, J = 8.1, 0.8 Hz, IH), 6.96 (dd, J = 8.2, 0.8 Hz, IH), 3.74 (s, 3H), 2.12-2.19 (m, IH), 1.62-1.90 (m, 7H), 1.47-1.53 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 157.1, 150.7, 144.5, 137.1, 134.3, 133.3, 129.5, 128.3, 123.3, 122.4, 118.9, 109.9, 84.1, 56.2, 41.7, 38.9, 23.5, 23.1; HRMS (EI+) calcd. for C₁₈H₁₈NO₄Cl (M+H) 347.0924, found 347.0934.
Example 15

This example provides detail concerning the synthesis of biaryl 4e (Table 2): To a pressure vessel containing 2e (77.2 mg, 0.276 mmol) and xylenes (0.55 mL) was added diene 3 (91.2 mg, 98.1 μL, 0.828 mmol) at r.t. The mixture was heated at 145°C for 18 h. The crude material was purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 4e (61.8 mg, 0.171 mmol, 62%) as a yellow oil. IR (neat) 3577, 2934, 1526, 1462 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.84 (dd, J = 8.1, 1.2 Hz, IH), 7.68 (dd, J = 8.1, 1.2 Hz, IH), 7.41 (t, J = 8.1 Hz, IH), 7.40 (t, J = 8.1 Hz, IH), 7.07 (dd, J = 8.1, 0.8 Hz, IH), 6.86 (dd, J = 8.2, 0.8 Hz, IH), 3.67 (s, 3H), 1.95-2.02 (m, 2H), 1.82-1.85 (m, IH), 1.67-1.75 (m, 2H), 1.51-1.63 (m, 4H), 1.40 (s, IH), 1.24-1.29 (m, IH); ¹³C NMR (100 MHz, CDCl₃) δ 156.6, 150.2, 148.4, 135.9, 135.5, 133.1, 129.4, 127.6, 121.8, 121.4, 119.3, 109.0, 75.6, 56.2, 39.2, 38.2, 25.5, 21.9, 21.8; HRMS (EI+) calcd. for C₁₉H₂₀NO₄Cl (M+H) 361.1081, found 361.1065.

Example 16

This example provides detail concerning the synthesis of Biaryl 4f: To a pressure vessel containing 2e (3.16 g, 8.69 mmol) and xylenes (17.4 mL) was added diene 3 (2.87 g, 3.01 mL, 26.1 mmol) at r.t. The mixture was heated at 145°C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10-40% CH₂Cl₂ / Hexanes to give 4f (2.78 g, 6.23 mmol, 72%) as a yellow crystalline solid. Mp 152-53°C; IR (neat) 3552, 3053, 1528, 1355 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.90 (dd, J = 8.2, 1.2 Hz, IH), 7.44 (dd, J = 8.0, 1.2 Hz, IH), 7.31-7.35 (m, 5H), 7.23-7.29 (m, 3H), 7.13-7.18 (m, 4H), 6.99 (d, J = 7.9 Hz, IH), 6.63 (dd, J = 8.0, 0.6 Hz, IH), 3.74 (s, 3H), 2.65 (s, IH); ¹³C NMR (100 MHz, CDCl₃) δ 157.6, 150.6, 147.0, 144.4, 144.3, 136.9, 133.8, 133.0, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 127.4, 127.0, 124.4, 123.4, 122.0, 109.9, 82.9, 56.3; HRMS (Cl+) calcd. for C₂₆H₂₀NO₄Cl (M+H) 445.1081, found 445.1078.
Example 17

This example provides detail concerning the synthesis of Biaryl 4g: To a pressure vessel containing 2 g (86.3 mg, 0.220 mmol) and xylenes (0.44 mL) was added diene 3 (72.8 mg, 78.3 μL, 0.661 mmol) at r.t. The mixture was heated at 145°C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 4g (82.2 mg, 0.174 mmol, 79%) as a yellow oil. IR (neat) 3556, 2923, 1529, 1460 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.87 (dd, J = 8.2, 1.3 Hz, IH), 7.43 (dd, J = 8.2, 1.3 Hz, IH), 7.32 (t, J = 8.0 Hz, IH), 7.28 (t, J = 8.1 Hz, IH), 6.98-7.10 (m, 8H), 6.96 (dd, J = 8.3, 0.9 Hz, IH), 6.63 (dd, J = 8.0, 0.9 Hz, IH), 3.72 (s, 3H), 2.52 (s, IH), 2.36 (s, 3H), 2.34 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 157.6, 150.5, 144.7, 144.3, 141.9, 137.2, 136.9, 136.5, 134.0, 132.9, 128.7, 128.3, 128.2, 127.9, 127.6, 127.3, 124.3, 123.4, 121.9, 109.8, 82.8, 56.3, 21.1; HRMS (EI+) calcd. for C₂₆H₂₄NO₄Cl (M+H) 473.1394, found 473.1398.

Example 18

This example provides detail concerning the synthesis of Biaryl 4h: To a pressure vessel containing 2h (63.1 mg, 0.146 mmol) and xylenes (0.29 mL) was added diene 3 (48.2 mg, 51.9 μL, 0.438 mmol) at r.t. The mixture was heated at 145°C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 4h (50.6 mg, 0.0982 mmol, 67%) as a yellow oil. IR (neat) 3565, 2947, 1528, 1488 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.88 (dd, J = 8.1, 1.2 Hz, IH), 7.45 (dd, J = 8.0, 1.2 Hz, IH), 7.19-7.37 (m, 6H), 7.06-7.10 (m, 4H), 6.99 (dd, J = 8.1, 0.7 Hz, IH), 6.59 (dd, J = 8.0, 0.8 Hz, IH), 3.72 (s, 3H), 2.78 (s, IH); ¹³C NMR (100 MHz, CDCl₃) δ 157.6, 150.5, 145.3, 143.7, 142.4, 136.7, 133.8, 133.4, 133.2, 133.1, 129.3, 128.7, 128.6, 128.3, 128.0, 127.9, 124.2, 123.0, 122.1, 110.4, 82.3, 56.3; HRMS (EI+) calcd. for C₂₆H₂₄NO₄Cl₃
Example 19

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\text{Example 19}
\]

This example provides detail concerning the synthesis of Biaryl 4i: To a pressure vessel containing 2i (72.6 mg, 0.201 mmol) and xylenes (0.40 mL) was added diene 3 (66.3 mg, 7.14 µL, 0.603 mmol) at r.t. The mixture was heated at 145°C for 36 h. The crude material was purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 4i (61.0 mg, 0.137 mmol, 68%) as a yellow crystalline solid. Mp 173-74°C; IR (neat) 3532, 2939, 1525, 1465 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.72 (dd, \(J = 8.3, 0.9\) Hz, 1H), 7.70 (bs, 1H), 7.51 (t, \(J = 8.1\) Hz, 1H), 7.33-7.37 (m, 2H), 7.26-7.31 (m, 2H), 7.19-7.24 (m, 5H), 7.09 (t, \(J = 8.2\) Hz, 1H), 6.99 (d, \(J = 8.3\) Hz, 1H), 3.67 (s, 3H), 2.17 (s, 1H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.1, 149.3, 149.1, 148.6, 139.4, 139.2, 139.0, 137.2, 133.3, 132.8, 129.3, 129.28, 128.9, 128.86, 128.3, 127.8, 125.3, 124.9, 123.0, 122.7, 120.1, 120.01, 119.5, 109.9, 83.3, 56.1; HRMS (EI+) calcd. for C\(_{26}\)H\(_{18}\)NO\(_4\)Cl (M+H) 443.0924, found 443.0940.

Example 20

This example provides detail concerning the synthesis of Biaryl 7: To a pressure vessel containing 2f (31.8 mg, 0.0874 mmol) and xylenes (0.18 mL) was added crude diene 6 (221 mg, 0.874 mmol) at r.t. The mixture was heated at 145°C for 24 h and purified by chromatography over silica gel, eluting with 10% EtOAc /
Hexanes to give 7 (22.0 mg, 0.0463 mmol, 53%) as a bright yellow oil. IR (neat)
3566, 2919, 1594, 1528, 1352 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.91 (dd, J = 8.0,
1.6 Hz, IH), 7.39 (dd, J = 7.9, 1.1 Hz, IH), 7.15-7.31 (m, HH), 6.73 (d, J = 2.1 Hz,
IH), 6.22 (d, J = 1.8 Hz, IH), 2.80 (s, IH), 2.39 (s, 6H), 0.93 (s, 9H), 0.059 (s, 3H),
0.057 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 155.1, 154.5, 151.1, 148.2, 145.2,
143.8, 137.6, 135.9, 133.3, 130.1, 128.6, 128.3, 128.0, 127.9, 127.5, 126.9, 125.1,
122.0, 112.2, 112.7, 83.2, 44.8, 25.7, 18.1, -4.4, -4.5; HRMS (ES⁺) calcd. for
C₃₃H₃₈N₂O₄SiCl (M+H) 589.2289, found 589.2297.

Example 21

This example provides detail concerning the synthesis of Biaryl 9: To a
pressure vessel containing 2f (34.1 mg, 0.0937 mmol) and xylenes (0.19 mL) was
added diene 8 (74.4 mg, 0.375 mmol) at r.t. The mixture was heated at 145°C for 24
h. To the mixture was added MeOH (0.47 mL) and K₂CO₃ (54.8 mg, 0.937 mmol).
After 30 min, the dark brown solution was quenched with sat. aq. NH₄Cl (15 mL),
diluted with EtOAc (15 mL) and washed with H₂O (15 mL) and sat. aq. NaCl (15
mL). The dried extract (MgSO₄) was purified by chromatography over silica gel,
eluting with 15-25% EtOAc / Hexanes to give 9 (40.9 mg, 0.0885 mmol, 95%) as a
bright yellow oil. IR (neat) 3468, 3061, 2943, 1599, 1526 cm⁻¹; ¹H NMR (300
MHz, CDCl₃) δ 7.83 (dd, J = 8.0, 1.3 Hz, IH), 7.40 (dd, J = 8.0, 1.3 Hz, IH), 7.20-
7.31 (m, 7H), 7.10-7.16 (m, 4H), 6.49 (d, J = 2.3 Hz, IH), 6.04 (d, J = 2.3 Hz, IH),
4.78 (s, IH), 3.69 (s, 3H), 2.68 (s, IH); ¹³C NMR (75 MHz, CDCl₃) δ 158.9, 155.6,
151.0, 146.7, 145.5, 144.1, 137.6, 133.5, 132.9, 128.1, 127.9, 127.7, 127.67, 127.65,
127.4, 127.1, 121.9, 116.8, 110.3, 98.4, 82.9, 56.3; HRMS (EI⁺) calcd. for
C₂₆H₂₀NO₃Cl (M+H) 461.1030, found 461.1042.
Example 22

This example provides detail concerning the synthesis of Biaryl 11: To a pressure vessel containing 2f (33.7 mg, 0.0926 mmol) and xylenes (0.19 mL) was added diene 10 (102 mg, 0.371 mmol) at r.t. The mixture was heated at 145°C for 24 h. To the mixture was added MeOH (0.46 mL) and K₂CO₃ (102 mg, 0.926 mmol). After 30 min, the dark brown solution was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (15 mL) and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was purified by chromatography over silica gel, eluting with 30% EtOAc / Hexanes to give 11 (36.0 mg, 0.0669 mmol, 72%) as a bright yellow oil. IR (neat) 3569, 2923, 2318, 1594, 1525 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.85 (dd, J = 8.1, 1.3 Hz, IH), 7.43 (dd, J = 8.0, 1.3 Hz, IH), 7.22-7.32 (m, 10H), 7.15-7.19 (m, 4H), 7.07-7.10 (m, 2H), 6.51 (d, J = 2.3 Hz, IH), 6.08 (d, J = 2.3 Hz, IH), 5.00 (s, 2H), 4.77 (s, IH), 2.75 (s, IH); ¹³C NMR (75 MHz, CDCl₃) δ 157.9, 155.4, 150.9, 146.7, 145.6, 144.1, 137.6, 136.9, 133.7, 132.9, 128.3, 128.1, 127.9, 127.72, 127.70, 127.68, 127.5, 127.4, 127.1, 126.2, 121.9, 117.1, 110.5, 99.7, 82.9, 70.4; HRMS (EI+) calcd. for C₃₂H₂₄NO₅Cl (M+H) 461.1030, found 461.1022.

Example 23

This example provides detail concerning the synthesis of Anilino Alcohol 12: To a stirred solution of 4f (2.78 g, 6.23 mmol) and glacial acetic acid (62.4 mL) was added Zn dust (2.04 g, 31.2 mmol) at r.t. After 2 h, the mixture was quenched with sat. aq. NaHCO₃ (250 mL), diluted with EtOAc (200 mL), and washed with NaHCO₃ (200 mL), H₂O (200 mL) and sat. aq. NaCl (200 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50-80% CH₂Cl₂ / Hexanes to give 12 (2.45 g, 5.86 mmol, 94%) as a white crystalline solid. Mp 110-111°C; IR (neat) 3528, 3333, 2825, 1623, 1572 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.16-7.31 (m, HH), 6.99 (t, J = 8.0 Hz, IH), 6.98
Example 24

This example provides detail concerning the synthesis of Anilino alcohol
15-(aR): To a pressure vessel was added 14-(aR) (878 mg, 1.47 mmol), KOH (825 mg, 14.7 mmol), H-BuOH (2.94 mL) and triethylene glycol (2.0 mL). The solution was heated at 115°C for 5 h, then quenched with 1 M HCl (30 mL), diluted with EtOAc (30 mL) and washed with H₂O (30 mL), and sat. aq. NaCl (30 mL). The dried extract (MgSO₄) was purified by silica gel chromatography, eluting with 20% EtOAc / Hexanes to yield 15-(aR) (479 mg, 1.15 mmol, 79%) as a white crystalline solid. Mp 110-11°C; [α]D²⁻³ = -78.1° (c=1.34, CHCl₃); IR (neat) 3528, 3333, 2825, 1623, 1572 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.16-7.31 (m, 1H), 6.99 (t, J = 8.0 Hz, IH), 6.98 (dd, J = 8.3, 1.0 Hz, IH), 6.73 (dd, J = 7.9, 1.0 Hz, IH), 6.66 (dd, J = 8.0, 1.0 Hz, IH), 6.54 (dd, J = 8.0, 1.1Hz, IH), 4.59 (bs, IH), 3.73 (s, 3H), 3.17 (bs, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 158.3, 147.1, 146.9, 146.3, 145.1, 135.8, 129.2, 128.7, 127.83, 127.6, 127.5, 126.9, 126.8, 124.1, 123.3, 123.1, 120.0, 114.2, 110.6, 82.9, 56.4; HRMS (Cl⁺) calcd. for C₂₆H₂₂NO₂Cl (M+H) 415.1339, found 415.1359.
Example 25

This example provides details concerning the synthesis of Dibenzopyran 16: To a pressure vessel was added the 14-(aS) (617 mg, 1.03 mmol), KOH (580 mg, 10.3 mmol), and n-BuOH (2.06 mL). The mixture was heated at 115°C for 22 h then quenched with 1 M HCl (30 mL), diluted with EtOAc (30 mL) and washed with H2O (30 mL) and sat. aq. NaCl (30 mL). The dried extract (MgSO4) was purified by silica gel chromatography, eluting with 20% EtOAc / Hexanes. The material was recrystallized from hot EtOAc / Hexanes to yield 16 (359 mg, 0.948 mmol, 92%) as a white crystalline solid. Mp 138-140°C; IR (neat) 3439, 3353, 3057, 1631, 1562, 1449 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.23-7.31 (m, 10H), 7.25 (t, J = 8.0 Hz, 1H), 7.10 (dd, J = 7.8, 1.2 Hz, 1H), 7.00 (t, J = 8.0 Hz, 1H), 6.61 (dd, J = 8.0, 1.0 Hz, 1H), 6.49 (dd, J = 7.6, 0.7 Hz, 1H), 6.30 (dd, J = 8.0, 1.0 Hz, 1H), 4.45 (bs, 2H), 3.97 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 155.2, 154.5, 145.2, 143.3, 143.2, 129.1, 129.0, 127.7, 127.65, 127.0, 121.5, 119.9, 112.5, 111.5, 110.5, 108.8, 87.4, 56.5; HRMS (CI⁺) calcd. for C₂₆H₂₁NO₂ (M+H) 379.1572, found 379.1576.

Example 26

This example provides details concerning the synthesis of Anilino Alcohol 15-(aS): To a stirred solution of 14-(aS) (205 mg, 0.343 mmol), dihydro-2H-pyran (288 mg, 3.11 µL, 3.43 mmol), and CH₂Cl₂ (1.14 mL) was added /Moulenesulfonic acid (6.5 mg, 0.343 mmol) at r.t. After 2h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL) and washed with H₂O (15 mL), and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was purified by column
chromatography in 10% EtOAc / Hexanes to give the DHP-protected product (212 mg, 0.311 mmol) which was taken directly on to the next step. To a pressure vessel was added the DHP-protected compound (212 mg, 0.311 mmol), KOH (576 mg, 10.3 mmol), n-BuOH (1.40 mL) and EtOH (2.1 mL). The mixture was heated at 140°C for 24 h. To this mixture was then added 1 M HCl (100 mL) and CH₂Cl₂ (20 mL) at r.t. After 3 h, the mixture was extracted with CH₂Cl₂ (2 x 100 mL), washed with H₂O (100 mL) and sat. aq. NaCl (100 mL). The dried extract (MgSO₄) was purified by silica gel chromatography, eluting with 20-50% EtOAc / Hexanes to yield 15-(a5) (80.7 mg, 0.194 mmol, 56% over 3 steps). Mp 110-111°C; [α]D₂ = -77.6° (c=2.08, CHCl₃); IR (neat) 3569, 3414, 2954, 1727, 1575 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.16-7.31 (m, 1H), 6.66 (dd, J = 8.0. 1.0 Hz, 1H), 6.54 (dd, J = 8.0, 1.1Hz, 1H), 4.59 (bs, 1H), 3.73 (s, 3H), 3.17 (bs, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 158.3, 147.1, 146.9, 146.3, 145.1, 135.8, 129.2, 128.7, 127.83, 127.81, 127.6, 127.5, 126.9, 126.8, 124.1, 123.3, 123.1, 120.0, 114.2, 110.6, 82.9, 56.4; HRMS (Cl+) calcd. for C₂₆H₂₂NO₂Cl (M+H) 415.1339, found 415.1359.

Example 27

This example provides details concerning the synthesis of Carbamate 14-(aR): To a stirred solution of 15-(aR) (32.2 mg, 0.0776 mmol), DMAP (0.95 mg, 0.00776 mmol) and pyridine (0.39 mL) was slowly added (-)-menthyl chloroformate (84.8 mg, 82.2 μL, 0.388 mmol) at 0°C. After 1 h, the mixture was quenched with NH₄Cl (15 mL), diluted with Et₂O (15 mL) and washed with NH₄Cl (15 mL), H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was purified by chromatography over silica gel, eluting with 50-75% CH₂Cl₂ / Hexanes to give 14-(aR) as a single diastereomer (36.9 mg, 0.0618 mmol, 86%). Mp 162-163°C; [α]D²⁺ = -77.6° (c=2.08, CHCl₃); IR (neat) 3569, 3414, 2954, 1727, 1575 cm⁻¹; ¹H
NMR (400 MHz, CDCl$_3$) δ 7.86 (d, $J = 7.7$ Hz, IH), 7.35 (t, $J = 8.1$ Hz, IH), 7.18-7.33 (m, 1H), 7.08 (d, $J = 7.9$ Hz, IH), 6.99 (d, $J = 7.7$ Hz, IH), 6.66 (d, $J = 7.9$ Hz, IH), 5.79 (s, IH), 4.54 (td, $J = 10.9$, 4.4 Hz, IH), 3.67 (s, 3H), 2.70 (s, IH), 2.03 (d, $J = 11.7$ Hz, IH), 1.65-1.72 (m, 3H), 1.27 (t, $J = 12.0$ Hz, IH), 0.97 (d, $J = 6.5$ Hz, 3H), 0.85 (d, $J = 7.0$ Hz, 3H), 0.81-1.10 (m, 3H), 0.74 (d, $J = 7.0$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 158.0, 153.1, 146.8, 146.1, 145.9, 138.0, 134.8, 128.9, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 126.9, 123.9, 123.5, 122.6, 117.9, 110.4, 83.5, 74.8, 56.2, 41.5, 34.3, 21.4, 26.7, 24.1, 22.1, 20.5, 17.40; HRMS (EI+) calcd. for C$_{37}$H$_{40}$NO$_4$Cl (M+H)$^+$ 597.2646, found 597.2642.

**Example 28**

![Chemical structure](image)

**Carbamate 14-(aS):** To a stirred solution of 15-(aS) (13.6 mg, 0.0328 mmol), DMAP (0.40 mg, 0.00328 mmol) and pyridine (0.16 mL) was slowly added (-)-menthyl chloroformate (35.8 mg, 34.8 μL, 0.164 mmol) at 0°C. After 1 h, the mixture was quenched with NH$_2$Cl (15 mL), diluted with Et$_2$O (15 mL) and washed with NH$_2$Cl (15 mL), H$_2$O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO$_4$) was purified by chromatography over silica gel, eluting with 50-75% CH$_2$Cl$_2$/Hexanes to give 14-(aS) as a single diastereomer (16.3 mg, 0.0273 mmol, 83%). Mp 88-90°C; [α]D$^{23}$ = +18.8° (c=2.14, CHCl$_3$); IR (neat) 3556, 3415, 2955, 1727, 1575 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.94 (bs, IH), 7.36 (t, $J = 8.1$ Hz, IH), 7.19-7.34 (m, HH), 7.05 (dd, $J = 7.9$, 0.7 Hz, IH), 7.01 (d, $J = 8.1$ Hz, IH), 6.68 (d, $J = 8.0$ Hz, IH), 6.01 (s, IH), 4.61 (td, $J = 10.9$, 4.3 Hz, IH), 3.70 (s, 3H), 2.73 (s, IH), 1.97-2.06 (m, 3H), 1.73 (d, $J = 11.7$ Hz, 2H), 1.49-1.54 (m, IH), 1.33-1.41 (m, IH)$_3$ LOI (d, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 6.4$ Hz, 3H), 0.88-1.16 (m, 2H), 0.85 (d, $J = 7.0$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 158.2, 153.2, 146.8, 146.4, 145.7, 138.3, 134.8, 128.9, 128.8, 128.1, 127.9, 127.8, 127.7, 127.4, 127.3, 126.8, 123.9, 123.4, 122.8, 117.7, 110.6, 83.5, 75.1, 56.3, 47.1, 41.1, 34.3, 31.4, 25.9, 23.2.
22.1, 21.1, 16.3; HRMS (EI+) calcd. for C_{37}H_{40}NO_4Cl (M+H) 597.2646, found 597.2651.

Example 29

This example describes the synthesis of Biaryl **14, Scheme 8.** To a pressure vessel containing 7 (2.24 g, 5.11 mmol) and PhMe (10.2 mL) was added 8 (4.14 g, 20.4 mmol) at rt. The mixture was heated at 80°C. After 18 h, the reaction was cooled to 0°C and Et_3N (2.59 g, 3.58 mL, 25.6 mmol) was slowly added. After stirring the orange solution for 6 h, the mixture was quenched with sat. aq. NH_4Cl (70 mL), diluted with EtOAc (70 mL), washed with H_2O (70 mL) and sat. aq. NaCl (70 mL). The dried extract (MgSO_4) was concentrated *in vacuo*. The crude product 12 was dissolved in DMF (25.6 mL) and cooled to 0°C. To this solution was added BnBr (17.5 g, 102 mmol, 11.8 mL) and NaH (1.02 g, 25.6 mmol, 60\% in mineral oil). After 8 h, the mixture was quenched with sat. aq. NH_4Cl (100 mL), diluted with EtOAc (100 mL), washed with H_2O (100 mL) and sat. aq. NaCl (100 mL). The dried extract (MgSO_4) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 50\% EtOAc / Hexanes to give 14 (2.26 g, 3.62 mmol, 70\%) as a bright yellow crystalline solid. MP 202-203°C; IR (neat) 2930, 1597, 1524, 1302; 1H NMR (400 MHz, CDCl_3) δ 8.09 (dd, J = 8.2, 1.2 Hz, IH), 7.87 (dd, J = 8.0, 1.2 Hz, IH), 7.33 (t, J = 8.6 Hz, IH), 7.25-7.31 (m, 3H), 7.18-7.19 (m, 2H), 6.75 (d, J = 2.1 Hz, IH), 6.51 (dd, J = 11.5, 2.2 Hz, IH), 5.10 (s, 2H), 3.87 (s, 3H), 1.20-1.96 (m, 22H); 13C NMR (100 MHz, CDCl_3) D 159.9 (d, J_{c-p}= 16 Hz, 1C), 158.2 (d, J_{c,p}= 14 Hz, 1C), 150.7, 136.7, 136.5, 134.1 (d, J_{c,p}= 1.9 Hz, 1C), 130.6, 129.8, 128.6, 128.4, 127.7, 127.6, 126.4, 125.8, 123.2, 107.6 (d, J_{c,p}= 12 Hz, 1C), 101.5 (d, J_{c,p}= 1.7 Hz, 1C), 70.6, 55.5, 38.2, 37.6 (d, J_{c,p}= 3.9 Hz, 1C), 36.9, 26.8 (d, J_{c,p}= 8.5 Hz, 1C), 26.7 (d, J_{c,p}= 8.9 Hz, 1C), 26.6 (d, J_{c,p}= 2.0 Hz, 1C), 26.5 (d, J_{c,p}= 3.3 Hz, 1C), 26.4 (d, J_{c,p}= 3.3 Hz, 1C), 25.9 (d, J_{c,p}= 1.4 Hz, 1C), 25.7 (d, J_{c,p}= 2.1 Hz, 1C), 25.0 (d, J_{c,p}= 3.3 Hz, 1C), 24.7 (d, J_{c,p}= 3.6 Hz, 1C); HRMS (FAB+) calcd. for C_{52}H_{38}NO_5PBr (M+H) 626.1671, found 626.1653.
Example 30

This example describes the synthesis of Acetylene 2a: To a stirred solution of 1 (456 mg, 2.50 mmol) in THF (12.5 mL) was added LDA (2.45 mL, 2.50 mmol, 1.02 M in THF) at -78°C. After 10 min, ClP(O)Ph₂ (473 mg, 380 µL, 2.00 mmol) was added. After 1h the solution was allowed to warm to rt then quenched with sat. aq. NH₄Cl (25 mL), diluted with CH₂Cl₂ (25 mL), and washed with H₂O (25 mL) and sat. aq. NaCl (25 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 0-30% EtOAc / CH₂Cl₂ to give 2a (720 mg, 1.88 mmol, 96%) as a yellow solid. MP 132-33°C; IR (neat) 2181. 1532 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.05 (d, J = 8.3 Hz, 1H), 7.95-8.01 (m, 4H), 7.77 (d, J = 8.1 Hz, IH), 7.51-7.59 (m, 7H); ¹³C NMR (100 MHz, CDCl₃) δ 151.5, 140.8 (d, Jc-p = 2.3 Hz, 1C), 134.8, 133.2, 133.0 (d, Jc-p = 2.9 Hz, 1C), 132.0, 131.6, 131.5, 131.3, 129.3, 129.1, 123.7, 116.2 (d, Jc-p = 4.3 Hz, 1C), 96.8 (d, Jc-p = 65 Hz, 1C), 95.6 (d, Jc-p = 8.5 Hz, 1C); HRMS (Cl⁺) calcd. for C₂₀H₁₄N₂O₃PCI (M+H) 382.0400, found 382.0427.

Example 31

This example describes the synthesis of Acetylene 2b: To a stirred solution of diisopropylamine (25.7 mg, 36.0 µL, 0.254 mmol) and THF (0.30 mL) was added «-BuLi (0.104 mL, 0.254 mmol, 2.45 M in hexane) at -78°C. After 30 min, the solution of 1 (46.3 mg, 0.254 mmol) in THF (0.50 mL) was added via cannula at -78°C. After an additional 30 min, the dark brown mixture was cannulated into a solution OfClP(O)(OEt)₂ (35.8 mg, 28.9 µL, 0.203 mmol) in THF (0.50 mL). After 30 min, the solution was allowed to warm to rt then quenched with sat. aq. NH₄Cl...
(10 mL), diluted with CH₂Cl₂ (15 mL), and washed with H₂O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 0-2% MeOH / CH₂Cl₂ to give 2b (62.0 mg, 0.194 mmol, 95%) as a yellow oil. IR (neat) 2192, 1536 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.04 (dd, J = 8.3, 1.4 Hz, IH), 7.77 (dd, J = 8.2, 1.2, IH), 7.55 (t, J = 8.2, IH), 4.29 (dq, J = 14.1, 7.9 Hz, IH), 1.43 (td, J = 7.1, 0.8, IH); ¹³C NMR (100 MHz, CDCl₃) δ 151.9, 140.5, 134.7, 131.2, 123.7, 116.0, 92.3 (d, Jₜ₋ₚ = 280 Hz, 1C), 89.6 (d, Jₜ₋ₚ = 50 Hz, 1C), 64.2 (d, Jₜ₋ₚ = 5.0 Hz, 4C), 16.5 (d, Jₜ₋ₚ = 7.0 Hz, 6C); HRMS (ES⁺) calcd. for C₁₂H₁₄NO₅PCl (M+H) 480.0768, found 480.0763.

Example 32

This example describes the synthesis of Biaryl 5a: To a pressure vessel containing 2a (720 mg, 1.88 mmol) and PhMe (3.76 mL) was added diene 3 (1.52 g, 7.52 mmol). The solution was stirred for 18 h at 100°C before TBAF (9.40 mL, 9.40 mmol, 1.0 M in THF) was added at 0°C. After 15 min, the dark brown solution was quenched with sat. aq. NH₄Cl (25 mL), diluted with CH₂Cl₂ (25 mL), and washed with H₂O (25 mL) and sat. aq. NaCl (25 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 0-50% EtOAc / CH₂Cl₂ to give 5a (763 mg, 1.50 mmol, 84%) as a yellow solid. MP > 250°C; IR (neat) 3102, 1600, 1531 cm⁻¹; ¹H NMR (300 MHz, 𝛾-DMSO) δ 10.0 (s, IH), 7.98 (dd, J = 7.9, 1.4 Hz, IH), 7.39-7.57 (m, 12H), 6.69 (d, J = 2.4, IH), 6.16 (dd, J = 14.8, 2.3 Hz, IH), 3.65 (s, 3H); ¹³C NMR (75 MHz, cf-DMSO) δ 159.9 (d, Jₜ₋ₚ = 30 Hz, 1C), 157.6 (d, Jₜ₋ₚ = 20 Hz, 1C), 151.2, 137.6, 134.2, 131.7-133.4 (m, 4C), 130.2, 129.3 (d, Jₜ₋ₚ = 10 Hz, 1C), 129.1 (d, Jₜ₋ₚ = 10 Hz, 1C), 123.5, 120.5 (d, Jₜ₋ₚ = 10 Hz, 1C), 111.2 (d, Jₜ₋ₚ = 10 Hz, 1C), 104.3, 55.8; HRMS (FAB⁺) calcd. for C₂₅H₂₀NO₅PCl (M+H) 480.0768, found 480.0763.
This example describes the synthesis of Biaryl 5b: To a pressure vessel containing 2b (70.6 mg, 0.221 mmol) and PhMe (0.44 mL) was added diene 3, before TBAF (1.0 mL, 1.0 mmol, 1.0 M in THF) was added at 0°C. After 20 min, the dark brown solution was quenched with sat. aq. NH₄Cl (20 mL), diluted with EtOAc (20 mL), and washed with H₂O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 100% CH₂Cl₂ to give 5b (55.0 mg, 0.133 mmol, 60%) as a yellow solid. MP > 250°C; IR (neat) 3135, 1599, 1532, 1320 cm⁻¹; ¹H NMR (400 MHz, /DMSO)  D 10.1 (s, 1H), 8.11 (dd, J = 8.3, 1.0 Hz, 1H), 7.91 (dd, J = 8.1, 1.0 Hz, 1H), 7.64 (t, J = 8.1 Hz, 1H), 6.86 (dd, J = 15.7, 2.5 Hz, 1H), 6.76 (d, J = 2.5 Hz, 1H), 3.82 (s, 3H), 3.76 (m, 4H), 1.06 (td, J = 16.8, 4 Hz, 6H), ¹³C NMR (100 MHz, /DMSO)  D 160.5 (d, J = 20 Hz, 1C), 157.5 (d, J = 20 Hz, 1C), 150.9, 138.0, 134.7, 132.4 (d, J = 10 Hz, 1C), 130.5, 129.6, 1278, 118.7 (d, J = 10 Hz, 1C), 109.1 (d, J = 8.0 Hz, 1C), 105.6, 65.44, 62.5 (d, J = 20 Hz, 1C), 62.4 (d, J = 20 Hz, 1C), 56.1, 16.7 (d, J = 30 Hz, 1C), 16.6 (d, J = 30 Hz, 1C); HRMS (ES+) calcd. for C₁₇H₂₀N₂O₇PCl (M+H) 416.0666, found 416.0678.

This example describes the synthesis of Biaryl 6: To a stirred solution of 5a (324 mg, 0.674 mmol) and DMF (3.4 mL) was added BnBr (1.15 g, 0.770 mL, 6.74 mmol), and NaH (55.9 mg, 1.35 mmol) at rt. After 1 h, the mixture was quenched...
with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (10 mL), washed with H₂O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO₄) was concentrated \textit{in vacuo} and purified by chromatography over silica gel, eluting with 70% EtOAc / Hexanes to give 6 (382 mg, 0.671 mmol, 98%) as a bright yellow crystalline solid.

MP 189-190°C; IR (neat) 3060, 2224, 1595 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.98 (dd, J = 8.2, 1.3 Hz, IH), 7.21-7.63 (m, 15H), 7.09-7.13 (m, 2H), 6.70 (d, J = 2.2, IH), 6.44 (dd, J = 14.4, 2.3 Hz, IH), 5.03 (s, 2H), 3.65 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 188.6, 148.4, 138.6, 132.9, 132.4, 123.4, 121.9.

HRMS (FAB+) calcd. for C₃₂H₂₆NO₅P(147.1215) [M+H]+ found 147.1215.

**Example 35**

This example describes the synthesis of Aldehyde 10: To a stirred solution of 9 (4.94 g, 22.3 mmol) and DMF (22.3 mL) was added DMF/DMA (8.18 g, 9.59 mL, 68.6 mmol). After heating at 135°C for 16 h, the dark red solution was cooled to 0°C and added to a rapidly stirred solution OfNaIO₄ (14.7 g, 68.6 mmol) in H₂O (46 mL) and DMF (23 mL) at 0°C. The reaction flask was washed with DMF (23 mL) at 0°C and added to NaIO₄ mixture. The reaction was stirred at 0°C for 4 h then allowed to warm to rt. After an additional 18 h, the orange solution was filtered over a pad of celite® and rinsed with EtOAc (200 mL) to remove precipitate. The filtrate was then washed with H₂O (3 x 150 mL) and sat. aq. NaCl (3 x 150 mL). The dried extract (MgSO₄) was concentrated \textit{in vacuo} and purified by chromatography over silica gel, eluting with 40% EtOAc / Hexanes to give the known aldehyde 10 (3.44 g, 14.8 mmol, 67%). ¹H NMR (400 MHz, CDCl₃) δ 10.3 (s, IH), 8.04 (dd, J = 1.0, 8.2 Hz, IH), 7.95 (dd, J = 1.0, 8.0 Hz, IH), 7.55 (t, J = 8.0 Hz, IH); ¹³C NMR (100 MHz, CDCl₃) δ 188.6, 148.4, 138.6, 132.9, 132.4, 123.4, 121.9.
Example 36

This example describes the synthesis of Acetylene 12: To a stirred solution of 10 (5.48 g, 23.6 mmol), K$_2$CO$_3$ (6.52 g, 47.2 mmol), and MeOH (236 mL) was added diazophosphonate reagent 11 (5.44 g, 28.3 mmol) at r.t. After 2 h, the solution was diluted with EtOAc (100 mL) and washed with sat. aq. NaHCO$_3$ (100 mL), H$_2$O (100 mL) and sat. aq. NaCl (100 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% CH$_2$Cl$_2$/Hexanes to give 12 (4.53 g, 20.0 mmol, 85%) as a pale yellow solid.

Example 37

This example describes the synthesis of Acetylene 13a: To a stirred solution of 12 (214 mg, 0.947 mmol) and THF (4.7 mL) was added LDA$_{\text{LDA Error! Bookmark not defined.}}$ (0.92 g mL$^{-1}$, 0.947 mmol, 1.02 M in THF / Hexanes) at -78°C. After 10 min, CIP(O)(Ph)$_2$ (179 mg, 145 mL, 0.758 mmol) was added to the dark brown mixture. After 30 min, the solution was allowed to warm to it. After an additional 30 min, the mixture was quenched with sat. aq. NH$_4$Cl (10 mL), diluted with EtOAc (10 mL), and washed with H$_2$O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 0-30% EtOAc / CH$_2$Cl$_2$ to give 13a (256 mg, 0.600 mmol, 80%) as a white solid. MP 120-121°C; IR (neat) 3060, 2180, 1530 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.11 (dd, $J = 8.3$, 1.1 Hz, IH), 7.97-8.03 (m, 5H), 7.53-7.63 (m, 6H), 7.49
(t, J = 8.2 Hz, IH); 13C NMR (100 MHz, CDCl 3 ) δ 151.4, 137.6, 132.5 (d, J c-P = 3.0 Hz, 1C), 131.6, 131.2 (d, Jc-P= 9.2 Hz, 1C), 131.0, 129.7 (d, J c-P = 2.4 Hz, 1C), 128.8 (d, Jc,P = 12.7 Hz, 1C), 123.8, 117.8 (d, J c-P = 3.7 Hz, 1C), 96.8 (d, J c-P = 89.2 Hz, 1C), 94.4 (d, Jc,P = 147 Hz, 1C); HRMS (FAB+) calcd. for C 20 H 14 NO 3 PBr (M+H) 425.9895, found 425.9901.

Example 38

This example describes the synthesis of Acetylene 13b: To a stirred solution of 12 (300 mg, 1.33 mmol) and THF (6.65 mL) was added LDA (1.25 mL, 1.33 mmol, 1.06 M in THF / Hexanes) at -78°C. After 10 min, ClP(O)(OEt) 2 (184 mg, 1.54 mL, 1.06 mmol) was added to the dark brown mixture. After 30 min, the solution was allowed to warm to rt. After an additional 30 min, the mixture was quenched with sat. aq. NH 4 Cl (30 mL), diluted with EtOAc (30 mL), and washed with H 2 O (30 mL) and sat. aq. NaCl (30 mL). The dried extract (MgSO 4 ) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 13b (369 mg, 1.02 mmol, 96%) as a brown oil. IR (neat) 2986, 2192, 1533 cm⁻¹; 1H NMR (400 MHz, CDCl 3 ) δ 8.09 (dd, J = 8.3, 1.1 Hz, 1H), 7.98 (dd, J = 8.1, 1.1 Hz, 1H), 7.50 (t, J = 8.2 Hz, 1H), 4.28-4.35 (m, 4H), 1.45 (t, J = 7.0 Hz, 3H); 13C NMR (100 MHz, CDCl 3 ) δ 151.5, 137.6, 131.5, 128.9 (d, J c-P = 3.1 Hz, 1C), 123.8, 117.0 (d, Jc-P = 6.1 Hz, 1C), 91.7 (d, J c-P = 140 Hz, 1C), 90.0 (d, Jc,P = 197 Hz, 1C), 63.8 (d, J c-P = 5.4 Hz, 4C), 16.1 (d, J c-P = 7.0 Hz, 6C); HRMS (FAB+) calcd. for C 20 H 14 NO 3 PBr (M+H) 361.9793, found 361.9799.
Example 39

This example describes the synthesis of Acetylene 13c: To a stirred solution of 12 (2.27 g, 10.0 mmol) and THF (40.2 mL) was added LDA (10.0 mL, 10.0 mmol, 1.0 M in THF / Hexanes) at -78°C. After 10 min, CIP(O)(C₆H₄)₂ (2.00 g, 8.03 mmol) in THF (10 mL) was added to the dark brown mixture. After 30 min, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (75 mL), diluted with EtOAc (50 mL), and washed with H₂O (75 mL) and sat. aq. NaCl (75 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 60-80% EtOAc / Hexanes to give 13c (3.15 g, 7.19 mmol, 90%) as a white solid. MP 193-193.5°C; IR (neat) 2928, 2181, 1531 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (dd, J = 8.2, 1.1 Hz, IH), 7.97 (dd, J = 8.2, 1.1 Hz, IH), 7.46 (t, J = 8.2 Hz, IH), 1.93-2.13 (m, 10H), 1.64-1.79 (m, 6H), 1.29-1.38 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 151.7, 137.3, 130.7, 129.3, 123.6, 118.0, 95.9, 94.4 (t, Jc-P = 20.3 Hz, 1C), 37.3, 36.5, 26.3 (d, Jc-P = 5.0 Hz, 1C), 26.1 (d, Jc-P = 4.6 Hz, 1C), 25.8, 25.5 (d, Jc-P = 2.5 Hz, 1C), 24.6 (d, Jc-P = 2.5 Hz, 1C); HRMS (FAB+) calcd. for C₂₀H₂₆NO₅PBr (M+H) 438.0834, found 438.0819.

Example 40

This example describes the synthesis of Phenol 54a: To a pressure vessel containing 13a (121 mg, 0.283 mmol) and PhMe (0.57 mL) was added diene 3 (230 mg, 1.14 mmol) at rt. The mixture was heated at 80°C. After 20 h, the reaction was cooled to 0°C and Et₃N (143 mg, 0.20 mL, 1.42 mmol) was slowly added. After stirring the orange solution 1.5 h, the mixture was quenched with sat. aq. NH₄Cl (10...
mL), diluted with EtOAc (10 mL), and washed with H₂O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO₄) was concentrated in vacuo. Due to solubility problems, the crude product 54a was used without further purification. MP > 225°C; IR (KBr) 3370, 1524, 13 16, 1140 cm⁻¹; ¹H NMR (300 MHz, d₆-DMSO) δ 9.98 (s, 1H), 8.00 (dd, J = 8.2, 0.7 Hz, 1H), 7.71 (dd, J = 8.2, 0.8 Hz, 1H), 7.35-7.49 (m, 1H), 6.67 (d, Jc-P = 2.4 Hz, 1H), 6.16 (dd, J = 14.7, 2.4 Hz, 1H), 3.65 (s, 3H); ¹³C NMR (75 MHz, d₆-DMSO) δ 159.5 (d, Jc-P = 18 Hz, 1C), 157.2 (d, Jc-P = 15 Hz, 1C), 150.7, 136.9, 133.0, 132.2, 131.9, 130.9, 130.0, 128.9 (t, Jc-P = 12 Hz, 1C), 128.5, 123.6, 110.6, 103.9, 55.5; HRMS (FAB+) calcd. for C₂₅H₂₀NO₃PBr (M+H) 524.0262, found 524.0272.

**Example 41**

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\[ \begin{align*}
\text{54a} & \quad \text{54a} \\
\text{Br} & \quad \text{Br} \\
\text{NO₂} & \quad \text{NO₂} \\
\text{O}_\text{Me} & \quad \text{O}_\text{Me} \\
\text{P(O)Ph₂} & \quad \text{P(O)Ph₂}
\end{align*} \]
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This example describes the synthesis of **Bromide 14a**: The crude product 54a (0.283 mmol) was dissolved in DMF (1.42 mL) and cooled to 0°C. To this solution was added BnBr (968 mg, 0.65 mL, 5.66 mmol) and NaH (56.8 g, 1.42 mmol, 60% in mineral oil). After 1.5 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 14a (112 mg, 0.182 mmol, 65% over 2 steps) as a bright yellow crystalline solid. MP 174-176°C; IR (neat) 3057, 1595 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.05 (dd, J = 8.2, 1.2 Hz, 1H), 7.70 (dd, J = 8.0, 1.2 Hz, 1H), 7.59-7.66 (m, 4H), 7.49-7.53 (m, 2H), 7.39-7.44 (m, 4H), 7.25-7.30 (m, 4H), 7.15-7.17 (m, 2H), 6.74 (d, J = 2.4 Hz, 1H), 6.48 (dd, J = 14, 2.3 Hz, 1H), 5.07 (s, 2H), 3.69 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.8 (d, Jc-P = 18 Hz, 1C), 157.6 (d, Jc-P = 16 Hz, 1C), 150.5, 136.5 (d, Jc-P = 3.6 Hz, 1C), 133.06 (t, Jc-P = 4.6 Hz, 1C), 132.8, 132.0 (d, Jc-P = 1.4 Hz, 1C), 132.0 (t, Jc-P = 1.5 Hz, 1C), 131.8 (t, Jc-P = 2.6 Hz, 1C), 131.6 (d, Jc-P = 2.5 Hz, 1C), 131.0, 129.1, 128.5, 128.4 (d, Jc-P = 6.7 Hz, 1C), 128.2 (d, Jc-P = 2.2... - 124 -
Hz, 1C), 126.5, 124.7 (d, Jc-P= 6.9 Hz, 1C), 123.3, 110.7 (d, Jc-P= 13 Hz, 1C), 102.6 (d, Jc-P = 2.2 Hz, 1C), 70.6, 55.3; HRMS (Cl+) calcd. for C_{38}H_{31}NO_3PBr (M+H) 612.19398, found 612.19190.

Example 42

This example describes the synthesis of Bromide 14b: To a pressure vessel containing 13b (60.0 mg, 0.166 mmol) and PhMe (0.33 mL) was added diene 3 (134 mg, 0.663 mmol) at rt. The mixture was heated at 80°C. After 20 h, the reaction was cooled to 0°C and Et_3N (83.9 mg, 116 µL, 0.830 mmol) was slowly added. After stirring the orange solution 1.5 h, the mixture was quenched with sat. aq. NH_4Cl (15 mL), diluted with EtOAc (15 mL), and washed with H_2O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO_4) was concentrated in vacuo to give crude 54b, which was used without further purification.

The crude product 54b was dissolved in DMF (0.83 mL) and cooled to 0°C. To this solution was added BnBr (568 mg, 3.32 mmol) and NaH (32.3 g, 0.830 mmol, 60% in mineral oil). After 1.5 h, the mixture was quenched with sat. aq. NH_4Cl (15 mL), diluted with EtOAc (15 mL), and washed with H_2O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO_4) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 14b (58.0 mg, 0.105 mmol, 64% over 2 steps) as a bright yellow crystalline solid. MP 111-1 13°C; IR (neat) 3468, 2981, 1596, 1528 cm\(^{-1}\); 1H NMR (400 MHz, CDCl_3) \(\delta\) 8.14 (dd, J = 8.2, 1.2 Hz, IH), 7.94 (dd, J = 8.0, 1.2 Hz, IH), 7.41 (t, J = 8.1 Hz, IH), 7.18-7.32 (m, 6H), 6.79 (d, J = 2.4 Hz, IH), 5.09 (s, 2H), 3.88-3.98 (m, 7H), 1.22 (t, J = 7.1 Hz, 3H), 1.15 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) \(\delta\) 160.5 (d, Jc-P = 21 Hz, 1C), 157.4 (d, Jc-P = 22 Hz, 1C), 150.3, 136.7, 136.5, 133.8 (d, Jc-P = 4.5 Hz, 1C), 129.2, 128.9, 128.7, 128.4, 127.7, 126.8, 126.5, 123.4, 122.9 (d, Jc-P = 8.1 Hz, 1C), 109.2 (d, Jc-P = 11 Hz, 1C), 104.2 (d, Jc-P = 2.5 Hz, 1C), 70.6, 62.3 (d, Jc-P = 5.7 Hz, 1C), 62.2 (d, Jc-P = 5.8 Hz, 1C), 55.6, 16.2 (d, Jc-P = 5.5 Hz,
1C), 16.0 (d, J_{C-P} = 6.7 Hz, 1C); HRMS (FAB+) calcd. for C_{24}H_{26}NO_{7}PBr (M+H) 550.0630, found 550.0633.

Example 43

This example describes the synthesis of Phenol 11: To a pressure vessel containing 7 (2.24 g, 5.11 mmol) and PhMe (10.2 mL) was added the diene 3 (4.14 g, 20.4 mmol) at rt. The mixture was heated at 80°C. After 18 h, the reaction was cooled to 0°C and Et_{3}N (2.59 g, 3.58 mL, 25.6 mmol) was slowly added. After stirring the orange solution 6 h, the mixture was quenched with sat. aq. NH_{4}Cl (70 mL), diluted with EtOAc (70 mL), and washed with H_{2}O (70 mL) and sat. aq. NaCl (70 mL). The dried extract (MgSO_{4}) was concentrated in vacuo. Due to solubility problems, the crude product 11 was used without further purification. MP > 225°C; IR (KBr) 2930, 1524, 1313 cm^{-1}; ^{1}H NMR (300 MHz, d_{6}-DMSO) δ 9.85 (s, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.1 Hz, 1H), 6.66 (d, J = 2.1 Hz, 1H), 6.45 (dd, J = 11.5, 2.2 Hz, 1H), 3.79 (s, 3H), 2.49-2.51 (m, 2H), 1.91-1.98 (m, 10H), 1.03-1.24 (m, 10H); ^{13}C NMR (75 MHz, d_{6}-DMSO) δ 159.7 (d, J_{C-P} = 15.9 Hz, 1C), 157.4 (d, J_{C-P} = 13 Hz, 1C), 150.9, 136.9, 134.7, 130.9, 129.8, 129.2, 127.8, 123.4, 122.9, 107.3 (d, J_{C-P} = 12 Hz, 1C), 103.3, 55.6, 37.5 (d, J_{C-P} = 66 Hz, 1C), 36.4 (d, J_{C-P} = 66 Hz, 1C), 26.7 (d, J_{C-P} = 0.9 Hz, 1C), 26.6, 26.4 (d, J_{C-P} = 3.6 Hz, 1C), 26.33 (d, J_{C-P} = 2.4 Hz, 1C), 26.3, 26.2, 26.1, 25.6 (d, J_{C-P} = 2.5 Hz, 1C), 25.1 (d, J_{C-P} = 2.5 Hz, 1C), 25.0 (d, J_{C-P} = 2.7 Hz, 1C), HRMS (FAB+) calcd. for C_{25}H_{32}NO_{5}PBr (M+H) 536.1201, found 536.1 192.
Example 44

This example describes the synthesis of Bromide 14c: The crude product 54c (5.11 mmol) was dissolved in DMF (25.6 mL) and cooled to 0°C. To this solution was added BnBr (17.5 g, 11.8 mL, 102 mmol) and NaH (1.02 g, 25.6 mmol, 60% in mineral oil). After 8 h, the mixture was quenched with sat. aq. NH₄Cl (100 mL), diluted with EtOAc (100 mL), and washed with H₂O (100 mL) and sat. aq. NaCl (100 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 14c (2.26 g, 1.41 mmol, 70% over 2 steps) as a bright yellow crystalline solid. MP 202-203°C; IR (neat) 2930, 1597, 1524, 1302 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (dd, J = 8.2, 1.2 Hz, 1H), 7.87 (dd, J = 8.0, 1.2 Hz, 1H), 7.33 (t, J = 8.6 Hz, 1H), 7.25-7.31 (m, 3H), 7.18-7.19 (m, 2H), 6.75 (d, J = 2.1 Hz, 1H), 6.51 (dd, J = 11.5, 2.2 Hz, 1H), 5.10 (s, 2H), 3.87 (s, 3H), 1.81-1.96 (m, 12H), 1.20-1.39 (m, 10H); ¹³C NMR (100 MHz, CDCl₃) δ 159.9 (d, J c-P = 16 Hz, 1C), 158.2 (d, J c-P = 14 Hz, 1C), 150.7, 136.7, 136.5, 134.1 (d, J c-P = 1.9 Hz, 1C), 130.6, 129.8, 128.6, 128.4, 127.7, 127.6, 126.4, 125.8, 123.2, 107.6 (d, J c-P = 12 Hz, 1C), 101.5 (d, J c-P = 1.7 Hz, 1C), 70.6, 55.5, 37.9 (d, J c-P = 66 Hz, 1C), 3.72 (d, J c-P = 66 Hz, 1C), 26.4-26.9 (m, 6C), 25.9 (d, J c-P = 1.4 Hz, 1C), 25.7 (d, J c-P = 2.1 Hz, 1C), 25.0 (d, J c-P = 3.3 Hz, 1C), 24.7 (d, J c-P = 3.6 Hz, 1C); HRMS (FAB+) calcd. for C₃₂H₃₈NO₅PBr (M+H) 626.1671, found 626.1653.

Example 45
This example describes the synthesis of Biaryl 16a: To a pressure vessel containing \(13a\) (61.8 mg, 0.145 mmol) and PhMe (0.29 mL) was added diene 15 (124 mg, 0.580 mmol) at rt. The mixture was heated at 120°C. After 16 h, the reaction was cooled to 0°C and TBAF (0.725 mmol, 0.725 mL, 1.0 M in THF) was slowly added. After stirring the solution for 20 min, the mixture was quenched with \(\text{H}_2\text{O} \ (10 \ \text{mL})\), diluted with \(\text{CH}_2\text{Cl}_2 \ (10 \ \text{mL})\), washed with \(\text{NaHCO}_3 \ (10 \ \text{mL})\) and sat. aq. \(\text{NaCl} \ (10 \ \text{mL})\). The dried extract (\(\text{MgSO}_4\)) was concentrated in vacuo. The crude product 17 was dissolved in DMF (0.29 mL) and cooled to 0°C. To this solution was added BnBr (496 mg, 0.330 mL, 2.90 mmol) and NaH (58.0 mg, 1.45 mmol, 60% in mineral oil). After 3 h, the mixture was quenched with sat. aq. \(\text{NH}_4\text{Cl} \ (15 \ \text{mL})\), diluted with \(\text{Et}_2\text{O} \ (15 \ \text{mL})\), washed with \(\text{H}_2\text{O} \ (3 \times 15 \ \text{mL})\) and sat. aq. \(\text{NaCl} \ (15 \ \text{mL})\). The dried extract (\(\text{MgSO}_4\)) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-50% \(\text{EtOAc} / \text{Hexanes}\) to give \(16a\) (58.3 mg, 0.0997 mmol, 69% over 2 steps) as a bright yellow crystalline solid. MP 127-129°C; IR (neat) 3049, 1596, 1525, 1436, 1349 cm\(^{-1}\); \(^1\)H NMR (300 MHz, \(\text{CDCl}_3\)) \(\delta\) 8.02 (dd, \(J = 8.2, 1.1 \ \text{Hz}, \ \text{IH}\)), 7.71 (dd, \(J = 8.1, 1.1 \ \text{Hz}, \ \text{IH}\)), 7.46-7.59 (m, 6H), 7.16-7.43 (m, 12H), 6.92 (dd, \(J = 14.5, 2.4 \ \text{Hz}, \ \text{IH}\)), 5.00 (s, 2H); \(^{13}\)C NMR (100 MHz, \(\text{CDCl}_3\)) \(\delta\) 157.5 (d, \(J_{c-p} = 16 \ \text{Hz}, \ \text{1C}\)), 150.0, 136.6, 136.2 (d, \(J_{c-p} = 3.4 \ \text{Hz}, \ \text{1C}\)), 136.0, 134.6 (d, \(J_{c-p} = 5.6 \ \text{Hz}, \ \text{1C}\)), 133.1 (d, \(J_{c-p} = 20 \ \text{Hz}, \ \text{1C}\)), 132.5 (d, \(J_{c-p} = 11 \ \text{Hz}, \ \text{1C}\)), 132.1 (d, \(J_{c-p} = 2.2 \ \text{Hz}, \ \text{1C}\)), 131.9 (d, \(J_{c-p} = 1.9 \ \text{Hz}, \ \text{1C}\)), 131.8 (d, \(J_{c-p} = 2.9 \ \text{Hz}, \ \text{1C}\)), 131.7 (d, \(J_{c-p} = 2.7 \ \text{Hz}, \ \text{1C}\)), 131.63 (d, \(J_{c-p} = 1.3 \ \text{Hz}, \ \text{1C}\)), 131.6, 130.5, 129.2, 128.7, 128.4 (d, \(J_{c-p} = 9.8 \ \text{Hz}, \ \text{1C}\)), 128.3, 128.2 (d, \(J_{c-p} = 9.8 \ \text{Hz}, \ \text{1C}\)), 127.7, 127.5 (d, \(J_{c-p} = 1.0 \ \text{Hz}, \ \text{1C}\)), 123.2, 120.0 (d, \(J_{c-p} = 13 \ \text{Hz}, \ \text{1C}\)), 117.8 (d, \(J_{c-p} = 2.6 \ \text{Hz}, \ \text{1C}\)), 70.4; HRMS (Cl+) calcd. for \(\text{C}_{31}\text{H}_{24}\text{NO}_4\text{PBr} \ (\text{M}+\text{H})\) 584.0626, found 584.0655.
Example 46

This example describes the synthesis of Biaryl 16b: To a pressure vessel containing 5 (111 mg, 0.307 mmol) and PhMe (0.62 mL) was added diene 15 (263 mg, 1.22 mmol) at rt. The mixture was heated at 120°C. After 16 h, the reaction was cooled to 0°C diluted with THF (0.62 mL). Next a solution of TBAF (1.54 mmol, 1.54 mL, 1.0 M in THF) was slowly added. After stirring the solution for 20 min, the mixture was quenched with H₂O (10 mL), diluted with CH₂Cl₂ (10 mL), washed with NaHCO₃ (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO₄) was concentrated in vacuo. The crude product 16 was dissolved in DMF (0.62 mL) and cooled to 0°C. To this solution was added BnBr (1.05 g, 0.707 mL, 6.14 mmol) and NaH (103 mg, 3.07 mmol, 60% in mineral oil). After 3 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with Et₂O (15 mL), washed with H₂O (3 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-40% EtOAc / Hexanes to give 16b (97.3 mg, 0.187 mmol, 61% over 2 steps) as a bright yellow crystalline solid. MP 104-105°C; IR (neat) 1598, 1528, 1348, 1247 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.12 (dd, J = 7.8, 0.52 Hz, IH), 7.95 (dd, J = 8.0, 1.1 Hz, IH), 7.65 (dd, J = 15.8, 2.7 Hz, IH), 7.37-7.52 (m, 6H), 7.29 (dd, J = 8.5, 2.7 Hz, IH), 7.22 (dd, J = 8.5, 3.2 Hz, IH), 5.19 (s, 2H), 3.86-4.00 (m, 6H), 1.23 (t, J = 7.0 Hz, 3H), 1.16 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 158.2 (d, Jc,P = 18 Hz, 1C), 149.9, 136.9, 136.6, 136.3, 132.9 (d, Jc,P = 7.0 Hz, 1C), 132.1 (d, Jc,P = 16 Hz, 1C), 129.4, 128.7, 128.2, 128.0, 127.7, 126.8, 123.3, 119.1, 119.0, 70.4, 62.3 (d, Jc,P = 5.0 Hz, 1C), 62.2 (d, Jc,P = 6.0 Hz, 1C), 16.2 (d, Jc,P = 10 Hz, 1C), 16.1 (d, Jc,P = 11 Hz, 1C); HRMS (FAB+) calcd. for C₂₃H₂₄NO₆PBr (M+H) 520.0525, found 520.0538.
Example 47

This example describes the synthesis of Biaryl 16c: To a pressure vessel containing 13c (95.2 mg, 0.217 mmol) and PhMe (0.44 mL) was added diene 15 (186 mg, 0.869 mmol) at rt. The mixture was heated at 120°C. After 16 h, the reaction was cooled to 0°C and TBAF (1.09 mmol, 1.09 mL, 1.0 M in THF) was slowly added. After stirring the solution for 20 min, the mixture was quenched with H₂O (15 mL), diluted with CH₂Cl₂ (15 mL), washed with NaHCO₃ (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo. The crude product 18 was dissolved in DMF (0.44 mL) and cooled to 0°C. To this solution was added BnBr (743 mg, 5.00 mL, 4.34 mmol) and NaH (87.0 mg, 2.17 mmol, 60% in mineral oil). After 3 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with Et₂O (15 mL), washed with H₂O (3 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-50% EtOAc / Hexanes to give 16c (86.0 mg, 0.144 mmol, 67% over 2 steps) as a bright yellow crystalline solid. MP 121-122°C; IR (neat) 2930, 2852, 1598, 1526, 1350 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (dd, J = 8.2, 1.2 Hz, IH), 7.87 (dd, J = 8.0, 1.2 Hz, IH), 7.39-7.53 (m, 5H), 7.34 (t, J = 8.0 Hz, IH), 7.28-7.29 (m, 3H), 6.90 (d, J = 1.4 Hz, IH), 5.18 (s, 2H), 1.57-1.91 (m, 12H), 1.14-1.38 (m, 10H); ¹³C NMR (100 MHz, CDCl₃) δ 157.6 (d, Jc-p = 13 Hz, 1C), 150.6, 136.9 (d, Jc-p = 3.0 Hz, 1C), 136.8, 135.6 (d, Jc-p = 3.0 Hz, 1C), 134.0 (d, Jc-p = 10 Hz, 1C), 130.0, 129.3, 128.8 (d, Jc-p = 6.0 Hz, 1C), 128.4, 127.7, 126.7, 123.0, 117.1 (d, Jc-p = 12.1 Hz, 1C), 116.7 (d, Jc-p = 2.2 Hz, 1C), 70.6, 37.9 (d, Jc-p = 65 Hz, 1C), 36.7 (d, Jc-p = 67 Hz, 1C), 26.4-26.8 (m, 7C), 25.9 (d, Jc-p = 2.0 Hz, 1C), 25.7 (d, Jc-p = 2.0 Hz, 1C), 25.3 (d, Jc-p = 3.1 Hz, 1C), 24.8 (d, Jc-p = 3.0 Hz, 1C), 24.7 (d, Jc-p = 3.1 Hz, 1C); HRMS (FAB+) calcd. for C₃₁H₃₆NO₄PBr (M+H) 596.1565, found 596.1593.
Example 48

![Chemical structure](image)

This example describes the synthesis of **Biaryl 18a**: To a pressure vessel containing 13a (88.2 mg, 0.207 mmol) was added diene 17 (45.6 mg, 0.0760 mL, 0.414 mmol) at rt. The mixture was heated at 155°C. After 24 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 18a (69.1 mg, 0.136 mmol, 66%) as a bright yellow crystalline solid. MP 203-205°C; IR (neat) 1634, 1525 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.09 (dd, \(J = 8.3, 1.2\) Hz, 1H), 7.69 (dd, \(J = 8.0, 1.2\) Hz, 1H), 7.57-7.63 (m, 4H), 7.48-7.53 (m, 2H), 7.37-7.44 (m, 5H), 7.30 (dd, \(J = 11, 8.2\) Hz, IH), 6.94 (ddd, \(J = 8.6, 7.7, 0.96\) Hz, IH), 3.77 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.3 (d, \(J_{c-P} = 13.1\) Hz, 1C), 150.0, 136.7, 133.2 (d, \(J_{c-P} = 22\) Hz, 1C), 132.9 (d, \(J_{c-P} = 21\) Hz, 1C), 132.2, 132.1 (d, \(J_{c-P} = 2.0\) Hz, 1C), 131.9 (d, \(J_{c-P} = 2.1\) Hz, 1C), 131.8, 131.7 (d, \(J_{c-P} = 2.5\) Hz, 1C), 131.6 (d, \(J_{c-P} = 2.5\) Hz, 1C), 131.2, 130.3, 129.2, 129.1, 128.9, 128.4, 128.3, 128.1, 127.6, 125.6 (d, \(J_{c-P} = 12\) Hz, 1C), 123.4, 114.3 (d, \(J_{c-P} = 2.4\) Hz, 1C), 56.2; HRMS (CI+) calcd. for C\(_{25}\)H\(_{20}\)NO\(_4\)PBr (M+H) 508.0313, found 508.0296.

Example 49

![Chemical structure](image)

This example describes the synthesis of **Biaryl 18b**: To a pressure vessel containing 13b (145 mg, 0.400 mmol) was added diene 17 (110 mg, 0.146 mL, 0.800 mmol) at rt. The mixture was heated at 155°C. After 24 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 18b (126 mg, 0.284 mmol, 71%) as a bright yellow crystalline solid. MP 138-139°C; IR (neat) 1644, 1528, 1349 cm\(^{-1}\); \(^1\)H NMR (400 MHz,
CDCl₃ δ 8.16 (dd, J = 8.3, 1.2 Hz, IH), 7.93 (dd, J = 8.0, 1.2 Hz, IH), 7.64 (ddd, J = 8.7, 7.7, 1.0 Hz, IH), 7.53 (td, J = 13, 7.9, 4.7 Hz, IH), 7.42 (t, J = 8.0 Hz, IH), 7.22 (d, J = 8.3 Hz, IH), 3.80-4. (m, 6H), 3.73 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H). **1.14** (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.0 (d, J=cm= 19 Hz, 1C), 149.8, 136.9, 133.8 (d, J=cm= 5.0 Hz, 1C), 130.0, 129.5 (d, J=cm= 17 Hz, 1C), 129.3, 128.1 (d, J=cm= 8.1 Hz, 1C), 126.3, 125.5 (d, J=cm= 8.9 Hz, 1C), 123.5, 115.0 (d, J=cm= 2.8 Hz, 1C), 62.2 (d, J=cm= 5.0 Hz, 1C), 62.0 (d, J=cm= 5.9 Hz, 1C), 56.3, 16.2 (d, J=cm= 6.0 Hz, 1C), 16.1 (d, J=cm= 5.9 Hz, 1C); HRMS (CI⁺) calcd. for C_{13}H_{32}NO_4PBr (M+H) 444.0212, found 444.0186.

**Example 50**

This example describes the synthesis of Biaryl **18c**: To a pressure vessel containing **13c** (38.0 mg, 0.0867 mmol) was added diene 17 (19.1 mg, 0.0320 mL, 0.173 mmol) at rt. The mixture was heated at 155°C. After 24 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give **18c** (31.1 mg, 0.598 mmol, 75%) as a bright yellow crystalline solid. MP 154-155°C; IR (neat) 2929, 1570, 1525, 1448 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.12 (dd, J = 8.2, 1.2 Hz, IH), 7.85 (dd, J = 8.0, 1.2 Hz, IH), 7.51 (td, J = 11, 8.0, 3.2 Hz, IH), 7.33 (dd, J = 16, 8.1 Hz, IH), 7.16 (d, J = 8.3 Hz, IH), 6.99 (ddd, J = 10.7, 7.7, 0.64 Hz, IH), 1.57-1.99 (m, 12H), 1.18-1.39 (m, 10H); ¹³C NMR (100 MHz, CDCl₃) δ 157.9 (d, J=cm= 11 Hz, 1C), 150.4, 136.7, 134.0 (d, J=cm= 3.9 Hz, 1C), 133.2 (d, J=cm= 4.6 Hz, 1C), 129.7, 129.0 (d, J=cm= 7.4 Hz, 1C), 128.8 (d, J=cm= 15.6 Hz, 1C), 126.7 (d, J=cm= 1.7 Hz, 1C), 123.2, 122.4 (d, J=cm= 11 Hz, 1C), 113.3 (d, J=cm= 2.3 Hz, 1C), 56.2, 37.9 (d, J=cm= 67 Hz, 1C), 37.2 (d, J=cm= 67 Hz, 1C), 26.4-26.9 (m, 5C), 25.9 (d, J=cm= 1.4 Hz, 1C), 25.8 (d, J=cm= 1.3 Hz, 1C), 25.4 (d, J=cm= 2.9 Hz, 1C), 25.0 (d, J=cm= 3.2 Hz, 1C), 24.7 (d, J=cm= 2.9 Hz, 1C); HRMS (CI⁺) calcd. for C_{25}H_{32}NO_4PBr (M+H) 520.1252, found 520.1238.
Example 5

This example describes the synthesis of Biaryl 20a: To a pressure vessel containing 13a (107 mg, 0.251 mmol) was added diene 19. The mixture was then cooled to 0°C and BnBr (342 mg, 2.00 mmol) and NaH (40.0 mg, 1.00 mmol, 60% in mineral oil) were added. After 1 h, the mixture was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-50% EtOAc / Hexanes to give 20a (103 mg, 0.168 mmol, 67% over 2 steps) as a bright yellow crystalline solid. MP 136-138°C; IR (neat) 1594, 1525, 1436 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.04 (dd, J = 8.2, 1.2 Hz, 1H), 7.67 (dd, J = 7.9, 1.2 Hz, 1H), 7.47-7.57 (m, 6H), 7.27 (t, J = 8.1 Hz, 1H), 6.84 (d, J = 2.2 Hz, 1H), 6.49 (dd, J = 14, 2.2 Hz, 1H), 4.97 (s, 2H), 3.74 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.1 (d, Jc-P = 18 Hz, 1C), 158.6 (d, Jc-P = 18 Hz, 1C), 150.5, 136.5, 136.2, 132.9 (d, Jc-P = 6.9 Hz, 1C), 123.8 (d, Jc-P = 10 Hz, 1C), 132.0 (d, Jc-P = 2.8 Hz, 1C), 131.9 (d, Jc-P = 2.8 Hz, 1C), 131.7 (d, Jc-P = 11.1 Hz, 1C), 131.6 (d, Jc-P = 1.8 Hz, 1C), 129.1, 128.8, 128.4, 128.3, 128.2, 127.7, 124.7 (d, Jc-P = 6.9 Hz, 1C), 123.3, 110.8 (d, Jc-P = 6.2 Hz, 1C), 102.6 (d, Jc-P = 1.8 Hz, 1C), 70.3, 56.3; HRMS (CI+) calcd. for C₃₂H₂₆NO₅PBr (M+H) 614.0731, found 614.0691.
Example 52

This example describes the synthesis of Biaryl 20b: To a pressure vessel containing 13b (88.3 mg, 0.244 mmol) was added diene 19 (145 mg, 0.731 mmol) at rt. The mixture was heated at 140°C for 17 h. The crude mixture was then cooled to 0°C and BnBr (333 mg, 0.224 mL, 1.95 mmol) and NaH (39.0 mg, 0.986 mmol, 60% in mineral oil) were added. After 1 h, the temperature was raised to rt. After 2 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with Et₂O (15 mL), washed with H₂O (3 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-40% EtOAc / Hexanes to give 20b (101 mg, 0.184 mmol, 75% over 2 steps) as a yellow solid. MP 35-38 0°C; IR (neat) 2980, 1595, 1528, 1348 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.14 (dd, J = 8.2, 1.2 Hz, 1H), 7.92 (dd, J = 7.9, 1.2 Hz, IH), 7.51 (dd, J = 8.4, 1.6 Hz, IH), 1.39-1.41 (m, 4H), 7.28 (dd, J = 15, 2.4 Hz, IH), 6.87 (d, J = 2.3 Hz, IH), 5.18 (s, 2H), 3.81-3.98 (m, 6H), 1.21 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.7 (d, Jc-P = 21 Hz, 1C), 158.3 (d, Jc-P = 22 Hz, 1C), 150.3, 136.7, 136.3, 133.7 (d, Jc-P = 4.0 Hz, 1C), 129.2, 128.9 (d, Jc-P = 1.2 Hz, 1C), 128.7, 128.6, 128.3, 127.9, 126.8, 123.4, 122.9 (d, Jc-P = 9.1 Hz, 1C), 109.6 (d, Jc-P = 9.8 Hz, 1C), 103.7 (d, Jc-P = 2.9 Hz, 1C), 70.5, 62.3 (d, Jc-P = 5.7 Hz, 1C), 62.2 (d, Jc-P = 5.8 Hz, 1C), 55.3, 16.2 (d, Jc-P = 5.7 Hz, 1C), 16.0 (d, Jc-P = 6.2 Hz, 1C); HRMS (FAB+) calcd. for C₂₄H₂₆NO₇PBr (M+H) 550.0631, found 550.0606.
Example 53

\[
\begin{array}{c}
\text{Br} \\
\text{NO}_2 \\
\text{P}([\text{O}]([\text{e-C}_6\text{H}_{11}]_2) \\
\text{MeO} \\
\text{O} \\
\text{Bn}
\end{array}
\]

This example describes the synthesis of Biaryl 20c: To a pressure vessel containing 13c (108 mg, 0.246 mmol) was added diene 19 (147 mg, 0.739 mmol) at rt. The mixture was heated at 140°C for 17 h. The crude mixture was then cooled to 0°C and BnBr (339 mg, 0.228 mL, 1.97 mmol) and NaH (39.0 mg, 0.986 mmol, 60% in mineral oil) were added. After 1 h, the temperature was raised to rt. After an additional 2 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with Et₂O (15 mL), washed with H₂O (3 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-50% EtOAc / Hexanes to give 20c (135 mg, 0.215 mmol, 88% over 2 steps) as a bright yellow crystalline solid. MP 143-144°C; IR (neat) 2930, 1596, 1524, 1450 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.08 (dd, J = 8.2, 1.2 Hz, 1H), 7.84 (dd, J = 8.0, 1.2 Hz, 1H), 7.38-7.53 (m, 5H), 7.32 (t, J = 8.2 Hz, 1H), 6.84 (d, J = 2.1 Hz, IH), 6.48 (dd, J = 12, 2.2 Hz, IH), 5.17 (s, 2H), 3.78 (s, 3H), 1.53-1.90 (m, 12H), 1.10-1.33 (m, 10H); ¹³C NMR (100 MHz, CDCl₃) δ 159.3 (d, Jc-P = 12 Hz, 1C), 159.1 (d, Jc-P = 11 Hz, 1C), 150.8, 136.5 (d, Jc-P = 4.2 Hz, 1C), 133.9 (d, Jc-P = 3.0 Hz, 1C), 130.3, 129.5, 128.9, 128.6, 128.3, 127.5, 125.9, 125.8, 123.2, 107.7 (d, Jc-P = 9.1 Hz, 1C), 101.6 (d, Jc-P = 2.4 Hz, 1C), 70.6, 56.5, 37.8 (d, Jc-P = 66 Hz, 1C), 37.1 (d, Jc-P = 67 Hz, 1C), 26.4-26.9 (m, 6C), 25.8 (d, Jc-P = 11.0 Hz, 1C), 25.4 (d, Jc-P = 1.8 Hz, 1C), 24.9 (d, Jc-P = 3.1 Hz, 1C), 24.7 (d, Jc-P = 3.2 Hz, 1C); HRMS (FAB+) calcd. for C₃₂H₃₈NO₅PBr (M+H) 626.1670, found 626.1641.

Example 54

\[
\begin{array}{c}
\text{Br} \\
\text{NO}_2 \\
\text{P}([\text{O}]([\text{e-C}_6\text{H}_{11}]_2) \\
\text{MeO} \\
\text{O} \\
\text{CO}_2\text{Me}
\end{array}
\]
This example describes the synthesis of Ester 21: To a pressure vessel containing 12 (107 mg, 0.473 mmol) and PhMe (0.95 mL) was added 3 (383 mg, 1.89 mmol). Heated at 80°C for 16 h. The mixture was purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to give 21 (69.1 mg, 0.194 mmol, 41%) as a yellow solid. Mp 52-3°C; IR (neat) 2955, 1739, 1637, 1530 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.89 (dd, J = 8.0, 1.2 Hz, IH), 7.85 (dd, J = 8.2, 1.2 Hz, IH), 7.32 (t, J = 6.1 Hz, IH), 6.67 (dd, J = 17.0, 10.6 Hz, IH), 4.75 (dd, J = 17.3, 10.7 Hz, IH), 3.80 (s, 3H), 3.59 (d, J = 4.4 Hz, IH), 3.55 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 169.19, 150.9, 148.7, 136.9, 132.7, 130.9, 128.9, 126.8, 122.9, 119.7, 114.1, 56.2, 52.5, 33.2; HRMS (Cl⁺) calcd. for C₁₄H₁₅NO₂Br (M+H) 356.01335, found 356.01475.

Example 55

This example describes the synthesis of Biaryl 27a: Procedure A (Suzuki) - To a pressure vessel was added 14a (81.1 mg, 0.132 mmol), PhB(OH)₂ (52.5 mg, 0.396 mmol), KF (58.1 mg, 1.19 mmol), (/-Bu,P)₂Pd (6.70 mg, 0.0132 mmol) and NMP (1.32 mL). The solution was sealed under Ar and heated to 95°C. After 24 h, the mixture was filtered over a pad of celite-®, eluting with EtOAc (25 mL) and concentrated in vacuo. The residue was purified by chromatography over silica gel, eluting with 0-20% EtOAc / CH₂Cl₂ to give 27a (49.0 mg, 0.0802 mmol, 61%) as a bright yellow crystalline solid.

Procedure B (Stille) - To a pressure vessel was added 14a (27.6 mg, 0.0449 mmol), PhSnBu₃ (49.6 mg, 62.2 µL, 0.135 mmol), CsF (61.4 mg, 0.404 mmol), (/-Bu,P)₂Pd (2.30 mg, 0.00449 mmol) and NMP (0.45 mL). The solution was sealed under Ar and heated to 60°C. After 20 h, the mixture was filtered over a pad of celite-®, eluting with EtOAc (25 mL) and concentrated in vacuo. The residue was purified by chromatography over silica gel, eluting with 0-10% EtOAc / CH₂Cl₂ to give 27a (16.5 mg, 0.0270 mmol, 61%) as a bright yellow crystalline solid.

- 136 -
To a pressure vessel was added a solution of PhZnCl (0.45 mL, 0.156 mmol, 0.34 M) followed by NMP (0.52 mL), (/-Bu3)2Pd (5.3 mg, 0.0104 mmol) and 14a (64.0 mg, 0.104 mmol). The solution was sealed under Ar and heated to 80°C. After 20 h, the mixture was filtered over a pad of celite®, eluting with EtOAc (10 mL) and was washed with sat. aq. NH4Cl (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO4) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 27a (54.0 mg, 0.0878 mmol, 52%) as a bright yellow crystalline solid. MP 184-187°C; IR (neat) 3422, 1596, 1525 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.98 (dd, J = 7.7, 1.9 Hz, IH), 7.22-7.56 (m, 13H), 6.99-7.04 (m, 9H), 6.57 (d, J = 2.3 Hz, IH), 6.21 (dd, J = 14.1, 2.4 Hz, IH), 5.01 (s, 2H), 3.59 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.1 (d, Jc-P= 18 Hz, 1C), 158.1 (d, Jc-P = 16 Hz, 1C), 149.5, 145.3, 140.3, 136.5, 134.5, 133.8 (d, Jc/>= 18 Hz, 1C), 132.7 (d, Jc/>= 18 Hz, 1C), 131.8 (d, Jc/>= 24 Hz, 1C), 131.7 (d, Jc/>= 4 Hz, 1C), 131.5 (d, Jc/>= 3 Hz, 1C), 131.4 (d, Jc/>= 3 Hz, 1C), 129.5, 128.5, 128.3, 128.1, 127.9, 127.7, 126.7, 126.4, 123.2, 110.8 (d, Jc/>= 13 Hz, 1C), 101.9, 70.3, 55.2; HRMS (Cl⁺) calcd. for C₃₈H₃₇iNO₅P (M+H) 612.1939, found 612.1919.

**Example 56**

This example describes the synthesis of Biaryl 27b: Procedure A (Suzuki) - To a pressure vessel was added 14b (61.0 mg, 0.111 mmol), PhB(OH)₂ (71.1 mg, 0.554 mmol), KF (96.7 mg, 1.67 mmol), (/-Bu3)2Pd (112 mg, 0.0222 mmol) and NMP (1.1 mL). The solution was sealed under Ar and heated to 95°C. After 24 h, the mixture was filtered over a pad of celite®, eluting with EtOAc (25 mL) and concentrated in vacuo. The residue was purified by chromatography over silica gel, eluting with 0-20% EtOAc / CH₂Cl₂ to give 27b (38.0 mg, 0.0694 mmol, 63%) as a bright yellow crystalline solid.
Procedure B (StUIe) - To a pressure vessel was added 14b (18.8 mg, 0.0342 mmol), PhSnBu₃ (37.7 mg, 33.5 μL, 0.102 mmol), CsF (46.8 mg, 0.308 mmol), (t-Bu₃P)₂Pd (1.70 mg, 0.00342 mmol) and NMP (0.34 mL). The solution was sealed under Ar and heated to 60°C. After 20 h, the mixture was filtered over a pad of celite®, eluting with EtOAc (25 mL) and concentrated in vacuo. The residue was purified by chromatography over silica gel, eluting with 0-20% EtOAc/CH₂Cl₂ to give 18 (11.0 mg, 0.0201 mmol, 60%) as a bright yellow crystalline solid.

Procedure C (Negishi) - To a pressure vessel was added a solution of PhZnCl (1.11 mL, 0.384 mmol, 0.35 M) followed by NMP (0.51 mL), (t-Bu₃P)₂Pd (13.1 mg, 0.0256 mmol), and 14b (140 mg, 0.256 mmol). The solution was sealed under Ar and heated to 80°C. After 18 h, the mixture was filtered over a pad of celite®, eluting with EtOAc (25 mL) and was washed with sat. aq. NH₄Cl (25 mL), H₂O (25 mL) and sat. aq. NaCl (25 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc/Hexanes to give 27b (77.0 mg, 0.141 mmol, 55%) as a bright yellow crystalline solid. MP 123-126°C; IR (neat) 3475, 2981, 1597, 1529 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.17 (dd, J = 7.6, 1.9 Hz, IH), 7.60 (dd, J = 7.6, 1.9 Hz, IH), 7.56 (t, J = 7.6 Hz, IH), 7.01-7.28 (m, 1IH), 6.45 (d, J = 2.4 Hz, IH), 4.85 (d, J = 12.6 Hz, IH), 4.72 (d, J = 12.6 Hz, IH), 3.80-4.89 (m, 4H), 3.79 (s, 3H), 1.24 (t, J = 7.0 Hz, 3H), 1.04 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.9 (d, J<sub>C-P</sub> = 21 Hz, 1C), 157.2 (d, J<sub>C-P</sub> = 22 Hz, 1C), 149.5, 145.6, 139.9, 136.7, 134.4, 131.1 (d, J<sub>C-P</sub> = 4.6 Hz, 1C), 129.5, 129.3, 128.4, 127.9, 127.7, 127.5, 127.3, 127.0, 126.1, 123.3, 122.1, 108.9 (d, J<sub>C-P</sub> = 10 Hz, 1C), 103.8 (d, J<sub>C-P</sub> = 2.6 Hz, 1C), 70.0, 62.4 (d, J<sub>C-P</sub> = 6.0 Hz, 1C), 61.8 (d, J<sub>C-P</sub> = 6.8 Hz, 1C), 55.5, 16.2 (d, J<sub>C-P</sub> = 6.8 Hz, 1C), 16.0 (d, J<sub>C-P</sub> = 6.7 Hz, 1C); HRMS (Cl⁺) calcd. for C₁₃₀H₁₃₀NO₇P (M+H) 547.1759, found 547.1761.
Example 57

This example describes the synthesis of Biaryl 27c: Procedure A (Suzuki) - To a pressure vessel was added 14c (49.1 mg, 0.0784 mmol), PhB(OH)_2 (28.7 mg, 0.235 mmol), KF (40.9 mg, 0.706 mmol), (/-Bu_3)Pd (4.00 mg, 0.0284 mmol) and NMP (0.78 mL). After 20 h at 95°C the mixture was filtered over a pad of celite-® and the residue was purified by chromatography over silica gel, eluting with 0-20% EtOAc / CH_2Cl_2 to give 27c (35.0 mg, 0.0562 mmol, 72%) as a bright yellow crystalline solid.

Procedure B (Stille) - To a pressure vessel was added 14c (39.8 mg, 0.0635 mmol), PhSnBu_3 (70.0 mg, 62.0 µL, 0.191 mmol), CsF (57.9 mg, 0.381 mmol), (/-Bu_3)Pd (3.24 mg, 0.00635 mmol) and NMP (0.64 mL). The solution was sealed under Ar and heated to 60°C. After 22 h, the mixture was filtered over a pad of celite-®, eluting with EtOAc (25 mL) and concentrated in vacuo. The residue was purified by chromatography over silica gel, eluting with 0-10% EtOAc / CH_2Cl_2 to give 27c (26.0 mg, 0.0417 mmol, 66%) as a bright yellow crystalline solid.

To a pressure vessel was added a solution of PhZnCl (0.35 mL, 0.0802 mmol, 0.35 M in THF) followed by NMP (0.27 mL), (/-Bu_3)Pd (2.7 mg, 0.00535 mmol), and 14c (33.5 mg, 0.0535 mmol). The solution was sealed under Ar and heated to 80°C. After 18 h, the mixture was filtered over a pad of celite-®, eluting with EtOAc (10 mL) and was washed with sat. aq. NH_4Cl (10 mL), H_2O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO_4) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 27c (20.0 mg, 0.0319 mmol, 60%) as a bright yellow crystalline solid. MP 209-211°C; IR (neat) 2930, 1700, 1525 cm⁻¹; ¹H NMR (300 MHz, CDCl_3) δ 8.05 (dd, J = 8.2, 1.4 Hz, IH), 7.60 (dd, J = 7.7, 1.4 Hz, IH), 7.50 (t, J = 8.0 Hz, IH), 7.25-7.31 (m, 5H), 7.15-7.18 (m, 5H), 6.67 (d, J = 2.2 Hz, IH), 6.27 (dd, J = 11.2, 2.2 Hz, IH), 5.16 (d, J = 12.3 Hz, IH), 5.08 (d, J = 12.3 Hz, IH), 3.81 (s, 3H), 1.40-1.74 (m, 1H); 0.75-1.30 (m, 1H); ¹³C NMR (75 MHz, CDCl_3) δ 159.6 (d, J_C-P = 11
Hz, 1C), 159.4 (d, Jc-P= 18 Hz, 1C), 149.7, 144.7, 140.8, 136.7, 134.6, 131.9, 130.8
(d, Jc P= 16 Hz, 1C), 129.9, 128.5, 127.5 (d, Jc-P = 39 Hz, 1C), 126.7, 126.4, 124.2
(d, Jc P= 18 Hz, 1C), 123.3, 107.4 (d, Jc-P = 48 Hz, 1C), 100.5 (d, Jc-P = 6.5 Hz, 1C),
70.4, 55.3, 38.5 (d, Jc-P= 65 Hz, 1C), 36.8 (d, Jc-P = 66 Hz, 1C), 26.4-26.9 (m, 5C),
25.8, 25.7 (d, Jc-P = 3.3 Hz, 1C), 25.6 (d, Jc-P = 3.8 Hz, 1C), 25.3 (d, Jc-P = 2.4 Hz,
1C), 25.0 (d, Jc-P = 3.0 Hz, 1C); HRMS (CI+) calcd. for C_{38}H_{43}NO_{5}P (M+H)
624.2879, found 624.2891.

Example 58

This example describes the synthesis of Biaryl 28a: To a pressure vessel
was added a solution of Grignard reagent (0.375 mL, 0.263 mmol, 0.70 M in THF)
and ZnCl₂ (0.282 mL, 0.282 mmol, 1.0 M in THF) at it. After 20 min, NMP (0.55
mL) was added to the solution. After 5 min, (t-Bu₃P)₂Pd (9.0 mg, 0.618 mmol), and
14c (110 mg, 0.176 mmol) were added sequentially. The solution was sealed under
Ar and heated to 80°C. After 18 h, the reaction was cooled and diluted with EtOAc
(20 mL). The mixture was then washed sequentially with 1 M HCl (5 x 20 mL),
H₂O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was
concentrated in vacuo and purified by chromatography over silica gel, eluting with
50% EtOAc / Hexanes to give 28a (65.0 mg, 0.101 mmol, 59%) as a bright yellow
crystalline solid. MP 109-111°C; IR (neat) 2929, 1525 cm⁻¹; ¹H NMR (400 MHz,
CDCl₃) δ 8.03 (dd, J = 8.0, 1.3 Hz, IH), 7.59 (dd, J = 7.7, 1.3 Hz, IH), 7.49 (t, J =
8.0 Hz, IH), 7.17-7.29 (m, 10H), 6.69-6.72 (m, 3H), 6.29 (dd, J = 12.0, 2.2 Hz, IH),
5.17 (d, J = 12.4 Hz, IH), 5.09 (d, J = 12.4 Hz, IH), 3.83 (s, 3H), 3.77 (s, 3H), 1.63-
1.74 (m, HH), 1.06-1.29 (m, HH); ¹³C NMR (100 MHz, CDCl₃) δ 159.6 (d, Jc-P =
7.6 Hz, 1C), 159.4 (d, Jc-P = 10 Hz, 1C), 158.6, 149.7, 144.4, 136.7, 134.5, 133.4,
131.8, 131.1, 130.9, 130.8 (d, Jc-P = 3 Hz, 1C), 128.5, 127.7 (d, Jc-P = 3.7 Hz, 1C),
127.1, 126.4, 124.4 (d, Jc-P = 4.4 Hz, 1C), 113.8, 113.0, 107.4 (d, Jc-P = 12 Hz, 1C),
100.6 (d, Jc-P = 1.8 Hz, 1C), 70.4, 55.4, 55.1, 38.6 (d, Jc-P = 65 Hz, 1C), 36.8 (d, Jc-P
= 66 Hz, 1C), 26.5-27.1 (m, 5C), 25.8, 25.7 (d, J = 3.0 Hz, 1C), 25.6 (d, Jc,p = 2.4 Hz, 1C), 25.3 (d, Jc,p = 2.9 Hz, 1C), 25.0 (d, Jc,p = 3.1 Hz, 1C); HRMS (CI+) calcd. for C39H45NO6P (M+H) 654.2985, found 654.2970.

**Example 59**

This example describes the synthesis of Biaryl 28b: To a pressure vessel was added a solution of Grignard reagent (0.300 mL, 0.223 mmol, 0.75 M in THF) and ZnCl2 (0.237 mL, 0.237 mmol, 1.0 M in THF) at rt. After 20 min, NMP (0.49 mL) was added to the solution. After 5 min, (t-Bu3P)2Pd (7.6 mg, 0.0148 mmol), and 14c (93.0 mg, 0.148 mmol) were added sequentially. The solution was sealed under Ar and heated to 80°C. After 18 h, the reaction was cooled and diluted with EtOAc (20 mL). The mixture was then washed sequentially with 1 M HCl (5 x 20 mL), H2O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO4) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 28b (55.0 mg, 0.0862 mmol, 58%) as a bright yellow crystalline solid. MP 143-146°C; IR (neat) 2929, 1525 cm^-1; 1H NMR (300 MHz, CDCl3) δ 8.05 (dd, J = 8.1, 1.4 Hz, IH), 7.62 (dd, J = 7.7, 1.4 Hz, IH), 7.49 (t, J = 8.0 Hz, IH), 7.15-7.29 (m, 3H), 7.05 (t, J = 7.6 Hz, IH), 6.88-6.90 (m, 2H), 6.68-6.73 (m, 2H), 6.27 (dd, J = 11, 2.2 Hz, IH), 5.16 (d, J = 12.3 Hz, IH), 5.09 (d, J = 12.3 Hz, IH), 3.81 (s, 3H), 3.65 (s, 3H), 0.73-1.30 (m, 1IH), 1.61-1.73 (m, HH); 13C NMR (75 MHz, CDCl3) δ 159.6 (d, Jc,P = 6.1 Hz, 1C), 159.4 (d, Jc,p = 9.4 Hz, 1C), 158.8, 149.7, 144.6, 142.1, 136.6, 134.5, 131.9, 130.8 (d, Jc,p = 9.0 Hz, 1C), 130.7, 128.5, 128.4, 127.7, 126.4, 124.3 (d, Jc,p = 5.4 Hz, 1C), 123.3, 122.4, 115.2, 113.0, 107.4 (d, Jc,p = 12.5 Hz, 1C), 100.5 (d, Jc,p = 2.6 Hz, 1C), 70.5, 55.4, 54.9, 38.5 (d, Jc,p = 65 Hz, 1C), 36.7 (d, Jc,p = 65 Hz, 1C), 26.4-26.9 (m, 3C), 25.9 (d, J = 1.3 Hz, 1C), 25.8 (d, J = 1.2 Hz, 1C), 25.7 (d, J = 3.1 Hz, 1C), 25.6 (d, J = 3.0 Hz, 1C), 25.6 (d, J = 3.0 Hz, 1C), 25.3 (d, Jc,p = 3.4 Hz, 1C), 24.9 (d, Jc,p = 3.3 Hz, 1C); HRMS (CI+) calcd. for C39H45NO6P (M+H) 654.2985, found 654.2970.
Example 60

This example describes the synthesis of Biaryl 28d: To a pressure vessel was added a solution of Grignard reagent (0.261 mL, 0.217 mmol, 0.83 M in THF) and ZnCl₂ (0.232 mL, 0.232 mmol, 1.0 M in THF) at rt. After 20 min, NMP (0.48 mL) was added to the solution. After 5 min, (lob₃P)₂Pd (8.0 mg, 0.0145 mmol), and 14c (91.0 mg, 0.145 mmol) were added sequentially. The solution was sealed under Ar and heated to 80°C. After 18 h, the reaction was cooled and diluted with EtOAc (20 mL). The mixture was then washed sequentially with 1 M HCl (5 x 20 mL), H₂O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 28d (56.0 mg, 0.0878 mmol, 61%) as a bright yellow crystalline solid. MP 128-130°C; IR (neat) 2930, 1524, 1254, 1152 cm⁻¹; ¹H NMR (300 MHz, CDCl₃, D₃:1 ratio atropisomers observed, major compound reported) δ 8.02 (dd, J = 8.0, 1.4 Hz, IH), 7.57 (dd, J = 7.7, 1.5 Hz, IH), 7.45 (t, J = 7.9 Hz, IH), 7.03-7.29 (m, 9H), 6.70 (d, J = 2.1 Hz, IH), 6.22 (dd, J = 12, 2.3 Hz, IH), 5.27 (d, J = 12.3 Hz, IH), 5.08 (d, J = 12.3 Hz, IH), 3.81 (s, 3H), 2.48 (s, 3H), 1.61-1.94 (m, HH), 1.01-1.47 (m, 1IH); ¹³C NMR (75 MHz, CDCl₃, D₃:1 ratio atropisomers observed, major compound reported) δ 159.8 (d, Jc-P = 14 Hz, 1C), 159.4 (d, Jc-P = 16 Hz, 1C), 150.1, 144.4, 142.6, 139.3, 137.5, 136.6, 135.9, 135.4, 134.9, 131.8 (d, Jc-P = 3.3 Hz, 1C), 130.9, 129.2, 128.4, 127.6, 126.9, 126.5, 126.2, 124.7, 123.3, 107.1 (d, Jc-P = 12.2 Hz, 1C), 100.5 (d, Jc-P = 2.1 Hz, 1C), 70.3, 55.4, 38.8 (d, Jc-P = 65 Hz, 1C), 36.9 (d, Jc-P = 65 Hz, 1C), 26.0-27.0 (m, 5C), 25.7-25.8 (m, 3C), 25.3 (d, Jc-P = 2.9 Hz, 1C), 24.7 (d, Jc-P = 3.3 Hz, 1C), 21.4; HRMS (Cl+) calcd. for C₃₉H₄₅NO₅P (M+H) 638.3035, found 638.3038.
Example 6

This example describes the synthesis of Biaryl 28e: To a pressure vessel was added a solution of Grignard reagent (0.394 mL, 0.335 mmol, 0.85 M in THF) and ZnCl₂ (0.357 mL, 0.357 mmol, 1.0 M in THF) at it. After 20 min, NMP (0.75 mL) was added to the solution. After 5 min, (t-Bu₃P)₂Pd (12.9 mg, 0.0223 mmol), and 14c (140 mg, 0.223 mmol) were added sequentially. The solution was sealed under Ar and heated to 80°C. After 18 h, the reaction was cooled and diluted with EtOAc (20 mL). The mixture was then washed sequentially with 1 M HCl (5 x 20 mL), H₂O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 28e (90.0 mg, 0.126 mmol, 57%) as a bright yellow crystalline solid. MP 176-178°C; IR (neat) 2930, 1521 cm⁻¹;¹H NMR (300 MHz, CDCl₃) δ 8.15-8.20 (m, 1H), 7.53-7.55 (m, 1H), 7.23-7.29 (m, 3H), 7.08-7.11 (m, 2H), 6.63 (d, J = 2.2 Hz, 1H), 6.32 (dd, J = 11, 2.2 Hz, 1H), 4.99 (s, 2H), 3.83 (s, 3H), 1.63-1.83 (m, 12H), 1.13-1.27 (m, 10H); ¹³C NMR (100 MHz, CDCl₃) δ 159.9 (d, Jc-p = 15 Hz, 1C), 159.2 (d, Jc-p = 13.8 Hz, 1C), 150.4, 136.5, 135.9, 133.7, 131.9, 131.2, 130.6, 128.4, 127.6 (d, Jc-p = 4.3 Hz, 1C), 126.3, 125.4, 122.0 (d, Jc-p = 3.4 Hz, 1C), 115.2 (t, Jc-p = 16 Hz, 1C), 107.4 (d, Jc-p = 11 Hz, 1C), 100.5, 70.2, 55.4, 39.2 (d, Jc-p = 65 Hz, 1C), 36.3 (d, Jc-p = 65 Hz, 1C), 27.0, 26.9, 26.7, 26.6, 26.5, 26.1, 25.9, 25.8, 25.4, 24.9; HRMS (CI+) calcd. for C₃₈H₃₈NO₅F₅P (M+H) 714.2408, found 714.2388.
Example 62

This example describes the synthesis of Biaryl 28f: To a pressure vessel was added a solution of Grignard reagent (1.55 mL, 1.32 mmol, 0.85 M in THF) and ZnCl₂ (1.41 mL, 1.41 mmol, 1.0 M in THF) at rt. After 20 min, NMP (1.93 mL) was added to the solution. After 5 min, (J-Bu₃P)₂Pd (45.0 mg, 0.0879 mmol), and 14c (551 mg, 0.879 mmol) were added sequentially. The solution was sealed under Ar and heated to 80°C. After 48 h, the reaction was cooled and diluted with EtOAc (40 mL). The mixture was then washed sequentially with 1 M HCl (5 x 40 mL), H₂O (40 mL) and sat. aq. NaCl (40 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50% EtOAc / Hexanes to give 28f (381 mg, 0.585 mmol, 66%) as a bright yellow crystalline solid. MP 199-200°C; IR (neat) 2929, 1525 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.07 (dd, J = 6.6, 2.9 Hz, IH), 7.42-7.45 (m, 2H), 7.26-7.30 (m, 3H), 7.03-7.09 (m, 4H), 6.83 (dd, J = 6.6, 2.3 Hz, IH), 6.58 (d, J = 2.2 Hz, IH), 6.31 (dd, J = 12, 2.3 Hz, IH), 4.94 (d, J = 12.0 Hz, IH), 4.87 (d, J = 12.0 Hz, IH), 3.81 (s, 3H), 2.35 (s, 3H), 1.84 (s, 3H), 1.71-1.93 (m, 14H), 0.92-1.62 (m, 8H); ¹³C NMR (100 MHz, CDCl₃) δ 159.1 (d, J = 16 Hz, 1C), 158.4 (d, J = 15 Hz, 1C), 151.0, 142.5, 139.2, 138.9, 136.8, 136.7, 136.3, 133.0, 132.5 (d, J = 28 Hz, 1C), 132.2, 128.4, 127.6, 127.3, 126.8, 126.4 (d, J = 6.7 Hz, 1C), 123.6 (d, J = 4.5 Hz, 1C), 123.4, 107.8 (d, J = 110 Hz, 1C), 100.3, 69.9, 55.3, 39.2 (d, J = 65 Hz, 1C), 38.1 (d, J = 64 Hz, 1C), 26.95 (d, J = 3.1 Hz, 1C), 26.9 (d, J = 2.0 Hz, 1C), 26.82 (d, J = 3.0 Hz, 1C), 26.8, 26.7, 26.4 (d, J = 2.8 Hz, 1C), 26.2 (d, J = 3.2 Hz, 1C), 26.1 (d, J = 2.2 Hz, 1C), 25.8, 25.5 (d, J = 3.4 Hz, 1C), 22.8, 20.0;
HRMS (Cl⁺) calcd. for C₄₀H₄₇NO₂P (M+H) 652.3192, found 652.3206.
This example describes the synthesis of **Biaryl 29**: To a stirred solution of 28e (100 mg, 0.153 mmol) in neat AcOH (0.64 mL) was added Zn powder (50.4 mg, 0.764 mmol) at it. After 16 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL) and washed with sat. aq. NaHCO₃ (15 mL), H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50-66% EtOAc / Hexanes to give 29 (80.4 mg, 0.129 mmol, 85%) as a white crystalline solid.

**Example 63**

![Diagram of the synthesis of Biaryl 29]

**Example 63**

This example describes the synthesis of **Biaryl 29**: To a stirred solution of 28e (100 mg, 0.153 mmol) in neat AcOH (0.64 mL) was added Zn powder (50.4 mg, 0.764 mmol) at it. After 16 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL) and washed with sat. aq. NaHCO₃ (15 mL), H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50-66% EtOAc / Hexanes to give 29 (80.4 mg, 0.129 mmol, 85%) as a white crystalline solid. MP 128-130°C; IR (neat) 3385, 2929, 1595, 1449, 1302, 1162 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.13-7.31 (m, 6H), 6.94-6.99 (m, 2H), 6.86 (dd, J = 7.7, 0.6 Hz, IH), 6.77-6.80 (m, 2H), 6.68 (dd, J = 7.6, 1.0 Hz, IH), 6.63 (d, J = 2.3 Hz), 6.38 (dd, J = 11, 1.6 Hz, IH), 5.07 (d, J = 12.3 Hz, IH), 4.90 (d, J = 12.3 Hz, IH), 3.81 (s, 3H), 2.39 (s, 3H), 1.89 (s, 3H), 1.82-1.99 (m, 12H), 0.98-1.70 (m, 10H); ¹³C NMR (75 MHz, CDCl₃) δ 159.1 (d, J_C-P = 16 Hz, 1C), 158.5 (d, J_C-P = 16 Hz, 1C), 144.2, 141.3, 140.6, 138.9, 136.8, 136.6, 133.8, 132.7, 128.3, 127.9, 127.3, 127.0 (d, J_C-P = 6.0 Hz, 1C), 126.0, 124.6, 123.5, 115.0, 108.0 (d, J_C-P = 12 Hz, 1C), 101.1, 69.3, 55.4, 39.0 (d, J_C-P = 29 Hz, 1C), 38.2 (d, J_C-P = 29 Hz, 1C), 26.9, 26.7 (d, J_C-P = 2.6 Hz, 1C), 26.6 (d, J_C-P = 3.1 Hz, 1C), 26.5 (d, J_C-P = 2.0 Hz, 1C), 26.4 (d, J_C-P = 1.3 Hz, 1C), 26.2 (d, J_C-P = 5.1 Hz, 1C), 26.1 (d, J_C-P = 3.3 Hz, 1C), 26.0 (d, J_C-P = 1.3 Hz, 1C), 25.8 (d, J_C-P = 4.8 Hz, 1C), 25.7 (d, J_C-P = 1.5 Hz, 1C), 22.7, 19.9; HRMS (ES+) calcd. for C₄₀H₄₉N₂O₃P (M+H) 622.3450, found 622.3473.
Example 64

This example describes the synthesis of Biaryl 30: A pressure vessel was charged with 29 (40.7 mg, 0.0655 mmol), Ti(O-Z-Pr)$_4$ (55.8 mg, 60 µL, 0.196 mmol), poly(methylhydrosiloxane) (118 mg, 117 µL, 1.97 mmol) and THF (0.13 mL). The solution was sealed under Ar and heated at 80°C. After 48 h, the crude mixture was transferred to a vigorously stirred solution of NaOH (100 mL, 2.5 M in H$_2$O) using THF (20 mL). After 20 h, the solution was extracted with EtOAc (2 x 60 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 30% EtOAc / Hexanes to yield 30 (24.0 mg, 0.0396 mmol, 61%) as a white solid. MP 76-79°C; IR (neat) 2922, 2268, 1590, 1446, 1302, 1156 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.17-7.33 (m, 6H), 6.99 (d, $J$ = 6.2 Hz, IH), 6.94 (t, $J$ = 7.4 Hz, IH), 6.73 (dd, $J$ = 7.9, 1.2 Hz, 2H), 6.61 (dd, $J$ = 7.6, 1.1 Hz, IH), 6.49-6.53 (m, 2H), 5.06 (d, $J$ = 12.3 Hz, IH), 4.96 (d, $J$ = 12.3 Hz, IH), 3.80 (s, 3H), 2.36 (s, 3H), 1.28 (s, 3H), 1.39-1.70 (m, HH), 0.85-1.30 (m, HH); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 158.8, 157.1 (d, $J_{C-P}$ = 11 Hz, 1C), 148.6, 146.5, 141.7, 141.1, 138.1, 137.3, 136.7, 128.4 (d, $J_{C-P}$ = 11 Hz, 1C), 127.2 (d, $J_{C-P}$ = 7.7 Hz, 1C), 126.7, 126.2, 125.9 (d, $J_{C-P}$ = 11 Hz, 1C), 122.4, 113.4, 109.2, 99.7, 69.2, 55.3, 37.3 (d, $J_{C-P}$ = 16 Hz, 1C), 33.3 (d, $J_{C-P}$ = 17 Hz, 1C), 32.8, 31.9, 30.7 (d, $J_{C-P}$ = 11 Hz, 1C), 30.4 (d, $J_{C-P}$ = 6.0 Hz, 2C), 29.6 (d, $J_{C-P}$ = 13 Hz, 1C), 27.9 (d, $J_{C-P}$ = 10 Hz, 1C), 27.6 (d, $J_{C-P}$ = 9.0 Hz, 1C), 27.2, 27.1 (d, $J_{C-P}$ = 6.1 Hz, 1C), 26.4, 23.9 (d, $J_{C-P}$ = 22.1 Hz, 1C), 23.9 (d, $J_{C-P}$ = 12 Hz, 1C), 19.8; $^{31}$P NMR (121 MHz, CDCl$_3$) $\delta$ -9.90 (s); HRMS (FAB+) calcd. for C$_{40}$H$_{49}$NO$_2$P (M+H) 606.3501, found 606.3481.
Example 65

This example describes the synthesis of Biaryl 32: To a stirred solution of 29 (47.0 mg, 0.0756 mmol) and CH₂Cl₂ (0.76 mL) was added BCl₃ (0.45 mL, 0.453 mmol, 1.0 M in heptane) at 0°C. After 3 h, the reaction was quenched with MeOH (1.8 mL) and concentrated in vacuo. The product was purified by chromatography over silica gel, eluting with 0-5% MeOH / CH₂Cl₂ to give 32 (28.0 mg, 0.0528 mmol, 70%) as a white insoluble powder. NMR analysis was performed on the salt by treatment of 32 with d₄-MeOD and one drop of TMSCl, followed by removal of solvent in vacuo to yield the more soluble salt. MP > 225°C; IR (KBr) 2929, 1591, 1447, 1311, 1211, 1132 cm⁻¹; ¹H NMR (300 MHz, d₄-MeOD) δ 7.49 (t, J = 7.7 Hz, IH), 7.37 (dd, J = 7.9, 1.4 Hz, IH), 7.29 (dd, J = 7.6, 1.3 Hz, IH), 7.03-7.05 (m, 2H), 6.84 (t, J = 5.4 Hz, IH), 6.70 (d, J = 2.3 Hz, IH), 6.40 (dd, J = 13.0, 2.4 Hz, IH), 3.82 (s, 3H), 1.26 (s, 3H), 1.69-2.30 (m, 12H), 1.17-1.30 (m, 10H); ¹³C NMR (75 MHz, d₄-MeOD) δ 160.5 (d, Jc-P = 17 Hz, 1C), 157.5 (d, Jc-P = 14 Hz, 1C), 142.7, 139.1, 137.9, 137.0, 132.6, 132.0, 131.5, 130.5, 128.3, 127.2, 126.9, 126.7, 120.5, 117.2, 109.6 (d, Jc-P = 12 Hz, 1C), 103.4, 54.6, 38.6 (d, Jc-P = 65 Hz, 1C), 37.4 (d, Jc-P = 64 Hz, 1C), 26.4, 26.2 (d, Jc-P = 3.2 Hz, 1C), 26.1 (d, Jc-P = 2.1 Hz, 1C), 26.0, 25.9, 25.73 (d, Jc-P = 2.7 Hz, 1C), 25.68 (d, Jc-P = 2.4 Hz, 1C), 25.6, 25.4, 25.0, 21.8, 19.1; HRMS (Cl⁺) calcd. for C₃₅H₄₃NO₃P (M+H) 532.29806, found 532.29768.
This example describes the synthesis of Biaryl 34: To a stirred mixture of 30 (35.8 mg, 0.0576 mmol), CH$_2$O (47.0 DL, 0.576 mmol, 12.3 M in H$_2$O), NaBH$_3$CN (10.9 mg, 0.173 mmol), and CH$_3$CN (0.30 mL) was slowly added AcOH (0.20 mL) at rt. After 2 h, the mixture was diluted with Et$_2$O (15 mL) and washed with sat. aq. NaHCO$_3$ (2 x 15 mL), H$_2$O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to yield 34 (29.4 mg, 0.0453 mmol, 80%) as a white crystalline solid. MP 148-150°C; IR (neat) 2923, 1592, 1561 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32 (t, $J$ = 7.7 Hz, IH), 7.20-7.29 (m, 3H), 7.06-7.10 (m, 3H), 6.98 (t, $J$ = 7.4 Hz, IH), 6.84 (t, $J$ = 7.0 Hz, IH), 6.78 (dd, $J$ = 7.5, 1.3 Hz, IH), 6.64 (t, $J$ = 2.0 Hz, IH), 6.25 (d, $J$ = 2.4 Hz, IH), 4.73 (s, 2H), 3.73 (s, 3H), 2.57 (s, 6H), 2.02 (s, 3H), 1.78 (s, 3H), 1.54-2.07 (m, 10H), 1.16-1.31 (m, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.9, 157.5 (d, $J_{c-p}$ = 11 Hz, 1C), 154.6, 142.6, 141.9, 139.5 (d, $J_{c-p}$ = 23 Hz, 1C), 137.5, 136.6, 130.4 (d, $J_{c-p}$ = 5.0 Hz, 1C), 128.3, 128.0, 127.7, 127.2 (d, $J_{c-p}$ = 2.0 Hz, 1C), 126.6 (d, $J_{c-p}$ = 5.1 Hz, 1C), 126.4, 125.9, 125.1, 116.1, 109.2, 98.9, 69.0, 55.0, 44.4, 36.1 (d, $J_{c-p}$ = 18 Hz, 1C), 33.8 (d, $J_{c-p}$ = 18 Hz, 1C), 33.2 (d, $J_{c-p}$ = 13 Hz, 1C), 30.7 (d, $J_{c-p}$ = 14 Hz, 1C), 30.3 (d, $J_{c-p}$ = 17 Hz, 1C), 28.5 (d, $J_{c-p}$ = 14 Hz, 1C), 28.0 (d, $J_{c-p}$ = 5.0 Hz, 1C), 27.8 (d, $J_{c-p}$ = 4.0 Hz, 1C), 27.7 (d, $J_{c-p}$ = 10 Hz, 1C), 27.4 (d, $J_{c-p}$ = 10 Hz, 1C), 26.6 (d, $J_{c-p}$ = 17 Hz, 1C), 23.6 (d, $J_{c-p}$ = 22 Hz, 1C), 21.1 (2C); HRMS (ESI+) calcd. for C$_{42}$H$_{53}$NO$_2$P (M+H) 634.3814 found 634.3803.

Example 67

This example describes the synthesis of Biaryl 37: To a pressure vessel was added 35 (34.6 mg, 0.231 mmol), K$_3$PO$_4$ (65.4 mg, 0.308 mmol), Pd(OAc)$_2$ (1.7 mg, 0.00776 mmol), 34 (10.0 mg, 0.0154 mmol) and PhMe (0.51 mL) followed by 36 (26.3 mg, 18.5 DL, 0.154 mmol). The solution was sealed under argon and heated to 100°C. After 20 h, the reaction was cooled and diluted with Et$_2$O (10 mL). The mixture was then washed sequentially with 1 M NaOH (10 mL) and sat. aq. NaCl.
The dried extract (MgSO$_4$) was concentrated \textit{in vacuo} and purified by chromatography over silica gel, eluting with 20\% EtOAc / Hexanes to give 37 (22.1 mg, 0.112 mmol, 73\%) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.28-7.39 (m, 3H), 7.17-7.25 (m, 3H), 7.07-7.10 (m, 1H), 2.05 (s, 3H), 2.02 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.1, 140.6, 135.9, 135.7, 130.0, 128.9, 127.3, 127.1, 126.9, 126.1, 20.4, 19.4.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{example68}
\caption{Example 68}
\end{figure}

This example describes the synthesis of Biaryl 37: To a pressure vessel was added 38 (88.9 mg, 0.654 mmol), K$_3$PO$_4$ (185 mg, 0.872 mmol), Pd(OAc)$_2$ (4.89 mg, 0.0219 mmol), 34 (28.3 mg, 0.0437 mmol) and PhMe (1.32 mL) followed by 39 (80.6 mg, 58.0 DL, 0.436 mmol). The solution was sealed under argon and heated to 100$^\circ$C. After 20 h, the reaction was cooled and diluted with Et$_2$O (15 mL). The mixture was then washed sequentially with 1 M NaOH (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO$_4$) was concentrated \textit{in vacuo} and purified by chromatography over silica gel, eluting with 10-20\% CH$_2$Cl$_2$ / Hexanes to give 37 (61.2 mg, 0.312 mmol, 73\%) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.28-7.39 (m, 3H), 7.17-7.25 (m, 3H), 7.07-7.10 (m, 1H), 2.05 (s, 3H), 2.02 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.1, 140.6, 135.9, 135.7, 130.0, 128.9, 127.3, 127.1, 126.9, 126.1, 20.4, 19.4.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{example69}
\caption{Example 69}
\end{figure}

This example describes the synthesis of Acetylene 40a: To a stirred solution of 12 (113 mg, 0.500 mmol) and THF (2.5 mL) was added LDA (0.500 mL, 0.500 mmol, 1.0 M in THF / Hexanes) at -78$^\circ$C. After 10 min, ClCO$_2$Me (94.5 mg, 0.773
mL, 1.00 mmol) was added to the dark brown solution. After 30 min, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over Florisil®, eluting with 10% EtOAc / Hexanes to give 40a (111 mg, 0.391 mmol, 92%) as a white crystalline solid. MP 91-92°C; IR (neat) 2981, 2228, 1713, 1524 cm⁻¹; ¹H NMR (400 MHz, CDCl₃)  δ 8.08 (dd, J = 8.3, 1.1 Hz, IH), 7.98 (dd, J = 8.1, 1.1 Hz, IH), 7.49 (t, J = 8.2 Hz, IH), 3.92 (3H); ¹³C NMR (100 MHz, CDCl₃)  δ 153.5, 151.8, 137.4, 130.9, 129.4, 123.7, 117.4, 91.1, 78.8, 53.2; HRMS (EI+) calcd. for C₁₀H₆NO₄Br (M+H) 282.94801, found 282.94768.

**Example 70**

![Diagram](image)

This example describes the synthesis of Acetylene 40b: To a stirred solution of 2 (317 mg, 1.40 mmol) and THF (7.00 mL) was added LDA (1.40 mL, 1.40 mmol, 1.0 M in THF / Hexanes) at -78°C. After 10 min, CICO₂Et (204 mg, 0.271 mL, 2.80 mmol) was added to the dark brown solution. After 30 min, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (20 mL), diluted with EtOAc (20 mL), and washed with H₂O (2 x 20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over Florisil®, eluting with 50-100% CH₂Cl₂ / Hexanes to give 40b (380 mg, 1.27 mmol, 91%) as a white crystalline solid. MP 62-63°C; IR (neat) 2983, 2241, 1707, 1531 cm⁻¹; ¹H NMR (400 MHz, C₆D₆)  δ 7.30 (dd, J = 8.3, 1.1 Hz, IH), 7.08 (dd, J = 8.1, 1.1 Hz, IH), 6.35 (t, J = 8.2 Hz, IH), 4.02 (q, J = 7.2 Hz, 2H), 0.98 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, C₆D₆)  δ 152.9, 151.1, 136.5, 130.3, 128.8, 123.1, 117.3, 92.0, 78.4, 62.2, 13.6; HRMS (ESI+) calcd. For C₁₀H₆NO₄Br (M+Na) 319.9534, found 319.9514.
Example 71

This example describes the synthesis of Acetylene 40c: To a stirred solution of 12 (45.3 mg, 0.200 mmol) and THF (1.0 mL) was added LDA (0.200 mL, 0.200 mmol, 1.0 M in THF / hexanes) at -78°C. After 10 min, ClCO₂CH₂CCl₃ (87.5 mg, 0.0569 mL, 0.400 mmol) was added to the dark brown solution. After 30 min, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over Florisil-® , eluting with 10% EtOAc / Hexanes to give 40c (54.4 mg, 0.135 mmol, 68%) as a yellow oil. IR (neat) 2994, 2234, 1731, 1532 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.13 (dd, J = 8.3, 1.0 Hz, IH), 8.06 (dd, J = 8.1, 1.0 Hz, IH), 7.53 (t, J = 8.2 Hz, IH), 4.95 (s, 2H); ¹³C NMR (100 MHZ, CDCl₃) δ 151.7, 151.4, 137.6, 131.4, 129.6, 123.8, 117.1, 93.9, 89.8, 83.4, 74.9; HRMS (EI+) calcd. for C₃₅H₅₅NO₄BrCl (M+H) 398.84679, found 398.84554.

Example 72

This example describes the synthesis of Acetylene 40d: To a stirred solution of 12 (51.6 mg, 0.228 mmol) and THF (1.14 mL) was added LDA Error! Bookmark not defined. (0.22g mL, 0.22g ml o i d, 1.0 M in THF / hexanes) at -78°C. After 10 min, the dark brown solution was slowly cannulated into freshly distilled pivaloyl chloride (137 mg, 0.140 mL, 1.14 mmol) in THF (2.28 mL) at -78°C. After 1 h, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in
vacuo and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 4Od (52.2 mg, 0.168 mmol, 74%) as a white crystalline solid. MP 120-21°C; IR (neat) 2964, 2204, 1663, 1529 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 8.06 (dd, J = 8.3, 1.1 Hz, IH), 7.96 (dd, J = 8.1, 1.1 Hz, IH), 7.47 (t, J = 8.2 Hz, IH), 1.32 (s, 9H); ¹³C NMR (100 MHz, C₆D₆) δ 193.0, 151.6, 137.2, 130.7, 129.3, 123.6, 118.1, 96.6, 83.5, 45.2, 25.8; HRMS (EI⁺) calcd. for C₁₃H₁₃NO₃Br (M+H) 310.00788, found 310.00635.

Example 73

This example describes the synthesis of Acetylene 40e: To a stirred solution of 12 (107 mg, 0.473 mmol) and THF (2.37 mL) was added LDA (0.473 mL, 0.473 mmol) in THF at -78°C. After 10 min the dark brown solution was slowly cannulated into freshly distilled benzoyl chloride (233 mg, 0.274 mL, 2.37 mmol) in THF (4.47 mL) at -78°C. After 1 h, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 50-60% CH₂Cl₂ /
Hexanes to give 40e (104 mg, 0.315 mmol, 67%) as a white crystalline solid. MP 109-1 10°C; IR (neat) 3230, 2204, 1643, 1528 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 8.47-8.49 (m, 2H), 7.27-7.30 (m, IH), 7.19-7.23 (m, 3H), 7.06 (dd, J = 8.0, 1.0 Hz, IH), 6.27 (t, J = 8.2 Hz, IH); ¹³C NMR (100 MHz, C₆D₆) δ 176.5, 151.3, 137.0, 136.5, 134.1, 130.2, 129.8, 129.4, 128.7, 123.1, 117.8, 97.4, 84.0; HRMS (EI⁺) calcd. for C₁₃H₉NO₃Br (M+H) 329.97658, found 329.97695.
This example describes the synthesis of Acetylene 4Of: To a stirred solution of 12 (102 mg, 0.451 mmol) and THF (2.25 mL) was added LDA derived from (0.289 mL, 0.289 mmol, 1.0 M in THF / hexanes) at -78°C. After 10 min, the dark brown solution was slowly cannulated into freshly distilled 4-chlorobenzoyl chloride (395 mg, 0.289 mL, 2.25 mmol) in THF (4.50 mL) at -78°C. After 1 h, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 25-40% CH₂Cl₂ / Hexanes to give 40f (60.8 mg, 0.165 mmol, 37%) as a white crystalline solid and recovered 2 (38.4 mg, 0.170 mmol, 59%) borsm. MP 146-47°C; IR (neat) 3094, 2206, 1646, 1530 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.26 (dt, J = 7.2, 1.4 Hz, 2H), 8.14 (dd, J = 8.2, 0.92 Hz, IH), 8.02 (dd, J = 8.2, 1.2 Hz, IH), 7.51-7.57 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 175.8, 151.6, 141.3, 137.5, 134.9, 131.2, 131.19, 129.9, 129.3, 123.9, 117.8, 96.7, 84.8; HRMS (EI⁺) calcd. for C₁₃H₇NO₃BrCl (M+H) 362.92978, found 362.92909.

This example describes the synthesis of Acetylene 40g: To a stirred solution of 12 (121 mg, 0.535 mmol) and THF (2.68 mL) was added LDA derived from (0.535 mL, 0.535 mmol, 1.0 M in THF / hexanes) at -78°C. After 10 min, ClC(O)NMe₂ (1.15 mg, 0.0985 mL, 1.07 mmol) was added to the dark brown solution. After 30 min, the solution was allowed to warm to rt. After an additional
1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-30% EtOAc / Hexanes to give 40g (104 mg, 0.350 mmol, 65%) as a white crystalline solid. MP 113-14°C; IR (neat) 3310, 2212, 1649, 1526 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.03 (dd, J = 8.3, 1.2 Hz, IH), 7.95 (dd, J = 8.1, 1.1 Hz, IH), 7.47 (t, J = 8.2Hz, IH), 3.34 (s, 3H), 3.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.1, 153.3, 151.3, 137.3, 130.6, 129.1, 123.6, 118.1, 92.9, 82.5, 60.3, 38.2, 34.2, 22.6, 20.9, 14.2; HRMS (EI+) calcd. for C₉H₆N₂O₃Br (M+H) found 296.98748, 296.98687.

**Example 76**

![Chemical structure](image)

This example describes the synthesis of Acetylene 40h: To a stirred solution of 12 (61.4 mg, 0.272 mmol) and THF (1.36 mL) was added LDA (0.272 mL, 0.272 mmol, 1.0 M in THF / hexanes) at -78°C. After 10 min, the dark brown solution was slowly cannulated into ClC(O)NPh₂ (504 mg, 2.18 mmol) in THF (2.18 mL) at -78°C. After 1 h, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-30% EtOAc / Hexanes to give 40h (64.3 mg, 0.153 mmol, 56%) as a yellow crystalline solid. MP 117-18°C; IR (neat) 3360, 2213, 1647, 1530 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.98 (dd, J = 8.3, 1.0 Hz, IH), 7.84 (dd, J = 8.0, 1.0 Hz, IH), 7.26-7.46 (m, HH); ¹³C NMR (100 MHz, CDCl₃) δ 152.5, 151.3, 141.3, 141.1, 137.1, 130.3, 129.6, 126.2, 129.1, 128.6, 128.5, 126.7, 125.8, 123.4, 118.1, 93.9; HRMS (EI+) calcd. for C₂H₄N₂O₃Br (M+H) 421.01878, found 421.01943.
Example 77

This example describes the synthesis of Acetylene 40i: To a stirred solution of 12 (103 mg, 0.456 mmol) and THF (2.28 mL) was added LDA (0.456 mL, 0.456 mmol, 1.0 M in THF / hexanes) at -78°C. After 10 min, N-morpholinylchloroformate (136 mg, 0.106 mL, 0.911 mmol) was added to the dark brown solution. After 30 min, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 30-40% EtOAc / Hexanes to give 40i (138 mg, 0.407 mmol, 89%) as a white crystalline solid. Mp 178-79°C; IR (neat) 2964, 2212, 1634, 1524 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.07 (dd, J = 8.2, 1.1 Hz, 1H), 7.97 (dd, J = 8.1, 1.2 Hz, IH), 7.48 (t, J = 8.2 Hz, IH), 8.09 (dd, J = 8.3, 1.1 Hz, IH), 3.93 (ddd, J = 6.0, 4.6, 1.3 Hz, 2H), 3.80 (ddd, J = 5.1, 3.8, 1.2 Hz, 2H), 3.75 (s, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 151.9, 151.3, 137.4, 130.7, 129.4, 123.7, 118.0, 92.1, 83.4, 66.9, 66.5, 47.2, 42.2; HRMS (EI+) calcd. for \( \text{C}_4\text{H}_n\text{N}_2\text{O}_4\text{Br} \) (M+H) 337.99022, found 337.98946.

Example 78

This example describes the synthesis of Acetylene 40j: To a stirred solution of 12 (107 mg, 0.473 mmol) and THF (2.4 mL) was added LDA (0.473 mL, 0.473 mmol, 1.0 M in THF / hexanes) at -78°C. After 10 min, (-)-menthylchloroformate (207 mg, 0.947 mL, 0.192 mmol) was added to the dark brown solution. After 30 min, the solution was allowed to warm to rt. After an
additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over Florisil®, eluting with 20-30% EtOAc / Hexanes to give 40j (132 mg, 0.323 mmol, 63%) as a white crystalline solid. MP 93-94°C; IR (neat) 2957, 2232, 1708, 1536 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.07 (dd, J = 8.2, 1.1 Hz, IH), 7.96 (dd, J = 8.1, 1.2 Hz, IH), 7.46 (t, J = 8.2 Hz, IH), 4.90 (td, J = 10.9, 4.5 Hz, IH), 2.09-2.17 (m, IH), 1.98 (dd, J = 7.0, 2.6 Hz, IH), 1.71-1.76 (m, IH), 1.55 (s, 3H), 1.47-1.53 (m, 2H), 1.09-1.21 (m, 2H), 0.89-1.05 (m, 7H), 0.94 (d, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) 6 152.8, 151.6, 13738, 130.9, 129.3, 123.7, 117.6, 91.8, 78.4, 46.8, 40.6, 34.1, 31.5, 26.4, 23.6, 21.9, 20.7, 16.5; HRMS (Cl+) calcd. for C₉H₂₃NO₄Br (M+H) 408.08104, found 408.07941.

**Example 79**

This example describes the synthesis of **Acetylene 40k**: To a stirred solution of 12 (111 mg, 0.493 mmol) and THF (2.47 mL) was added LDA (0.493 mmol, 1.0 M in THF / Hexanes) at -78°C. After 10 min, the brown solution was cannulated into a stirred solution of (S)-benzyloxazolidinylcarbamyl chloride (236 mg, 0.985 mmol) in THF (0.500 mL) at -78°C. After 30 min, the solution was allowed to warm to rt. After an additional 1 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL), and washed with H₂O (2 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-40% EtOAc / Hexanes to give 40k (129 mg, 0.300 mmol, 61%) as a white crystalline solid. MP 93-94°C; IR (neat) 3410, 2217, 1793, 1659 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.08 (dd, J = 8.3, 1.1 Hz, IH), 7.96 (dd, J = 8.1, 1.1 Hz, IH), 7.47 (t, J = 8.2 Hz, IH), 7.24-7.40 (m, 6H), 4.73-4.81 (m, IH), 4.23-4.34 (m, 2H), 3.40 (dd, J = 13.5, 3.3Hz, IH), 2.91 (dd, J = 13.5, 9.5 Hz, IH); ¹³C
NMR (100 MHz, CDCl₃) δ 151.7, 151.5; 149.9, 137.4, 134.7, 131.1, 129.5, 129.0, 128.9, 127.5, 123.7, 117.7, 91.3, 87.2, 66.1, 55.1, 37.6; HRMS (CI+) calcd. for C₉H₁₄N₂O₅Br (M+H) 429.00860, found 429.00877.

Example 80

This example describes the synthesis of Biaryl 42a: To a pressure vessel containing 40a (34.0 mg, 0.117 mmol) was added diene 17 (39.9 mg, 0.0429 mL, 0.361 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to give 42a (34.9 mg, 0.0956 mmol, 82%) as a bright yellow crystalline solid. MP 144-45°C; IR (neat) 2943, 1717, 1525, 1272 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.08 (dd, J = 8.3, 1.2 Hz, IH), 7.93 (dd, J = 8.0, 1.2 Hz, IH), 7.76 (dd, J = 7.8, 1.0 Hz, IH), 7.52 (t, J = 8.2Hz, IH), 7.41 (t, J = 8.2 Hz, IH), 7.21 (dd, J = 8.3, 0.92 Hz, IH), 3.76 (s, 3H), 3.71 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.2, 156.4, 149.7, 136.9, 134.3, 129.9, 129.7, 128.8, 127.8, 125.9, 123.2, 122.7, 115.1, 56.3, 52.2; HRMS (EI+) calcd. for C₁₅H₁₂N₂O₅Br (M+H) 364.98987, found 364.99104.

Example 81

This example describes the synthesis of Biaryl 42b: To a pressure vessel containing 40b (93.0 mg, 0.312 mmol) was added diene 17 (96.1 mg, 0.114 mL, 0.106 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 42b (101 mg, 0.266 mmol, 85%) as a bright yellow crystalline solid. MP 80-81°C; IR (neat) 2880, 1717, 1527 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ - 158 -
8.06 (dd, J = 8.2, 1.2 Hz, IH), 7.92 (dd, J = 8.0, 1.2 Hz, IH), 7.78 (dd, J = 7.9, 1.0 Hz, IH), 7.52 (t, J = 8.1 Hz, IH), 7.41 (dd, J = 8.1 Hz, IH), 7.20 (dd, J = 8.3, 0.92 Hz, IH), 4.08-4.19 (m, 2H), 3.75 (s, 3H), 1.11 (t, J = 7.1 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 165.8, 156.5, 149.8, 136.8, 134.6, 130.4, 129.8, 128.8, 127.5, 126.1, 123.1, 122.8, 115.0, 61.0, 56.3, 13.8; HRMS (ESI+) calcd. for C₁₆H₁₄NO₅BrNa (M+Na) 401.9953, found 401.9933.

Example 82

This example describes the synthesis of Biaryl 40c: To a pressure vessel containing 40c (42.1 mg, 0.103 mmol) was added diene 17 (35.4 mg, 0.0381 mL, 0.321 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 20-30% CH₂Cl₂ / Hexanes to give 42c (32.3 mg, 0.0668 mmol, 64%) as a yellow oil. IR (neat) 2939, 1736, 1527, 1349 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (dd, J = 8.2, 1.2 Hz, IH), 7.94 (dd, J = 8.0, 1.2 Hz, IH), 7.91 (dd, J = 8.0, 1.0 Hz, IH), 7.58 (t, J = 8.3 Hz, IH), 7.42 (dd, J = 8.1 Hz, IH), 7.27 (dd, J = 8.4, 0.80 Hz, IH), 4.80 (dd, J = 16.1, 2.0 Hz, IH), 3.77 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.1, 156.5, 149.7, 137.2, 133.8, 129.9, 129.0, 128.5, 126.0, 123.4, 123.2, 116.0, 94.7, 74.6, 56.3; HRMS (FAB+) calcd. for C₁₆H₁₄NO₅Cl₂Br (M+H) 480.88865, found 480.88866.

Example 83

This example describes the synthesis of Biaryl 6d: To a pressure vessel containing 40d (43.0 mg, 0.139 mmol) was added diene 17 (47.0 mg, 0.0506 mL,
0.426 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes to give 42d (44.1 mg, 0.112 mmol, 81%) as a bright yellow crystalline solid. MP 165-66°C; IR (neat) 2935, 1680, 1526, 1469 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (dd, J = 8.2, 1.0 Hz, IH), 7.88 (dd, J = 8.0, 1.0 Hz, IH), 7.47 (t, J = 8.2Hz, IH), 7.38 (t, J = 8.0 Hz, IH), 7.22 (dd, J = 7.8, 0.92 Hz, IH), 7.11 (dd, J = 8.3, 0.64 Hz, IH), 3.82 (s, 3H), 1.19 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 210.7, 157.4, 150.8, 138.6, 136.7, 133.3, 129.0, 128.8, 126.9, 125.1, 123.2, 118.5, 112.3, 56.2, 44.4, 28.4; HRMS (EI+) calcd. for C₁₄H₉NO₂Br (M+H) 333.97149, found 333.97106.

**Example 84**

This example describes the synthesis of Biaryl 42e: To a pressure vessel containing 40e (37.1 mg, 0.112 mmol) was added diene 17 (38.1 mg, 0.0410 mL, 0.345 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes to give 42e (33.0 mg, 0.0800 mmol, 71%) as a bright yellow crystalline solid. MP 185-86°C; IR (neat) 3011, 1654, 1528, 1490 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.02 (dd, J = 8.2, 1.2 Hz, IH), 7.84 (dd, J = 8.0, 1.2 Hz, IH), 7.57-7.78 (m, 2H), 7.39-7.57 (m, 5H), 7.34 (t, J = 8.1 Hz, IH), 7.20 (dd, J = 8.3, 0.90 Hz, IH); ¹³C NMR (100 MHz, CDCl₃) δ 195.9, 156.9, 150.4, 137.7, 137.3, 136.9, 133.2, 132.8, 130.4, 129.5, 129.0, 128.1, 126.8, 126.6, 123.2, 122.7, 113.9, 56.3; HRMS (EI+) calcd. for C₂₀H₁₄N₂O₄Br (M+H) 411.01061, found 411.01209.
This example describes the synthesis of Biaryl 42f: To a pressure vessel containing 40f (45.0 mg, 0.123 mmol) was added diene 17 (41.8 mg, 0.0450 mL, 0.379 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes to give 42f (35.7 mg, 0.0799 mmol, 64%) as a bright yellow crystalline solid. MP 85-86°C; IR (neat) 3420, 3935, 1662, 1585, 1526 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.04 (dd, J = 8.2, 1.2 Hz, IH), 7.86 (dd, J = 8.1, 1.2 Hz, IH), 7.73 (ddd, J = 7.8, 4.2, 2.3 Hz, 2H), 7.52 (t, J = 8.1 Hz, IH), 7.41 (ddd, J = 8.6, 4.2, 2.3 Hz, 2H), 7.37 (t, J = 8.1 Hz, IH), 7.23 (dd, J = 8.3, 0.64 Hz, IH), 7.15 (dd, J = 7.8, 1.0 Hz, IH), 3.84 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 194.7, 157.0, 150.3, 139.3, 137.4, 136.9, 135.6, 132.9, 131.8, 129.2, 129.1, 128.5, 126.7, 126.6, 123.3, 122.4, 114.1, 56.3; HRMS (EI+) calcd. for C₂₀H₁₅NO₄Br (M+H) 444.97164, found 444.97286.

This example describes the synthesis of Biaryl 40g: To a pressure vessel containing 40g (72.5 mg, 0.244 mmol) was added diene 17 (82.7 mg, 0.0890 mL, 0.751 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 20-40% EtOAc / Hexanes to give 42g (69.3 mg, 0.183 mmol, 75%) as a bright yellow crystalline solid. MP 153-54°C; IR (neat) 3290, 1635, 1530, 1353 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.01 (dd, J = 8.2, 1.2 Hz, IH), 7.90 (dd, J = 8.1, 1.2 Hz, IH), 7.45 (t, J = 8.2 Hz, IH), 7.38 (t, J = 8.1 Hz, IH), 7.07 (dd, J = 8.3, 0.80 Hz, IH),
6.95 (dd, J = 7.7, 0.96 Hz, IH), 3.83 (s, 3H), 2.93 (s, 3H), 2.87 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.8, 157.4, 150.4, 136.8, 135.2, 132.8, 129.5, 129.3, 127.3, 125.2, 123.3, 119.1, 111.6, 56.1, 39.3, 34.8; HRMS (EI+) calcd. for C$_{16}$H$_{16}$N$_2$O$_4$Br (M+H) 379.02934, found 379.03057.

Example 87

This example describes the synthesis of Biaryl 42h: To a pressure vessel containing 40h (28.5 mg, 0.0677 mmol) was added diene 17 (22.9 mg, 0.208 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes to give 42h (24.6 mg, 0.0489 mmol, 72%) as a bright yellow crystalline solid. MP 147-48°C; IR (neat) 3435, 1660, 1527, 1359 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.08 (dd, J = 8.2, 1.2 Hz, IH), 7.92 (dd, J = 8.0, 1.2 Hz, IH), 7.37 (t, J = 8.1 Hz, IH), 7.26-7.29 (m, 4H), 7.11-7.19 (m, 7H), 6.97 (dd, J = 7.3, 0.84 Hz, IH), 6.92 (dd, J = 7.2, 1.0 Hz, IH), 3.78 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.9, 157.2, 150.7, 143.7, 136.9, 133.7, 133.0, 130.3, 129.0, 128.6, 127.6, 127.3, 126.9, 126.3, 123.5, 122.5, 112.4, 56.1; HRMS (EI+) calcd. for C$_{26}$H$_{19}$N$_2$O$_4$Br (M+H) 502.05282, found 502.05157.

Example 88

This example describes the synthesis of Biaryl 42i: To a pressure vessel containing 40i (340 mg, 1.00 mmol) was added diene 17 (340 mg, 0.366 mL, 3.09 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 30-50% EtOAc /
Hexanes to give 42i (349 mg, 0.829 mmol, 83%) as a bright yellow crystalline solid. MP 121-22°C; IR (neat) 2858, 1635, 1530, 1430 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (d, J = 8.0 Hz, IH), 7.92 (dd, J = 8.0, 0.88 Hz, IH), 7.46 (t, J = 7.7 Hz, IH), 7.41 (t, J = 8.1 Hz, IH), 7.09 (dd, J = 8.4, 0.84 Hz, IH), 6.93 (dd, J = 7.6, 0.84 Hz, IH), 3.84 (s, 3H), 3.42-3.65 (m, 8H); ¹³C NMR (100 MHz, CDCl₃) δ 167.6, 157.5, 150.5, 136.8, 134.2, 134.1, 132.6, 129.6, 129.5, 125.6, 123.5, 118.8, 111.9, 66.8, 56.2, 47.9, 42.0; HRMS (EI+) calcd. for C₁₈H₁₇N₂O₅Br (M+H) 420.03208, found 420.03275.

**Example 89**

This example describes the synthesis of Biaryl 44: To a pressure vessel containing 40b (39.4 mg, 0.132 mmol) was added diene 43 (88.9 mg, 0.528 mmol) and xylenes (0.26 mL) at rt. The mixture was heated at 130°C for 20 h. The crude mixture was then cooled to rt and BnBr (226 mg, 0.152 mL, 1.32 mmol) and K₂CO₃ (91.2 mg, 0.660 mmol) were added. The mixture was heated at 60°C for 6 h and directly purified by chromatography over silica gel, eluting with 10-25% EtOAc / Hexanes to give 44 (32.2 mg, 0.0708 mmol, 54% over 2 steps) as a bright yellow oil. IR (neat) 2988, 1717, 1527, 1285 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.95 (dd, J = 8.2, 1.1 Hz, IH), 7.89 (dd, J = 8.1, 1.2 Hz, IH), 7.81 (d, J = 2.7 Hz, IH), 7.37-7.52 (m, 6H), 7.22 (dd, J = 8.5, 2.7 Hz, IH), 7.06 (d, J = 8.5 Hz, IH), 5.17 (s, 2H), 4.14 (dd, J = 8.9, 7.2, 1.2 Hz, 2H), 1.09 (t, J = 7.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 165.5, 158.9, 149.8, 137.7, 136.4, 136.3, 130.9, 130.7, 130.3, 128.73, 128.71, 128.3, 127.7, 126.3, 122.8, 118.9, 116.7, 70.4, 61.1, 13.8; HRMS (EI+) calcd. for C₂₂H₁₈NO₅Br (M+H) 455.03682, found 455.03703.
Example 90

This example describes the synthesis of Biaryl 45: To a pressure vessel containing 40b (77.8 mg, 0.261 mmol) was added diene 19 (155 mg, 0.783 mmol) at rt. The mixture was heated at 125°C for 20 h. The crude mixture was then cooled to rt and BnBr (447 mg, 0.300 mL, 2.61 mmol) and K₂CO₃ (180 mg, 1.31 mmol) and DMF (1.31 mL) were added. After 3 h, the mixture was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (15 mL), washed with H₂O (3 x 15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes to give 45 (80.3 mg, 0.165 mmol, 63% over 2 steps) as a bright yellow oil.

IR (neat) 3280, 1718, 1606, 1526 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.02 (dd, J = 8.2, 1.2 Hz, 1H), 7.91 (dd, J = 8.0, 1.2 Hz, 1H), 7.38 (t, J = 2.0 Hz, 1H), 7.26-7.32 (m, 4H), 7.14-7.17 (m, 2H), 5.03 (s, 2H), 4.09-4.17 (m, 2H), 3.90 (s, 3H), 1.08 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.8, 160.6, 156.6, 150.2, 136.6, 136.4, 134.7, 131.1, 128.6, 128.5, 127.8, 126.5, 123.0, 120.3, 106.7, 104.3, 70.6, 61.1, 55.6, 13.8; HRMS (CI+) calcd. for C₂₃H₂₀NO₆Br (M+H) 485.04739, found 485.04690.

Example 91

This example describes the synthesis of Biaryl 47: To a pressure vessel containing 40b (46.4 mg, 0.156 mmol) was added diene 46 (169 mg, 0.623 mmol) and xylenes (0.31 mL) at rt. The mixture was heated at 130°C for 20 h. The crude mixture was then cooled to rt and MeI (221 mg, 0.0969 mL, 1.56 mmol) and K₂CO₃ (108 mg, 0.780 mmol) were added. The mixture was heated at 60°C for 2 h and directly purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes to give 47 (31.1 mg, 0.0640 mmol, 41% over 2 steps) as a bright yellow
oil. IR (neat) 2980, 1717, 1605, 1528 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.00 (dd, J = 8.2, 1.2 Hz, IH), 7.90 (dd, J = 8.1, 1.2 Hz, IH), 7.28-7.52 (m, 7H), 6.83 (d, J = 3.4 Hz, IH), 5.16 (s, 2H), 4.11 (dddd, J = 14.3, 7.1, 2.4 Hz, 2H), 3.71 (s, 3H), 1.06 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.8, 160.0, 157.6, 150.2, 136.6, 136.3, 134.4, 131.0, 128.7, 128.6, 128.4, 127.9, 126.9, 123.0, 120.5, 107.1, 103.6, 70.5, 61.1, 56.3, 13.7; HRMS (Cl⁺) calcd. for C₂₃H₂₀NO₅Br (M+H) 485.04739, found 485.04806.

Example 92

This example describes the synthesis of Biaryl 48: To a pressure vessel containing 40j (92.4 mg, 0.226 mmol) was added diene 17 (49.9 mg, 0.0537 mL, 0.453 mmol) at rt. The mixture was heated at 130°C. After 20 h, the reaction was cooled to rt and purified by chromatography over silica gel, eluting with 10% EtOAc

/ Hexanes to give 48 (86.1 mg, 0.176 mmol, 78% as a 1:1 mix of atropic diastereomers) as a bright yellow crystalline solid. MP 107-08°C; IR (neat) 2956, 1711, 1528, 1467 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (dd, J = 8.2, 1.2 Hz, IH), 8.05 (dd, J = 8.2, 1.2 Hz, IH), 7.92 (d, J = 1.2 Hz, IH), 7.90 (d, J = 1.2 Hz, IH), 7.80 (dd, J = 8.0, 1.1 Hz, IH), 7.76 (dd, J = 7.9, 1.0 Hz, IH), 7.52 (t, J = 8.0 Hz, IH), 7.51 (t, J = 8.1 Hz, IH), 7.41 (t, J = 8.2 Hz, IH), 7.41 (t, J = 7.9 Hz, IH), 7.20 (dd, J = 3.8, 1.0 Hz, IH), 7.17 (dd, J = 3.70, 0.92 Hz, IH), 4.74 (dddd, J = 14.9, 10.5, 4.43 Hz, IH), 3.76 (s, 3H), 3.75 (s, 3H), 1.88-1.93 (m, IH), 1.61-1.74 (m, 3H), 1.38-1.44 (m, IH), 0.95-1.15 (m, 2H), 0.88 (d, J = 6.5 Hz, IH), 0.84 (dd, J = 7.0, 3.1 Hz, IH), 0.69 (dd, J = 8.2, 6.9 Hz, IH); ¹³C NMR (100 MHz, CDCl₃) δ 165.5, 165.4, 156.5, 156.4, 149.8, 149.7, 149.7, 136.8, 136.7, 134.9, 134.8, 131.0, 130.8, 129.7, 129.6, 128.7, 128.6, 127.4, 127.2, 126.4, 126.2, 123.2, 122.3, 122.1, 122.9, 122.8, 124.9, 74.8, 56.3, 56.2, 47.0, 46.9, 40.3, 40.2, 34.2, 34.18, 31.34, 31.32, 25.9, 25.8, 23.1, 22.9, 22.0, 20.9, 20.8, 16.0, 15.8; HRMS (Cl⁺) calcd. for C₂₄H₂₉NO₅Br (M+H) 490.12290, found 490.12445.
Example 93

This example describes the synthesis of Biaryls 49-(aS) and (aR): To a

5 pressure vessel containing 40k (90.7 mg, 0.211 mmol) was added diene 17 (69.8
mg, 0.0752 mL, 0.634 mmol) at rt. The mixture was heated at 130°C. After 20 h,
the reaction was cooled to rt and purified by chromatography over silica gel, eluting
with 10-20% EtOAc / Hexanes to give 49 (95.1 mg, 0.186 mmol, 88% as a 1:1 mix
of atropic diastereomers) as a bright yellow crystalline solid. The diastereomers can
be separated via chromatography over silica gel, eluting with 50-65% CH₂Cl₂ /
PhMe to give 49-(aS) (42.9 mg, 0.0841 mmol, 40%) and 49-(aR) (43.8 mg, 0.0867
mmol, 41%) as yellow crystalline solids. 49-(aS): MP 71-72°C; [D]D 2.3 = +14.5°
(c=1.03, CHCl₃); IR (neat) 3430, 1971, 1682, 1530 cm⁻¹; ¹H NMR (400 MHz,
CDCl₃) δ 8.05 (dd, J = 8.2, 1.2 Hz, IH), 7.89 (dd, J = 8.0, 1.2 Hz, IH), 7.49 (t, J =
7.8 Hz, IH), 7.40 (t, J = 8.1 Hz, IH), 7.16-7.40 (m, 3H), 4.63-4.72 (m, 4H), 4.12-
4.23 (m, 2H), 3.81 (s, 3H), 3.20 (dd, J = 13.4, 3.4 Hz, IH), 2.77 (dd, J = 13.5, 9.6
Hz, IH); ¹³C NMR (100 MHz, CDCl₃) δ 167.7, 156.8, 152.3, 151.1, 137.0, 134.9,
132.3, 132.29, 129.5, 129.4, 128.96, 128.92, 127.4, 125.8, 127.4, 126.1, 121.6,
113.9, 65.9, 56.2, 54.9, 37.3; HRMS (Cl⁺) calcd. for C₉₄H₇₂N₂O₄Br (M⁺H)

20 511.05047, found 511.04948. 49-(aR): MP 74-75°C; [D]D 2.3 = +65.3° (c=0.91,
CHCl₃); IR (neat) 3434, 1790, 1676, 1529 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.98
(dd, J = 8.2, 1.2 Hz, IH), 7.92 (dd, J = 8.0, 1.2 Hz, IH), 7.49 (t, J = 7.8 Hz, IH),
7.39 (t, J = 8.1 Hz, IH), 7.28-7.32 (m, 3H), 7.10-7.18 (m, 4H), 4.56-4.64 (m, IH),
4.22 (t, J = 9.0 Hz, IH), 4.13 (dd, J = 9.1, 3.0 Hz, IH), 3.81 (s, 3H), 3.09 (dd, J =
13.3, 3.3 Hz, IH), 2.70 (dd, J = 13.4, 9.4 Hz, IH); ¹³C NMR (100 MHz, CDCl₃) δ
167.4, 156.8, 151.9, 151.0, 136.6, 135.0, 132.5, 132.2, 129.5, 129.4, 129.0, 128.9,
127.4, 126.8, 127.4, 126.8, 125.3, 123.1, 120.9, 113.7, 65.9, 56.2, 55.7, 37.0; HRMS

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(CI+) calcd. for C_{24}H_{20}N_{2}O_{6}Br (M+H) 511.05047, found 511.04767.

**Example 94**

This example describes the synthesis of Biaryl 50: To a stirred solution of 49-(aS) (49.1 mg, 0.0961 mmol) in MeOH (0.961 mL) was added LiBH4 (0.240 mL, 0.480 mmol, 2.0 M in THF) at 0°C. After 1 h, the mixture was quenched with 1 M HCl (1 mL), diluted with CH2C12 (15 mL) and washed with H2O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO4) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 25% EtOAc / Hexanes to give 50 (24.2 mg, 0.0785 mmol, 75%) as a white crystalline solid. MP 70-71°C; [D]D^2^3 = -107° (c=2.45, CHCl3); IR (neat) 3378, 2931, 1527, 1471 cm^-1; 1H NMR (400 MHz, CDCl3) δ 7.96 (d, J = 8.2 Hz, 2H), 7.48 (t, J = 8.1 Hz, IH), 7.45 (t, J = 7.9 Hz, IH), 7.22 (d, J = 7.7 Hz, IH), 6.97 (d, J = 8.4 Hz, IH), 4.40 (ddd, J = 18.6, 12.8, 6.1 Hz, 2H), 3.74 (s, 3H), 1.72 (t, J = 6.1 Hz, IH); 13C NMR (100 MHz, CDCl3) δ 156.1, 151.1, 139.8, 136.9, 132.6, 130.4, 129.5, 126.9, 124.4, 123.1, 120.7, 110.6, 63.5, 55.9; HRMS (Cl+) calcd. for C_{14}H_{12}NO_4Br (M+H) 336.9950, found 336.9945.

**Example 95**

This example describes the synthesis of Amino Alcohol 51: To a stirred solution of 49-(aS) (43.7 mg, 0.0855 mmol) in THF (0.428 mL) and MeOH (14.1 mL) was added LiBH_4 (0.214 mL, 0.427 mmol, 2.0 M in THF) at 0°C. The solution was heated at 80°C for 30 min, then degassed. This was repeated once more then
stirred for 5 h. The mixture was then quenched with 1 M HCl (15 mL), diluted with CH$_2$Cl$_2$ (15 mL) and washed with H$_2$O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (Na$_2$SO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 25-40% EtOAc / Hexanes to give 51 (16.8 mg, 0.0547 mmol, 64%) as an oil. [D]D$^2$ = -87.2° (c=1.0, CHCl$_3$); IR (neat) 3375, 2935, 1610, 1579, 1469 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.49 (t, $J$ = 8.0 Hz, IH), 7.25 (dd, $J$ = 7.1, 0.32 Hz, IH), 7.16 (dd, $J$ = 8.0, 1.1 Hz, IH), 7.09 (t, $J$ = 8.0 Hz, IH), 7.03 (dd, $J$ = 7.7, 0.64 Hz, IH), 6.78 (dd, $J$ = 7.9, 1.1 Hz, IH), 4.33 (dd, $J$ = 24.1, 12.2 Hz, 2H); 3.81 (s, 3H), 3.56 (bs, 2H), 2.84 (bs, IH); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.0, 145.3, 141.2, 130.2, 129.8, 125.4, 124.9, 123.8, 123.1, 121.8, 114.6, 110.9, 63.8, 56.1; HRMS (EI+) calcd. for C$_{14}$H$_{10}$NO$_2$Br (M+H) 307.0206, found 307.0206.

**Example 96**

This example describes the synthesis of **Lactam 52**: To a stirred solution of **49-(aS)** (26.5 mg, 0.0519 mmol) in glacial AcOH (0.21 mL) was added Zn dust (10.2 mg, 0.153 mmol) at rt. After 2 h, the mixture was quenched with sat. aq. NaHCO$_3$ (15 mL), diluted with EtOAc (15 mL) and washed with sat. aq. NaHCO$_3$ (15 mL), H$_2$O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by trituration with EtOAc to give 52 (7.5 mg, 0.0247 mmol, 48%) as a white solid. [D]D$^2$ = +1.4° (c=0.98, DMSO); Mp >225°C; IR (neat) 2923, 1708, 1669, 1558 cm$^{-1}$; $^1$H NMR (400 MHz, d$_6$-OMSO) $\delta$ 11.65 (s, IH), 7.87 (dd, $J$ = 7.7, 0.9 Hz, IH), 7.67 (t, $J$ = 8.0, IH), 7.47-7.50 (m, 2H), 7.28-7.34 (m, 2H), 3.97 (s, 3H); $^{13}$C NMR (100 MHz, d$_6$-OMSO) $\delta$ 160.9, 156.2, 139.0, 130.1, 129.6, 129.5, 128.1, 122.8, 122.5, 118.7, 117.1, 155.3, 114.8, 55.5; HRMS (EI+) calcd. for C$_{14}$H$_{10}$NO$_2$Br (M+H) 302.9895, found 302.9906.
Example 97

![Diagram of molecule conversion from 49-(aS) to S3]

This example describes the synthesis of Lactam 53: To a stirred solution of 49-(aS) (33.8 mg, 0.0661 mmol) in glacial AcOH (0.26 mL) and H₂O (0.26 mL) was added Zn dust (21.6 mg, 0.331 mmol) at rt. After 3 h, the mixture was quenched with sat. aq. NaHCO₃ (15 mL), diluted with EtOAc (15 mL) and washed with sat. aq. NaHCO₃ (15 mL), H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by trituration with EtOAc to give 53 (8.6 mg, 0.0389 mmol, 51%) as a white solid. MP >225°C; [D]D²⁺ = +11.7° (c=0.02, DMSO); IR (neat) 3418, 2923, 1662, 1635, 1456 cm⁻¹; ¹H NMR (300 MHz, c⁶-DMSO) δ 11.72 (s, IH), 9.08 (d, J = 7.5 Hz, IH), 8.02 (dd, J = 7.8, 1.5 IH), 7.62 (td, J = 7.8 IH), 7.44-7.54 (m, 2H), 7.37 (dd, J = 8.4, 1.5 IH), 7.23 (dd, J = 8.4, 1.5 IH), 3.43 (s, 3H); ¹³C NMR (75 MHz, c⁶-DMSO) δ 160.9, 158.1, 136.8, 129.1, 128.8, 128.7, 128.3, 123.7, 122.4, 120.0, 117.7, 116.2, 115.8, 56.6; HRMS (EI⁺) calcd. for C₉₄H₅₈NO₂ (M+H) 225.0790, found 225.0798.

Example 98

This example concerns the synthesis of triaryl 34 and provides a representative procedure for palladium coupling using pd₂(dba)₃ / (c-c⁶-hii)₃P: To a pressure vessel was added 16 (1.162 g, 3.141 mmol), PhB(OH)₂ (1.350 g, 11.07 mmol), Cs₂CO₃ (1.767 g, 5.245 mmol), Pd₂(dba)₃ (73.3 mg, 80.0 µmol), PCy₃ (76.6 mg, 0.273 mmol), and dry dioxane (5.80 mL). The solution was sealed under Ar and heated to 80°C. After 48 h, the mixture was filtered over a pad of Celite®, eluting with Et₂O (200 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 10% Et₂O/hexanes, to give 34 (1.267 g, 3.078 mmol, 98%) as a bright yellow crystalline solid. MP 124-126°C; IR (thin film) 3031, 2934, 1612, 1582, 1529, 1511, 1359, 1048 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.87 (dd, J = 8.0, 1.2 Hz, IH), 7.63 (dd, J = 7.6, 1.6 Hz, IH), 7.53 (t, J = 7.6, IH), 7.37-7.25 (m, 3H), 7.25-7.17 (m, 5H), 7.10-7.02 (m, 2H), 6.83 (dd, J =...
8.4 Hz, IH), 6.40 (d, J = 2.4 Hz, IH), 6.39 (dd, J = 8.4, 2.4 Hz, IH), 4.99 (d, J = 12.4, IH), 4.87 (d, J = 12.4, IH), 3.74 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 160.7, 156.8, 151.2, 144.6, 140.1, 137.0, 133.9, 131.5, 129.2, 128.4, 127.8, 127.7, 127.6, 127.0, 126.7, 122.5, 117.5, 104.8, 99.9, 70.0, 55.2; HRMS (FAB+)
calcld. for C26H2iNO₄ (M+) 411.1471, found 411.1462.

Example 99

This example concerns the synthesis of triaryl 37, and provides a representative procedure for palladium couplings using (t-bu₂P)₂Pd: To a pressure vessel containing 30 (552 mg, 1.49 mmol), was sequentially added KF (783 mg, 13.5 mmol), C₆H₅-B(OH)₂ (732 mg, 6.00 mmol), (t-Bu₂P)₂Pd (38.4 mg, 0.0750 mmol), and NMP (15.0 mL). The solution was sealed under Ar and heated to 80°C. After 48 h, the reaction was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (100 mL), and washed with H₂O (50 mL) and sat. aq. NaCl (50 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5-25% EtOAc / Hexanes to give 37 (582 mg, 1.42 mmol, 95%) as a yellow crystalline solid. MP 107-108 °C; IR (neat) 3063, 2930, 1608, 1534 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 7.57 (t, J = 7.6 Hz, IH), 7.46-7.42 (m, 7H), 7.37-7.30 (m, 5H), 7.22 (d, J = 8.0 Hz, IH), 6.60-6.57 (m, 2H), 5.08 (s, 2H), 3.82 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 161.2, 156.9, 150.4, 137.2, 137.0, 134.6, 131.8, 131.6, 130.9, 129.9, 129.7, 128.7, 128.5, 128.3, 128.1, 127.7, 126.8, 118.6, 105.3, 100.7, 70.5, 55.4; HRMS (FAB+) calcd. for C₂₆H₂iNO₄ (M+H) 411.1471, found 411.1491.

Example 100

This example concerns representative procedure for debenzylation using bcl₃: To a stirred solution of benzyl ether 34 or 37 (0.1 mmol) in CH₂Cl₂ (1.2 M) was added BCl₃ (5.45 equiv, 1.0 M in heptane) at 0°C. After 4 h, the reaction was quenched with MeOH, concentrated in vacuo, and purified via flash chromatography over silica gel, eluting with 10-30% EtOAc / hexanes to give the phenol 56 or 57 (82-92%).
56 (92%): IR (neat) 3522, 1620, 1592, 1526, 1360, 1264, 1040, 877, 764 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.85 (dd, J = 8.0, 1.4 Hz, IH), 7.68 (dd, J = 8.0,1.4 Hz, IH), 7.60 (t, J = 8.0 Hz, IH), 7.28-7.21 (m, 3H), 7.19-7.12 (m, 2H), 6.77(d, J = 8.0 Hz, IH), 6.41-6.32 (m, 2H), 4.95 (br, IH), 3.65 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.8, 154.0, 151.7, 145.2, 139.5, 134.1, 131.5, 129.7, 129.1, 128.5, 128.0, 127.4, 122.6, 115.0, 106.7, 101.7, 55.2; HRMS (EI+) calcd. for C₁₉H₁₅NO₄ 321.1001, found 321.0999.

57 (82%): MP 166-167°C; IR (neat) 3409, 2921, 1617, 1530 cm⁻¹; ¹H NMR (400 MHz, MeOD) δ 7.62 (t, J = 7.7 Hz, IH), 7.46-7.38 (m, 7H), 7.05 (d, J = 8.0 Hz, IH), 6.50-6.47 (m, 2H), 3.81 (s, 3H); ¹³C NMR (100 MHz, MeOD) δ 161.3, 155.6, 152.8, 150.5, 137.4, 134.4, 132.0, 131.5, 130.5, 129.5, 128.2, 127.9, 127.8, 116.6, 104.7, 101.0, 54.3; HRMS (EI+) calcd. for C₁₉H₁₅NO₄ (M+H) 321.1001, found 321.1004.

Example 101
This example concerns a representative procedure for nitro reduction using Zn/HOAc: To a stirred solution of nitroarene 34 or 37 (0.1 mmol) in glacial HOAc (0.25 M) was added Zn dust (6.3 equiv.) at rt. After 20 h, the mixture was quenched with sat. aq. NaHCO₃, diluted with EtOAc and washed with H₂O and sat. aq. NaCl. The dried extract (Na₂SO₄) was concentrated in vacuo and purified via flash chromatography over silica gel, eluting with 15-25% EtOAc/Hexanes to give the aniline 58 or 59 (90%-97%).

58 (90%): IR (neat) 3471, 3379, 3058, 2835, 1609, 1580, 1266, 1044 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.13 (m, 1IH), 7.01 (d, J = 9.0 Hz, IH), 6.87 (dd, J = 8.0,1.1 Hz, IH), 6.83 (dd, J = 8.0, 1.1 H, IH), 6.54-6.41 (m, 2H), 5.02 (d, J = 12.8 Hz, IH), 4.92 (d, J = 12.8 Hz, IH), 3.76 (s, 3H), 3.52 (br, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 160.2, 157.2, 145.0, 143.2, 142.4, 137.4, 132.9, 129.3, 128.4, 128.1, 127.5, 127.4, 126.6, 126.0, 122.9, 120.2, 119.4, 114.3, 105.4, 100.6, 69.9, 55.3; HRMS (EI+) calcd. for C₂₆H₂₅NO₂ 381.1729, found 381.1721.

59 (97%): IR (neat) 3471, 3385, 3057, 2933, 1611, 1503, 1163 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.56-7.48 (m, 4H), 7.41 (dt, J = 1.5, 1.5, 7.2 Hz, IH), 7.38-7.32 (m, 6H), 7.20 (dd, J = 1.2, 7.2 Hz, 2H), 6.93 (t, J = 7.5 Hz, IH), 6.71-6.67
(m, 2H), 5.12 (s, 2H), 3.88 (s, 3H), 3.85 (broad s, 2H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 160.5, 156.9, 142.0, 140.2, 137.2, 132.4, 130.7, 129.5, 129.4, 128.8, 128.5, 127.8, 127.7, 127.1, 126.9, 125.0, 122.0, 117.9, 106.0, 101.3, 70.7, 55.5. HRMS (EI+) calcd. for C\(_{26}\)H\(_{23}\)N\(_2\)O\(_2\) (M+H) 382.1729, found 381.1728.

**Example 102**

This example concerns a representative procedure for hydrogenation using Pd/c: To a stirred solution of benzylated nitro arene 34 or 37 (0.1 mmol) and EtOH (0.28 M, absolute) was added Pd/C (475 mg / mmol, 10% Pd). After stirring under an atmosphere of H\(_2\) for 21 h, the mixture was filtered over a pad of Celite-® with EtOAc and concentrated in vacuo. The product was purified via flash chromatography over silica gel, eluting with 15-20% EtOAc / Hexanes to give the anilino phenol 60 or 61 (67%-85%).

60 (67%): IR (neat) 3472, 3382, 3187, 3057, 2959, 1617, 1578, 1549, 1447, 1440, 1413, 1326, 1291, 1291, 1277, 1265, 1214, 1206, 1159, 1149, 1073, 1016, 55.2; HRMS (EI+) calcd. for C\(_9\)H\(_7\)N\(_2\)O\(_2\) 291.1259, found 291.1251.

**Phenol 61:** MP 87-89°C; IR (neat) 3394, 3301, 2921, 1731, 1617, 1160 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.30 (t, \(J = 7.9\) Hz, IH), 7.25-7.10 (m, 5H), 6.95 (dd, \(J = 7.6, 1.0\) Hz, IH), 6.86 (dd, \(J = 8.0, 1.0\) Hz, IH), 6.80 (d, \(J = 8.5\) Hz, IH), 6.54 (d, \(J = 2.5\) Hz, IH), 6.38 (dd, 8.5, 2.5 Hz, IH), 3.78 (s, 3H), 4.70-3.40 (br, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 160.7, 154.7, 144.7, 144.0, 141.3, 132.6, 129.1, 129.1, 127.7, 126.5, 121.4, 120.6, 115.9, 114.9, 107.3, 101.6, 55.2; HRMS (EI+) calcd. for C\(_{19}\)H\(_{17}\)N\(_2\)O\(_2\) (M+H) 291.1259, found 291.126.

**Example 103**

This example concerns a representative procedure for Cadogan cyclization using PPh\(_3\): To a pressure vessel containing 20, 21, 22 or 32 (0.1 mmol) and \(o\)-C\(_6\)H\(_4\)Cl\(_2\) (0.5 M) was added PPh\(_3\) (2.5 equiv.) at rt. The mixture was heated to
180°C. After 24 h, the reaction was cooled to rt and purified via flash chromatography over silica gel, eluting with 10-30% EtOAc / Hexanes and recrystallization afforded the carbazole 62, 63, 64 or 65 (65-89%) as an off-white solid.

62 (75%): MP 158-160°C; IR (thin film) 3387, 1177 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.48 (d, J = 8.7 Hz, IH), 8.02 (br s, IH), 7.52 (d, J = 7.2 Hz, 2H), 7.45 (t, J = 7.2 Hz, 2H), 7.38 (t, J = 7.2 Hz, IH), 7.33-7.18 (m, 3 H), 7.03 (dd, J = 8.7, 2.2 Hz, IH), 6.97 (d, J= 0.9 Hz, IH), 5.19 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 158.5, 140.8, 140.6, 137.0, 128.7, 128.0, 127.8, 127.5, 125.0, 123.9, 120.9, 120.3, 116.4, 109.3, 108.6, 95.7, 70.4; HRMS (EI+) calcd. for C₁₉H₁₄ClNO (M⁺) 307.0764, found 307.0775.

63 (89%): MP 222-224°C; IR (KBr) 3390, 2916, 1624, 1225, 1176, 1027, 816, 728 cm⁻¹; ¹H NMR (400 MHz, d₆-DMSO) δ 11.30 (s, IH), 8.11 (s, IH), 8.04 (d, J = 7.8 Hz, IH), 7.68-7.19 (m, 7H), 7.08 (s, IH), 6.89 (d, J = 7.8 Hz, IH), 5.22 (s, 2H); ¹³C NMR (100 MHz, d₆-DMSO) δ 158.5, 142.2, 138.7, 137.7, 128.9, 128.3, 128.2, 124.5, 124.3, 123.4, 122.0, 119.4, 116.0, 112.5, 109.4, 96.2, 70.0; HRMS (EI+) calcd. for C₁₉H₁₄NOCl (M⁺) 307.0764, found 307.0775.

64 (84%): MP 235-238°C; IR (KBr) 3396, 2923, 1605, 1016, 797 cm⁻¹; ¹H NMR (400 MHz, d₆-DMSO) δ 11.29 (s, IH), 8.02 (d, J = 3.3 Hz, IH), 8.00 (d, J = 3.7 Hz, IH), 7.52 (d, J = 7.2 Hz, 2H), 7.46 (d, J = 1.8 Hz, IH), 7.43 (t, J = 7.1 Hz, 2H), 7.35 (t, J = 7.3 Hz, IH), 7.14 (dd, J = 8.3, 1.9 Hz, IH), 7.09 (d, J = 2.3 Hz, IH), 6.90 (dd, J = 8.6, 2.3 Hz, IH), 5.21 (s, 2H); ¹³C NMR (100 MHz, d₆-DMSO) δ 158.3, 141.9, 140.9, 137.7, 129.0, 128.9, 128.3, 128.2, 122.0, 121.6, 121.1, 119.1, 116.2, 110.8, 109.4, 96.4, 70.0; HRMS (EI+) calcd. for C₁₉H₁₄NOCl (M⁺) 307.0764, found 307.0772.

65 (65%): MP 145-146T; IR 3419, 2911, 1419, 735; ¹H NMR (400 MHz, CDCl₃) δ 8.21 (bs, IH), 7.96 (d, J = 8.6 Hz, IH), 7.89 (d, J = 7.8 Hz, IH), 7.52 (d, J = 7.2 Hz, 2H), 7.45 (t, J = 7.1, 7.6 Hz, 2H), 7.38 (t, J = 7.2, 7.8 Hz, 2 H), 7.18 (t, J = 7.8 Hz, IH), 7.07 (d, J = 2.0 Hz, IH), 7.00 (dd, J = 2.2 Hz, 8.6 Hz, IH); ¹³C NMR (100 MHz, CDCl₃) δ 158.7, 140.5, 137.0, 136.7, 128.7, 128.1, 127.5, 125.0, 123.9, 121.6, 120.4, 117.9, 117.6, 115.8, 109.8, 96.2, 70.5; HRMS (FAB+) calcd. For C₁₉H₁₄ClNO (M+H) 308.0842, found 308.0846.
Example 104

This example concerns the synthesis of **Toluene 73**: To a pressure vessel containing 13 (1.294 g, 7.126 mmol) and xylenes (14.0 mL) was added known diene 71 (4.831 g, 28.70 mmol) at it. The mixture was heated at 140°C. After 10 h, the reaction was cooled to 0°C and TBAF (29.0 mL, 29.0 mmol, 1 M in THF) was added. After 15 min, the brown mixture was quenched with sat. aq. NH₄Cl (100 mL), diluted with EtOAc (200 mL), washed with H₂O (2 x 50 mL), and sat. aq. NaCl (2 x 50 mL). The dried (Na₂SO₄) extract was concentrated *in vacuo* and purified via flash chromatography over silica, eluting with 0-35% EtOAc/Hexanes to give the phenol 70 (1.928 g) as an impure yellow oil. To a pressure vessel containing the impure phenol 70 (1.928 g), Cs₂CO₃ (4.637 g, 14.23 mmol), Pd₂(dba)₃ (35.8 mg, 39.1 mmol), PCy₃ (41.1 mg, 146 mmol), methyl boroxine (2.44 g, 2.70 mL, 19.4 mmol) and dioxane (20 mL). The solution was sealed under Ar and heated to 80°C. After 10 h, the vessel was cooled to rt and filtered over a pad of Celite®, eluting with EtOAc (150 mL) and concentrated *in vacuo*. The residue was purified by flash chromatography over silica gel, eluting with 0-20% EtOAc / PhMe, to give 73 (1.226 g, 5.348 mmol, 76% over two steps) as a bright yellow crystalline solid. MP 94-97°C; IR (thin film) 3407, 1612, 1517, 1350, 1216, 758 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, J = 8.2 Hz, IH), 7.29-7.19 (m, 4H), 6.93-6.87 (m, 2H), 4.96 (br s, IH), 2.48 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 155.8, 146.9, 143.5, 136.2, 132.7, 129.9, 129.3, 128.3, 124.4, 115.7, 21.4; HRMS (EI+) calcd. for C₁₃H₁₁NO₃ (M⁺) 229.0739, found 229.0732.

Example 105

This example concerns the synthesis of **Phenol 77**: To a stirred solution of 68 (43.2 mg, 160.4 mmol) in CH₂Cl₂ (500 μL) and 2-methyl-2-butene (596.0 mg, 0.90 mL, 8.49 mmol) was added Grubbs’ 2nd generation catalyst (4.0 mg, 4.7 μmol) at rt. After stirring for 18 h, the mixture was concentrated *in vacuo* and purified directly via flash chromatography over silica gel, eluting with 0-10% EtOAc / PhMe to give 77 (40.1 mg, 135.0 μmol, 73%) as a yellow oil. IR (neat) 3472, 1608, 1582, 1520, 1352, 824, 755 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, J = 8.8, Hz, IH),
7.25 (d, J = 7.1 Hz, 2H), 7.09 (dd, J = 6.0, 2.1 Hz, 2H), 6.86 (d, J = 8.8 Hz, IH),
5.48-5.31 (m, 2H), 3.41 (d, J = 7.1 Hz, 2H), 2.48 (s, 3H), 1.81 (s, 6H); 13C NMR
(100 MHz, CDCl 3 ) 5154.5, 147.1, 143.1, 136.3, 135.2, 132.6, 130.0, 129.5, 128.1,
127.2, 127.1, 124.3, 121.4, 116.0, 29.7, 25.8, 21.4, 17.9; HRMS (EI+) calcd. for
5 C 8 H 19 NO 3 (M+) 297.1365, found 297.1364.

Example 106
This example concerns the synthesis of Aniline 78: To a stirred solution of
77 (196.7 mg, 660.4 µmol) in glacial HOAc (6.0 mL) was added Zn dust (314.2 mg, 4.803 mmol) at rt. After 3 h, the mixture was quenched with sat. aq. NaHCO 3 (20 mL), diluted with EtOAc (100 mL) and washed with H 2 O (10 mL) and sat. aq. NaCl (2 x 20 mL). The dried extract (Na 2 SO 4 ) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 0-40% EtOAc / Hexanes to give 78
(151.7 mg, 551.0 µmol, 86%) as an off white solid. MP 126-132°C; IR (thin film)
3363, 3276, 2920, 1604, 1431, 1279, 1233 cm⁻¹; 1H NMR (400 MHz, CDCl 3 ) 7.23
(d, J=2.0 Hz, IH), 7.21 (dd, J = 8.3, 2.1Hz, IH), 7.00 (d, J = 9.1 Hz, 2H), 6.87 (d, J = 8.0 Hz, IH), 6.74 (d, J = 7.8 Hz, IH), 5.40 (tt, J = 5.9, 1.3 Hz, IH), 4.18 (br s, IH), 3.44 (d, J = 7.2 Hz, 2H), 2.32 (s, 3H), 1.83 (s, 3H), 1.82 (s, 3H); 13C NMR (100 MHz, CDCl 3 ) 153.6, 140.9, 134.8, 131.9, 131.1, 130.7, 128.6, 128.1, 128.0, 127.4, 121.7, 115.9, 115.9, 29.8, 25.9, 20.5, 17.9; HRMS (EI+) calcd. for C 8 H 9 NO (M+) 267.1623, found 267.1629.

Example 107
This example concerns the synthesis of Azide 79: To a stirred solution of
78 (150.2 mg, 562.1 mmol) and dioxane (2.00 mL) at -10°C was added aq. H 2 SO 4
(5.60 mL, 1.98 M). After stirring for 5 min at -10°C, NaN 3 (82.8 mg, 400 µL, 1.20 mmol, 3.00 M) was added via syringe. After 20 min at -10 °C, NaN 3 (117.0 mg, 600 µL, 1.80 mmol, 3.01 M) was added to the deep yellow solution and effervescence evolved. After 30min, the mixture was warmed to rt, and diluted with
30 Et 2 O (30 mL). The organic extract was washed with NaHCO 3 (3 x 15 mL) and sat aq. NaCl (2 x 10 mL). The dried extract (Na 2 SO 4 ) was concentrated in vacuo to give 79 (114.0 mg, 542.8 µmol, 97%) as a brown oil and used without further
purification. IR (thin film) 3419, 2115, 2068, 1608, 1263, 808 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.13 (m, 5H), 6.89 (d, J = 7.9 Hz, IH), 5.41 (tt, J = 7.4, 1.3 Hz, IH), 5.24 (d, J = 1.9 Hz, IH), 3.45 (d, J = 7.2 Hz, 2H), 2.40 (s, 3H), 1.84 (s, 3H), 1.83 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 5154.0, 135.0, 134.6, 134.3, 133.4, 131.8, 131.1, 130.8, 128.9, 128.6, 126.5, 121.1, 118.7, 115.5, 30.0, 25.8, 20.9, 17.9; HRMS (EI⁺) calcd. for C₈H₁₆N₃O (M⁺) 293.1528, found 293.1518.

Example 108

This example concerns the synthesis of Siamenol 66 and Carbazole 67: To a stirred solution of 74 (57.4 mg, 195.6 mmol) and PhMe (1.96 mL) and 2-methyl-2-butene (300 µL) at -10°C was added MeLi (160 µL, 216 µmol, 1.35M in Et₂O). After 5 min, BCl₃ (600 µL, 600 µmol, 1 M in hexanes) was added to the red mixture, and slight effervescence was observed. After stirring for 24 h at -10°C, the mixture was quenched with MeOH (1 mL) at -10°C, and then warmed to rt. The mixture was diluted with CH₂Cl₂ (30 mL) and washed with sat. aq. NH₄Cl (10 mL), H₂O (10 ml) and sat aq. NaCl (2 x 10 mL). The dried extract (Na₂SO₄) was concentrated in vacuo and purified via flash chromatography over silica gel, eluting with 0-20% EtOAc / Hexanes to give sequentially 67 (21.1 mg, 79.5 µmol, 41%) and 66 (19.2 mg, 72.3 µmol, 37%) as white solids. 66: MP 140-143°C; IR (thin film) 3406, 3252, 2920, 2852, 1636, 1617, 1465, 1319, 1210, 1014, 802 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (m, 3H), 7.27 (d, J = 8.0 Hz, IH), 7.17 (d, J=8.0 Hz, IH), 6.86 (s, IH), 5.44 (tt, J = 7.2, 1.2 H, IH), 5.30 (s, IH), 3.55 (d, J = 7.2 Hz, 2H), 2.54 (s, 3H), 1.88 (s, 3H), 1.85 (s, 3H); ¹H NMR (400 MHz, d₆-MeOO) δ 7.64 (dd, J = 1.6, 0.8 Hz, IH), 7.60 (s, IH), 7.19 (d, J = 8.2 Hz, IH), 7.04 (dd, J = 8.1, 1.0 Hz, IH), 6.79 (s, IH), 5.43 (t-sept, J = 7.3, 1.4 Hz, IH), 3.41 (d, J = 7.3 Hz, 2H), 2.45 (s, 3H), 1.78 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 153.7, 139.9, 137.7, 134.7, 128.6, 125.7, 123.7, 122.6, 120.8, 119.4, 117.2, 109.9, 97.2, 30.5, 25.8, 21.4, 17.9; ¹³C NMR (100 MHz, CDCl₃) δ 154.16, 140.4, 138.5, 131.1, 127.3, 124.7, 124.0, 123.9, 120.5, 119.7, 118.5, 116.1, 109.7, 95.9, 28.5, 24.9, 20.4, 16.7; HRMS (EI⁺) calcd. for C₈H₁₉NO 265.1467 (M⁺), found 265.1471. 67: MP 126-128°C; IR (thin film) 3524, 3424, 3261, 2919, 2853, 1614, 1227, 1211, 1032, 802 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.85 (br s, IH), 7.78 (d, J = 1.0 Hz, IH), 7.76 (d, J = 3.6 Hz, IH), 7.56 (d, J = 8.0 Hz, IH),...
7.31 (d, J = 8.2 Hz, IH), 7.18 (dd, J = 8.4, 1.1 Hz, IH), 6.76 (d, J = 8.3 Hz, IH), 5.41 (d-quint, J = 6.9, 1.4 Hz, IH), 5.11 (br s, IH), 3.64 (d, J = 6.9 Hz, 2H), 2.54 (s, 3H), 1.94 (s, 3H), 1.82 (d, J = 1.2 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 152.2, 140.4, 137.8, 134.9, 128.8, 125.8, 124.2, 121.5, 119.5, 118.6, 117.4, 110.1, 109.0, 108.3, 25.8, 24.4, 21.5, 18.1; HRMS (EI+) calcd. for C6H5NO 237.154 (M+), found 237.155.

Example 109

This example concerns the synthesis of Aldehyde 4: To a stirred solution of 1 (18.53 g, 108.0 mmol) in dry DMF (240 mL) was added NJV-dimethylformamide dimethyl acetal (DMF'DMA) (39.5 g, 44.0 mL, 331 mmol). After heating at 140°C for 16 h, the dark red solution was cooled to 0°C and added slowly, over 1 h via cannula, to a rapidly stirred solution OfNaIO4 (83.0 g, 388.0 mmol) in H2O (291 mL) and DMF (77 mL) at 0°C. The reaction flask was washed with DMF (20 mL) at 0°C and added to NaIO4 mixture. The reaction was stirred at 0°C for 2 h then allowed to warm to rt. After an additional 6 h, the orange solution was filtered and rinsed with PhMe/EtOAc (1:1, 200 mL). The filtrate was then washed with H2O (3 x 150 mL) and sat. aq. NaCl (3 x 150 mL). The dried (MgSO4) extract was concentrated in vacuo to a dark red oil, and hexanes (40 mL) were added. Solids were isolated and recrystallized in PhMe to give the known aldehyde 4 (17.23 g, 92.88 mmol, 86%). 1H NMR (400 MHz, CDCl3) δ 10.42 (s, IH), 8.01 (dd, J = 1.0, 8.2 Hz, IH), 7.79 (dd, J = 1.0, 8.1 Hz3 IH), 7.65 (t, J = 8.1 Hz, IH); 13C NMR (100 MHz, CDCl3) δ 188.6, 148.4, 138.6, 132.9, 132.4, 123.4, 121.9.
Example 110

This example concerns the synthesis of Aldehyde 5: To a stirred solution of 2 (5.248 g, 30.59 mmol) in dry DMF (172 mL) was added N,N-dimethylformamide dimethyl acetal (DMF•DMA) (13.7 g, 12.0 mL, 88.5 mmol). After heating at 140°C for 16 h, the dark red solution was cooled to 0°C and added slowly, over 20 min via cannula, to a rapidly stirred solution of NaIO₄ (18.7 g, 87.4 mmol) in H₂O (69 mL) and DMF (23 mL) at 0°C. The reaction flask was washed with DMF (20 mL) at 0°C and added to NaIO₄ mixture. The reaction was stirred at 0°C for 30 min then allowed to warm to rt. After an additional 4 h, the orange solution was filtered and rinsed with PhMe (200 mL). The filtrate was then washed with H₂O (2 x 200 mL) and sat. aq. NaCl (2 x 100 mL). The dried (MgSO₄) extract was filtered, concentrated in vacuo to a dark red oil, and purified by flash chromatography over silica gel, eluting with 20-50% EtOAc / Hexanes to give known aldehyde 5 (4.737 g, 25.53 mmol, 84%). ¹H NMR (400 MHz, CDCl₃) δ 10.41 (s, 1H), 8.13 (d, J = 2.0 Hz, 1H), 7.97 (dd, J = 8.3 Hz, 1H), 7.78 (dd, J = 2.0, 8.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 186.9, 150.1, 140.2, 134.2, 130.9, 129.3, 124.8.

Example 111

This example concerns the synthesis of Acetylene 7: To a stirred solution of 4 (16.64 g, 89.67 mmol), K₂CO₃ (25.14 g, 181.9 mmol), and MeOH (1.34 L) was added diazophosphonate 6 (24.33 g, 208.7 mmol) at rt. After 4 h, the solution was quenched with sat. aq. NaHCO₃ (500 mL) and concentrated in vacuo to remove the MeOH. The solution was diluted with EtOAc (700 mL) and washed with H₂O (3 x 200 mL), and sat. aq. NaCl (2 x 150 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting...
with 1% EtOAc/Hexanes, to give 7 (13.84 g, 76.22 mmol, 85%) as a pale yellow solid. MP 94-95°C; IR (thin film) 3286, 1521, 1351, 808, 756, 736, 681 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.92 (dd, J = 8.2, 1.1 Hz, IH), 7.74 (dd, J = 8.2, 1.1 Hz, IH), 7.47 (t, J = 8.2, IH), 3.86 (s, IH); ¹³C NMR (100 MHz, CDCl₃) δ 139.8, 134.0, 129.6, 123.1, 117.6, 109.9, 91.7, 75.3; HRMS (CI+) calcd. for C₈H₅NO₂Cl (M+H) 182.0009, found 182.0005.

Example 112

![Chemical structure](image)

This example concerns the synthesis of Acetylene 8: To a stirred solution of 5 (3.667 g, 19.76 mmol), K₂CO₃ (5.510 g, 39.87 mmol), and MeOH (330 mL) was added diazophosphonate 6 (5.168 g, 26.90 mmol) at rt. After 4 h, the solution was quenched with sat. aq. NaHCO₃ (200 mL) and concentrated in vacuo to remove the MeOH. The solution was diluted with EtOAc (200 mL) and washed with H₂O (3 x 50 mL), and sat. aq. NaCl (2 x 50 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 1% EtOAc/Hexanes, to give 8 (2.870 g, 15.81 mmol, 81%) as a pale yellow solid. MP 68-70°C; IR (thin film) 3285, 1555, 1528, 1345, 891, 840, 791, 761 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (d, J = 2.0 Hz, IH), 7.67 (dd, J = 8.4 Hz, IH), 7.60 (dd, J = 8.4, 2.0, IH), 3.59 (s, IH); ¹³C NMR (75 MHz, CDCl₃) δ 150.5, 136.4, 135.3, 133.1, 124.9, 115.9, 86.3, 77.6; HRMS (CI+) calcd. for C₈H₅NO₂Cl (M+H) 183.9979, found 183.9980.

Example 113

![Chemical structure](image)

This example concerns the synthesis of Methyl ester 80: To a stirred solution of 9 (9.393 g, 46.60 mmol) in dry DMF (155 mL) at 0°C was added K₂CO₃..
(13.23 g, 95.72 mmol) and MeI (19.38 g, 8.5 mL, 136.5 mmol) and warmed to 40°C. After 1 h, the solution was cooled to rt and diluted with EtOAc (115 mL). The solution was washed with H₂O (3 x 100 mL), and sat. aq. NaCl (3 x 100 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica gel, eluting with 40-60% EtOAc/Hexanes, to give the known methyl ester 80 (9.244 g, 42.87 mmol, 92%) as a pale yellow solid. 

Example 114

This example concerns the synthesis of Aldehyde 11: To a stirred solution of 80 (8.20 g, 38.0 mmol) and dry CH₂Cl₂ (205 mL) was added DIBAL-H (48.0 mL, 48.0 mmol, 1.0 M in CH₂Cl₂) at -78°C. After 45 min, MeOH (20 mL) was added and the solution was allowed to warm to rt. Next, aq. sodium tartrate (200 mL, 10% w/v) was added and the suspension was left to stir vigorously until a bilayer was distinct. The solution was diluted with CH₂Cl₂ (100 mL) and washed with H₂O (2 x 100 mL), sat. aq. NaCl (2 x 100 mL). The dried (Na₂SO₄) extract was purified via flash chromatography over silica gel, eluting with 20-50% EtOAc/Hexanes to give the known aldehyde 13 (6.80 g, 36.7 mmol, 97%). 

$^1$H NMR (400 MHz, CDCl₃) δ 10.46 (s, IH), 8.15 (d, $J$ = 8.7 Hz, IH), 7.94 (d, $J$ = 2.3 Hz, IH), 7.74 (dd, $J$ = 2.4, 8.7 Hz, IH); $^{13}$C NMR (100 MHz, CDCl₃) δ 187.0, 147.5, 141.0, 133.5, 132.7, 129.4, 126.2.
Example 115

This example concerns the synthesis of Methyl ester 81: To a stirred solution of 10 (5.01 g, 24.9 mmol), K$_2$CO$_3$ (10.3 g, 74.7 mmol), and DMF (25 mL) was added MeI (3.10 mL, 7.07 g, 49.8 mmol). The reaction mixture was heated to 40°C. After 1 h, the reaction was quenched with H$_2$O (30 mL), diluted with EtOAc (50 mL), and washed with H$_2$O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO$_4$) was concentrated in vacuo to give known ester 81 (5.31 g, 24.6 mmol, 99%) as a white crystalline solid. MP 101-103°C; $^1$H NMR (300 MHz, CDCl$_3$) δ 8.01 (dd, J = 1.2, 7.8 Hz, 1H), 7.74 (dd, J = 1.2, 8.1 Hz, 1H), 7.55 (dd, J = 7.8, 8.1 Hz, 1H), 3.94 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.6, 148.4, 134.8, 130.7, 129.7, 126.4, 124.5, 53.4.

Example 116

This example concerns the synthesis of Aldehyde 12: To a stirred solution of 81 (2.91 g, 13.5 mmol) and CH$_2$Cl$_2$ (134 mL) at -78°C was added DIBAL-H (16.0 mL, 16.0 mmol, 1.0 M in CH$_2$Cl$_2$) over 15 min. After an additional 10 min, the reaction was quenched with MeOH (1.0 mL) and warmed to rt. Next, a solution of aq. sodium potassium tartrate (190 mL, 10% w/v) was added and vigorously stirred. After 4 h, the reaction mixture was diluted with CH$_2$Cl$_2$ (50 mL) and washed with H$_2$O (3 x 100 mL) and sat. aq. NaCl (100 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by recrystallization with EtOAc / Hexanes (1:3) to give known aldehyde 12 (2.32 g, 12.7 mmol, 94%) as a white crystalline solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 9.90 (s, 1H), 7.92 (dd, J = 1.4, 7.7 Hz, 1H), 7.80 (dd, J = 1.4, 8.1 Hz, 1H), 7.67 (dd, J = 7.7, 8.1 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 186.0, 148.1 136.0, 131.7, 130.1, 128.5, 126.6.
Example 117

\[
\begin{array}{c}
\text{Cl} & \text{NO}_2 \\
\text{O} & \text{Cl} \\
\text{H} & \text{NO}_2
\end{array}
\quad +
\begin{array}{c}
\text{O} & \text{P} & \text{OMe}_2 \\
\text{N}_2 & \text{O} & \text{P} & \text{OMe}_2
\end{array}
\rightarrow
\begin{array}{c}
\text{Cl} & \text{NO}_2 \\
\text{O} & \text{Cl} \\
\text{H} & \text{NO}_2
\end{array}
\]

This example concerns the synthesis of Acetylene 13: To a stirred solution of 11 (3.694 g, 19.90 mmol), K₂CO₃ (5.528 g, 40.00 mmol), and dry MeOH (350 mL) was added diazophosphonate 6 (5.088 g, 26.48 mmol) at rt. After 4 h, the solution was quenched with sat. aq. NaHCO₃ (200 mL) and concentrated in vacuo to remove the MeOH. The solution was diluted with EtOAc (300 mL) and washed with H₂O (3 x 100 mL), and sat. aq. NaCl (2 x 100 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 1% EtOAc / Hexanes, to give 13 (2.891 g, 15.92 mmol, 80%) as a pale yellow solid. MP 70-73°C; IR (thin film) 3286, 2112, 1599, 1559, 1516, 883, 753 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.04 (d, J = 8.7 Hz, IH), 7.68 (d, J = 2.3 Hz, IH), 7.49 (dd, J = 8.7, 2.3 Hz, IH), 3.60 (s, IH); ¹³C NMR (75 MHz, CDCl₃) δ 148.5, 139.5, 135.2, 129.6, 126.0, 119.2, 86.6, 77.5; HRMS (Cl⁺) calcd. for C₈H₈NO₂⁻Cl (M+H) 183.9979, found 183.9977.

Example 118

\[
\begin{array}{c}
\text{Cl} & \text{NO}_2 \\
\text{O} & \text{Cl} \\
\text{H} & \text{NO}_2
\end{array}
\quad +
\begin{array}{c}
\text{O} & \text{P} & \text{OMe}_2 \\
\text{N}_2 & \text{O} & \text{P} & \text{OMe}_2
\end{array}
\rightarrow
\begin{array}{c}
\text{Cl} & \text{NO}_2 \\
\text{O} & \text{Cl} \\
\text{H} & \text{NO}_2
\end{array}
\]

This example concerns the synthesis of Acetylene 14: To a stirred solution of 12 (1.02 g, 5.59 mmol), K₂CO₃ (1.54 g, 11.1 mmol), and MeOH (56.0 mL) was added diazophosphonate reagent 6 (1.39 g, 1.07 mL, 7.26 mmol) at rt. After 2 h, the reaction was quenched with aq. NaHCO₃ (60 mL, 5% w/v), and the MeOH was removed in vacuo. The reaction mixture was diluted with EtOAc (30 mL) and washed with aq. NaHCO₃ (25 mL, 5% w/v), H₂O (25 mL), and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5 - 20% EtOAc/Hexanes, to give 14 (1.01 g, 4.94 mmol, 88%) as a pale yellow solid. MP 42-43°C; IR (neat) 3289, 3072, 1549 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.56 (dd, J = 1.4, 7.9 Hz, IH), 7.54 - 182 -
Example 119

This example concerns the synthesis of Phenol 82: To a pressure vessel containing 7 (1.739 g, 9.578 mmol) and PhMe (20 mL) was added diene 15 (8.423 g, 41.63 mmol) at rt. The mixture was heated at 80°C. After 24 h, the reaction was cooled to 0°C and DABCO (4.414 g, 39.35 mmol) was added and gradually warmed to 40°C over 30 min. After 1 h at 40°C, the brown mixture was cooled to rt and quenched with aq. HCl (1 M) until pH = 2, diluted with EtOAc (100 mL), washed with H₂O (50 mL), and sat. aq. NaCl (2 x 50 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0-20% EtOAc/Hexanes to give 82 (1.795 g, 6.417 mmol, 67%) as a yellow solid. MP 134-135°C; IR (thin film) 3423, 1620, 1529, 1444, 1356 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.78 (dd, J = 8.1, 1.0 Hz, IH), 7.73 (dd, J = 8.1, 1.0, Hz, IH), 7.46 (t, J = 8.1, IH), 7.00 (d, 8.5 Hz, IH), 6.58 (dd, J = 8.5, 2.4 Hz, IH), 6.49 (d, J = 2.4 Hz, IH), 5.05 (s, IH), 3.82 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.8, 154.2, 152.2, 137.6, 134.0, 131.3, 131.2, 129.6, 122.6, 114.2, 107.1, 102.5, 55.8; HRMS (CI⁺) calcd. for C₈H₄NO₂Cl (M+) 182.0009, found 182.0001.

Example 120

This example concerns the synthesis of Chloride 16: To a stirred solution of 82 (1.245 g, 4.500 mmol) and dry DMF (22.0 mL) was added NaH (397.2 mg, 9.93
mmol, 60% dispersion in mineral oil) at 0°C. To this dark red solution was added
BnBr (7.76 g, 5.40 mL, 45.4 mmol). After 10 min, the yellow solution was
quenched with sat. aq. NH₄Cl (100 mL), diluted with EtOAc (150 mL), washed with
H₂O (50 mL), and sat. aq. NaCl (2 x 100 mL). The dried (MgSO₄) extract was
concentrated in vacuo and purified by flash chromatography over silica gel, eluting
with 0-10% Et₂O/Hexanes to give 16 (1.582 g, 4.277 mmol, 95%) as a bright yellow
crystalline solid. MP 99-100°C; IR (thin film) 2936, 1612, 1583, 1529, 1441 cm⁻¹;
¹H NMR (400 MHz, CDCl₃) δ 7.82 (dd, J = 8.1, 1.2 Hz, IH), 7.73 (dd, J = 8.1, 1.2
Hz, IH), 7.443 (t, J = 8.1 Hz, IH), 7.36-7.23 (m, 5H), 7.13 (d, J = 8.3 Hz, IH), 6.63
(dd, J = 8.3, 2.3 Hz, IH), 6.60 (d, J = 2.3 Hz, IH), 5.05 (s, 2H), 3.85 (s, 3H); ¹³C
NMR (100 MHz, CDCl₃) δ 161.4, 156.6, 151.4, 136.8, 136.7, 133.4, 132.0, 130.7,
128.6, 128.4, 127.7, 126.8, 122.2, 116.2, 105.1, 100.3, 70.3, 55.3; HRMS (FAB+)
calcd. for C₂₀H₁₆NO₄Cl (M+) 369.0768, found 369.0759.

Example 121

This example concerns the synthesis of Phenol 83: To a pressure vessel
containing 13 (189.3 mg, 1.043 mmol) and PhMe (2.0 mL) was added diene 15
(872.8 mg, 4.313 mmol) at rt. The mixture was heated at 80°C. After 24 h, the
reaction was cooled to 0°C and DABCO (670.8 mg, 5.980 mmol) was added and
gradually warmed to 40°C over 30 min. After 30 min at 40°C, the brown mixture
was cooled to rt and quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (25
mL), washed with H₂O (10 mL), and sat. aq. NaCl (2 x 20 mL). The dried (Na₂SO₄)
extract was concentrated in vacuo and purified via flash chromatography over silica,
eluting with 0-20% EtOAc / Hexanes to give 83 (178.9 mg, 646.6 mmol, 62%) as a
yellow oil. IR (thin film) 3389, 2933, 1622, 1600, 1561, 1518, 865, 830, 727 cm⁻¹;
¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, J = 8.5 Hz, IH), 7.46 (dd, J = 8.5, 2.3, Hz,
IH), 7.43 (d, J = 2.3, IH), 7.17 (d, 8.5 Hz, IH), 6.63 (dd, J = 8.5, 2.4 Hz, IH), 6.41
(d, J = 2.4 Hz, IH), 4.94 (s, IH), 3.84 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.4,
This example concerns the synthesis of Chloride 17: To a stirred solution of 83 (100 mg, 361.4 mmol) and dry DMF (1.8 mL) was added NaH (30.8 mg, 0.77 mmol, 60% dispersion in mineral oil) at 0°C. To this dark red solution was added BnBr (7.19 mg, 500 mL, 4.20 mmol). After 10 min, the yellow solution was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (20 mL), washed with H₂O (15 mL), and sat. aq. NaCl (2 x 25 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 0-10% Et₂O / Hexanes to give 17 (124.3 mg, 336.2 mmol, 93%) as a bright yellow crystalline solid. MP 121-124°C; IR (thin film) 2925, 2851, 1617, 1595, 1531, 1268, 1049 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.91 (dd, J = 0.3, 8.6 Hz, IH), 7.45-7.39 (m, 2H), 7.37-7.33 (m, 3H), 7.27-7.22 (m, 3H), 6.65 (dd, J = 8.4, 2.4 Hz, IH), 6.55 (d, J = 2.4 Hz, IH), 5.00 (s, 2H), 3.85 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.5, 156.2, 147.9, 138.6, 136.3, 135.1, 132.6, 130.2, 128.5, 127.9, 127.6, 127.2, 125.5, 119.2, 105.6, 100.3, 70.7, 55.4; HRMS (EI+) calcd. for C₂₀H₁₆NO₄Cl (M+) 369.0768, found 369.0776.

Example 123

This example concerns the synthesis of Phenol 84 and Chloride 18: To a pressure vessel containing 8 (185.2 mg, 1.020 mmol) and PhMe (2.0 mL) was added...
diene 15 (834.1 mg, 4.102 mmol) at rt. The mixture was heated at 80°C. After 24 h, the reaction was cooled to 0°C and DABCO (493.6 mg, 4.401 mmol) was added and gradually warmed to 40°C over 30 min. After 1 h, the brown mixture was cooled to rt and quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (20 mL), washed with H₂O (20 mL), and sat. aq. NaCl (2 x 15 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0-20% EtOAc/Hexanes to give impure 84 (363.0 mg) as a yellow oil and used without further purification.

**Chloride 18:** To a stirred solution of 84 (363.0 mg) and dry DMF (3.6 mL) was added NaH (93.2 mg, 2.33 mmol, 60% dispersion in mineral oil) at 0°C. To this dark red solution was added BnBr (1.22 g, 0.85 mL, 7.15 mmol). After 10 min, the yellow solution was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (30 mL), washed with H₂O (10 mL), and sat. aq. NaCl (2 x 10 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 0-10% Et₂O / Hexanes to give 18 (233.9 mg, 0.632 mmol, 62% over 2 steps) as a bright yellow crystalline solid. MP 126-128°C; IR (thin film) 3032, 2925, 1608, 1527, 1260, 1050 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, J = 2.2 Hz, IH), 7.58 (dd, J = 8.3, 2.2 Hz, IH), 7.44-7.20 (m, 7H), 6.63 (dd, J = 8.4, 2.4 Hz, IH), 6.54 (d, J = 2.4 Hz, IH), 5.00 (s, 2H), 3.84 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.4, 156.1, 149.7, 136.3, 133.8, 133.3, 132.6, 131.7, 130.2, 128.5, 127.9, 127.1, 124.2, 119.2, 105.6, 100.3, 70.6, 55.4; HRMS (EI+) calcd. for C₂₀H₁₆NO₄Cl (M+) 369.0768, found 369.0766.

**Example 124**

This example concerns the synthesis of Phenol 85: To a pressure vessel containing 7 (147.1 mg, 810.2 mmol) and PhMe (1.3 mL) was added diene 19 (630 mg, 700 mL, 2.94 mmol) at rt. The mixture was heated at 120°C. After 24 h, the reaction was cooled to 0°C and TBAF (3.0 mL, 3.0 mmol, 1.0 M in THF) was...
added. After 15 min, the brown mixture was quenched with sat. aq. NH₄Cl (10 mL),
diluted with EtOAc (20 mL), washed with H₂O (10 mL), and sat. aq. NaCl (2 x 10 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0-20% EtOAc/Hexanes to give 85 (161.0 mg, 644.9 mmol, 80%) as a yellow solid. MP 83-84 °C; IR (thin film) 3423, 1614,
1529, 1361, 1201 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 8.0, 2H), 7.45 (t, J = 8.0 Hz, 1H), 7.18 (d, J = 8.5, 2H), 6.94 (d, 8.5 Hz, 2H), 5.00 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 156.3, 151.9, 136.5, 134.7, 133.5, 130.7, 129.1, 126.5, 122.2, 115.9; HRMS (Cl+) calcd. for C₁₉H₁₄NO₃Cl (M+H) 250.0271, found 250.0277.

**Example 125**

![Chemical Structure](image)

This example concerns the synthesis of Chloride 20: To a stirred solution of 85 (111.4 mg, 446.2 mmol) and dry DMF (2.0 mL) was added NaH (48.1 mg, 1.20 mmol, 60% dispersion in mineral oil) at 0 °C. To this dark red solution was added BnBr (790.9 mg, 550 mL, 4.624 mmol). After 10 min, the yellow solution was quenched with sat. aq. NH₄Cl (20 mL), diluted with EtOAc (20 mL), washed with H₂O (10 mL), and sat. aq. NaCl (2 x 10 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 0-10% Et₂O/Hexanes to give 20 (137.2 mg, 403.8 mmol, 90%) as a bright yellow crystalline solid. MP 85-89 °C; IR (thin film) 3088, 2873, 1610, 1531, 1244, 1027 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, J = 8.1 Hz, 2H), 7.55-7.35 (m, 6H), 7.20 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 5.14 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 151.6, 136.7, 136.1, 134.4, 133.2, 130.2, 128.7, 128.7, 128.1, 127.7, 126.2, 121.9, 114.8, 70.1; HRMS (FAB+) calcd. for C₁₉H₁₄NO₃Cl 339.0662, found 339.0669.
Example 126

This example concerns the synthesis of Phenol 86 and Chloride 21: To a pressure vessel containing 13 (116.8 mg, 643.3 mmol) and PhMe (1 mL) was added diene 19 (495 mg, 550 mL, 2.32 mmol) at rt. The mixture was heated at 120°C. After 24 h, the reaction was cooled to O°C and THF (3.6 mL, 3.6 mmol, 1.0 M in THF) was added. After 15 min, the brown mixture was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (30 mL), washed with H₂O (15 mL), and sat. aq. NaCl (2 x 10 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0-20% EtOAc/Hexanes to give impure 86 (171.3 mg) as a yellow oil, and was used without further purification.

Chloride 21: To a stirred solution of 86 (171.3 mg) and dry DMF (3.2 mL) was added NaH (101.5 mg, 2.538 mmol, 60% dispersion in mineral oil) at 0°C. To this dark red solution was added BnBr (1.44 g, 1.00 mL, 8.41 mmol). After 10 min, the yellow solution was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (30 mL), washed with H₂O (15 mL), and sat. aq. NaCl (2 x 10 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 0-10% Et₂O/Hexanes to give 21 (170.6 mg, 502.0 mmol, 78% over 2 steps) as a bright yellow crystalline solid. MP 144-147°C; IR (thin film) 3087, 2888, 1609, 1653, 1249, 1028 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, J = 2.2 Hz, 1H), 7.60 (dd, J = 8.3, 2.2 Hz, 1H), 7.53-7.36 (m, 6H), 7.27 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 8.8 Hz, 2H), 5.14 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 149.5, 136.7, 134.3, 133.5, 133.0, 132.3, 129.2, 128.7, 128.6, 128.2, 127.6, 124.2, 115.3, 70.1; HRMS (EI+) calcd. for C₁₉H₁₄NO₃Cl (M+) 339.0662, found 339.0660.
Example 127

This example concerns the synthesis of **Phenol 87** and **Chloride 22**: To a pressure vessel containing 8 (123.7 mg, 681.3 μmol) and PhMe (1 mL) was added diene 19 (495 mg, 550 μL, 2.203 mmol) at rt. The mixture was heated at 120°C. After 24 h, the reaction was cooled to 0°C and TBAF (3.7 mL, 3.7 mmol, 1.0 M in THF) was added. After 10 min, the brown mixture was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (30 mL), washed with H₂O (15 mL), and sat. aq. NaCl (2 x 10 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0-20% EtOAc / Hexanes to give 87 (169.4 mg) as a yellow oil, with minor impurities, and used without further purification.

**Chloride 22**: To a stirred solution of 87 (169.4 mg) and dry DMF (3.0 mL) was added NaH (155.6 mg, 3.89 mmol, 60% dispersion in mineral oil) at 0°C. To this dark red solution was added BnBr (1.44 g, 1.0 mL, 8.41 mmol). After 10 min, the yellow solution was quenched with sat. aq. NH₄Cl (15 mL), diluted with EtOAc (20 mL), washed with H₂O (15 mL), and sat. aq. NaCl (2 x 10 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 0-10% Et₂O/Hexanes to give 22 (175.9 mg, 517.6 mmol, 76% over 2 steps) as a bright yellow crystalline solid. MP 147-148°C; IR (thin film) 3067, 1609, 1531, 1249, 1028 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, J = 2.0 Hz, IH), 7.60 (dd, J = 8.3, 2.0 Hz, IH), 7.55-7.35 (m, 6H), 7.27 (d, J = 8.6 Hz, 2H), 7.08 (d, J = 8.6 Hz, 2H), 5.14 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 149.5, 136.7, 134.3, 133.5, 133.0, 132.3, 129.2, 128.7, 128.6, 128.2, 127.6, 124.2, 115.3, 70.1; HRMS (EI+) calcd. for C₁₉H₁₄NO₃Cl (M+) 339.0662, found 339.0652.
Example 128

This example concerns the synthesis of Phenol 88: To a pressure vessel containing 7 (52.6 mg, 289.7 mmol) was added diene 23 (269.9 mg, 1.361 mmol) at rt. The mixture was heated at 140°C. After 24 h, the reaction was cooled to 0°C and TBAF (1.4 mL, 1.4 mmol, 1M in THF) was added. After 10 min, the brown mixture was quenched with sat. aq. NH₄Cl (20 mL), diluted with EtOAc (30 mL), washed with H₂O (20 mL), and sat. aq. NaCl (2 x 20 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0-20% EtOAc/Hexanes to give 88 (53.6 mg, 191.6 mmol, 66%) as a bright yellow solid. MP 136-138°C; IR (thin film) 3432, 3080, 2929, 1613, 1587, 1531, 1355, 1303 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.84 (dd, J = 8.1, 1.2 Hz, IH), 7.73 (dd, J = 8.1, 1.2, IH), 7.44 (t, J = 8.1, IH), 7.05 (d, 8.8 Hz, IH), 6.56-6.50 (m, 2H), 3.74 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 157.8, 157.6, 151.5, 136.7, 133.5, 131.8, 130.9, 128.5, 122.1, 115.3, 107.4, 99.4, 55.6; HRMS (EI+) calcd. for C₁₃H₁₀NO₄Cl (M+H) 279.0298, found 279.0293.

Example 129

This example concerns the synthesis of Chloride 24: To a stirred solution of 88 (26.4 mg, 94.4 mmol) and dry DMF (50 mL) was added NaH (8.2 mg, 0.205 mmol, 60% dispersion in mineral oil) at 0°C. To this dark red solution was added BnBr (187 mg, 130 mL, 1.07 mmol). After 10 min, the yellow solution was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (20 mL), washed with H₂O (10 mL), and sat. aq. NaCl (2 x 10 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting...
with 0-10% Et₂O/Hexanes to give 24 (18.1 mg, 48.9 mmol, 96%) as a bright yellow crystalline solid. MP 104-106°C; IR (thin film) 2959, 1614, 1583, 1530, 1025, 1037 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.80 (dd, J = 8.1, 1.3 Hz, IH), 7.72 (dd, J = 8.1, 1.3 Hz, IH), 7.53-7.34 (m, 6H), 7.12 (d, J = 8.3 Hz, IH), 6.69 (dd, J = 8.3, 2.3 Hz, IH), 6.65 (d, J = 2.3 Hz, IH), 5.11 (s, 2H), 3.73 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.9, 157.5, 151.5, 136.7, 136.7, 133.5, 131.8, 130.8, 128.7, 128.5, 128.2, 127.8, 122.2, 115.9, 105.4, 99.6, 70.3, 55.6; HRMS (EI+) calcd. for C₂₀H₁₆NO₄Cl (M⁺) 369.0768, found 369.0760.

Example 130

This example concerns the synthesis of Phenol 89: To a pressure vessel containing 7 (106.8 mg, 588.2 mmol) was added diene 23 (364.7 mg, 1.839 mmol) at rt. The mixture was heated at 140°C. After 24 h, the reaction was cooled to 0°C and TBAF (1.8 mL, 1.8 mmol, 1 M in THF) was added. After 10 min, the brown mixture was quenched with sat. aq. NH₄Cl (20 mL), diluted with EtOAc (30 mL), washed with H₂O (20 mL), and sat. aq. NaCl (2 x 20 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0-20% EtOAc/Hexanes to give 89 (124.6 mg, 445.5 mmol, 76%) as a bright yellow solid. MP 178-181°C; IR (thin film) 3458, 1613, 1596, 1523, 1350, 1037 cm⁻¹; ¹H NMR (400 MHz, DMSO-J) δ 9.83 (s, 1H), 7.95 (dd, J = 8.4, 1.3 Hz, IH), 7.61 (dd, J = 8.4, 2.4, IH), 7.51 (d, 2.4 Hz, IH), 7.19 (d, J = 8.4 Hz, IH), 6.50 (dd, J = 8.4, 2.4 Hz, IH), 6.45 (d, J = 2.0, IH), 3.58 (s, 3H); ¹³C NMR (100 MHz, DMSO-J) δ 160.2, 157.1, 148.3, 137.8, 134.8, 132.3, 130.9, 128.1, 126.2, 116.1, 108.4, 99.5, 55.4; HRMS (EI+) calcd. for C₁₃H₁₀NO₄Cl (M⁺) 279.0298, found 279.0303.
Example 131

This example concerns the synthesis of Chloride 25: To a stirred solution of 89 (28.9 mg, 103.3 mmol) and dry DMF (50 mL) was added NaH (12.0 mg, 300 mmol, 60% dispersion in mineral oil) at 0°C. To this dark red solution was added BnBr (186.9 mg, 130 mL, 1.07 mmol). After 10 min, the yellow solution was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (30 mL), washed with H₂O (10 mL), and sat. aq. NaCl (2 x 10 mL). The dried (MgSO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with 0-10% Et₂O/Hexanes to give 25 (36.1 mg, 97.6 mmol, 94%) as a bright yellow crystalline solid. MP 98-99°C; IR (thin film) 3062, 2941, 1612, 1582, 1526, 1273, 1040 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, J = 8.4 Hz, 1H), 7.58-7.34 (m, 7H), 7.25 (d, J = 8.4 Hz, 1H), 6.72 (dd, J = 8.4, 2.3 Hz, 1H), 6.60 (d, J = 2.3 Hz, 1H), 5.14 (s, 2H), 3.70 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.93, 157.0, 148.0, 138.6, 136.6, 134.7, 132.4, 130.1, 128.7, 128.2, 127.7, 127.6, 125.4, 118.8, 106.0, 99.5, 70.3, 55.2; HRMS (El+) calcd. for C₂₀H₁₆NO₄Cl (M+) 369.0768, found 369.0762.

Example 132

This example concerns the synthesis of Phenol 82Phenol 90: To a pressure vessel containing 7 (103.0 mg, 567.3 mmol) was added diene 23 (353.4 mg, 1.782 mmol) at rt. The mixture was heated at 140°C. After 24 h, the reaction was cooled to 0°C and TBAF (1.8 mL, 1.8 mmol, IM in THF) was added. After 10 min, the brown mixture was quenched with sat. aq. NH₄Cl (20 mL), diluted with EtOAc (30
mL), washed with H₂O (20 mL), and sat. aq. NaCl (2 x 20 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica, eluting with 0-20% EtOAc / Hexanes to give 90 (115.8 mg, 414.0 mmol, 73%) as a bright yellow solid. MP 90-92°C; IR (thin film) 3385, 1617, 1531, 1359, 1265, 1037 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 9.81 (s, IH), 8.04 (d, J = 2.0 Hz, IH), 7.81 (dd, J = 8.4, 2.0, IH), 7.47 (d, 8.4 Hz, IH), 7.14 (d, J = 8.4 Hz, IH), 6.51 (dd, J = 8.4, 2.4 Hz, IH), 6.45 (d, J = 2.4 Hz, IH), 3.58 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 160.1, 157.0, 150.1, 134.4, 133.2, 132.2, 131.3, 130.8, 124.1, 116.2, 108.4, 99.5, 55.3; HRMS (EI+) calcd. for C₁₂H₁₀NO₄Cl (M) 279.0298, found 279.0293.

**Example 133**

This example concerns the synthesis of Chloride 26: To a stirred solution of 26 (32.2 mg, 87.1 mmol, 92%) as a bright yellow crystalline solid. MP 94-97°C; IR (thin film) 2933, 1613, 1532, 1357, 1261, 1036 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, J = 2.2 Hz, IH), 7.61 (dd, J = 8.3, 2.2 Hz, IH), 7.52-7.32 (m, 6H), 7.23 (d, J = 8.4 Hz, IH), 6.72 (dd, J = 8.4, 2.3 Hz, IH), 6.60 (d, J = 2.3 Hz, IH), 5.14 (s, 2H), 3.70 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.8, 156.9, 149.8, 136.6, 133.6, 133.3, 132.6, 131.3, 130.2, 128.7, 128.2, 127.7, 124.2, 118.8, 106.0, 99.5, 70.31, 55.2; HRMS (EI+) calcd. for C₂₀H₁₆ NO₄Cl (M) 369.0768, found 369.0756.
This example concerns the synthesis of **Enol Ether 29**: To a pressure vessel containing 14 (144 mg, 0.790 mmol) was added diene 15 (642 mg, 3.17 mmol) and heated to 110°C. After 24 h, the reaction was cooled to 0°C, diluted with toluene (0.79 mL) and DABCO (357 mg, 3.17 mmol) was added. After 2 h, the reaction mixture was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (25 mL), and washed with H₂O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO₄) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 15-35% EtOAc/Hexanes, to sequentially give impure 28 (40.0 mg) and impure 29 (44.5 mg) as a yellow oil. 29 was further purified by chromatography over silica gel containing silver nitrate, eluting with 10 - 20% EtOAc/Hexanes. 29: IR (neat) 2915, 1735, 1537, 1027 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.54 (dd, J = 1.2, 8.1 Hz, IH), 7.48 (dd, J = 7.7, 8.1 Hz, IH), 7.30 (dd, J = 1.2, 7.7 Hz, IH), 7.01 (ddd, J = 6.8, 10.8, 17.6 Hz, IH), 5.09 (d, J = 10.8 Hz, IH), 4.52 (d, J = 17.6 Hz, IH), 3.73 (s, 3H), 3.71 (s, 3H), 3.26 (d, J = 16.7 Hz, IH), 3.03 (d, J = 16.7 Hz, IH); ¹³C NMR (100 MHZ, CDCl₃) δ 169.7, 150.2, 149.8, 131.6, 131.4, 131.3, 130.9, 130.0, 125.1, 119.8, 115.8, 57.3, 52.3, 35.4; HRMS (EI+) calcd. for C₁₄H₁₄NO₅Cl (M+H) 311.0560, found 311.0567.

**Example 135**

This example concerns the synthesis of **Biaryl 30**: To a stirred solution of 28 (40.0 mg, 0.143 mmol) and DMF (0.900 mL) at 0°C was added NaH (10.6 mg, 0.265 mmol, 60% in mineral oil). After bubbling ceased, BnBr (376 mg, 0.263 mL, 2.20 mmol) was added dropwise to the deep red solution. After 15 min, the reaction was warmed to rt. After 1 h, the reaction was quenched with sat. aq. NH₄Cl (5 mL), diluted with EtOAc (15 mL), washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was concentrated *in vacuo* and purified by
chromatography over silica gel, eluting with 3-10% EtOAc/Hexanes, to give 30
(41.2 mg, 0.11 mmol, 14% over two steps) as a yellow solid. MP 110-111°C; IR
(neat) 2921, 1530 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.49 (dd, J = 1.8, 8.0 Hz,
IH), 7.43 (dd, J = 7.6, 8.0 Hz, IH), 7.36 (dd, J = 1.8, 7.6 Hz, IH), 7.33-7.27
(m, 5H), 7.14 (dd, J = 1.7, 7.5 Hz, IH), 6.56 (dd, J = 2.4, 7.5 Hz, IH), 6.54
(dd, J = 1.7 Hz, IH), 5.05 (s, 2H), 3.80 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ
161.5, 156.7, 149.6, 136.6, 133.4, 131.0, 130.8, 130.2, 129.1, 128.5, 127.8,
126.8, 125.1, 117.4, 110.7, 70.5, 55.4; HRMS (CI⁺) calcd. for C₂₀H₁₆NO₄Cl
(M+H) 370.0846, found 370.0849.

Example 136

![Diagram](image)

This example concerns the synthesis of **Enone 92**: To a stirred solution of
91 (1.07 g, 9.53 mmol) and PhMe (48.0 mL) was added BnOH (1.96 mL, 2.06 g,
19.1 mmol), and/or-TSA (45.4 mg, 0.238 mmol). The reaction flask was equipped
with a Dean Stark trap and heated at 140°C. After 12 h, the reaction was cooled to
rt, concentrated *in vacuo* and purified by chromatography over silica gel, eluting
with 20-50% EtOAc/Hexanes to give known enone 92 (1.65 g, 8.16 mmol, 86%)
as a yellow crystalline solid. ¹H NMR (300 MHz, CDCl₃) δ 7.44-7.28 (m, 5H), 5.50
(s, IH), 4.91 (s, 2H), 2.50 (t, J = 6.3 Hz, 2H), 2.39 (t, J = 6.3 Hz, 2H), 2.03
(q, J = 6.3 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 199.7, 177.5, 135.2, 128.7,
128.6, 127.9, 103.4, 70.5, 36.8, 29.1, 21.2.

Example 137

![Diagram](image)

This example concerns the synthesis of **Diene 31**: To a flask containing
LDA (15.7 mL, 13.4 mmol, 0.86 M in THF/hexanes) was added a solution of 92
(2.56 g, 12.8 mmol) in THF (6.7 mL) at -78°C. After 10 min, TMSCl (1.67 g, 1.95
mL, 15.3 mmol) was added. After 1 h, the reaction was warmed to rt, poured into a cold solution of aq. NaHCO$_3$ (50 mL, 5% w/v), extracted with Et$_2$O (100 mL), and washed with H$_2$O (75 mL) and sat. aq. NaCl (75 mL). The dried extract (MgSO$_4$) was concentrated in vacuo to give 31 (3.51 g, 12.8 mmol, 99%) as a pale yellow oil.

IR (neat) 2943, 1605, 1361 cm$^{-1}$, $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.42-7.31 (m, 5H), 4.88 (s, IH), 4.81 (s, 2H), 4.61-4.59 (m, IH), 2.31-2.25 (m, 4H), 0.23 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 160.1, 149.0, 136.6, 128.5, 128.0, 127.7, 96.0, 94.7, 69.4, 27.4, 21.8, 0.21; HRMS (Cl$^+$) calcd. for C$_{19}$H$_{14}$N$_2$O$_4$Cl (M+H) 355.0611, found 355.0624.

Example 138

This example concerns the synthesis of Phenol 93: To a pressure vessel containing 14 (1.88 g, 13.4 mmol) was added diene 31 (8.02 g, 29.2 mmol) and heated to 140°C. After 5 h, the reaction was cooled to -30°C, diluted with THF (20 mL) and TBAF (31.1 mL, 31.1 mmol, 1.0 M in THF) was added. After 15 min, the reaction was quenched with sat. aq. NH$_4$Cl (30 mL), diluted with EtOAc (50 mL), and washed with H$_2$O (30 mL) and sat. aq. NaCl (30 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 15-50% EtOAc/Hexanes, to give 93 (2.90 g, 8.16 mmol, 79%) as an orange oil. MP 98-100°C; IR (neat) 3443, 1614, 1537 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.48 (dd, $J = 1.5$, 8.0 Hz, IH), 7.44 (dd, $J = 7.7$, 8.0 Hz, IH), 7.34 (dd, $J = 1.6$, 7.7 Hz, IH), 7.26-7.33 (m, 5H), 7.04 (d, $J = 8.2$ Hz, IH), 6.48 (d, $J = 2.3$ Hz, IH), 6.43 (dd, $J = 2.3$, 8.2 Hz, IH), 5.58 (s, IH), 4.99 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.7, 156.8, 149.5, 136.5, 133.4, 131.1, 131.0, 130.4, 129.2, 128.5, 127.8, 126.8, 125.1, 117.1, 108.0, 101.1, 70.4; HRMS (Cl$^+$) calcd. for C$_9$H$_4$NO$_4$Cl (M+H) 355.0611, found 355.0624.
This example concerns the synthesis of Chloride 30: To a stirred solution of 93 (2.23 g, 6.27 mmol) and DMF (31.0 mL) at 0°C, was added NaH (300 mg, 7.5 mmol, 60% in mineral oil). After bubbling ceased, MeI (0.780 mL, 12.5 mmol) was added dropwise to the deep red solution. After 30 min, the reaction mixture was warmed to it. After an additional 20 min, the reaction was quenched with sat. aq. NH₄Cl (20 mL), diluted with EtOAc (50 mL), and washed with H₂O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by recrystallization with Et₂O / Hexanes (2:1) to give 30 (1.68 g, 4.55 mmol, 73%) as a yellow solid. MP 110.1-11.5°C; IR (neat) 2921, 1530 cm⁻¹; 1H NMR (300 MHz, CDCl₃) δ 7.49 (dd, J = 1.8, 8.0 Hz, IH), 7.43 (dd, J = 7.6, 8.0 Hz, IH), 7.36 (dd, J = 1.8, 7.6 Hz, IH), 7.33-7.27 (m, 5H), 7.14 (dd, J = 1.7, 7.5 Hz, IH), 6.56 (dd, J = 2.4, 7.5 Hz, IH), 6.54 (dd, J = 1.7 Hz, IH), 5.05 (s, 2H), 3.80 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 161.5, 156.7, 149.6, 136.6, 133.4, 131.0, 130.8, 130.2, 129.1, 128.5, 127.8, 126.8, 125.1, 117.4, 105.3, 100.7, 70.5, 55.4; HRMS (Cl+) calcd. for C₂₀H₁₆NO₄Cl (M+H) 370.0846, found 370.0849.

This example concerns the synthesis of Phenol 94: To a pressure vessel containing 14 (59.2 mg, 0.325 mmol) and PhMe (0.650 mL) was added diene 19 (277 mg, 0.308 mL, 1.30 mmol) and heated to 115°C. After 14 h, the reaction was cooled to 0°C and TBAF (1.95 mL, 1.95 mmol, 1.0 M in THF) was added. After 15 min, the reaction was quenched with sat. aq. NH₄Cl (8 mL), diluted with Et₂O (15 mL), and washed with H₂O (10 mL) and sat. aq. NaCl (10 mL). The dried extract...
(MgSO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 20-50% EtOAc/Hexanes, to yield 94 (64.2 mg, 0.258 mmol, 78%) as a white crystalline solid. MP 132-134°C; IR (neat) 3518, 1610, 1534, 1459, 1369, 1199 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.51 (dd, $J = 2.1, 8.1$ Hz, IH), 7.48 (t, $J = 8.1$ Hz, IH), 7.37 (dd, $J = 2.1, 7.0$ Hz, IH), 7.27 (dt, $J = 2.2, 8.8$ Hz, 2H), 6.90 (dt, $J = 2.2, 8.8$ Hz, 2H), 5.19 (s, IH); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 156.8, 149.4, 136.2, 131.1, 129.9, 129.4, 128.2, 125.6, 116.3; HRMS (CI+) calcd. for C$_{12}$H$_8$NO$_3$Cl (M+H) 250.0271, found 250.0269.

Example 141

This example concerns the synthesis of Chloride 32: To a stirred solution of 94 (34.0 mg, 0.140 mmol) and DMF (0.70 mL) at 0°C, was added NaH (6.72 mg, 0.168 mmol, 60% in mineral oil). After bubbling ceased, BnBr (0.170 mL, 1.40 mmol) was added dropwise to the deep red solution. After 30 min, the reaction mixture was warmed to rt and stirred for 20 min. The reaction was quenched with sat. aq. NH$_4$Cl (10 mL), diluted with EtOAc (20 mL), and washed with H$_2$O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 3-10% EtOAc / Hexanes to give 32 (46.3 mg, 0.136 mmol, 97%) as a white crystalline solid. MP 125-127°C; IR (neat) 2927, 1537, 1249 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.51 (dd, $J = 2.0, 8.0$ Hz, IH), 7.49-7.42 (m, 5H), 7.39 (dt, $J = 1.2, 7.6$ Hz, IH), 7.37 (dd, $J = 2.0, 6.8$ Hz, IH), 7.33 (dt, $J = 2.0, 8.8$ Hz, 2H), 7.06 (dt, $J = 2.0, 8.8$ Hz, 2H), 5.13 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.5, 149.1, 136.6, 135.8, 130.6, 129.5, 129.3, 128.9, 128.7, 128.2, 127.9, 127.6, 125.2, 115.3, 70.1; HRMS (EI+) calcd. for C$_{12}$H$_8$NO$_3$Cl (M+H) 339.0662, found 339.0670.
Example 142

This example concerns the synthesis of **Phenol 95**: To a pressure vessel containing 14 (87.1 mg, 0.480 mmol) was added diene 23 (286 mg, 1.44 mmol) and heated to 140°C. After 3.5 h, the reaction was cooled to rt and the crude oil was purified by chromatography over silica gel, eluting with 5-40% EtOAc/Hexanes, to give 95 (103 mg, 0.370 mmol, 76%) as an orange solid. IR (neat) 3385, 2924, 1534 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.51 (dd, J = 1.6, 8.2 Hz, IH), 7.46 (dd, J = 7.5, 8.2 Hz, IH), 7.33 (dd, J = 1.6, 7.5 Hz, IH), 7.08 (dd, J = 2.4, 6.5 Hz, IH), 6.49 (s, IH), 6.48 (dd, J = 2.4, 6.5 Hz, IH) 4.94 (s, 2H), 3.79 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.7, 150.9, 133.6, 131.1, 130.8, 130.5, 129.2, 125.3, 124.9, 115.5, 107.5, 99.3, 55.4; HRMS (EI+) calcd. For C₁₃H₁₀ClNO₄ (M+H) 279.0298, found 279.0288.

Example 143

This example concerns the synthesis of **Chloride 33**: To a stirred solution of 95 (54.0 mg, 0.190 mmol) and DMF (0.97 mL) at 0°C, was added NaH (9.26 mg, 0.232 mmol, 60% in mineral oil). After bubbling ceased, BnBr (0.230 mL, 1.93 mmol) was added dropwise to the deep red solution. After 30 min, the reaction mixture was warmed to rt and stirred for 1 h. The reaction was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (20 mL), and washed with H₂O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO₄) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 3-10% EtOAc/Hexanes to give 33 (71.3 mg, 0.190 mmol, 99%) as a yellow solid. MP 126-127°C; IR (neat) 1611, 1534, 1200 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.51 (dd, J = 1.5, 8.1 Hz, IH), 7.48-7.37 (m, 6H), 7.34 (dd, J = 1.5, 7.6 Hz, IH), 7.15 (d, J = 8.4 Hz, IH), 6.65
(dd, $J = 2.2$, 8.4 Hz, IH), 6.62 (d, $J = 2.2$ Hz, IH), 5.1 1 (s, 2H), 3.74 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 160.9, 157.5, 149.4, 136.6, 133.6, 130.9, 130.8, 130.5, 129.2, 128.7, 128.2, 127.7, 125.4, 117.4, 105.7, 99.7, 70.3, 55.4; HRMS (EI+) calcd. for C$_{20}$H$_{16}$NO$_4$Cl (M+) 369.0768, found 369.0771.

**Example 144**

\[ \begin{align*}
\begin{array}{c}
\begin{array}{c}
O_{2}N \quad BnO \\
\text{Cl} \quad \text{O}Me \\
17 \quad 35
\end{array}
\end{array}
\end{align*} \]

This example concerns the synthesis of Triaryl 35: To a pressure vessel was added 17 (36.7 mg, 99.2 mmol), PhB(OH)$_2$ (53.0 mg, 435 mmol), Cs$_2$CO$_3$ (82.9 mg, 254 mmol), Pd$_2$(dba)$_3$ (3.4 mg, 3.8 mmol), PCy$_3$ (8.1 mg, 29 mmol), and dry dioxane (300 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the mixture was filtered over a pad of Celite-®, eluting with Et$_2$O (60 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 10% Et$_2$O/hexanes, to give 35 (37.3 mg, 96.1 mmol, 84%) as a bright yellow crystalline solid. MP 127-131°C; IR (thin film) 3067, 2932, 1611, 1586, 1519, 1348, 1050 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.06 (d, $J = 8.4$ Hz, IH), 7.75-7.57 (m, 4H), 7.57-7.4 (m, 3H), 7.4-7.2 (m, 6H), 6.67 (dd, $J = 8.3$, 2.0 Hz, IH), 6.60 (d, $J = 2.0$, IH), 5.05 (s, 2H), 3.86 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 161.2, 156.3, 148.4, 145.6, 139.0, 136.5, 133.8, 131.4, 130.3, 129.1, 128.6, 128.5, 127.8, 127.4, 127.1, 126.1, 124.8, 120.6, 105.5, 100.4, 70.7, 55.4; HRMS (EI+) calcd. for C$_{26}$H$_{24}$NO$_4$ (M+) 411.1471, found 411.1475.
Example 145

This example concerns the synthesis of Triaryl 36: To a pressure vessel was added 18 (13.2 mg, 35.7 mmol), PhB(OH)$_2$ (17.6 mg, 144 mmol), Cs$_2$CO$_3$ (24.8 mg, 76.1 mmol), Pd$_2$(dba)$_3$ (0.1 mg, 1.2 mmol), PCy$_3$ (1.1 mg, 3.9 mmol), and dry dioxane (60 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the mixture was filtered over a pad of Celite®, eluting with Et$_2$O (40 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 0-10% Et$_2$O/hexanes, to give 36 (12.2 mg, 31.5 mmol, 88%) as a bright yellow crystalline solid. MP 130-2°C; IR (thin film) 3054, 2925, 1610, 1520, 1356, 1091, 1024 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.18 (d, $J = 1.9$ Hz, 1H), 7.86 (dd, $J = 8.0$, 1.9 Hz, IH), 7.74-7.63 (m, 2H), 7.58-7.42 (m, 4H), 7.38-7.23 (m, 6H), 6.67 (dd, $J = 8.4$, 2.3 Hz, IH), 6.58 (d, $J = 2.3$ Hz, IH), 5.04 (s, 2H), 3.85, (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 161.1, 156.3, 149.9, 140.9, 138.6, 136.5, 133.2, 131.8, 130.8, 130.3, 129.1, 128.5, 128.3, 127.8, 127.1, 127.0, 122.5, 120.1, 105.5, 100.4, 70.7, 55.4; HRMS (EI+) calcd. for C$_{26}$H$_{21}$NO$_4$ (M+) 411.1471, found 411.1455.

Example 146

This example concerns the synthesis of Triaryl 38: To a pressure vessel was added 16 (43.8 mg, 118 mmol), P-MeO-C$_6$H$_4$-B(OH)$_2$ (68.9 mg, 453 mmol), Cs$_2$CO$_3$ (69.6 mg, 214 mmol), Pd$_2$(dba)$_3$ (2.3 mg, 2.5 mmol), PCy$_3$ (4.3 mg, 15 mmol), and dry dioxane (250 mL). The solution was sealed under Ar and heated to
80°C. After 24 h, the mixture was filtered over a pad of Celite®, eluting with Et₂O (60 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 10% Et₂O/hexanes, to give 38 (47.0 mg, 107 mmol, 90%) as a bright yellow crystalline solid. MP 131-133°C; IR (thin film) 2957, 2923, 2853, 1610, 1581, 1527, 1514, 1356, 1246 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.83 (dd, J = 8.0, 1.4 Hz, IH), 7.61 (dd, J = 7.7, 1.4 Hz, IH), 7.51 (t, J = 8.0 Hz, IH), 7.40-7.24 (m, 3H), 7.18 (d, J = 6.3 Hz, 2H), 6.98 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.3 Hz, IH), 6.73 (d, J = 8.9 Hz, 2H), 6.41 (d, J = 2.3 Hz, IH), 6.39 (dd, J = 8.3, 2.4 Hz, IH), 4.98 (d, J = 12.6 Hz, IH), 4.88 (d, J = 12.5 Hz, IH), 3.80 (s, 3H), 3.76 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.6, 158.6, 156.8, 151.3, 144.3, 137.0, 133.9, 132.5, 131.5, 130.9, 130.4, 128.4, 127.7, 127.6, 126.7, 122.2, 117.7, 113.3, 104.9, 99.9, 70.0, 55.2, 55.2; HRMS (Cl⁺) calcd. for C₂₇H₂₄NO₅ (M+H) 442.1654, found 442.1668.

Example 147

This example concerns the synthesis of Triaryl 39: To a pressure vessel was added 16 (47.3 mg, 128 mmol), W-MeO-C₆H₄-B(OH)₂ (65.5 mg, 431 mmol), Cs₂CO₃ (92.0 mg, 282 mmol), Pd₂(dba)₃ (2.9 mg, 3.2 mmol), PCy₃ (1.8 mg, 6.4 mmol), and dry dioxane (300 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the mixture was filtered over a pad of Celite®, eluting with Et₂O (60 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 10% Et₂O/hexanes, to give 39 (51.4 mg, 116 mmol, 91%) as a crystalline yellow, 1:1 mixture of atropisomers. MP 127-129°C; IR (thin film) 2929, 1612, 1583, 1528, 1512, 1360, 1227, 1042, 753 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.91-7.85 (m, IH), 7.69-7.63 (m, IH), 7.57-7.50 (m, IH), 7.39-7.19 (m, 5H), 7.13 (t, J = 7.6 Hz, IH), 6.89-6.84 (m, IH), 6.80-6.76 (m, IH), 6.64-6.68 (m, IH), 6.63-6.58 (m, IH), 6.47-6.38 (m, 2H), 4.99 (d, J = 12.4 Hz, IH), 4.87 (d, J = 12.4 Hz, IH), 3.75 (s, 3H), 3.60 (s, 3H); ¹³C NMR (100 MHz, - 202 -
CDCl₃ δ 160.8, 158.9, 156.8, 151.2, 144.4, 141.4, 137.0, 133.8, 131.4, 131.0, 128.8, 128.4, 127.8, 127.6, 126.7, 121.8, 117.6, 114.4, 113.4, 104.9, 99.9, 70.1, 55.3, 55.0; HRMS (CI+) calcd. for C₂₇H₂₃NO₅ 441.1576, found 441.1577.

Example 148

This example concerns the synthesis of Triaryl 40: To a pressure vessel was added 16 (42.3 mg, 114 mmol), 0-MeO-C₆H₄-B(OH)₂ (64.4 mg, 432 mmol), Cs₂CO₃ (74.3 mg, 228 mmol), Pd₂(dba)₃ (2.5 mg, 2.7 mmol), PCy₃ (3.3 mg, 12 mmol), and dry dioxane (230 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the mixture was filtered over a pad of Celite®, eluting with Et₂O (60 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 10% Et₂O/hexanes, to give 40 (40.4 mg, 91.5 mmol, 80%) as a bright yellow crystalline solid. MP 123-124°C; IR (thin film) 3003, 2954, 1613, 1582, 1512, 1358, 1274, 1242, 1039, 1026, 755 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.90 (dd, J = 8.0, 1.3 Hz, IH), 7.63-7.55 (br, IH), 7.50, (t, J = 8.0 Hz, IH), 7.39-7.16 (m, 6H), 7.04-6.59 (br, 4H), 6.48-6.21 (br, 2H), 4.98, (d, J = 12.4 Hz, IH), 4.92 (d, J = 12.4 Hz, IH), 3.719 (s, 3H), 3.5-3.2 (br, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.4, 156.5, 156.1, 150.1, 141.7, 137.0, 134.8, 132.3, 131.0, 130.9, 128.9, 128.4, 127.8, 127.6, 127.3, 126.7, 122.7, 120.0, 118.1, 110.3, 104.2, 99.5, 70.0, 55.2, 55.0; HRMS (FAB+) calcd. for C₂₇H₂₃NO₅ 441.1576, found 441.1595.

Example 149
This example concerns the synthesis of Triaryl 41: To a pressure vessel was added 16 (39.0 mg, 105 mmol), 0-Me-C₆H₄-B(OH)₂ (69.5 mg, 511 mmol), Cs₂CO₃ (112.3 mg, 344.7 mmol), Pd₂(dba)₃ (2.4 mg, 2.6 mmol) and dry dioxane (300 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the mixture was filtered over a pad of Celite-®, eluting with Et₂O (60 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 10% Et₂O/hexanes, to give 41 (40.0 mg, 93.9 mmol, 89%) as a crystalline yellow, 1:1 mixture of atropisomers. MP 72-75°C; IR (thin film) 3062, 2924, 1613, 1578, 1528, 1512, 1269, 1049, 757 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.93 (t, J = 4.8 Hz, 1H), 7.83-7.80 (m, 3H), 7.39-7.10 (m, 8H), 7.06-6.89 (m, IH), 6.83-6.72 (m, IH), 6.37 (dd, J = 10.0, 2.4 Hz, IH), 6.28 (dt, J = 8.5, 2.3 Hz, IH), 5.05-4.85 (m, 2H), 3.71 (s, 3H), 2.19 (s, 1.3 H), 1.80 (s, 1.7 H); ¹³C NMR (100 MHz, CDCl₃) δ 160.5, 160.4, 156.6, 156.3, 151.2, 151.1, 144.4, 144.4, 139.5, 139.4, 137.0, 136.8, 136.1, 135.1, 134.5, 134.3, 132.2, 131.8, 131.5, 130.4, 130.1, 129.7, 129.6, 128.5, 128.4, 127.7, 127.6, 127.4, 127.3, 126.8, 126.7, 125.1, 125.0, 122.7, 122.6, 117.8, 117.0, 104.6, 104.4, 99.5, 70.1, 70.0, 55.1, 20.4, 19.3; HRMS (EI+) calcd. for C₂₇H₂₃NO₄ 425.1627, found 425.1612.

Example 150

This example concerns the synthesis of Triaryl 42: To a pressure vessel was added 16 (41.0 mg, 111 mmol), 7-CN-C₆H₄-B(OH)₂ (64.2 mg, 437 mmol), KF (58.4 mg, 1.00 mmol), Pd[Bu₃P]₂ (4.0 mg, 7.8 mmol) and NMP (300 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the mixture was filtered over a pad of Celite-®, eluting with Et₂O (60 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting with 10% Et₂O/hexanes, to give 42 (40.0 mg, 91.5 mmol, 80%) as a bright yellow crystalline solid. MP 142-144°C; IR (thin film) 2950, 2918, 2228, 1610, 1582 1531, 1513, 1272, 1242, 1048, 737 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.93 (t, J = 4.8 Hz, IH),
7.85-7.78 (m, 1H), 7.75-7.70 (m, 1H), 7.60-7.54 (m, 2H), 7.50-7.45 (m, 2H), 7.37-
7.28 (m, 1H), 7.19-7.10 (m, 4H), 6.80 (d, J = 8.4 Hz, 1H), 6.42 (d, J = 2.3 Hz, 1H),
6.39 (dd, J = 8.4, 2.3 Hz, 1H), 4.96 (d, J = 12.4 Hz, 1H), 4.84 (d, J = 12.4 Hz, 1H),
3.77 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 161.1, 156.6, 151.2, 144.9, 142.7,
136.6, 133.3, 132.9, 131.6, 131.3, 130.0, 128.5, 128.2, 127.8, 126.8, 123.5, 118.7,
116.6, 110.9, 105.1, 100.0, 70.1, 55.3; HRMS (Cl+) calcd. for C₂₇H₂₀F₃N₂O₄
436.2423, found 436.1426.

Example 151

This example concerns the synthesis of Triaryl 45: To a pressure vessel was
added 16 (110.3 mg, 298.2 mmol), W-CF₃-C₆H₄-B(OH)₂ (235.8 mg, 1.241 mmol),
KF (155.5 mg, 2.676 mmol), Pd[18Bu₃P]₂ (9.0 mg, 18 mmol) and NMP (600 mL).
The solution was sealed under Ar and heated to 80°C. After 48 h, the mixture was
filtered over a pad of Celite®, eluting with Et₂O (60 mL) and concentrated in vacuo. The residue was purified by flash chromatography over silica gel, eluting
with 50-75% PhMe/hexanes, to give 45 (100.2 mg, 229.6 mmol, 77%) as a bright yellow crystalline solid. MP 121-124°C; IR (thin film) 3067, 2938, 1613, 1582,
1531, 1513, 1539, 1335, 1271, 1061, 756 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 7.93,
(dd, J = 8.0, 1.4 Hz, 1H), 7.63 (dd, J = 8.0, 1.4 Hz, 1H), 7.57 (t, J = 7.8, 1H) 7.49
(d, J = 7.7 Hz, 1H), 7.36-7.20 (m, 8H), 6.83 (d, J = 8.3 Hz, 1H), 6.42 (d, J = 2.2 Hz,
IH), 6.39 (dd, J = 8.3, 2.2 Hz, 1H), 4.97 (d, J = 12.4 Hz, 1H), 4.86 (d, J = 12.4 Hz,
IH), 3.74 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 161.1, 156.7, 151.2, 143.1, 140.7,
136.7, 133.5, 132.5, 131.4, 131.3, 130.0 (q, J_C-F= 32 Hz), 128.4, 128.2, 128.1,
127.7, 126.7, 126.1 (q, J_C,F= 4 Hz), 123.9 (q, J_C,F= 273 Hz), 123.9 (q, J_C,F= 4
Hz), 123.2, 122.6, 119.9, 116.9, 105.1, 99.9, 70.1, 55.3; HRMS (EI+) calcd. for
C₂₇H₂₀F₃N₂O₄ 479.1344, found 479.1334.
Example 152

This example concerns the synthesis of Triaryl 47: To a pressure vessel containing 30 (41.9 mg, 0.110 mmol), was sequentially added KF (57.4 mg, 0.990 mmol), 7-OMe-C₆H₄-B(OH)₂ (68.9 mg, 0.450 mmol), (t-Bu₃P)₂Pd (2.8 mg, 0.0060 mmol), and NMP (1.10 mL). The solution was sealed under Ar and heated to 80°C. After 48 h, the reaction was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (25 mL), and washed with H₂O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5-20% EtOAc / Hexanes to give 47 (42.0 mg, 0.0950 mmol, 86%) as a yellow crystalline solid. MP 102-103°C; IR (neat) 2927, 1608, 1530, 1246 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.54 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 7.6 Hz, 2H), 7.36 (dt, J = 2.0, 3.2, 8.4 Hz, 2H), 7.36-7.27 (m, 5H), 7.20 (d, J = 8.4 Hz, 1H), 6.98 (dt, J = 1.6, 3.2, 8.4 Hz, 2H), 6.57 (dd, J = 2.4, 8.4 Hz, 1H), 6.56 (d, J = 2.4 Hz, 1H), 5.08 (s, 2H), 3.87 (s, 3H), 3.81 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.2, 159.7, 156.8, 150.4, 137.0, 134.2, 131.7, 131.1, 130.9, 130.0, 129.5, 129.4, 129.3, 128.4, 127.6, 126.8, 118.6, 114.2, 105.2, 100.8, 70.5, 55.4, 55.3; HRMS (TOF-MS/ES+) calcd. for C₂₇H₂₃NO₅(M+Na) 464.1474, found 464.1460.

Example 153

This example concerns the synthesis of Triaryl 48: To a pressure vessel containing 30 (23.4 mg, 0.0630 mmol), was sequentially added KF (32.9 mg, 0.570 mmol), W-OMe-C₆H₄-B(OH)₂ (38.3 mg, 0.250 mmol), (t-Bu₃P)₂Pd (1.6 mg, 0.0030
mmol), and NMP (0.63 mL). The solution was sealed under Ar and heated to 80°C. After 48 h, the reaction was quenched with sat. aq. NH₄Cl (10 mL), diluted with EtOAc (25 mL), and washed with H₂O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5-20% EtOAc/Hexanes to give 48 (17.9 mg, 0.0410 mmol, 64%) as a yellow crystalline solid. MP 107-108°C; IR (neat) 3063, 2930, 1608, 1534 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.56 (dd, J = 7.6, 7.7 Hz, IH), 7.45 (dd, J = 1.4, 5.2 Hz, IH), 7.43 (dd, J = 1.4, 5.2 Hz, IH), 7.38-7.27 (m, 6H), 7.21 (d, J = 8.4 Hz, IH), 7.00 (d, J = 7.6 Hz, IH), 6.97 (dd, J = 2.0, 4.0 Hz, 2H), 6.58 (dd, J = 2.4, 8.4 Hz, IH), 6.56 (d, J = 2.4 Hz, IH), 5.07 (s, 2H), 3.85 (s, 3H), 3.82 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.2, 159.6, 156.8, 150.3, 138.4, 136.9, 134.4, 131.7, 131.6, 130.9, 129.8, 129.7, 129.6, 128.4, 127.6, 126.8, 120.5, 118.6, 114.2, 113.6, 105.2, 100.8, 70.5, 55.4, 55.3; HRMS (EI+) calcd. for C₂₇H₂₃NO₅ (M+H) 441.1576, found 441.1569.

Example 154

This example concerns the synthesis of Triaryl 49: To a pressure vessel containing 30 (36.2 mg, 0.0980 mmol) was sequentially added KF (51.2 mg, 0.880 mmol), 0-OMe-C₆H₄-B(OH)₂ (62.3 mg, 0.390 mmol), and (t-Bu₃P)₂Pd (2.5 mg, 0.0050 mmol), and NMP (0.98 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the reaction was quenched with sat. aq. NH₄Cl (5 mL), diluted with EtOAc (15 mL), and washed with H₂O (5 mL) and sat. aq. NaCl (5 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 3-10% EtOAc/Hexanes to give 49 (19.1 mg, 0.0430 mmol, 44%) as a pale yellow solid. MP 156-157°C; IR (neat) 2924, 1610, 1530 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.57 (dd, J = 7.6, 8.0 Hz, IH), 7.41 (dd, J = 7.6, 8.0 Hz, 3H), 7.34-7.25 (m, 7H), 7.08 (t, J = 7.6 Hz, IH), 6.96 (d, J = 8.4 Hz, IH), 6.61
Example 155

This example concerns the synthesis of Triaryl 50: To a pressure vessel containing 30 (59.5 mg, 0.160 mmol) was sequentially added KF (83.5 mg, 1.44 mmol), 0-Me-C_{6}H_{4}B(OH)_{2} (87.0 mg, 0.640 mmol), (i-Bu_{3})_{2}Pd (4.1 mg, 0.0080 mmol), and NMP (1.60 mL). The solution was sealed under Ar and heated to 80°C. After 48 h, the reaction was quenched with sat. aq. NH_{4}Cl (5 mL), diluted with EtOAc (20 mL), and washed with H_{2}O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO_{4}) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 3-10% EtOAc / Hexanes followed by recrystallization with Et_{2}O/Hexanes (1:2) to give 50 (22.8 mg, 0.0540 mmol, 34%) as a pale yellow solid. MP 126-127°C; IR (neat) 3062, 2860, 1617, 1531 cm^{-1}; ^{1}H NMR (400 MHz, CDCl_{3}) δ 7.53 (t, \( J = 7.6 \) Hz, IH), 7.42 (dd, \( J = 1.6, 8.0 \) Hz, IH), 7.32-7.26 (m, 8H), 7.24 (d, \( J = 8.0 \) Hz, IH), 7.19 (dd, \( J = 2.0, 6.8 \) Hz, IH), 7.16 (dd, \( J = 1.6, 8.0 \) Hz, IH), 6.58 (dd, \( J = 2.4, 8.4 \) Hz, IH), 6.56 (d, \( J = 2.4 \) Hz, IH), 5.02 (s, 2H), 3.82 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, CDCl_{3}) δ 161.2, 156.6, 150.6, 136.8, 136.5, 134.5, 131.7, 131.4, 131.0, 130.0, 129.8, 129.5, 128.8, 128.5, 128.4, 128.3, 127.7, 127.0, 125.5, 118.9, 105.3, 100.5, 70.4, 55.4, 20.1; HRMS (TOF/ES+) calcd. for C_{27}H_{23}NO_{4} (M+Na) 448.1525, found 448.1512.

C_{27}H_{23}NO_{4} (M+Na) 448.1525, found 448.1512.
Example 156

This example concerns the synthesis of Triaryl 51: To a pressure vessel containing 30 (48.6 mg, 0.130 mmol), was sequentially added KF (68.4 mg, 1.18 mmol), CN-C₆H₄-B(OH)₂ (76.1 mg, 0.520 mmol),-(Bu₃P)₂Pd (3.4 mg, 0.0070 mmol), and NMP (1.30 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the reaction was quenched with sat. aq. NH₄Cl (5 mL), diluted with EtOAc (15 mL), and washed with H₂O (5 mL) and sat. aq. NaCl (5 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5-20% EtOAc/Hexanes to give 51 (34.8 mg, 0.0800 mmol, 61%) as a pale yellow solid. MP 178-179.5°C; IR (neat) 2921, 2223, 1610, 1530 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, J = 8.0 Hz, 2H), 7.61 (dd, J = 8.0, 7.6 Hz, IH), 7.52 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 7.6 Hz, IH), 7.38 (dd, J = 1.2, 7.6 Hz, IH), 7.34-7.28 (m, 5H), 7.20 (d, J = 8.4 Hz, IH), 6.60 (dd, J = 2.4, 8.4 Hz, IH), 6.57 (d, J = 2.4 Hz, IH), 5.06 (s, 2H), 3.82 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.4, 156.6, 149.9, 141.9, 136.8, 132.9, 132.7, 132.5, 132.4, 130.8, 130.1, 129.4, 128.9, 128.5, 127.7, 126.8, 118.5, 118.1, 112.4, 105.4, 100.6, 70.4, 55.4; HRMS (FAB+) calcd. for C₂₇H₂₀N₂O₄ (M⁺) 436.1423, found 436.1440.

Example 157

This example concerns the synthesis of Triaryl 53: To a pressure vessel containing 30 (36.2 mg, 0.0980 mmol), was sequentially added KF (51.2 mg, 0.880 mmol), CF₃-C₆H₄-B(OH)₂ (74.5 mg, 0.390 mmol), -(Bu₃P)₂Pd (2.5 mg, 0.0050 mmol), and NMP (1.30 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the reaction was quenched with sat. aq. NH₄Cl (5 mL), diluted with EtOAc (15 mL), and washed with H₂O (5 mL) and sat. aq. NaCl (5 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5-20% EtOAc/Hexanes to give 53 (34.8 mg, 0.0800 mmol, 61%) as a pale yellow solid. MP 178-179.5°C; IR (neat) 2921, 2223, 1610, 1530 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, J = 8.0 Hz, 2H), 7.61 (dd, J = 8.0, 7.6 Hz, IH), 7.52 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 7.6 Hz, IH), 7.38 (dd, J = 1.2, 7.6 Hz, IH), 7.34-7.28 (m, 5H), 7.20 (d, J = 8.4 Hz, IH), 6.60 (dd, J = 2.4, 8.4 Hz, IH), 6.57 (d, J = 2.4 Hz, IH), 5.06 (s, 2H), 3.82 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.4, 156.6, 149.9, 141.9, 136.8, 132.9, 132.7, 132.5, 132.4, 130.8, 130.1, 129.4, 128.9, 128.5, 127.7, 126.8, 118.5, 118.1, 112.4, 105.4, 100.6, 70.4, 55.4; HRMS (FAB+) calcd. for C₂₇H₂₀N₂O₄ (M⁺) 436.1423, found 436.1440.
mmol), and NMP (0.98 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the reaction was quenched with sat. aq. NH₄Cl (5 mL), diluted with EtOAc (15 mL), and washed with H₂O (10 mL) and sat. aq. NaCl (10 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 3-5% EtOAc / Hexanes followed by recrystallization with Et₂O / Hexanes (2:1) to give 55 (10.1 mg, 0.0210 mmol, 22%) as a yellow crystalline solid. MP 102-104°C; IR (neat) 3063, 2933, 1530 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.78 (dd, J = 2.4, 7.2 Hz, IH), 7.57-7.52 (m, 2H), 7.47 (dd, J = 1.8, 7.8 Hz, IH), 7.34-7.28 (m, 5H), 7.24 (d, J = 8.4 Hz, IH), 6.59 (dd, J = 2.4, 8.4 Hz, IH), 6.55 (d, J = 2.4 Hz, IH), 5.01 (s, 2H), 3.82 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.2, 156.6, 150.1, 136.7, 135.4, 132.3, 132.1, 131.3, 131.2, 131.1, 130.9, 129.9, 129.8, 129.3, 128.5, 128.4, 127.6, 126.9, 126.4, 126.3, 119.0, 105.4, 100.5, 70.5, 55.4; HRMS (EI⁺) calcd. for C_{27}H_{20}F_{3}NO_{4} (M⁺) 479.1344, found 479.1323.

Example 158

![Example diagram]

This example concerns the synthesis of Triaryl 54: To a pressure vessel containing 30 (39.4 mg, 0.107 mmol), was sequentially added KF (55.9 mg, 0.960 mmol), W-CF₃-C₆H₄-B(OH)₂ (81.3 mg, 0.430 mmol), (t-Bu₃P)₂Pd (2.7 mg, 0.0050 mmol), and NMP (1.07 mL). The solution was sealed under Ar and heated to 80°C. After 48 h, the reaction was quenched with sat. aq. NH₄Cl (5 mL), diluted with EtOAc (15 mL), and washed with H₂O (5 mL) and sat. aq. NaCl (5 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 3-5% EtOAc/Hexanes to give 54 (36.3 mg, 0.0800 mmol, 71%) as a pale yellow oil. IR (neat) 2921, 1527, 1339 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.69-7.67 (m, 2H), 7.58 (t, J = 7.5 Hz, IH), 7.56 (t, J = 5.7 Hz, IH), 7.48 (dd, J = 1.5, 7.8 Hz, IH), 7.39 (dd, J = 1.2, 7.5 Hz, IH), 7.35-7.25 (m, 6H), 7.20 (d, J = 8.4 Hz, IH), 6.58 (dd, J = 2.4, 8.4 Hz, IH), 6.55 (d, J = 2.4 Hz, IH), 5.05 (s, 3H).
2H), 3.81 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 161.3, 156.8, 150.2, 137.9, 136.8, 133.2, 132.3, 132.2, 131.4, 131.3, 130.9, 130.2, 129.9, 129.8, 129.1, 128.4, 127.7, 126.9, 125.3, 125.2 (q, $J = 3.8$ Hz, 1C), 118.3, 105.3, 100.6, 70.5, 55.4; HRMS (EI+) calcd. for C$_{27}$H$_{20}$F$_3$NO$_4$ (M+) 479.1344, found 479.1324.

### Example 159

![Chemical Structure](image)

This example concerns the synthesis of Triaryl 55: To a pressure vessel containing 30 (48.5 mg, 0.130 mmol), was sequentially added KF (68.4 mg, 1.18 mmol), 7-CF$_3$-C$_6$H$_4$-B(OH)$_2$ (99.5 mg, 0.520 mmol), (J-Bu$_3$P)$_2$Pd (3.4 mg, 0.0070 mmol), and NMP (1.31 mL). The solution was sealed under Ar and heated to 80°C. After 24 h, the reaction was quenched with sat. aq. NH$_4$Cl (5 mL), diluted with EtOAc (15 mL), and washed with H$_2$O (5 mL) and sat. aq. NaCl (5 mL). The dried extract (MgSO$_4$) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 5-20% EtOAc/Hexanes to give 55 (37.5 mg, 0.0780 mmol, 60%) as a yellow crystalline solid. MP 113-1 14°C; IR (neat) 2918, 1527, 1323 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.70 (d, $J = 8.2$ Hz, 2H), 7.59 (t, $J = 7.7$ Hz, IH), 7.52 (d, $J = 8.2$ Hz, 2H), 7.49 (dd, $J = 1.4$, 7.7 Hz, IH), 7.39 (dd, $J = 1.4$, 7.7 Hz, IH), 7.33-7.27 (m, 5H), 7.20 (d, $J = 8.3$ Hz, IH), 6.58 (dd, $J = 2.4$, 8.3 Hz, IH), 6.55 (d, $J = 2.4$ Hz, IH), 5.06 (s, 2H), 3.81 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 161.3, 156.7, 150.2, 140.8, 136.8, 133.3, 132.4, 132.2, 130.8, 130.3, 129.9, 129.6, 128.6, 128.5, 127.7, 126.8, 125.7, 125.6, 118.3, 105.3, 100.7, 70.5, 55.4; HRMS (EI+) calcd. for C$_{27}$H$_{20}$NO$_4$F$_3$ (M+) 479.1344, found 479.1353.
Example 160

This example concerns the synthesis of Phenol 56: To a stirred solution of 34 (45.3 mg, 110 mmol) in CH₂Cl₂ (98 mL) was added BCl₃ (600 mL, 600 mmol, 1.0 M in heptane) at 0°C. After 4 h, the reaction was quenched with MeOH (2.0 mL), concentrated in vacuo, and purified via flash chromatography over silica gel, eluting with 10-30% EtOAc/hexanes to give 56 (32.9 mg, 102 mmol, 92%) as a bright yellow oil. IR (neat) 3522, 1620, 1592, 1526, 1360, 1264, 1040, 877, 764 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.85 (dd, J = 8.0, 1.4 Hz, 1H), 7.68 (dd, J = 8.0, 1.4 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.28-7.21 (m, 3H), 7.19-7.12 (m, 2H), 6.77 (d, J = 8.0 Hz, 1H), 6.41-6.32 (m, 2H), 4.95 (br, 1H), 3.65 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.8, 154.0, 151.7, 145.2, 139.5, 134.1, 131.5, 129.7, 129.1, 128.5, 128.0, 127.4, 122.6, 115.0, 106.7, 101.7, 55.2; HRMS (EI⁺) calcd. for C₁₉H₁₉NO₄ 321.1001, found 321.0999.

Example 161

This example concerns the synthesis of Phenol 57: To a stirred solution of 37 (45.2 mg, 0.110 mmol) in CH₂Cl₂ (98 mL) was added BCl₃ (660 mL, 660 mmol, 1.0 M in hexanes) at 0°C. After 4 h, the reaction was quenched with MeOH (2.0 mL), concentrated in vacuo, and purified via recrystallization with CH₂Cl₂ to yield 57 (29.0 mg, 0.0900 mmol, 82%) as a yellow crystalline solid. MP 166-167°C; IR (neat) 3409, 2921, 1617, 1530 cm⁻¹; ¹H NMR (400 MHz, MeOD) δ 7.62 (t, J = 7.7 Hz, 1H), 7.46-7.38 (m, 7H), 7.05 (d, J = 8.0 Hz, 1H), 6.50-6.47 (m, 2H), 3.81 (s, 3H); ¹³C NMR (100 MHz, MeOD) δ 161.3, 155.6, 152.8, 150.5, 137.4,
134.4, 132.0, 131.5, 130.5, 129.5, 128.2, 127.9, 127.8, 116.6, 104.7, 101.0, 54.3; HRMS (EI+) calcd. for C_{19}H_{15}NO_{4} (M+H) 321.1001, found 321.1004.

Example 162

This example concerns the synthesis of Aniline 58: To a stirred solution of 34 (44.6 mg, 101 mmol) in glacial HOAc (410 mL) was added Zn dust (41.0 mg, 627 mmol) at rt. After 20 h, the mixture was quenched with sat. aq. NaHCO_{3} (15 mL), diluted with EtOAc (20 mL) and washed with H_{2}O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (Na_{2}SO_{4}) was concentrated in vacuo and purified via flash chromatography over silica gel, eluting with 15-25% EtOAc/Hexanes to give 58 (34.2 mg, 90.9 mmol, 90%) as a colorless oil. IR (neat) 3471, 3379, 3058, 2835, 1609, 1580, 1266, 1044 cm^{-1}; {^1}H NMR (400 MHz, CDCl_{3}) \delta 7.38-7.13 (m, HH), 7.01 (d, J = 9.0 Hz, IH), 6.87 (dd, J = 8.0, 1.1 Hz, IH), 6.83 (dd, J = 8.0, 1.1 H, IH), 6.54-6.41 (m, 2H), 5.02 (d, J = 12.8 Hz, IH), 4.92 (d, J = 12.8 Hz, IH), 3.76 (s, 3H), 3.52 (br, 2H); {^{13}}C NMR (100 MHz, CDCl_{3}) \delta 160.2, 157.2, 145.0, 143.2, 142.4, 137.4, 132.9, 129.3, 128.4, 128.1, 127.5, 127.4, 126.6, 126.0, 122.9, 120.2, 119.4, 114.3, 105.4, 100.6, 69.9, 55.3; HRMS (EI+) calcd. for C_{26}H_{23}NO_{2} 381.1729, found 381.1721.

Example 163

This example concerns the synthesis of Aniline 59: To a stirred solution of 37 (54.4 mg, 0.132 mmol) in glacial HOAc (0.55 mL) was added Zn dust (43.2 mg, 0.660 mmol) at rt. After 20 h, the mixture was quenched with sat. aq. NaHCO_{3} (15 mL)
mL), diluted with EtOAc (20 mL) and washed with H₂O (20 mL) and sat. aq. NaCl (20 mL). The dried extract (MgSO₄) was concentrated in vacuo and purified by chromatography over silica gel, eluting with 15-25% EtOAc / Hexanes to give 59 (49.0 mg, 0.128 mmol, 97%) as a yellow oil. IR (neat) 3471, 3385, 3057, 2933, 1611, 1503, 1163 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.56-7.48 (m, 4H), 7.41 (dt, J = 1.5, 1.5, 7.2 Hz, IH), 7.38-7.32 (m, 6H), 7.20 (dd, J = 1.2, 7.2 Hz, 2H), 6.93 (t, J = 7.5 Hz, IH), 6.71-6.67 (m, 2H), 5.12 (s, 2H), 3.88 (s, 3H), 3.85 (broad s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 160.5, 156.9, 142.0, 140.2, 137.2, 132.4, 130.7, 129.4, 128.8, 128.5, 127.8, 127.7, 127.1, 126.9, 125.0, 122.0, 117.9, 106.0, 101.3, 70.7, 55.5; HRMS (EI+) calcd. for C₂₆H₂₃NO₂ (M+H) 382.1729, found 381.1728.

Example 164

This example concerns the synthesis of Phenol 60: To a stirred solution of 34 (54.7 mg, 132.3 mmol) and EtOH (460 mL, absolute) was added Pd/C (62.3 mg, 10% Pd). After stirring under an atmosphere of H₂ for 21 h, the mixture was filtered over a pad of Celite® with EtOAc (50 mL) and concentrated in vacuo. The product was purified via flash chromatography over silica gel, eluting with 15-20% EtOAc/Hexanes to give 60 (26.1 mg, 89.6 mmol, 67%) as a colorless oil; IR (neat) 3472, 3382, 3187, 3059, 1621, 1573, 1265, 1161, 1039 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.30 (t, J = 7.9 Hz, IH), 7.25-7.10 (m, 5H), 6.95 (dd, J = 7.6, 1.0 Hz, IH), 6.86 (dd, J = 8.0, 1.0 Hz, IH), 6.80 (d, J = 8.5 Hz, IH), 6.54 (d, J = 2.5 Hz, IH), 6.38 (dd, 8.5, 2.5 Hz, IH), 3.78 (s, 3H), 4.70-3.40 (br, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.7, 154.7, 144.7, 144.0, 141.3, 132.6, 129.1, 129.1, 127.7, 126.5, 121.4, 120.6, 115.9, 114.9, 107.3, 101.6, 55.2; HRMS (EI+) calcd. for C₁₉H₁₉NO₂ 291.1259, found 291.1251.
Example 165

\[
\begin{align*}
\text{BnO} & \quad \text{NO}_2 \\
\text{OMe} & \quad \text{HO} \\
\text{OMe} & \quad \text{NH}_2 \\
37 & \quad \text{61}
\end{align*}
\]

This example concerns the synthesis of Phenol 61: To a stirred solution of 37 (25.6 mg, 0.0620 mmol) and EtOH (0.31 mL) was added Pd/C (29.9 mg, 10% Pd). After stirring under an atmosphere of H\textsubscript{2} for 21 h, the mixture was filtered over a pad of celite-® with EtOAc (50 mL) and concentrated \textit{in vacuo}. The product was purified by chromatography over silica gel, eluting with 15-20% EtOAc/Hexanes to give 61 (15.3 mg, 0.0530 mmol, 85%) as a white solid. MP 87-89°C; IR (neat) 3394, 3301, 2921, 1731, 1617, 1160 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.55-7.50 (m, 4H), 7.45 (m, 1H), 7.29 (d, \(J = 2.0\) Hz, 1H), 7.26 (dd, \(J = 1.6, 7.6\) Hz, 1H), 7.23 (dd, \(J = 1.6, 8.4\) Hz, 1H), 7.05 (t, \(J = 7.6\) Hz, 1H), 6.69 (m, 2H), 3.87 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 161.1, 154.9, 139.0, 138.9, 131.9, 131.1, 129.9, 129.8, 129.3, 129.1, 127.7, 126.3, 120.6, 118.8, 107.9, 103.1 55.4; HRMS (EI+) calcd. for C\textsubscript{19}H\textsubscript{17}NO\textsubscript{2} (M+H) 291.1259, found 291.126.

Example 166

\[
\begin{align*}
\text{Cl} & \quad \text{NO}_2 \\
\text{OBn} & \quad \text{Cl} \\
\text{OBn} & \quad \text{NH} \\
20 & \quad \text{62}
\end{align*}
\]

This example concerns the synthesis of Carbazole 62: To a pressure vessel containing 20 (38.7 mg, 114 \(\mu\)mol) and 0-C\textsubscript{6}H\textsubscript{4}Cl\textsubscript{2} (230 \(\mu\)L) was added PPh\textsubscript{3} (75.5 mg, 289 \(\mu\)mol) at rt. The mixture was heated to 180°C. After 24 h, the reaction was cooled to rt and purified via flash chromatography over silica gel, eluting with 10-30% EtOAc/Hexanes to give impure 62 (40.2 mg) as a brown solid. Recrystallization from CHCl\textsubscript{3}/Pentane afforded 61 (26.3 mg, 85.5 \(\mu\)mol, 75%) as an off-white solid. MP 158-160°C; IR (thin film) 3387, 1177 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.48 (d, \(J = 8.7\) Hz, 1H), 8.02 (br s, 1H), 7.52 (d, \(J = 7.2\) Hz, 2H),...
7.45 (t, J = 7.2 Hz, 2H), 7.38 (t, J = 7.2 Hz, IH), 7.33-7.18 (m, 3 H), 7.03 (dd, J = 8.7, 2.2 Hz, IH), 6.97 (d, J = 0.9 Hz, IH), 5.19 (s, 2H); 13C NMR (100 MHz, CDCl3) δ 158.5, 140.8, 140.6, 137.0, 128.7, 128.0, 127.5, 125.0, 123.9, 120.9, 120.3, 116.4, 109.3, 108.6, 95.7, 70.4; HRMS (EI+) calcd. for C19H14NOCl (M+) 307.0764, found 307.0775.

Example 167

This example concerns the synthesis of Carbazole 63: To a pressure vessel containing 21 (49.9 mg, 147 µmol) and 0-C6H4Cl2 (300 µL) was added PPh3 (119.4 mg, 455 µmol) at rt. The mixture was heated to 180°C. After 24 h, the reaction was cooled to rt and purified via flash chromatography over silica gel, eluting with 10-30% EtOAc/Hexanes to give impure 63 (50.4 mg) as a brown solid. Recrystallization from CHCl3/Pentane afforded 63 (43.7 mg, 142 µmol, 89%) as an off-white solid. MP 222-224°C; IR (KBr) 3390, 2916, 1624, 1225, 1176, 1027, 816, 728 cm−1; 1H NMR (400 MHz, d6-DMSO) δ 1.30 (s, IH), 8.11 (s, IH), 8.04 (d, J = 7.8 Hz, IH), 7.68-7.19 (m, 7H), 7.08 (s, IH), 6.89 (d, J = 7.8 Hz, IH), 5.22 (s, 2H); 13C NMR (100 MHz, d6-DMSO) δ 158.5, 142.2, 138.7, 137.7, 128.9, 128.3, 128.2, 124.5, 124.3, 123.4, 122.0, 119.4, 116.4, 112.5, 109.4, 96.2, 70.0; HRMS (EI+) calcd. for C19H14NOCl (M+) 307.0764, found 307.0764.

Example 168

This example concerns the synthesis of Carbazole 64: To a pressure vessel containing 22 (18.7 mg, 55.0 mmol) and 0-C6H4Cl2 (150 µL) was added PPh3 (44.1
mg, 168 µmol) at rt. The mixture was heated to 180°C. After 24 h, the reaction was cooled to rt and purified via flash chromatography over silica gel, eluting with 10-30% EtOAc / Hexanes to give impure 64 (17.6 mg) as a brown solid.

Recrystallization from CHCl₃ / Pentane afforded 64 (14.2 mg, 46.1 µmol, 84%) as an off-white solid. MP 235-238°C; IR (KBr) 3396, 2923, 1605, 1016, 797 cm⁻¹; ¹H NMR (400 MHz, d₆-DMSO) 11.29 (s, IH), 8.02 (d, J = 3.3 Hz, IH), 8.00 (d, J = 3.7 Hz, IH), 7.52 (d, J = 7.2 Hz, 2H), 7.46 (d, J = 1.8 Hz, IH), 7.43 (t, J = 7.1 Hz, 2H), 7.35 (t, J = 7.3 Hz, IH), 7.14 (dd, J = 8.3, 1.9 Hz, IH), 7.09 (d, J = 2.3 Hz, IH), 6.90 (dd, J = 8.6, 2.3 Hz, IH), 5.21 (s, 2H); ¹³C NMR (100 MHz, d₆-DMSO) δ 158.3, 141.9, 140.9, 137.7, 129.0, 128.9, 128.3, 128.2, 122.0, 121.6, 121.1, 119.1, 116.2, 110.8, 109.4, 96.4, 70.0; HRMS (EI+) calcd. for C₁₉H₁₆ClNO (M+) 307.0764, found 307.0772.

Example 169

This example concerns the synthesis of Carbazole 65: To a pressure vessel containing 32 (17.2 mg, 0.0510 mmol) and o-dichlorobenzene (100 µL) was added PPh₃ (66.4 mg, 0.254 mmol) at rt. The mixture was heated at 180°C. After 48 h, the reaction was purified via flash chromatography over silica gel, eluting with 0-20% EtOAc / Hexanes to give 65 (10.2 mg, 0.033 mmol, 65%) as a white solid. MP 145-146°C; IR 3419, 2911, 1419, 735 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.21 (bs, IH), 7.96 (d, J = 8.6 Hz, IH), 7.89 (d, J = 7.8 Hz, IH), 7.52 (d, J = 7.2 Hz, 2H), 7.45 (t, J = 7.1, 7.6 Hz, 2H), 7.38 (t, J = 7.2, 7.8 Hz, 2 H), 7.18 (t, J = 7.8 Hz, IH), 7.07 (d, J = 2.0 Hz, IH), 7.00 (dd, J = 2.2 Hz, 8.6 Hz, IH); ¹³C NMR (100 MHz, CDCl₃) δ 158.7, 140.5, 137.0, 136.7, 128.7, 128.1, 127.5, 125.0, 123.9, 121.6, 120.4, 117.9, 117.6, 115.8, 109.8, 96.2, 70.5; HRMS (FAB+) calcd. For C₁₉H₁₄ClNO (M+H) 308.0842, found 308.0846.
Example 170

This example concerns the synthesis of AHyI ether 96: To a stirred solution of 73 (843.0 mg, 3.677 mmol) and dry DMF (18.0 mL) was added NaH (320.9 mg, 8.022 mmol, 60% dispersion in mineral oil) at 0°C. To this dark red solution was added allyl iodide (3.12 g, 1.70 mL, 18.59 mmol). After 10 min, the yellow solution was quenched with sat. aq. NH₄Cl (20 mL), diluted with EtOAc (100 mL), washed with H₂O (10 mL), and sat. aq. NaCl (2 x 10 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified by flash chromatography over silica gel, eluting with PhMe to give 96 (990 mg, 3.68 mmol, 99%) as a bright yellow oil. IR (neat) 1610, 1516, 1353, 734 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.782 (d, J = 8.9, 1H), 7.31-7.22 (m, 4H), 7.03-6.97 (m, 2H), 6.18-6.05 (m, 1H), 5.48 (dq, J = 17.2, J = 1.5 Hz, 1H), 5.34 (dq, J = 10.5, 1.3 Hz, 1H), 4.60 (dt, J = 5.3, 1.5 Hz, 2H), 2.47 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 6158.6, 147.1, 143.3, 136.1, 133.2, 132.6, 130.1, 129.1, 128.3, 124.3, 117.8, 114.9, 68.9, 21.4; HRMS (EI⁺) calcd. for C₁₄H₁₂NO₃ (M⁺) 269.1052, found 269.1042.

Example 171

This example concerns the synthesis of Phenol 68: To a stirred solution of 96 (990 mg, 3.68 mmol) in CH₂Cl₂ (37.0 mL) was added BCl₃ (11.1 mL, 11.1 mmol, 1.0 M in hexanes) at -78°C. After 2 h, the reaction was quenched with MeOH (2.0 mL) at -78°C and warmed to rt. The solution was diluted with CH₂Cl₂ (45 mL) and washed with H₂O (2 x 20 mL) and sat. aq. NaCl (2 x 20 mL). The dried (Na₂SO₄) extract was concentrated in vacuo and purified via flash chromatography over silica gel, eluting with 10-30% Et₂O/PhMe to give 68 (845.7 mg, 3.141 mmol, 85%) as a...
yellow crystalline solid. MP 82-83°C; IR (thin film) 3486, 1609, 1520, 1351, 1215,
758 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 8.1 Hz, IH), 7.28-7.22 (m, 2H), 7.14-7.08 (m, 2H), 6.88 (d, J = 8.0 Hz, IH), 6.06 (m, IH), 5.24 (dq, J = 5.25,
1.5 Hz, IH), 5.21 (t, J = 1.6 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ; HRMS (EI+)
calcd. for C₁₉H₁₆N₂O₄ (M+) 269.1052, found 269.1053.

Example 172

This example concerns the synthesis of Carbazoles 74 and 75 and Aniline

METHOD A: To a pressure vessel containing 68 (5.16 mg, 191.6 mmol) and
0-C₆H₄Cl₂ (2.00 mL) was added PPh₃ (205 mg, 782 µmol) at rt. The mixture was
heated at 180°C. After 30 h at 180°C, the reaction was cooled to rt and passes
trough a silica plug. Purification via flash chromatography over silica gel, eluting
with 10-15% EtOAc/Hexanes gave sequentially 75 (23.2 mg, 97.8 µmol, 51%), 76
(5.3 mg, 22.1 µmol, 11%), and 74 (14.5 mg, 61.1 µmol, 32%) as off-white solids.

METHOD B: To a pressure vessel containing 68 (26.6 mg, 98.8 mmol) and
0-C₆H₄Cl₂ (1.00 mL) was added P"Bu₃ (81 mg, 100 µL, 400 µmol) at rt. The
mixture was heated at 180°C. After 12 h at 180°C, the reaction was cooled to rt and
purified via flash chromatography over silica gel, eluting with 10-25%
EtOAc/Hexanes to give sequentially 75 (5.6 mg, 24 µmol, 23%), 76 (9.4 mg, 39
µmol, 38%), and 74 (6.5 mg, 27 µmol, 27%) as off-white solids.

74: MP 131-133°C; IR (thin film) 3412, 3212, 2920, 2851, 1639, 1615,
1211, 909, 802 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 4.9 Hz, 3H), 7.27
(d, J = 8.2 Hz, IH), 7.18 (dd, J = 8.2, 1.1 Hz, IH), 6.86 (s, IH), 6.15 (ddt, J = 16.5,
10.1, 6.3 Hz, IH), 5.26 (dq, J = 12.2, 1.6 Hz, IH), 5.23 (dt, J = 4.9, 1.7 Hz, IH), 5.19
(br s, IH), 3.61 (d, J = 3.6 Hz, 2H), 2.54 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ
153.4, 140.1, 137.8, 137.3, 128.7, 125.8, 123.7, 121.5, 119.5, 117.9, 117.4, 116.4,
110.0, 97.4, 35.7, 21.5; HRMS (EI+) calcd. for C_{6}H_{15}NO 237.1 154 (M+), found 237.1 149.

75: MP 154-156°C; IR (thin film) 3459, 3356, 2918, 2850, 1614, 1211, 912, 804 cm^{-1}; ¹H NMR (400 MHz, CDCl₃) δ 7.91 (br s, IH), 7.80 (d, J= 8.1 Hz, IH), 7.79 (s, IH), 7.32 (d, J= 8.2 Hz, IH), 7.19 (dd, J= 8.2, 1.3 Hz, IH), 6.76 (d, J= 8.3 Hz, IH), 6.13 (ddt, J= 16.0, 10.1, 6.0 Hz, IH), 5.29-5.19 (m, 2H), 4.96 (br s, IH), 3.72 (dt, J= 5.9, 1.6 Hz, 2H), 2.54 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 152.0, 140.8, 137.9, 135.6, 128.9, 125.9, 124.1, 119.5, 119.0, 117.5, 116.3, 110.2, 108.9, 106.5, 29.4, 21.5; HRMS (EI+) calcd. for C_{6}H_{15}NO 237.1 154 (M+), found 237.1 149.

76: MP 136-138°C; IR (thin film) 3376, 3311, 1607, 1270 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.91-7.18 (m, 2H), 7.06-6.97 (m, 2H), 6.85 (d, J= 8.0 Hz, IH), 6.76 (d, J= 7.8 Hz, IH), 6.09 (m, IH), 5.29-5.17 (m, 2H), 3.92 (br s, IH), 3.49 (d, J= 6.4 Hz, 2), 2.34 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 153.4, 140.6, 136.4, 131.9, 131.1, 128.7, 128.4, 128.1, 126.1, 116.6, 116.1, 116.0, 35.1, 20.5. HRMS (EI+) calcd. for C_{6}H_{15}NO 239.1310 (M+), found 239.1321.

Example 173

This example concerns the synthesis of Siamenol 66, Carbazole 67 and Amine 78: To a pressure vessel containing 77 (50.4 mg, 169 mmol) and 0-C₆H₄Cl₂ (400 µL) was added P'Bu₃ (138 mg, 170 µL, 681 µmol) at rt. The mixture was heated at 100°C. After 12 h at 100°C, the reaction was cooled to rt and purified via flash chromatography over silica gel, eluting with 10-25% EtOAc/Hexanes to give sequentially 67 (19.2 mg, 72.3 µmol, 43%), 78 (10.8 mg, 40.4 µmol, 24%), and 66 (12.4 mg, 46.7 µmol, 28%) as white solids.

66: MP 140-143°C; IR (thin film) 3406, 3252, 2920, 2852, 1636, 1617, 1465, 1319, 1210, 1014, 802 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (m, 3H), 7.29-7.18
(d, J = 8.0 Hz, IH), 7.17 (d, J=8.0 Hz, IH), 6.86 (s, IH), 5.44 (tt, J = 7.2, 1.2 H, IH), 5.30 (s, IH), 3.55 (d, J = 7.2 Hz, 2H), 2.54 (s, 3H), 1.88 (s, 3H), 1.85 (s, 3H); 1H NMR (400 MHz, CDCl₃) δ 7.64 (dd, J = 1.6, 0.8 Hz, IH), 7.60 (s, IH), 7.19 (d, J = 8.2 Hz, IH), 7.04 (dd, J = 8.1, 1.0 Hz, IH), 6.79 (s, IH), 5.43 (t-sept, J = 7.3, 1.4 Hz, IH), 3.41 (d, J = 7.3 Hz, 2H), 2.45 (s, 3H), 1.78 (s, 6H); 13C NMR (100 MHz, CDCl₃) δ 153.7, 139.9, 137.7, 134.7, 128.6, 125.7, 123.7, 122.6, 120.8, 119.4, 117.2, 109.9, 97.2, 30.5, 25.8, 21.4, 17.9; 13C NMR (100 MHz, CDCl₃) δ 154.16, 140.4, 138.5, 131.1, 127.3, 124.7, 124.0, 123.9, 120.5, 119.7, 118.5, 116.1, 109.7, 95.9, 28.5, 24.9, 20.4, 16.7 HRMS (EI+) calcd. for C₁₄H₁₈N₆O 265.1467 (M+), found 265.1471.

67: MP 126-128°C; IR (thin film) 3524, 3424, 3261,2919, 2853, 1614, 1227, 1211, 1032, 802 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 7.85 (br s, IH), 7.78 (d, J = 1.0 Hz, IH), 7.76 (d, J = 3.6 Hz, IH), 7.31 (d, J = 8.2 Hz, IH), 7.18 (dd, J = 8.4, 1.1 Hz, IH), 6.76 (d, J = 8.3 Hz, IH), 5.41 (d-sept, J = 6.9, 1.4 Hz, IH), 5.11 (br s, IH), 3.64 (d, J = 6.9 Hz, 2H), 2.54 (s, 3H), 1.94 (s, 3H), 1.82 (d, J = 1.2 Hz, 3H); 13C NMR (100 MHz, CDCl₃) δ 152.2, 140.4, 137.8, 134.9, 128.8, 125.8, 124.2, 121.5, 119.5, 118.6, 117.4, 110.1, 109.0, 108.3, 25.8, 24.4, 21.5, 18.1; HRMS (EI+) calcd. for C₁₄H₁₈N₆O 237.1154 (M+), found 237.1155.

78: MP 126-132°C; IR (thin film) 3363, 3276, 2920, 1604, 1431, 1279, 1233 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 7.23 (d, J = 2.0 Hz, IH), 7.21 (dd, J = 8.3, 2.1Hz, IH), 7.00 (d, J = 9.1 Hz, 2H), 6.87 (d, J = 8.0 Hz, IH), 6.74 (d, J = 7.8 Hz, IH), 5.40 (tt, J = 5.9, 1.3 Hz, IH), 4.18 (br s, IH), 3.44 (d, J = 7.2 Hz, 2H), 2.32 (s, 3H), 1.83 (s, 3H), 1.82 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 153.6, 140.9, 134.8, 131.9, 131.1, 130.7, 128.6, 128.1, 128.0, 127.4, 121.7, 115.9, 115.9, 29.8, 25.9, 20.5, 17.9; HRMS (EI+) calcd. for C₁₈H₂₁N₆O (M+) 267.1623, found 267.162.
Example 174

To a pressure vessel containing acetylene 13 (105 mg, 0.564 mmol) was added diene 11 (234 mg, 1.69 mmol) and xylenes (1.1 mL) at rt. The mixture was heated at 140°C for 6 h then allowed to cool to rt. The mixture was loaded directly onto silica gel and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes, and recrystallized from Et₂O / petroleum ether to give 14 (66.1 mg, 0.227 mmol, 40%) as a yellow crystalline solid and bicyclo-[4.2.0]-octadiene 15 (52.8 mg, 0.166 mmol, 29%) as a yellow crystalline solid. Biaryl: Mp = 72-73°C; IR (neat) 2958, 1722, 1528, 1350, 1264 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.20 (dd, J = 7.8, 1.4 Hz, 1H), 8.00 (dd, J = 8.3, 1.1 Hz, 1H), 7.75 (dd, J = 8.0, 1.1 Hz, 1H), 7.65 (td, J = 7.5, 1.4 Hz, 1H), 7.56 (td, J = 7.8, 1.4 Hz, 1H), 7.51 (t, J = 8.2 Hz, 1H), 7.19 (dd, J = 7.6, 1.0 Hz, 1H), 3.76 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.2, 149.3, 136.6, 136.1, 135.4, 133.6, 132.6, 130.8, 129.7, 129.0, 128.7, 128.6, 122.5, 52.2; HRMS (CI+) calcd. for C₄₅H₄₁NO₄Cl (M+H) 292.0377, found 292.0382.

Cyclobutene: Mp = 94-95°C; IR (neat) 2928, 1711, 1532, 1435, 1368, 1250 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (dd, J = 8.2, 1.2 Hz, 1H), 7.56 (dd, J = 8.2, 1.2 Hz, 1H), 7.33 (t, J = 8.1 Hz, 1H), 6.98 (dd, J = 5.8, 2.8 Hz, 1H), 6.51 (s, 1H), 4.06 (ddd, J = 5.6, 4.1, 1.4 Hz, 1H), 3.73 (s, 3H), 2.67-3.25 (m, -lH), 2.06-2.15 (m, 1H), 1.98-2.03 (m, 1H), 1.48 (dddd, J = 12.3, 9.6, 5.4, 4.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 167.3, 150.5, 140.9, 137.7, 137.2, 135.1, 133.3, 133.28, 128.7, 127.0, 121.6, 51.7, 44.1, 39.7, 25.2, 20.8; HRMS (CI+) calcd. for C₁₆H₁₅NO₄Cl (M+H) 320.06896, found 320.06881.
Example 175

![Chemical structure of the reactants and product](image)

To a pressure vessel containing the acetylene (47.2 mg, 0.258 mmol) was added the diene (85.8 mg, 92.3 µL, 0.775 mmol) at rt. After heating at 140°C for 2 h, the crude mixture was cooled to rt and purified by chromatography over silica gel, eluting with 10% EtOAc/Hexanes to give the biaryl (56.0 mg, 0.212 mmol, 82%) as a crystalline solid. Mp = 69-70°C; IR (neat) 2944, 1530, 1358, 1261 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.74 (dd, J = 8.2, 1.3 Hz, IH), 7.73 (dd, J = 8.0, 1.2 Hz, IH), 7.45 (t, J = 8.1 Hz, IH), 7.44 (ddd, J = 7.3, 6.4, 1.7 Hz, IH), 7.19 (dd, J = 7.5, 1.8 Hz, IH), 7.07 (td, J = 7.5, 1.0 Hz, IH), 7.00 (dd, J = 8.4, 1.0Hz, IH), 3.76 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 156.3, 151.1, 136.3, 133.6, 132.1, 130.4, 130.2, 128.7, 123.3, 122.3, 120.7, 111.0, 55.6; HRMS (Cl+) calcd. for C₁₃H₁₀NO₃Cl (M+H) 263.03492, found 263.03508.

Example 176

![Chemical structure of the reactants and product](image)

To a pressure vessel containing the acetylene (61.7 mg, 0.273 mmol) was added the diene (113 mg, 0.819 mmol) and xylene (0.55 mL). After heating at 140°C for 6 h, the mixture was cooled to rt, loaded directly onto silica gel and purified via silica gel chromatography, eluting with 75-100% Hexanes/PhMe to give the biaryl (33.0 mg, 0.0981 mmol, 36%) as a yellow oil and the cyclobutene (26.8 mg, 0.0737 mmol, 27%) as a yellow oil. Biaryl: IR (neat) 2952, 1723, 1528, 1434,
1350, 1265 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.19 (dd, J = 7.8, 1.3 Hz, IH), 8.03 (dd, J = 8.2, 1.2 Hz, IH), 7.93 (dd, J = 8.0, 1.0 Hz, IH), 7.64 (td, J = 7.6, 1.4 Hz, IH), 7.56 (td, J = 7.8, 1.4 Hz, IH), 7.42 (t, J = 8.2 Hz, IH), 7.16 (dd, J = 7.6, 1.2 Hz, IH), 3.75 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.1, 149.2, 138.6, 137.8, 136.8, 132.6, 130.8, 129.7, 129.2, 128.9, 128.7, 125.5, 123.1, 52.2. 

Cyclobutene: IR (neat) 2919, 1716, 1525, 1438, 1371, 1248, cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.79 (dd, J = 8.0, 1.0 Hz, IH), 7.61 (dd, J = 8.1, 1.1 Hz, IH), 7.26 (t, J = 8.0 Hz, IH), 6.97 (dd, J = 5.8, 2.8 Hz, IH), 6.48 (s, IH), 4.08 (t, J = 4.0 Hz, IH), 3.73 (s, 3H), 3.23 (s, IH), 2.69 (d, J = 16 Hz, IH), 2.09-2.18 (m, IH), 1.97-2.03 (m, IH), 1.44-1.51 (m, IH); ¹³C NMR (100 MHz, CDCl₃) δ 167.4, 150.5, 140.7, 138.9, 137.6, 136.6, 133.3, 129.2, 129.0, 124.6, 122.2, 51.7, 44.2, 39.5, 25.2, 20.9.

**Example 177**

![Diagram](image.png)

To a pressure vessel containing the acetylene (52.6 mg, 0.358 mmol) was added the diene (148 mg, 1.07 mmol) at rt. The mixture was heated at 140°C for 6 h then allowed to cool to rt. The crude mixture was loaded directly onto silica gel and purified by chromatography over silica gel, eluting with 10% EtOAc/Hexanes, to give a mixture of the biaryl and the cyclobutene as observed by ¹H NMR. To this mixture (0.358 mmol) was added Zn dust (117 mg, 1.79 mmol) and AcOH (1.79 mmol) at rt. After 30 min, the reaction was filtered over celite, eluting with EtOAc (20 mL). The organic phase was basified with sat. aq. NaHCO₃ and washed with H₂O (15 mL) and sat. aq. NaCl (15 mL). The dried extract (MgSO₄) was purified by chromatography over silica gel, eluting with 0-50% EtOAc / CH₂Cl₂, to give the lactam (35.2 mg, 0.180 mmol, 51%) as a white crystalline solid. ¹H NMR (400 MHz, d₆-DMSO) δ 11.7 (s, IH), 8.52 (d, J = 8.2 Hz, IH), 8.40 (d, J = 7.8 Hz, IH), 8.34 (dd, J = 7.4, 1.3 Hz, IH), 7.87 (td, J = 7.2, 1.4 Hz, IH), 7.66 (td, J = 8.0, 1.1 Hz, IH).
Hz, IH), 7.50 (td, $J = 8.3$, 1.2 Hz, IH), 7.38 (d, $J = 8.1$, 1.0 Hz, IH), 7.28 (td, $J = 8.2$, 1.2 Hz, IH); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (dd, $J = 8.2$, 1.2 Hz, IH), 7.67 (dd, $J = 8.1$, 1.3 Hz, IH), 7.22 (d, $J = 4.8$ Hz, IH), 6.03 (dt, $J = 9.9$, 5.0 Hz, IH), 5.78-5.83 (m, 2H), 3.80 (s, 3H), 2.65-2.91 (m, 2H), 2.61-2.66 (m, 2H); $^13$C NMR (100 MHz, CDCl$_3$) $\delta$ 167.9, 150.6, 137.5, 136.4, 136.12, 136.1, 135.5, 135.3, 133.8, 128.8, 126.5, 124.9, 122.4, 52.0, 28.7, 25.7; HRMS (EI+) calcd. for C$_{16}$H$_{14}$NO$_4$Cl (M+) 319.0613, found 319.06050.

Procedure C. To a pressure vessel was added the cyclobutene (48.3 mg, 0.151 mmol) and xylenes (0.30 mL). After heating at 160°C for 6 h in the absence

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Example 178

Cyclooctatriene: Procedure A. To a pressure vessel was added the cyclobutene (174 mg, 0.544 mmol) and xylenes (1.09 mL) and heated at 160°C for 20 h. The mixture was cooled to rt then purified by chromatography over silica gel, eluting with 5-10% EtOAc / Hexanes, to give the biaryl (66.8 mg, 0.229 mmol, 42%) and the cyclooctatriene (65.2 mg, 0.204 mmol, 37%) as yellow crystalline solids.

Procedure B. To a pressure vessel containing the cyclobutene (16.9 mg, 0.0529 mmol) was added xylenes (0.2 mL). The solution was irradiated (120 W halogen bulb) with heating at 140°C. After 40 h, the solution was cooled to rt and loaded directly onto silica gel. The reaction was purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes to give the cyclooctatriene (14.0 mg, 0.0438 mmol, 83%) as a yellow solid: Mp = 86-87°C; IR (neat) 2952, 1711, 1532, 1434, 1357 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (dd, $J = 8.2$, 1.2 Hz, IH), 7.67 (dd, $J = 8.1$, 1.3 Hz, IH), 7.22 (d, $J = 4.8$ Hz, IH), 6.03 (dt, $J = 9.9$, 5.0 Hz, IH), 5.78-5.83 (m, 2H), 3.80 (s, 3H), 2.65-2.91 (m, 2H), 2.61-2.66 (m, 2H); $^13$C NMR (100 MHz, CDCl$_3$) $\delta$ 161.3, 137.0, 134.7, 133.3, 130.1, 128.4, 127.9, 126.2, 123.7, 123.1, 122.7, 118.0, 116.6.
of light, the mixture cooled to rt, loaded directly onto silica gel and purified via silica gel chromatography, eluting with 5-10% EtOAc / Hexanes to give the biaryl (20.7 mg, 0.0709 mmol, 47%) as a yellow oil and cyclooctatriene (12.6 mg, 0.0393 mmol, 26%) as a yellow oil.

In view of the many possible embodiments to which the principles of the disclosed invention may be applied, it should be recognized that the illustrated embodiments are only preferred examples of the invention and should not be taken as limiting the scope of the invention. Rather, the scope of the invention is defined by the following claims. We therefore claim as our invention all that comes within the scope and spirit of these claims.
We claim:

1. A dienophile having a formula

   \[
   \begin{array}{c}
   \text{R}_1 \\
   \text{R}_2 \\
   \text{R}_3 \\
   \text{R}_4 \\
   \text{R}_5 \\
   \text{R}_6
   \end{array}
   \]

   where \( \text{R}_i \) is a nitrogen-containing moiety, \( \text{R}_2 \) and \( \text{R}_4-\text{R}_6 \) independently are alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties, cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties, phosphorus-containing moieties, silicon, silicon-containing moieties, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, and \( \text{R}_3 \) is halide or hydrogen, but excluding compounds where (a) \( \text{R}_1 \) is nitro, \( \text{R}_2 \) is H-pentyl, and \( \text{R}_3 \) is bromide, and (b) \( \text{R}_1 \) is nitro, \( \text{R}_2 \) is carboxylic acid or methyl ester, and \( \text{R}_3 \) is chloride or bromide.

2. The compound according to claim 1 comprising a dihalide, where at least one halogen is other than fluorine, and where \( \text{R}_2 \) is other than aryl.

3. The compound according to claim 1 where at least one of \( \text{R}_4-\text{R}_6 \) is halide.

4. The compound according to claim 1 where \( \text{R}_3 \) is bromide or chloride.

5. The compound according to claim 1 where \( \text{R}_i \) is nitro, nitroso, or nitrogen oxide.
6. The compound according to claim 1 where \( R_3 \) is bromide or chloride, and \( R_i \) is nitro, nitroso, or nitrogen oxide.

7. The compound according to claim 5 where \( R_i \) is nitro.

8. The compound according to claim 1 where \( R_i \) is nitro, \( R_3 \) is chloride or bromide, and \( R_4-R_6 \) independently are hydrogen and halide.

9. The compound according to claim 1 where \( R_2 \) is a phosphorus-containing moiety.

10. An unsymmetrical, tetra-or t/z/o-substituted biaryl compound having a formula

![Diagram]

where \( R_3, R_4, R_8 \) and \( R_9 \) are different, and where \( R_i-R_{10} \) are independently selected from alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, aroylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties, cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties, phosphorus-containing moieties, silicon, silicon-containing moieties, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties.
11. The biaryl compound according to claim 10 where R3 is a nitrogen-containing moiety, and R9 is halide or hydrogen.

12. The compound according to claim 10 where R9 is bromide or chloride.

13. The compound according to claim 12 where R3 is bromide or chloride, and R4 is nitro, nitroso, or nitrogen oxide.

14. The compound according to claim 12 having a formula

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\begin{center}
\includegraphics[width=0.5\textwidth]{formula.png}
\end{center}
```

where R1-R2, R5-R7, and R10 groups independently are aliphatic, substituted aliphatic, aryl, alkyl aryl, carboxylic acid, ester, heteroaliphatic, heteroaryl, heterocyclic, or hydrogen, Rn is selected from lower alkyl, aryl, substituted aryl or haloaryl, R12 is aliphatic, substituted aliphatic, aryl, alkyl aryl, heteroaliphatic, heteroaryl, heterocyclic, X is bromide or chloride, and any and all combinations thereof.

15. The compound according to claim 14 where R1-R2, R5-R7 and R10 are hydrogen, R12 is lower alkyl, aryl or substituted aryl, and X is chloride.

16. The compound according to claim 12 having a formula
where $R_i-R_2$, $R_5-R_7$ and $R_{10}$ groups independently are aliphatic, substituted aliphatic, aryl, alkyl aryl, carboxylic acid, ester, heteroaliphatic, heteroaryl, heterocyclic, or hydrogen, $R_n$ is selected from lower alkyl, aryl, substituted aryl or haloaryl, $R_{12}$ is aliphatic, substituted aliphatic, aryl, alkyl aryl, heteroaliphatic, heteroaryl, heterocyclic, $X_i$ is bromide or chloride, $R_{13}$ is selected from lower aliphatic, lower alkoxy, aryl, substituted aryl, and haloaryl, $X$ is bromide or chloride, and any and all combinations thereof.

17. A method for making a tetra-or t/zo-substituted biaryl compound comprising reacting a diene with a dienophile under reaction conditions that promote a cycloaddition reaction.

18. The method according to claim 17 where the dienophile is an alkyne.

19. The method according to claim 18 where the alkyne is an aryl alkyne.

20. The method according to claim 17 where the biaryl compound has a formula

\[
\begin{align*}
R_1 & \quad R_2 \\
\text{NO}_2 & \\
R_7 & \quad R_5 \\
P(O)R_{13} & \\
R_{12}O & \\
\end{align*}
\]
where R₃, R₄, R₈ and R₉ are different, and where R₁-R₁₀ are independently selected from alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties (such as aldehydes, amides, carboxylic acids, esters, ketones and thioesters), cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties, phosphorus-containing moieties, silicon, silicon-containing moieties, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties.

21. The method according to claim 20 where R₃ is a nitrogen-containing moiety, and R₉ is halide or hydrogen.

22. The method according to claim 21 where R₃ is nitro, nitroso, or nitrogen oxide, and R₉ is bromide or chloride.

23. The method according to claim 17 where the dienophile has a formula
where $R_i$ is a nitrogen-containing moiety, $R_2$ and $R_4$-$R_6$ independently are alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, aryl, substituted aryl, arylalkyl, carbonyl-containing moieties, cyclic, substituted cyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, and phosphorus-containing moieties, and $R_3$ is halide.

24. The compound according to claim 23 comprising a dihalide, where at least one halogen is other than fluorine.

25. The compound according to claim 23 where at least one of $R_4$-$R_6$ is halide.

26. The compound according to claim 23 where $R_3$ is bromide or chloride.

27. The compound according to claim 23 where and $R_i$ is nitro, nitroso, or nitrogen oxide, and $R_3$ is bromide or chloride.

28. The compound according to claim 27 where $R_i$ is nitro.

29. The compound according to claim 23 where $R_i$ is nitro, $R_3$ is chloride or bromide, and $R_4$-$R_6$ independently are hydrogen and halide.
30. The compound according to claim 23 where R₂ is a phosphorus-containing moiety.

31. A method for making a biaryl compound, comprising:

providing a diene;

providing a dienophile having a formula

\[
\begin{align*}
\text{R}_1 & \quad \text{R}_2 \\
\text{R}_3 & \quad \text{R}_4 \\
\text{R}_5 & \quad \text{R}_6
\end{align*}
\]

where R₁ and R₃ are independently selected from halide, hydrogen, and nitrogen-containing moieties, R₂ is selected from aliphatic, substituted aliphatic, carbonyl bearing moieties, halogen, hydrogen, and phosphorus-containing moieties, and R₄-R₆ are independently selected from hydrogen, halide, aliphatic, substituted aliphatic, substituted aliphatic, aryl, substituted aryl, arylalkyl, carbonyl bearing moieties, cyclic, substituted cyclic, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; and

making a biaryl compound by combining the diene with the dienophile under reaction conditions that facilitate a cycloaddition reaction between the diene and the dienophile.

32. A method, comprising:

making a biaryl compound by combining a diene with a dienophile under reaction conditions that facilitate a Diels-Alder reaction between the diene and the dienophile; and

reacting the biaryl compound to form a second compound.

33. The method according to claim 32 where the dienophile has a formula
where \( R_p R_6 \) are independently selected from alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties, cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties, phosphorus-containing moieties, silicon, silicon-containing moieties, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties.

34. The method according to claim 33 where \( R_i \) and \( R_3 \) are independently selected from hydrogen, halide, and nitrogen-containing moieties, \( R_2 \) is selected from aliphatic, substituted aliphatic, aryl, substituted aryl, carbonyl bearing moieties, cyclic, heteroaryl, heterocyclic, hydrogen, halogen, phosphorus-containing moieties, and \( R_4 - R_6 \) independently are selected from hydrogen, halide, aliphatic, substituted aliphatic, aryl, substituted aryl, carbonyl bearing moieties, cyclic, heteroaryl, and substituted heteroaryl.

35. The method according to claim 32 where the diene has a formula
where \( R_i \) to \( R_6 \) independently are selected from aliphatic; substituted aliphatic; alkoxy; amino; amine; substituted amine; aryl; substituted aryl; arylalkyl; carbonyl-bearing groups, halogens; hydrogen; nitriles; phosphorous, silyl; silyl ether; sulfide; sulfones; or sulfoxide, and where \( R_i \) and \( R_6 \) also can be a carbon atom or a heteroatom in cyclic or heterocyclic compounds having 5 or more atoms in a ring, and where \( R_7 \) and \( R_8 \) are carbon atoms or heteroatoms.

36. The method according to claim 32 where the biaryl compound is a tetra-or \( t/t \)-substituted biaryl compound having a formula

where \( R_3, R_4, R_8 \) and \( R_9 \) are other than hydrogen, and where \( R_i \) to \( R_{10} \) are independently selected from alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties, cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic,
hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties, phosphorus-containing moieties, silicon, silicon-containing moieties, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties.

37. The method according to claim 36 where $R_3$, $R_4$, $R_8$ and $R_9$ are different, and where remaining $R_p R_2$, $R_5-R_7$ and $R_i$ groups are selected from amino, amine, substituted amine, aliphatic, substituted aliphatic, aryl, substituted aryl, arylalkyl, cyclic, substituted cyclic, halogen, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, and combinations thereof.

38. The method according to claim 32 where the alkyne is produced from a carboxylic acid having a formula

\[
\begin{array}{c}
\text{CO}_2\text{H} \\
\text{NO}_2
\end{array}
\]

where $R_i$ and $R_2$ independently are hydrogen or halogen.

39. The method according to claim 38 where the dienophile is produced from a 6-chloro-2-nitro-toluene or 4-chloro-2-nitro-toluene by oxidation to the corresponding benzaldehyde, followed by alkyne formation.

40. The method according to claim 39 where the alkyne is formed using an Ohira-Bestmann reagent.

41. The method according to claim 32 where the dienophile is a propargyl alcohol.

42. The method according to claim 41 where the propargyl alcohol has a formula
where $R_i$ and $R_2$ independently are hydrogen, lower alkyl, aryl or substituted aryl.

43. The method according to claim 42 where $R_i$ and $R_2$ independently are methyl, ethyl, propyl, butyl, pentyl, phenyl or halophenyl.

44. The method according to claim 32 further comprising aromatizing a Diels-Alder reaction product.

45. The method according to claim 44 comprising aromatizing using 1,8-diazabicyclo [5.4.0] undec-7-ene (DBU), 1,4-diazabicyclo [2.2.2] octane (DABCO), tetra-n-butylammonium fluoride (TBAF), trialkyl amines, and potassium carbonate ($K_2CO_3$).

46. The method according to claim 32 where the diene is a cyclohexadiene.

47. The method according to claim 46 where the cyclohexadiene includes at least one oxygen substituent.

48. The method according to claim 32 where the dienophile has a formula
where \( R_1 - R_2 \) and \( R_4 - R_6 \) independently are selected from aliphatic, substituted aliphatic, aryl, substituted aryl, cyclic, substituted cyclic, halide, heterocyclic, substituted heterocyclic, heteroaryl, substituted heteroaryl, and \( R_3 \) is a nitrogen bearing moiety.

49. The method according to claim 48 where \( R_1 - R_2 \) and \( R_4 - R_6 \) independently are halide, hydrogen, lower alkyl or lower alkoxy, and \( R_3 \) is nitro or nitroso.

50. The method according to claim 32 where the biaryl compound has a formula

where \( R_1 - R_2 \) and \( R_9 - R_{10} \) independently are hydrogen or halogen, and \( R_6 \) and \( R_8 \) are lower alkoxy, aryloxy, hydroxy or protected alcohol.

51. The method according to claim 50 where the biaryl compound has a formula
52. The method according to claim 32 where the diene has a formula
where $R_1$ and $R_2$ independently are lower alkoxy, aryloxy, hydrogen or silyl ether, and where the biaryl compound has a formula

![Chemical Structure](image)

where $R_i$ and $R_0-R_i$ independently are hydrogen or halogen, and $R_6$ and $R_8$ are lower alkoxy, aryloxy, hydroxyl, or protected alcohol.

53. The method according to claim 52 where the biaryl compound has a formula
54. The method according to claim 32 where the biaryl is a tetra-ortho-substituted biaryl compound.

55. The method according to claim 32 where the diene is a propargyl alcohol, and the biaryl compound has a formula

\[
\begin{align*}
\text{R}_1 & \text{R}_2 \\
\text{X} & \\
\text{NO}_2 & \\
\text{R}_{12} & \text{O} \\
\end{align*}
\]

where \( \text{R}_n \) is methyl, ethyl, \((\text{CH}_2)_3\), \((\text{CH}_3)_4\), \((\text{CH}_2)_5\), phenyl, \(/7\text{-Me-C}_6\text{H}_4\), or \(/?\text{-Cl-C}_6\text{H}_4\), \text{R}_{12} \) is lower alkyl, and \text{X} \) is halide.
56. The method according to claim 32 where the diene has a formula

\[
NR_1R_2
\]

Silyl ether

where \( R_1 \) and \( R_2 \) independently are hydrogen, lower alkyl, and oxygen-containing moiety, a silicon-containing moiety, or combinations thereof.

57. The method according to claim 56 where the biaryl compound has a formula

\[
\begin{array}{c}
\text{NO}_2 \\
\text{OH} \\
\text{Ph} \\
\text{Silyl ether}
\end{array}
\]

where \( R_1 \) and \( R_2 \) are independently hydrogen or lower alkyl, and \( X \) is a halide.

58. The method according to claim 32 where the diene has a formula

\[
\begin{array}{c}
\text{OCH}_3 \\
\text{Silyl ether}
\end{array}
\]

59. The method according to claim 32 where the diene has a formula

\[
\begin{array}{c}
\text{Silyl ether} \\
\text{or Silyl ether}
\end{array}
\]
60. The method according to claim 32 where the diene has a formula

\[
\begin{array}{c}
\text{OR} \\
\text{RO}
\end{array}
\]

where R independently is lower alkyl or aryl.

61. The method according to claim 32 where the diene has a formula

\[
\begin{array}{c}
\text{NR}_1\text{R}_2 \\
\text{RO}
\end{array}
\]

where R is independently is lower alkyl or aryl and R_i and R_2 independently are hydrogen, lower alkyl, oxygen-containing moiety, a silicon-containing moiety, or combinations thereof.

62. The method according to claim 32 where the dienophile is a propargyl alcohol, and the diene has a formula

\[
\begin{array}{c}
\text{OR}_1 \\
\text{Silyl ether}
\end{array}
\]

where R_i is lower alkyl or aryl.

63. The method according to claim 62 where the biaryl compound has a formula
64. The method according to claim 32 where the biaryl compound is chiral.

65. The method according to claim 23 where the dienophile is a phosphorus-containing dienophile or a carbonyl-containing dienophile.

66. The method according to claim 65 where the dienophile has a formula

\[
\begin{align*}
  &R_3 &R_4 &R_5 &R_6 \\
\end{align*}
\]

where \( R_3 \) is halide or hydrogen, and \( R_4-R_6 \) are hydrogen.

67. The method according to claim 66 where \( R_3 \) is halide or hydrogen, and \( R_4-R_6 \) are hydrogen.

68. The method according to claim 67 where \( R_3 \) is bromo.
69. The method according to claim 67 where the diene has a formula

\[ \begin{align*}
\text{R}_2 & \quad \text{R}_3 \\
\quad & \quad \text{R}_1 \\
\end{align*} \]

where \( \text{R}_\text{pR}_3 \) independently are lower alkoxy, hydrogen or silyl ether.

70. The method according to claim 69 where the diene has a formula

\[ \begin{align*}
\text{Silyl ether} & \quad \text{OR} \\
\quad & \quad \text{OR} \\
\end{align*} \]

71. The method according to claim 70 where the diene has a formula

\[ \begin{align*}
\text{TMSO} & \quad \text{OCH}_3 \\
\quad & \quad \text{OCH}_3 \\
\end{align*} \]

and the biaryl compound has a formula

\[ \begin{align*}
\text{Br} & \quad \text{NO}_2 \\
\text{HO} & \quad \text{P(OR)}_\text{R}_1 \\
\quad & \quad \text{OCH}_3 \\
\end{align*} \]

where \( \text{R}_\text{i} \) is lower alkoxy or aryl.

72. The method according to claim 66 where the diene has a formula
where $R_i$ is lower alkoxy and $R_2$ is hydrogen or silyl ether.

73. The method according to claim 66 where the diene has a formula

\[
\begin{align*}
R_1O
\end{align*}
\]

where $R_i$ is lower alkoxy and $R_2$ is hydrogen or silyl ether.

74. The method according to claim 66 where the diene has a formula

\[
\begin{align*}
\text{Silyl ether}
\end{align*}
\]

and the biaryl compound has a formula

\[
\begin{align*}
\text{P(O)R}_1
\end{align*}
\]

74. The method according to claim 66 where the diene has a formula

\[
\begin{align*}
\text{P(O)R}_1
\end{align*}
\]

where $R_i$ is lower alkyl, lower alkoxy, or aryl.
75. The method according to claim 66 where the diene has a formula

\[
\begin{align*}
\text{CH}_3\text{O} & \quad \text{Silyl ether} \\
\end{align*}
\]

and the biaryl compound has a formula

\[
\begin{align*}
\text{Br} & \quad \text{NO}_2 \\
\text{CH}_3\text{O} & \quad \text{P(O)R}_1 \\
\text{OH} & \\
\end{align*}
\]

where R is lower alkyl, lower alkoxy, or aryl.

76. The method according to claim 32 further comprising performing a functional group transformation on the biaryl compound.

77. The method according to claim 32 further comprising coupling the biaryl compound with an aryl compound using a metal-mediated coupling reaction.

78. The method according to claim 77 where the biaryl compound is a tetra ortho substituted biaryl.

79. The method according to claim 77 comprising using Buchwald's ligands, \( P(C=\text{C}_6\text{H}_4\text{H}_2)_3/Pd_2\text{dba}_3, Pd(dppf)\text{Cl}_2, Pd(OAc)_2/dppp), \ Pd(P-t-\text{Bu}_3)_2. \)
80. The method according to claim 77 comprising performing a Suzuki coupling, a Stille coupling, a Negishi coupling, a Heck reaction, a Sonogashiri coupling, a carbonylation reaction, or combinations thereof.

81. The method according to claim 11 comprising forming a compound having a formula

where at least one of $R_1$-$R_{10}$ is an aryl compound, with remaining $R$ groups independently being alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties, cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties, phosphorus-containing moieties, silicon, silicon-containing moieties, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties
82. The method according to claim 81 where $R_3$ is a nitrogen-containing moiety, and $R_9$ is an aryl compound.

83. The method according to claim 82 where the compound includes two or more halogen atoms.

84. The method according to claim 81 where the compound is an unsymmetric tetra-or tri-substituted biaryl.

85. The method according to claim 81 where the compound has a formula

![Chemical structure](image)

where $R_9$ is aryl or hydrogen, $R_{13}$ is aliphatic or aryl, $R_{i4}$ is aliphatic or hydrogen, and $R_{i3}$ is hydrogen, an alcohol protecting group, aliphatic, or an ester.

86. The method according to claim 85 where the compound has a formula

![Chemical structure](image)

where $R_{i3}$ is aliphatic or aryl.
87. The method according to claim 85 where R₉ is alkoxyphenyl, alkylphenyl, or phenyl halide.

88. The method according to claim 85 where R₉ is lower alkoxyphenyl, lower alkylphenyl, or a phenyl group having two or more halogen atoms.

89. The method according to claim 85 where R₉ is 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-methylphenyl, or 2,3-dimethylphenyl.

90. The method according to claim 81 where R₃ is nitro and the method comprises converting the nitro group into an amine.

91. The method according to claim 90 where the method further comprises reductive amination to form an alkyl amine.

92. The method according to claim 32 where the diene and the dienophile undergo a Diels-Alder reaction to provide enantioenriched products.

93. The method according to claim 92 where the diene has a formula

\[
\text{Silyl ether}
\]

94. The method according to claim 92 where the diene has a formula

\[
\text{Silyl ether}
\]

where R is aliphatic or hydrogen.

95. The method according to claim 94 where R is hydrogen or lower alkyl.
96. The method according to claim 93 where the dienophile has a
formula

\[
\begin{align*}
X & \text{-} & \text{NO}_2 \\
\text{CO}_2R & \\
\end{align*}
\]

and the biaryl compound has a formula

\[
\begin{align*}
X' & \text{-} & \text{NO}_2 \\
\text{Silyl ether} & \text{-} & \text{CO}_2R \\
\end{align*}
\]

where R is aliphatic or hydrogen and X is a halide.

97. The method according to claim 96 where the biaryl compound is produced in approximately 70% ee.

98. The method according to claim 81 where R₄ is a phosphine oxide and the method further comprises converting the phosphine oxide into a phosphine.

99. The method according to claim 32 further comprising forming a phosphorus-containing alkyne dienophile by deprotonating an alkyne using lithium diisopropylamide and reacting the alkyne with a phosphorus-containing electrophile.

100. The method according to claim 32 comprising using arylboronic acids.

101. The method according to claim 100 where the arylboronic acid is a phenylboronic acid, and the compounds have a formula
where $R_1$-$R_2$ and $R_9$-$R_{10}$ are phenyl or substituted phenyl, $R_{14}$-$R_{15}$ are hydrogen, alcohol protecting group, or aliphatic.

102. The method according to claim 32 where the dienophile is a carbonyl-containing alkyne.

103. The method according to claim 102 comprising providing an alkyne having a formula

where $R_4$-$R_6$ independently are selected from hydrogen and halide, and $X$ is halide, and the method further comprises forming a carbonyl-containing dienophile by deprotonating the alkyne and reacting it with a carbonyl-containing electrophile.
104. The method according to claim 103 where the electrophile is
ClCO₂Me, ClCO₂Et, ClCO₂CH₂CCl₃, ClC(O)-^Bu, ClC(O)Ph, ClC(O)-P-Cl-C₆H₄,
ClC(O)NMe₂, ClC(O)NPh₂, ClC(O)-N-morpholinyl, (-)-ClCO₂-menthyl, or

![Chemical Structures](image)

105. The method according to claim 102 comprising reacting the
dienophile with a diene under conditions that facilitate producing Diels-Alder
products having a formula

![Chemical Structure](image)

where RpR₂ and R₅-R₇ and Rᵢ₀ independently are aliphatic, substituted aliphatic,
hydrogen or halogen, are phenyl or substituted phenyl, R₁₅ is hydrogen, alcohol
protecting group, or aliphatic, and where R is aliphatic, aminoaliphatic, cyclic,
heterocyclic, aryl or heteroaryl.

106. The method according to claim 105 where R is OMe, OEt,
OCH₂CCl₃, t-Bu, Ph, /7-Cl-C₆H₄, NMe₂, NPh₂, N-morpholinyl, O-menthol and N-
oxazolidinone.

107. The method according to claim 32 where the biaryl compound has a
formula
where $R_3$, $R_4$, $R_8$ and $R_9$ are different, $R_3$ is a nitrogen-containing moiety, $R_9$ is halide, and remaining $R_i$-$R_2$, $R_4$-$R_8$ and $R_i_0$ groups are selected alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, arylalkyl, substituted arylalkyl, boron, boron-containing moieties, carbonyl-containing moieties, cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties, phosphorus-containing moieties, silicon, silicon-containing moieties, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, and the method further comprises forming a carbazole.

108. The method according to claim 107 where $R_3$ is a nitro group, and the method further comprises forming a carbazole using a Cadogan cyclization.

109. The method according to claim 108 where the carbazole is a halogenated carbazole.

110. The method according to claim 107 where the carbazole is a naturally occurring, synthetic or semisynthetic compound having biological activity.

111. The method according to claim 107 where the biaryl compound has a formula
where $R_1-R_2$, $R_4-R_5$ and $R_7-R_0$ independently are halogen, hydrogen, aliphatic or substituted aliphatic, and $R_6$ is hydrogen, alcohol protecting group, or aliphatic, and the carbazole has a formula

112. The method according to claim 111 where $R_1-R_2$, and $R_9-R_0$ independently are halogen or hydrogen.

113. The method according to claim 111 where $R_5$ and $R_7-R_8$ are hydrogen.

114. The method according to claim 107 where the carbazole is Siamenol.

115. The method according to claim 114 where Siamenol is formed by a method comprising:

- forming a biaryl compound by a Diels-Alder reaction;
forming a Claisen precursor and subsequently performing a Claisen rearrangement; and
forming Siamenol by a Cadogan cyclization.

5. A method for performing an organocatalyst reaction, comprising:
providing an organic biaryl compound made by a cycloaddition reaction; and
using the biaryl compound as an organic catalyst.

117. The method according to claim 116 where providing comprises
making the biaryl compound.

118. The method according to claim 116 where the biaryl compound is a
dialkylamino phosphine.

15. The method according to claim 118 where the dialkylamino phosphine has a formula

\[
\begin{align*}
R_1 & \quad R_2 \\
R_9 & \quad NR_{13}R_{14} \\
R_8 & \quad PR_{15}R_{16} \\
R_7 & \quad R_6 \\
\end{align*}
\]

where \( R_i \) independently are alcohols, protected alcohols, substituted alcohols, aldehydes, protected aldehydes, substituted aldehydes, aliphatic, substituted aliphatic, alkoxy, amino, amines, substituted amines, protected amines, aryl, substituted aryl, aryalkyl, substituted aryalkyl, boron, boron-containing moieties, carbonyl-containing moieties, cyclic, substituted cyclic, ethers, substituted ethers, halide, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, hydrogen, hydroxyl, hydroxylamine, nitrogen-containing moieties, phosphorus-containing moieties, silicon, silicon-containing moieties, including particularly silyl.
ethers, sulfur, sulfur-containing moieties, tin, tin-containing moieties, including trialkyl tin or triaryl tin moieties, or combinations thereof.

120. The method according to claim 118 where the dialkylamino phosphine has a formula

![Chemical Structure](image)

where R1-R2, R5, R7, R9 and R10 independently are aliphatic, aryl or hydrogen, R6 and R8 independently are hydrogen, alcohol protecting group, aliphatic or aryl, and R13-R16 independently are lower alkyl.

121. The method according to claim 120 where the dialkylamino phosphine is used as a ligand in palladium-mediated processes.

122. A compound having a formula

![Chemical Structure](image)

where R1-R8 are independently selected from hydrogen, halogen, hydroxyl, aliphatic, and substituted aliphatic.
123. The compound according to claim 1 where $R_1$-$R_{8}$ are independently selected from hydrogen, chlorine, bromine, hydroxyl, and aliphatic.

124. The compound according to claim 122 selected from the following or analogs thereof.
125. The compound according to claim 122 selected from the following or analogs thereof.

![Chemical structures](image)

126. A method for treating a subject, comprising:

providing a compound having a formula

![Chemical structure](image)

where R<sub>i</sub>-R<sub>8</sub> are independently selected from hydrogen, halogen, hydroxyl, aliphatic, and substituted aliphatic; and

administering a therapeutically effective amount of the compound to a subject.

127. The method according to claim 126 for treating HIV.
128. The method according to claim 126 where the effective amount is a concentration ranging from about 0.005 µg/mL to at least about 5 µg/mL.
FIG. 2
FIG. 5