TRANSITION METAL-CATALYZED REACTIONS OF ARYLMETAL REAGENTS AND ALKYNES INVOLVING REMOTE C–H ACTIVATION

NANYANG TECHNOLOGICAL UNIVERSITY
SINGAPORE

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List of Abbreviations

δ	chemical shift (ppm)
°C	degree centigrade
Ac	acetyl
Ad	adamantyl
Ar	aryl (substituted aromatic ring)
aq	aqueous
br	broad
Bn	benzyl
Bz	benzoyl
Boc	*tert*-butyloxycarbonyl
*n*Bu	butyl
*t*Bu	*tert*-butyl
cod	1,5-cyclooctadiene
coe	cyclooctene
Cp*	1,2,3,4,5-pentamethylcyclopentadienyl
Cy	cyclohexyl
d	doublet
dd	doublet of doublet
dt	doublet of triplet
dppb	1,4-bis(diphenylphosphino)butane
dppbz	1,2-bis(diphenylphosphino)benzene
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1'-bis(diphenylphosphino)ferrocene

Dppp	1,3-bis(diphenylphosphino)propane
DMI	1,3-dimethyl-2-imidazolidinone
ESI	electrospray ionization
eq /equiv.	equivalent
EtOAc	ethyl acetate
Et	ethyl
EtCN	propionitrile
g	gram
h	hour
H	hydrogen
HOAc	acetic acid
HRMS	high resolution mass spectrometry
Hz	hertz
J	coupling constants
m	multiple
m/z	mass per charge ratio
M	concentration (mol/L)
M^+	parent ion peak (mass spectrum)
Me	methyl
mg	milligram
MHz	mega hertz
min	minute
mL	milliliter
mmol	millimole
m.p.	melting point
NMP	*N*-methylpyrrolidone

NMR	nuclear magnetic resonance
Ph	phenyl
PMP/*p*-An	*p*-methoxylphenyl
ppm	parts per million
*i*Pr	*iso*-propyl
Py	pyridine
q	quartet
s	singlet
sat	saturated
rt/r.t.	room temperature
t	triplet
td	triplet of doublet
TBS	*tert*-butyldimethylsilyl
TEA	triethylamine
Temps	temperature
Tf	trifluoromethyl
THF/thf	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
p-Tol	*p*-toluene
Ts	*p*-toluenesulfonyl
p-TSA	*p*-toluenesulfonic acid
vol	volume

Abstract

Selective C–H bond activation is a highly demanding task due to the presence of multiple C–H bonds of strong and similar bond strength in a complex molecule. Over the last three decades, a variety of approaches based on transition metal catalysis have been developed to enable efficient and selective C–H activation. Among them, one of the most successful approaches capitalizes on the use of a heteroatom-containing directing group, which allows transition metal catalysts to activate the proximal C–H bond.

While the "directed C–H activation" uses dative bond (coordination) to achieve site-selectivity, analogous approach, termed remote C–H activation/metal migration, employs metal–carbon covalent bond as a steppingstone. Thus, an organotransition metal species may undergo activation of the proximal C–H bond in an intramolecular fashion, which may result in formation of a metalacycle and/or complete migration of the transition metal center. In this context, noble metals (Pd, Rh) have been extensively employed to enable numerous reactions involving 1,4-metal migration, while the use of base metals remains underdeveloped.

This thesis research aimed at development of new base metal-catalyzed transformations involving remote C–H activation/metal migration. In particular, the present research was focused on transition metal-catalyzed reactions between arylmetal reagents and alkynes. Chapter 2 describes a cascade arylative cyclization reaction between ester- or ketone-tethered alkynes and arylzinc reagents that involves 1,4-cobalt migration as a key step. The reaction was achieved by a cobalt catalyst bearing an appropriately chosen biaryl-diphosphine ligand, which displayed unique reactivity in comparison with previously reported rhodium and iridium catalysts. Chapter 3 reports on the discovery of 1,4-chromium migration. Investigation into a chromium-catalyzed alkyne arylmagnesiation reaction unexpectedly indicated the feasibility of 1,4-chromium migration and allowed us to establish effective chromium catalyst systems for “migratory” arylmagnesiation of

alkynes to afford *ortho*-alkenylaryl Grignard reagent. Stimulated by this discovery, we further developed a chromium-catalyzed [4+2] benzannulation reaction between 2-biaryl Grignard reagents and internal alkynes to afford phenanthrene derivatives, which is described in Chapter 4.

Chapter 1. Introduction

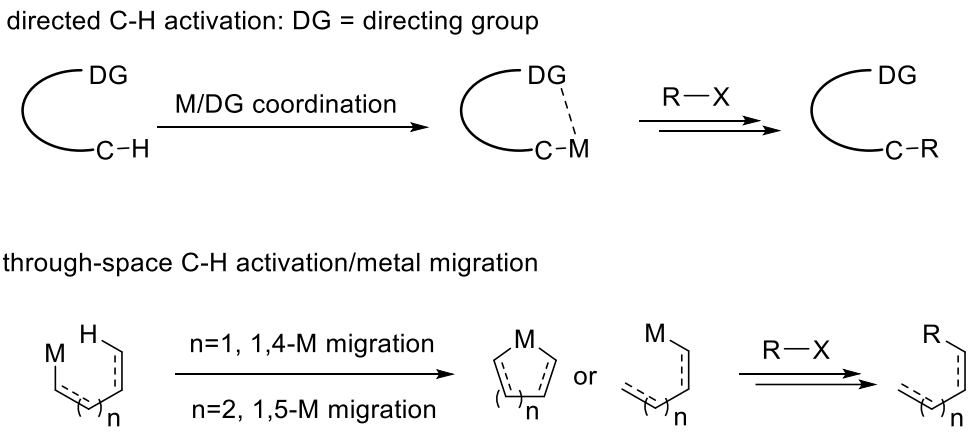
The selective activation of a specific C–H bond in a complex molecule is a highly demanding task in synthetic organic chemistry because of the high bond dissociation energies of typical C–H bonds and the presence of multiple C–H bonds of similar bond strength in a single molecule, among other reasons.[1] While daunting, "C–H activation/functionalization" has been a subject of extensive research of chemists over the world. As many of pharmaceuticals and fine chemicals are currently derived ultimately from fossil resources, which contain only C–H and C–C bonds, efficient and selective C–H functionalization processes could potentially benefit or even revolutionize the industrial manufacturing of these chemicals. Over the last three decades, a growing number of approaches, many of which are based on transition metal catalysis, have been developed to enable efficient and selective C–H functionalization.

One of the most successful approaches to selective C–H functionalization capitalizes on the use of a heteroatom-containing coordinating group, which allow transition metal catalysts to activate the proximal C–H bond through several different mechanisms such as oxidative addition, electrophilic substitution, and concerted metalation-deprotonation.[2] This approach has enabled an extremely broad range of *ortho* C(sp^2)–H functionalization of functionalized arenes, and more recently, *meta*- and *para*-selective arene C(sp^2)–H functionalization as well as C(sp^3)–H functionalization of functionalized alkanes.[3]

While the above-mentioned "directed C–H functionalization" uses dative bond (coordination) to achieve site-selectivity in C–H activation, an analogous approach employing metal–carbon covalent bond as a steppingstone in selective C–H functionalization has also been explored. Thus, an organotransition metal species, often formed in situ in a catalytic manner, may undergo activation of the proximal C–H bond,

which may result in formation of a metalacycle intermediate and/or complete migration of the transition metal center from the original position to the proximal position (Scheme 1.1). Such processes, when coupled with other appropriate elementary steps, would offer unique catalytic transformations involving remote C–H functionalization, which would not be achieved by other means. This type of remote C–H activation/metal migration is known to occur most commonly in a 1,4-fashion[4] and sometimes in a 1,5-fashion,[5] while a rare example of 1,7-palladium migration was also reported.[6] In the following sections, representative examples of Remote 1,4-C–H activation/metal migration are discussed.

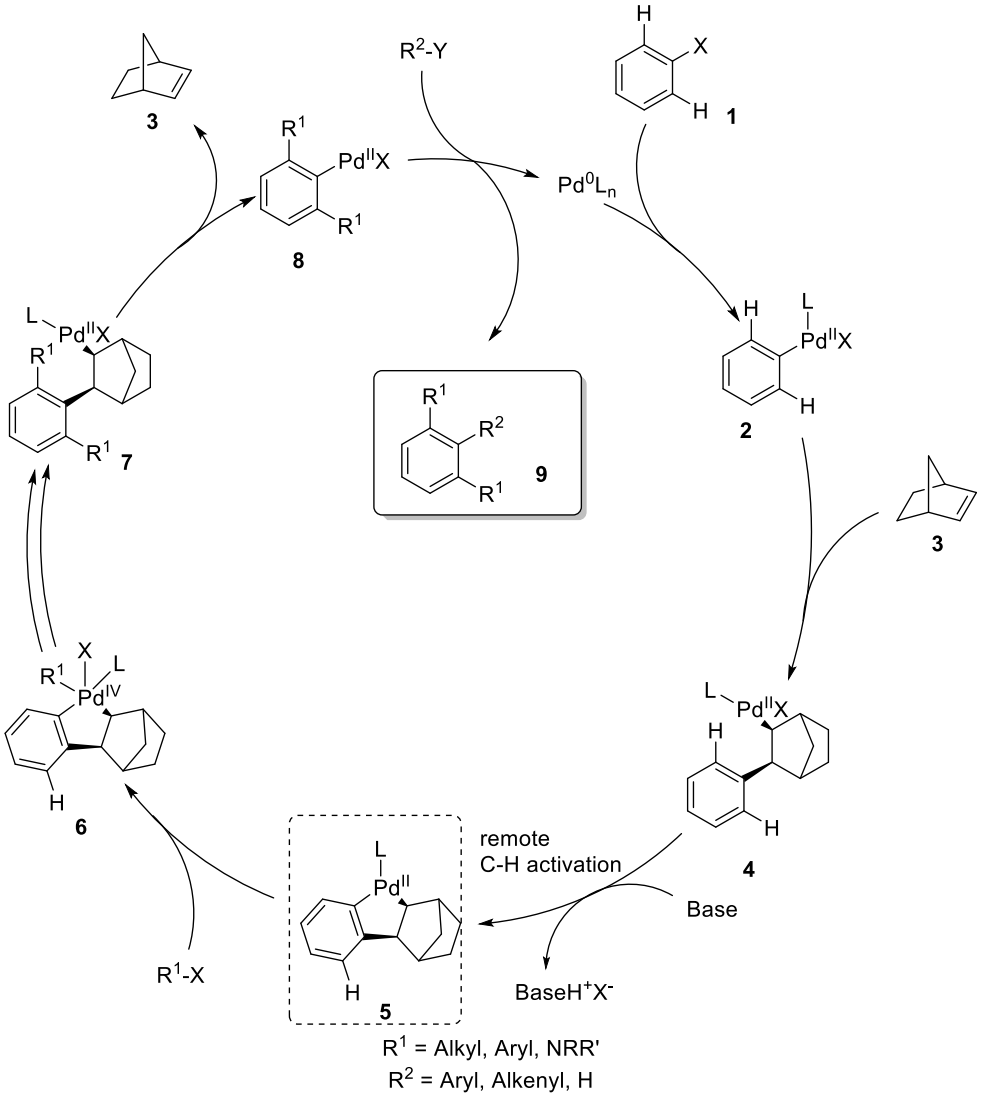
Scheme 1.1. Site-Selective Remote C–H Activation/Metal Migration



1.1 Remote C–H Activation/Metal Migration: Early Discoveries

The remote C–H activation/metal migration dates back to the discovery and development of Catellani reaction,[7] a palladium-catalyzed, norbornene-mediated *ipso*- and *ortho*-functionalization of an aryl halide, a prototypical catalytic cycle of which is illustrated in Scheme 1.2. The reaction is initiated by oxidative addition of the aryl halide **1** to a Pd(0) species to form an aryl–Pd species **2**. Migratory insertion of norbornene into the aryl–Pd bond of **2** generates a norbornyl–Pd species **4**, which then undergoes remote C–H activation of the *ortho* C–H bond to generate a five-membered palladacycle **5**. Subsequent oxidative addition of an electrophile (R^1–X) occurs to give an organopalladium(IV) species **6**, which undergoes reductive elimination to form *ortho* C–R^1 bond while liberating the norbornyl–Pd bond. Repetition of this C–H activation/oxidative addition/reductive elimination process leads to the formation of another *ortho* C–R^1 bond. The resulting norbornyl–Pd species **7** extrudes norbornene via β-carbon elimination to afford a new aryl–Pd species **8**, which may participate in another bond-forming event such as Heck olefination. Capitalizing on this general principle, numerous cascade reactions have been developed to date.[8]

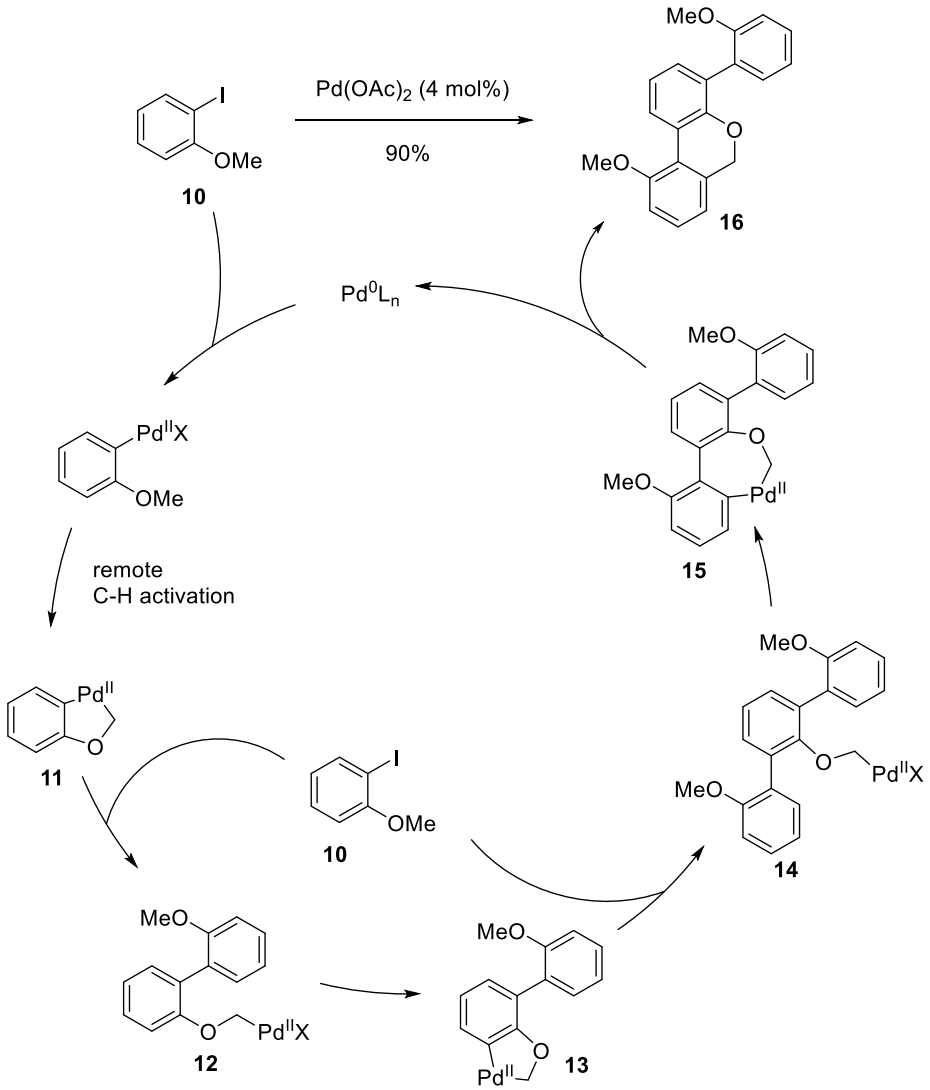
Scheme 1.2. Catalytic Cycle of Pd-Catalyzed Norbornene-Mediated *ipso*- and *ortho*-Functionalization of Aryl Halide (Catellani Reaction)



Organopalladium species can also undergo remote C–H activation without assistance of norbornene. An early example of such reactions, a three-fold condensation of *ortho*-iodoanisole, is shown in Scheme 1.3.[9] Oxidative addition of iodoanisole to Pd(0) generates an *ortho*-methoxyphenylpalladium species, which undergoes cyclometalation of the methoxy C(sp^3)–H bond to afford a five-membered palladacycle **11**. The species **11** reacts with a second molecule of iodoanisole, presumably via oxidative addition and reductive elimination, to generate an alkyl–Pd species **12** upon biaryl bond formation. Cyclometalation of **12** at the *ortho* C–H bond of the aromatic ring generates a new

palladacycle **13**, which undergoes biaryl coupling with a third molecule of iodoanisole to form a symmetric alkyl–Pd species **14**. Cyclometalation of **14** takes place in a 1,6-fashion to form a seven-membered palladacycle **15**, which releases the condensation product **16** upon C–C reductive elimination.

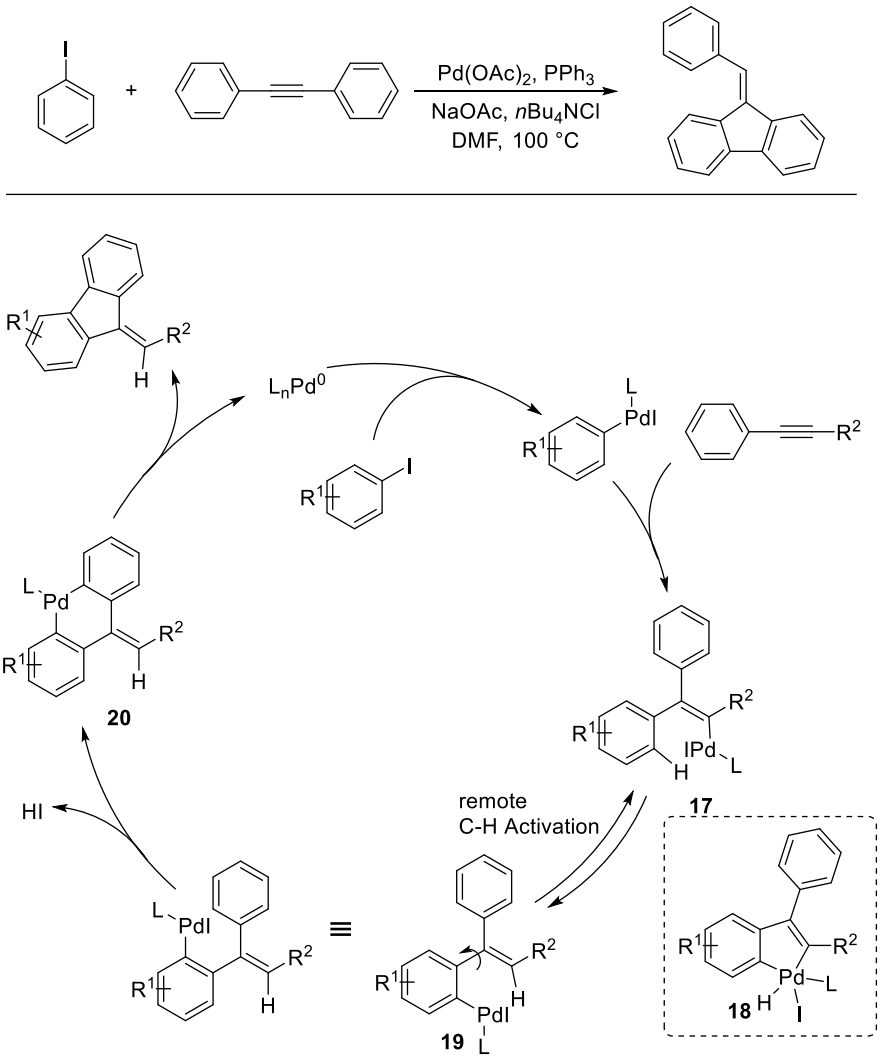
Scheme 1.3. Palladium-Catalyzed Condensation Reaction of *ortho*-Iodoanisole Involving Remote C–H Activation



The above-discussed examples do not involve a "genuine" metal migration. Thus, the remote C–H activation only gives a "half-migrated" metallacycle species, or C–C coupling occurs prior to migration (e.g., **11** to **12** in Scheme 1.3). In 2000, an early example

of remote C–H activation/metal migration was reported by Larock and co-workers, where 1,4-palladium migration is involved as a fundamental step in the palladium-catalyzed synthesis of 9-alkylidene-9*H*-fluorenes (Scheme 1.4).[10] This cascade annulation reaction starts with the formation of an arylpalladium(II) species generated by oxidative addition of an aryl iodide to Pd(0), which is followed by insertion of an alkyne to afford an alkenylpalladium species **17**. At this stage, the Pd center undergoes remote 1,4-migration to the *ortho* position of the aromatic ring, resulting in an *ortho*-alkenylarylpalladium species **19**. While Larock proposed a five-membered pallada(IV)cycle **18**, formed by intramolecular C–H oxidative addition, as a possible intermediate, the author is tempted to suggest an alternative mechanism without redox on Pd, which involves concerted metalation-deprotonation and its reverse process. Subsequent rotation of the aryl–alkenyl C–C bond of **19** relocates the Pd center to the proximity of another pendant aromatic ring, leading to another C–H activation to afford a six-membered palladacycle **20**. This palladacycle undergoes reductive elimination to furnish the fluorene product and regenerate the Pd(0) catalyst.

Scheme 1.4. Palladium-Catalyzed Fluorene Synthesis Involving Remote C–H Activation/Palladium Migration



Following this seminal work, the remote C–H activation/palladium migration has found substantial applications in cascade bond forming reactions to provide rapid synthetic routes for various heterocycles.[11] In particular, a number of examples of 1,4-palladium migration in catalytic cascade transformations have been reported, demonstrating the utility of 1,4-palladium migration as a strategy to introduce a palladium moiety into a position where direct palladium introduction may not be feasible.[12] Furthermore, along with the development of palladium migrations, other organotransition metal species have also

proved to be capable of undergoing remote C–H activation/metal migration, as described in the next section.

1.2 Remote C–H Activation/1,4-Migration of Noble Transition Metal Species

In this section, selected representative examples of 1,4-metal migration involving noble transition metals (i.e., second- or third-row transition metals) are briefly discussed.[13] Thus far, palladium and rhodium have been most extensively explored for such reactions, while 1,4-migrations of iridium and ruthenium have emerged recently.

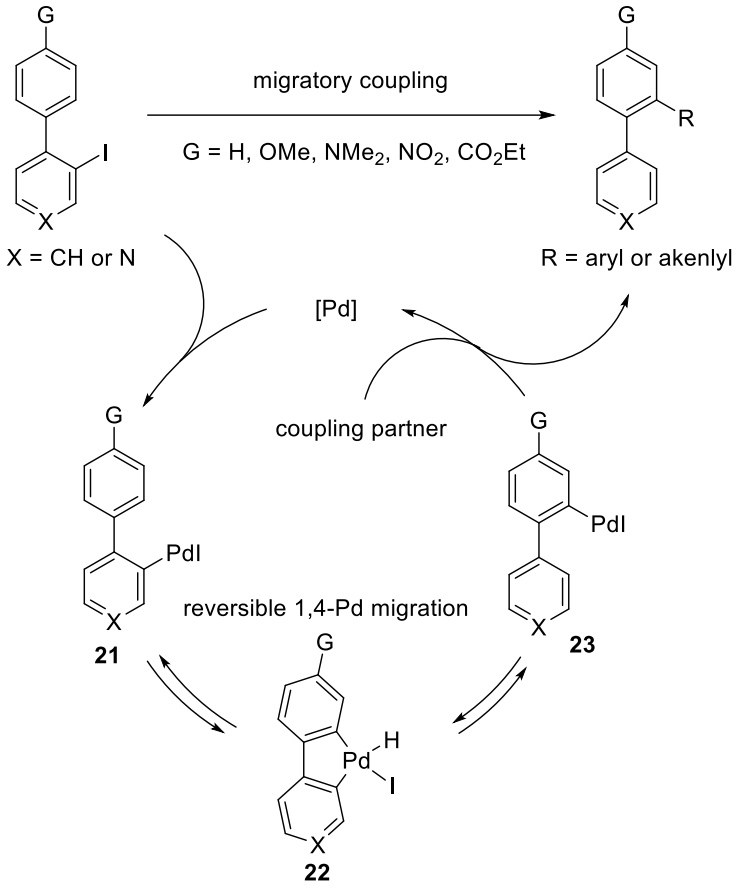
1,4-Palladium Migration

1,4-Palladium migration has been widely exploited as a key step in cascade reactions involving remote C–H functionalization. Biaryl is one of the most popular scaffolds to carry out 1,4-palladium migrations, as illustrated in Scheme 1.5.[14] In these reactions, a 2-biarylpalladium species **21** initially formed by the oxidative addition of 2-iodobiaryl to Pd(0) undergoes activation of the *ortho* C–H bond on the adjacent aryl ring, affording a new 2-biarylpalladium species **23**. This migration possibly proceeds through reversible oxidative addition and reductive elimination (or reversible deprotonative metalation and protodemetalation), with a five-membered palladacycle **22** (or an analogous complex lacking hydrido and iodo ligands) as the intermediate.

Owing to the intramolecular nature, the energy barriers for 1,4-palladium migration, both forward and reverse, are generally modest, and often lower compared with the barriers required for subsequent steps. Thus, because of the reversibility of 1,4-palladium migration, both of the biarylpalladium species **21** and **23** are capable of participating in subsequent transformations such as Suzuki and Heck reactions. The site selectivity of the reaction is sensitive to the relative C–H acidity. While a 2-iodobiaryl substrate bearing a strong electron-withdrawing group on the distal aryl group (labeled as G, Scheme 1.5) undergoes preferential C–C coupling upon migration with moderate selectivity (up to 77:23 when G

= NO_2), electron-donating groups or more weakly electron-withdrawing groups at this position result in unselective coupling.[14d] While these results alone may not sound synthetically very useful, more selective 1,4-palladium migration has been achieved and productively utilized with elaborately designed substrates.[15]

Scheme 1.5. Catalytic 1,4-Migrations in Biaryl Systems Involving Pd.

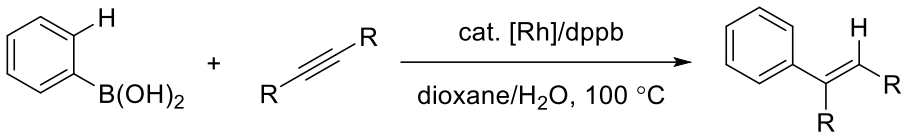


1,4-Rhodium Migration

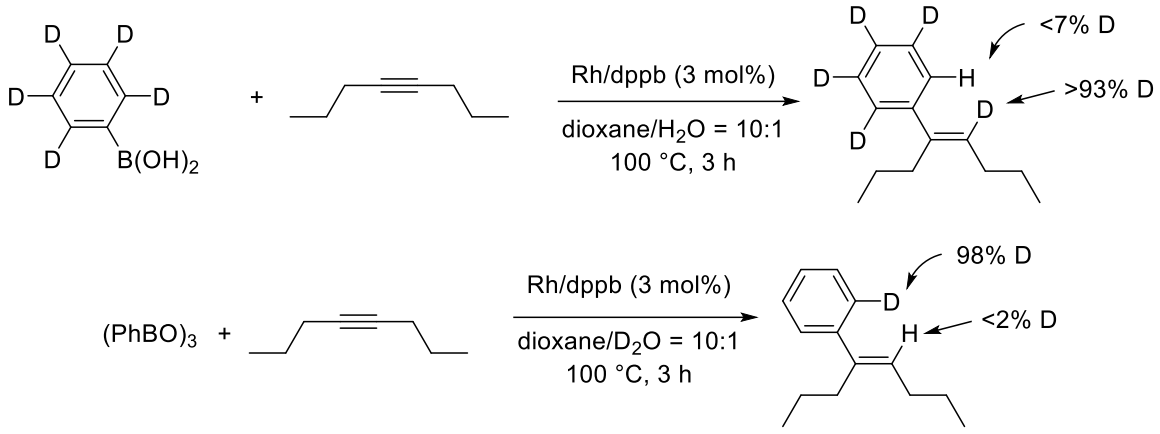
In addition to 1,4-palladium migration, 1,4-rhodium migration has also been studied extensively.[16] Seminal publications from the groups of Miura[16a] and Hayashi[16b] revealed the ability of rhodium to undergo a 1,4-migration in catalytic addition of arylboron compounds to unsaturated substrates such as norbornene and alkyne. The latter case, the

rhodium-catalyzed hydroarylation of an internal alkyne with phenylboronic acid, affords the corresponding alkene product with exclusive *syn* geometry (Scheme 1.6). The original mechanistic hypothesis, which involved protodemetalation of an alkenylrhodium species by water in the solvent system, turned out to be completely wrong according to deuterium labeling experiments (Scheme 1.7). The reaction of pentadeuterated phenylboronic acid performed in dioxane/H_2O afforded the adduct with substantial (93%) migration of one of the *ortho*-deuterium atoms into the vinyl position. On the other hand, the reaction of parent phenylboroxine performed in dioxane/D_2O delivered the corresponding product in which 98% deuterium incorporation was observed at the *ortho* position of the aromatic ring. The observed deuterium incorporation clearly indicates the involvement of a 1,4-rhodium migration process. Thus, a catalytic cycle involving transmetalation between rhodium hydroxide and phenylboronic acid, insertion of the alkyne into phenylrhodium species, vinyl-to-aryl 1,4-rhodium migration, and protodemetalation of the *ortho*-alkenylarylrhodium species was proposed (Scheme 1.8).

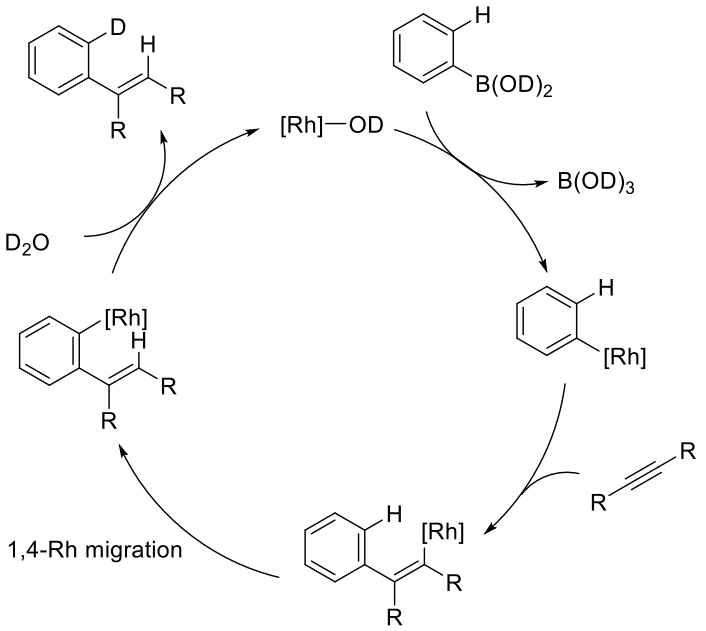
Scheme 1.6. Rhodium-Catalyzed *syn*-Selective Alkyne Hydroarylation



Scheme 1.7. Deuterium-Labeling Experiments for Alkyne Hydroarylation



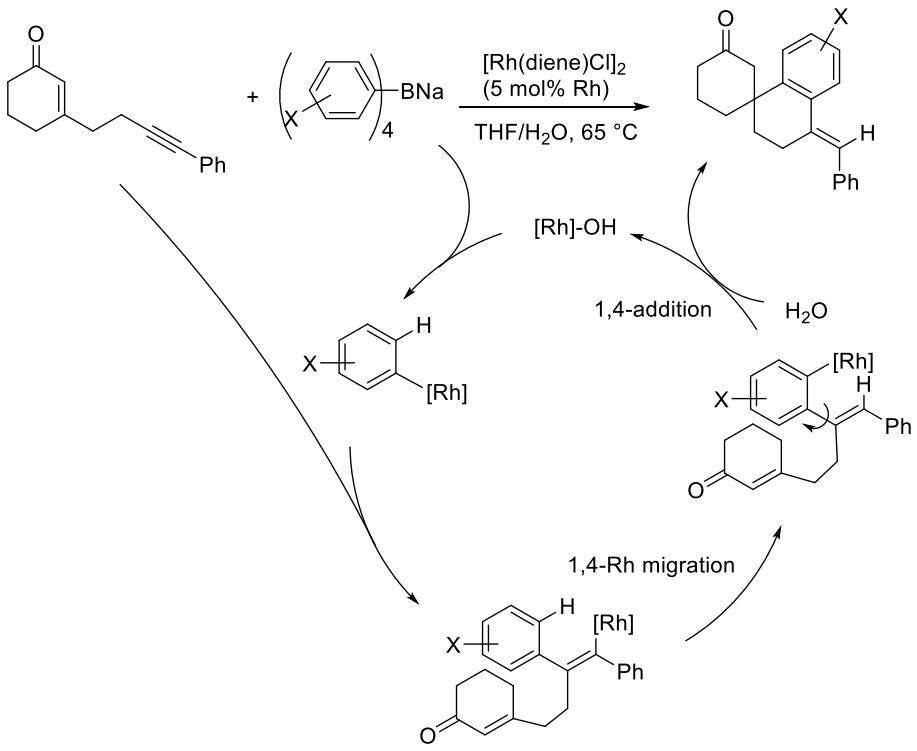
Scheme 1.8. Catalytic Cycle for Alkyne Hydroarylation Involving 1,4-Rhodium Migration



After this seminal report, a variety of substrates have been designed to achieve novel cascade reactions featuring 1,4-rhodium migrations. While the above-discussed hydroarylation involves protodemetalation as the turnover step to intercept the organorhodium species upon 1,4-migration, one can utilize electrophilic trapping such as conjugate addition [17] and intramolecular acylation [18] to achieve more complex and sophisticated cascade reactions. For example, a challenging spirocycle synthesis was

achieved by merging 1,4-migration and intramolecular conjugate addition as key steps, using an alkyne–enone bifunctional substrate (Scheme 1.9).[19] A plausible mechanism of the reaction involves initial addition of aryl–[Rh] complex across the triple bond to generate a vinyl–[Rh] intermediate. Subsequent alkenyl-to-aryl 1,4-rhodium migration relocates the Rh center to the *ortho* position of the phenyl group to afford an *ortho*-alkenylaryl–[Rh] species, which undergoes, upon single bond rotation, conjugate addition to the pendant α,β-unsaturated ketone moiety to close the six-membered ring.

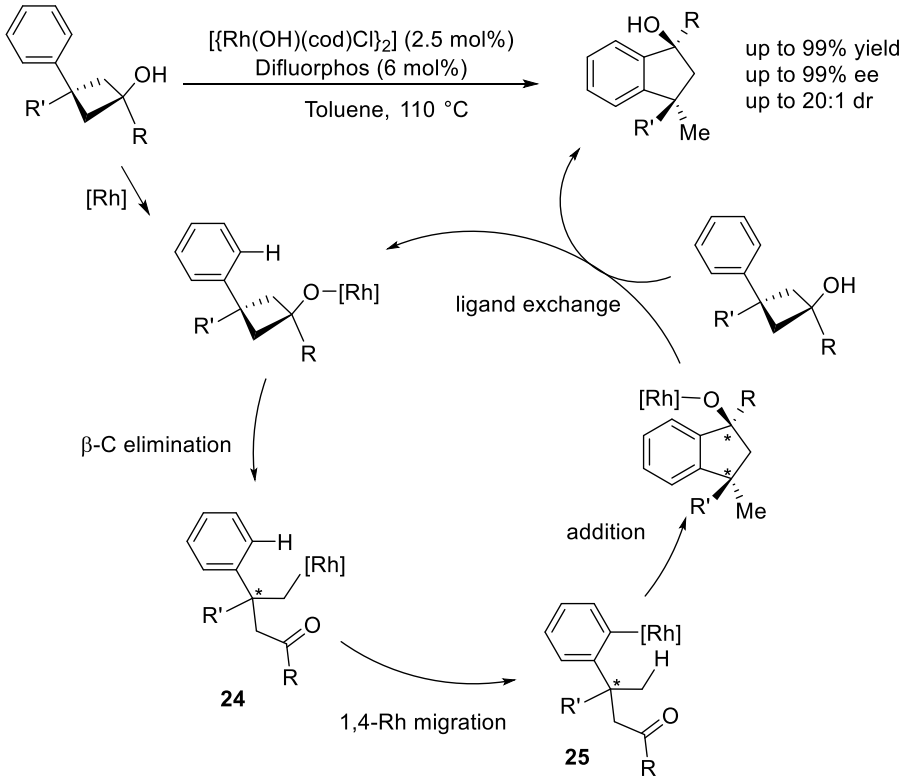
Scheme 1.9. Spirocycle Synthesis via Rhodium-Catalyzed Tandem Alkenyl-to-Aryl 1,4-Migration/1,4-Addition



1,4-Rhodium migrations have also been incorporated into cascade reactions leading to ring expansions.[20] As a representative case, alkyl-to-aryl 1,4-rhodium migration was employed as a fundamental step to enable highly enantio- and diastereoselective ring expansion of phenyl substituted *tert*-cyclobutanol (Scheme 1.10).[21] The reaction is initiated

by the generation of a rhodium alkoxide species from the cyclobutanol. Selective β-carbon elimination cleaves one of the enantiotopic C–C bonds of the cyclobutane ring, forming a primary alkyl rhodium species **24**. The quaternary carbon of the species **24** prevents undesired β-hydride elimination. Alkyl-to-aryl 1,4-rhodium migration leads to a more stable arylrhodium species **25**, which would readily undergo an intramolecular nucleophilic addition to the tethered carbonyl group enantioselectively to furnish the ring-expanded indane product.

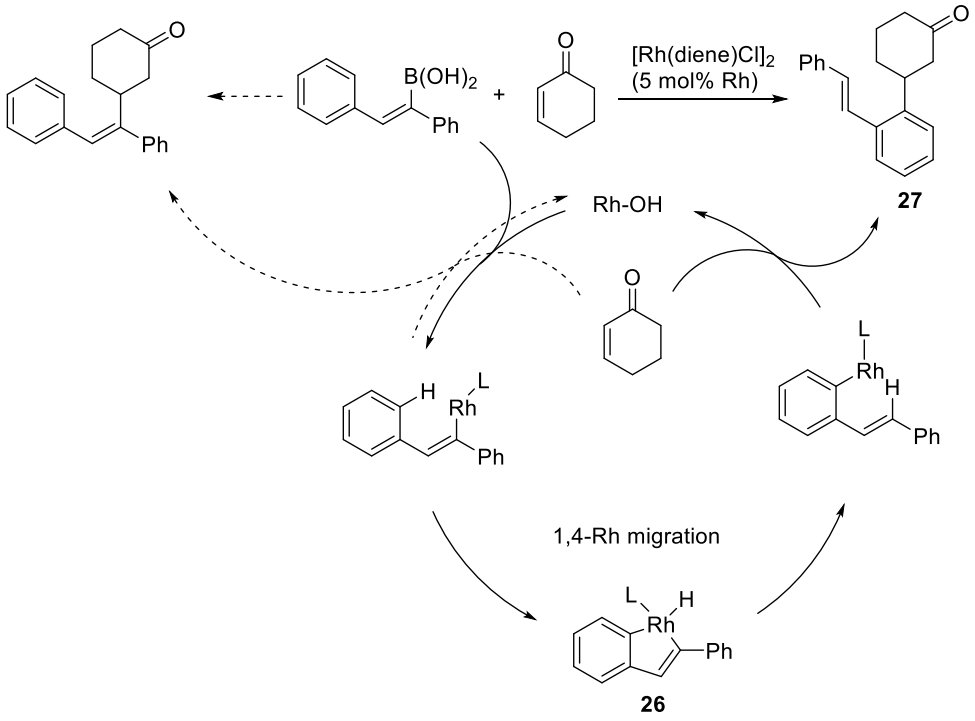
Scheme 1.10. Enantioselective Ring Expansion via Rhodium-Catalyzed Tandem C–C Activation/Alkyl-to-Aryl 1,4-Migration



The mechanistic aspect of 1,4-rhodium migration has been studied both theoretically and experimentally (Scheme 1.11). DFT calculations revealed detailed reaction pathways of alkenyl-to-aryl rhodium migration[22] as well as the alkyl-to-aryl rhodium migration.[23] In both cases, five-membered rhoda(III)cycle intermediates (such as

26 for the former case) are formed by intramolecular C–H oxidative addition, which is followed by reductive elimination to complete the 1,4-migration process. The greater thermodynamic stability of aryl–rhodium species than that of alkenyl–rhodium or alkyl–rhodium species is ascribed to the possible driving force of 1,4-migration. The former computational work was also supported by experiments on the conjugate addition of (*E*)-1,2-diphenylethenylboronic acid to 2-cyclohexenone in the presence of rhodium/diene catalyst. Selective formation of a rearranged product **27** (>99:1) bearing a 2-((*E*)-2-phenylethenyl)phenyl group suggests that 1,4-Rh migration occurs prior to 1,4-addition.

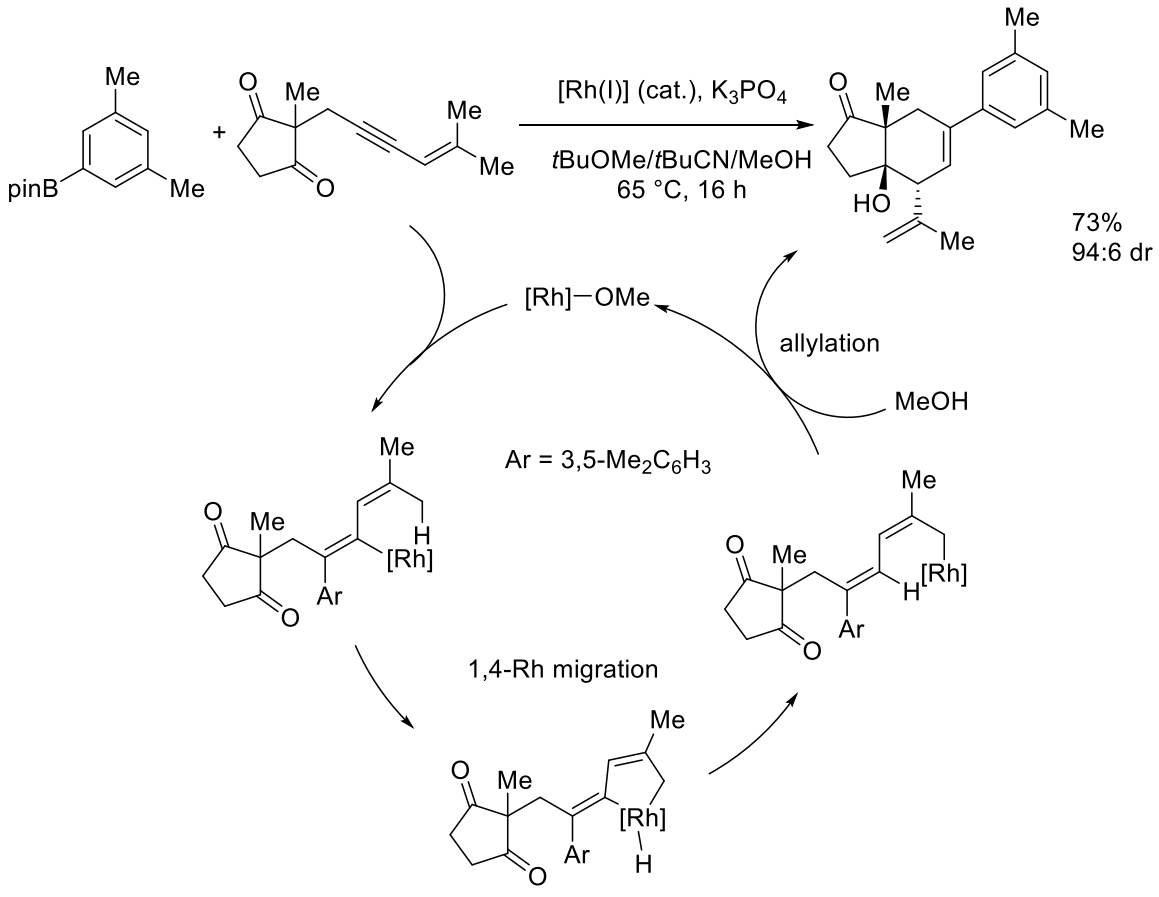
Scheme 1.11. Rhodium-Catalyzed Tandem 1,4-Migration/1,4-Addition



Recently, alkenyl-to-allyl 1,4-rhodium(I) migration was reported by Lam and coworkers to generate nucleophilic allylrhodium(I) species (Scheme 1.12).[24] Such mode of reactivity enables the diastereoselective arylative allylation of 1,3-enynes bearing a tethered cyclic diketone moiety, affording products containing three contiguous stereocenters. The use of *meta*-substituted arylboron reagents enables the preferential alkenyl-to-allyl 1,4-

rhodium(I) migration over alkenyl-to-aryl 1,4-rhodium(I) migration due to steric hindrance. The reaction can also proceed in a highly enantioselective fashion using a chiral sulfur-alkene ligand. Deuterium-labeling experiments support that the alkenyl-to-allyl 1,4-rhodium(I) migration occurs by C–H oxidative addition/reductive elimination mediated by a five-membered rhoda(III)cycle species, as is also the case with the alkenyl-to-aryl 1,4-rhodium(I) migration.[22]

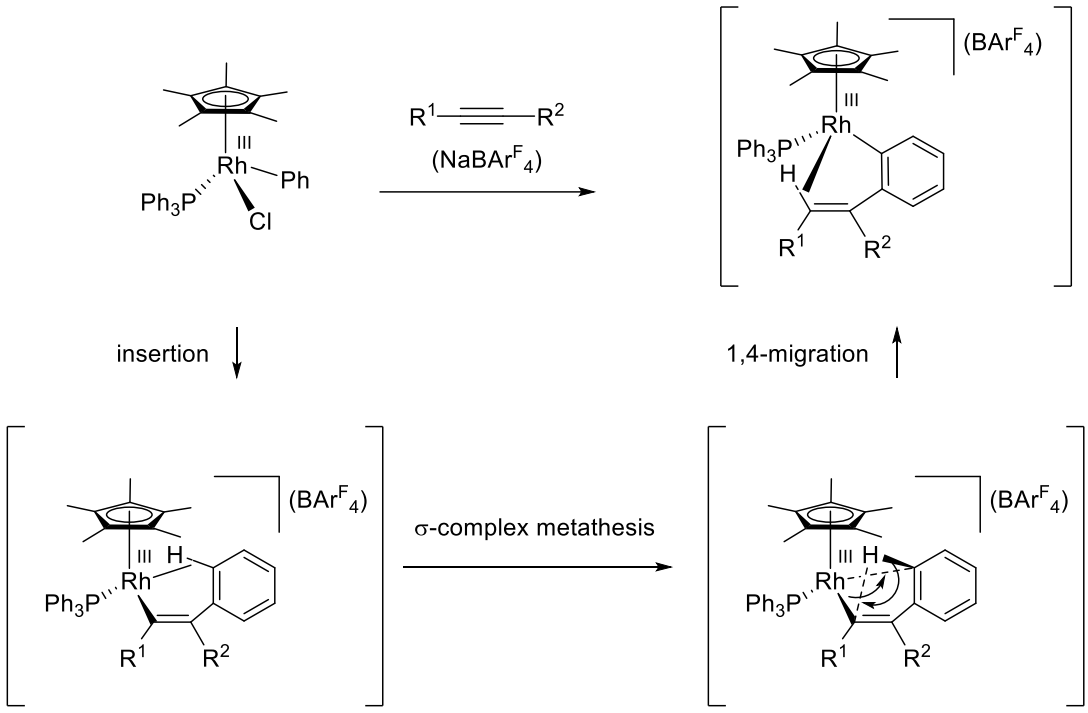
Scheme 1.12. Arylative Intramolecular Allylation of Ketones with 1,3-Enynes via Alkenyl-to-Allyl 1,4-Rhodium(I) Migration



Ishii group reported the first example of alkenyl-to-aryl 1,4-Rh(III) migration in their study on a stoichiometric reaction of [Cp*RhCl(Ph)(PPh_3)] with an internal alkyne (Scheme 1.13).[25] Migratory insertion of the alkyne into a cationic Rh(III)–Ph species,

generated with the assistance of a borate additive, and following 1,4-rhodium migration affords an *ortho*-alkenylaryl–rhodium(III) complex stabilized by the presence of Rh•••vinyl C–H agostic interaction. In contrast to the oxidative addition/reductive elimination mechanism accepted for 1,4-Rh(I) migration (Scheme 1.11), a σ-complex-assisted metathesis (σ-CAM) mechanism is considered plausible for this 1,4-Rh(III) migration.

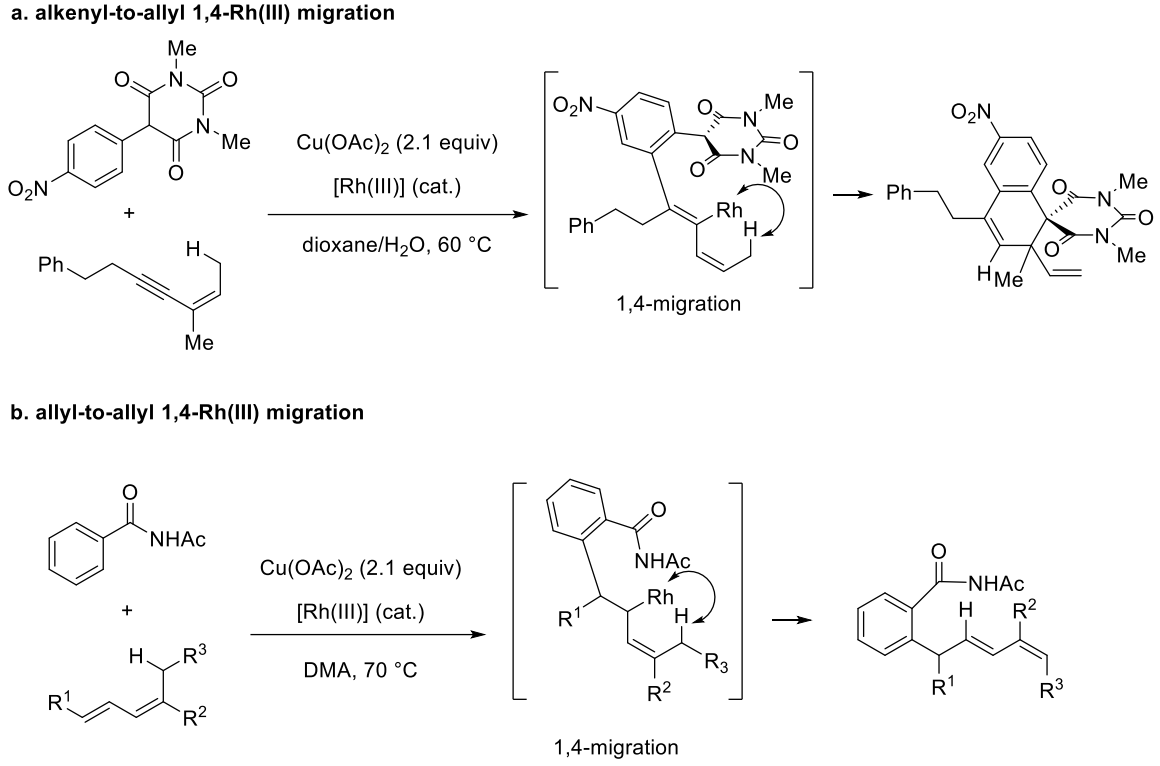
Scheme 1.13. Stoichiometric Alkenyl-to-Aryl 1,4-Migration of Rhodium((III)) Complex



Related 1,4-Rh(III) migration processes have been employed by Lam and coworkers to enable various catalytic reactions initiated by directing group-assisted C−H activation. For example, alkenyl-to-allyl 1,4-Rh(III) migration was employed as an elementary step in a [3+3] oxidative annulation reaction between a 2-aryl cyclic 1,3-dicarbonyl compound and a 1,3-enyne derivative (Scheme 1.14a).[26] The migration step is proposed to occur via a concerted metalation-deprotonation/reprotonation sequence. In their related work, allyl-to-allyl 1,4-Rh(III) migration served as a key step to achieve

Rh(III)-catalyzed oxidative C−H allylation of N-acetylbenzamides with 1,3-dienes.[27] The presence of allylic C−H bonds *cis* to the less substituted alkene moiety of the 1,3-diene is essential for this migration (Scheme 1.14b). In contrast to the alkenyl-to-allyl 1,4-Rh(III) migration, mechanistic experiments suggest that allyl-to-allyl 1,4-Rh(III) migration is more likely to occur via C−H oxidative addition/reductive elimination or σ-complex-assisted metathesis (σ-CAM).

Scheme 1.14. Catalytic Reactions Involving 1,4-Migration of Rhodium((III)) Complex

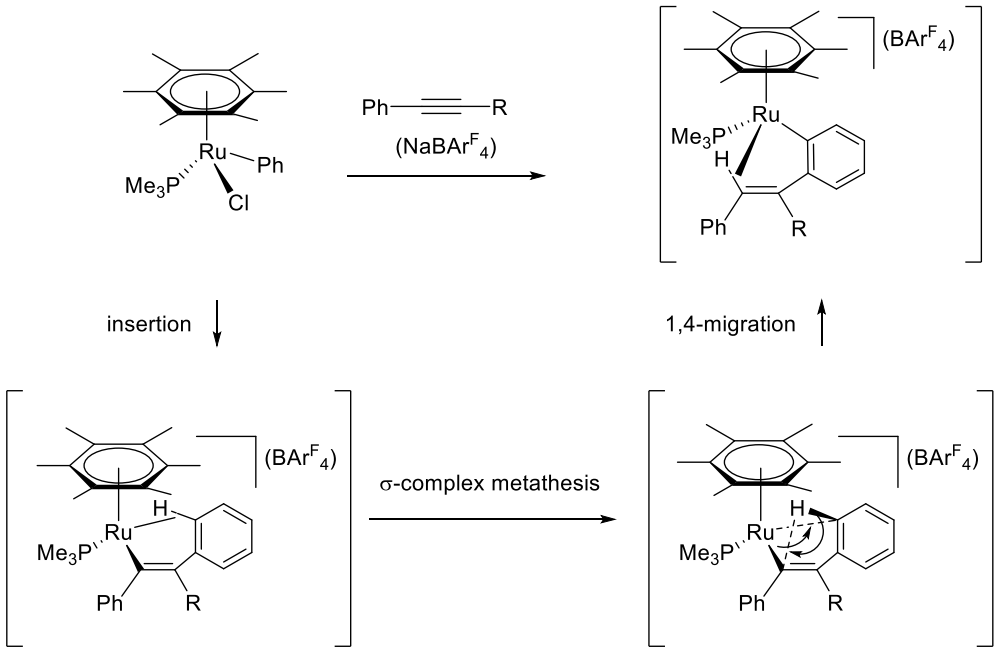


Iridium and Ruthenium 1,4-Migration

Following their initial report on the Cp*Rh(III)–phenyl complex (Scheme 1.13, vide supra), Ishii and coworkers reported that a Cp*Ir(III)–phenyl complex also participate in an analogous alkyne insertion/1,4-iridium migration sequence.[28] They further disclosed

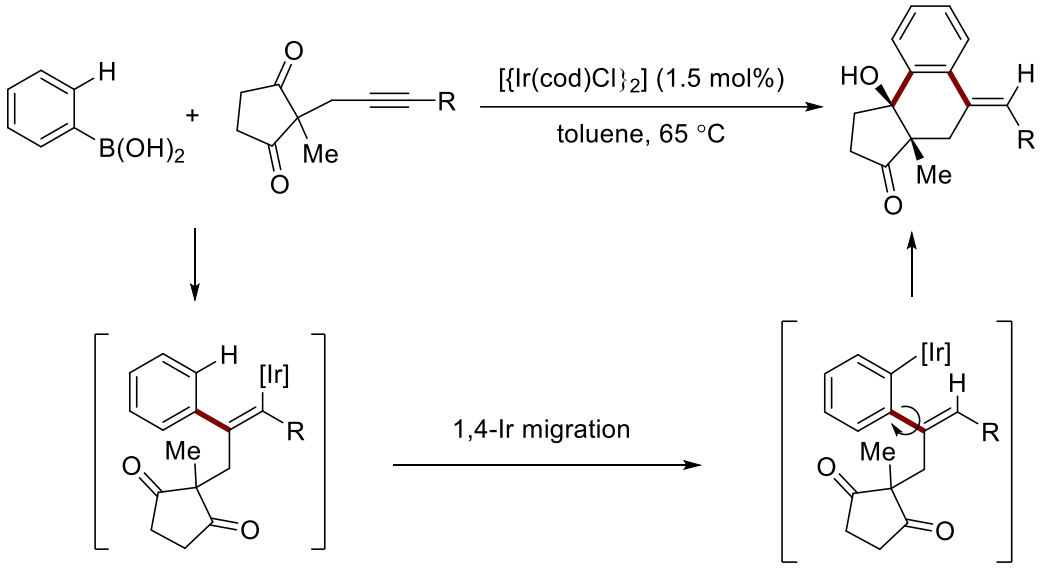
the same reaction pattern of an arene-coordinated ruthenium(II)–phenyl complex, demonstrating the feasibility of 1,4-ruthenium migration (Scheme 1.15).[29] In these stoichiometric examples of 1,4-metal migration, insertion of the alkyne into the metal–aryl bond results in vinyl-metal complex. Next, activation of the *ortho* C–H bond on the aryl group proceeds to promote 1,4-migration, in which the metal center and the hydrogen atom exchange their positions to afford the more stable aryl–metal complex.

Scheme 1.15. Stoichiometric Alkenyl-to-Aryl 1,4-Migration of Ruthenium(II)) Complex



Lam and coworkers reported a catalytic example of 1,4-iridium(I) migration, which is involved in diastereoselective synthesis of benzo-fused carbocycles (Scheme 1.16).[30] Thus, an Ir(I) catalyst promotes arylative cyclization of an alkyne bearing a cyclic 1,3-diketone moiety with an arylboronic acid. Being mechanistically analogous to related cascade reactions catalyzed by Rh(I) (cf. Scheme 1.9), the reaction likely proceeds via insertion of the alkyne into an aryliridium species, alkenyl-to-aryl 1,4-iridium(I) migration, and nucleophilic attack of the resulting aryl–iridium moiety to the carbonyl group, thus furnishing the polycyclic product.

Scheme 1.16. Cascade Arylative Cyclization Enabled by 1,4-Iridium Migration



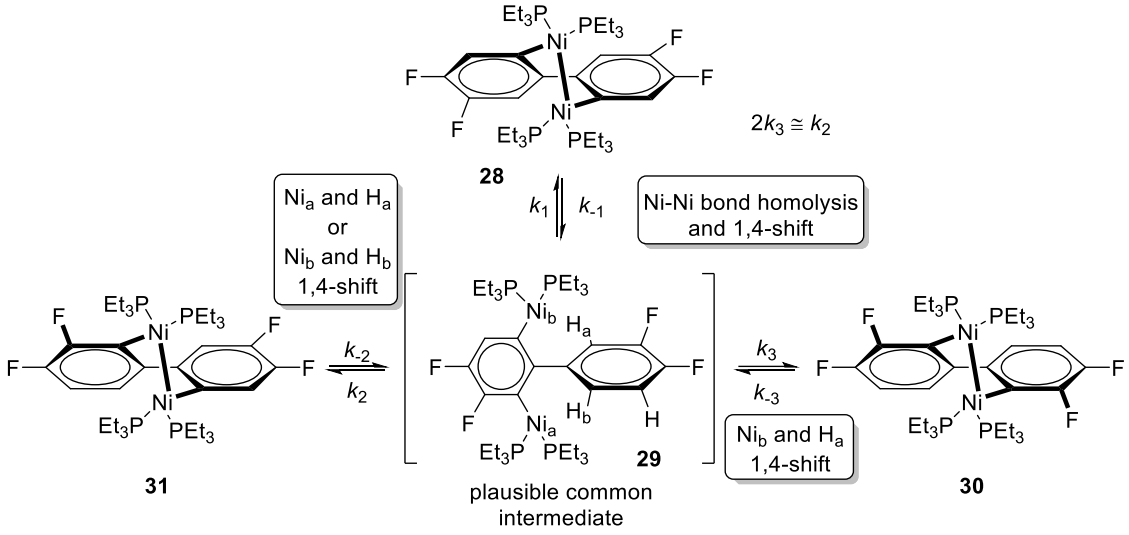
1.3 Remote C–H Activation/1,4-Migration of Earth-Abundant Transition Metal Species

As described above, most of reported remote C–H activation/1,4-migration reactions involve precious transition metals of the second- or third-row (Pd, Pt, Rh, Ir, Ru; vide supra).[31] However, earth-abundant transition metals of the first row, such as Ni, Co, and Fe, have recently been reported to mediate such C–H activation processes.

1,4-Nickel Migration

In 2007, Johnson and coworkers reported the first and thus far only example of 1,4-Ni migration (Scheme 1.17).[32] A bimetallic Ni(I) complex **28** featuring a 3,3',4,4'-tetrafluorobiphenyl backbone bridged by a di-Ni(I) fragment isomerized to analogous Ni(I) biarylyl complexes **30** and **31** in 1:2 ratio upon standing for 48 h at room temperature. The isomerization is proposed to proceed via a 2,6-dinickelated biaryl species **29** as a common intermediate, which undergoes interchange of the nickel center and the hydrogen at the 2'- or 6'-position (H_a or H_b) via 1,4-Ni migration. The formation of **29** from **28** probably involves homolytic cleavage of the Ni–Ni bond and subsequent 1,4-migration of one of the Ni(I) center. From a thermodynamic point of view, this isomerization would be driven by the formation of more stable aryl–Ni bond at the *ortho* position of the fluorine atom.

Scheme 1.17. Isomerization of Dinuclear Ni(I) Biarylyl Complex via 1,4-Ni(I) Migration

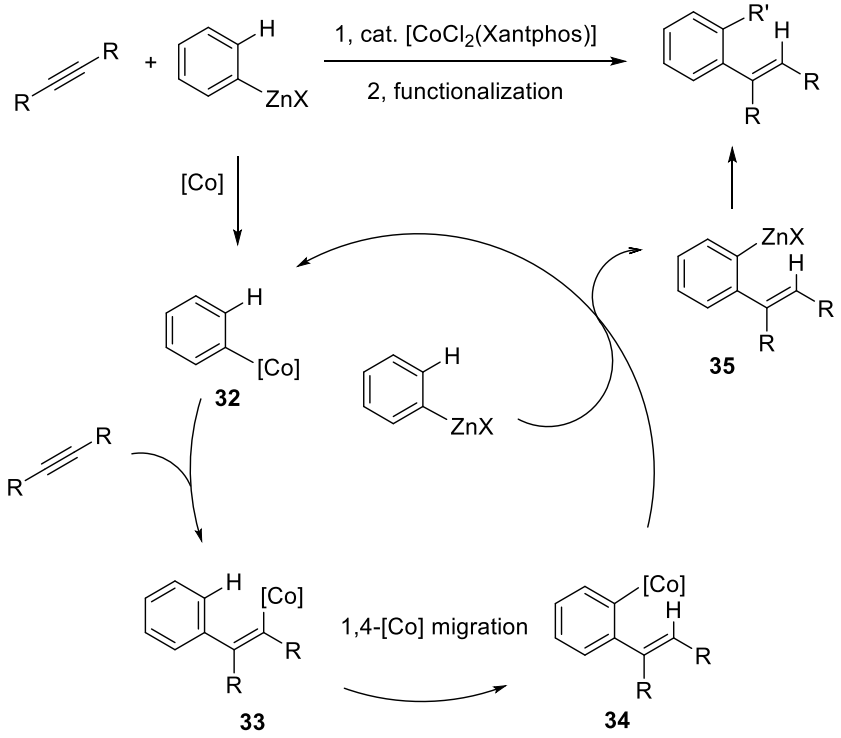


1,4-Cobalt Migration

In 2012, our group reported a cobalt-catalyzed addition reaction of an arylzinc reagent to an internal alkyne to afford an *ortho*-alkenylarylzinc species, which represents the first example of 1,4-cobalt migration (Scheme 1.18).[33] The reaction is proposed to involve a catalytic cycle analogous to that of the rhodium-catalyzed alkyne hydroarylation (Scheme 1.8, vide supra). An arylcobalt species **32** formed by transmetalation from the arylzinc reagent undergoes migratory insertion of the alkyne, followed by vinyl-to-aryl 1,4-cobalt migration of the alkenylcobalt species **33** to generate the *ortho*-alkenylarylcobalt species **34**. Unique about this reaction is the last step, that is, transmetalation between **34** and the arylzinc reagent to furnish the *ortho*-alkenylarylzinc species **35** while regenerating **32**. It should be mentioned that this "migratory" arylzincation is uniquely catalyzed by a cobalt–diphosphine (Xantphos) catalyst. In fact, earlier report by Yorimitsu and Oshima[34] and later report by Gosmini[35] demonstrated the ability of cobalt to promote "normal" arylzincation under different conditions. The product **35** not only allows preparation of various 1-alkenyl-2-functionalized arenes through electrophilic trapping, but also serves as

a valuable common precursor to a series of benzo-fused heterocycles.[36] As a follow-up work, the feasibility of migratory arylzincation of a norbornene derivative involving alkyl-to-aryl 1,4-cobalt migration have also been demonstrated.[37]

Scheme 1.18. Cobalt-Catalyzed Migratory Arylzincation of Alkyne via Vinyl-to-Aryl 1,4-Cobalt Migration

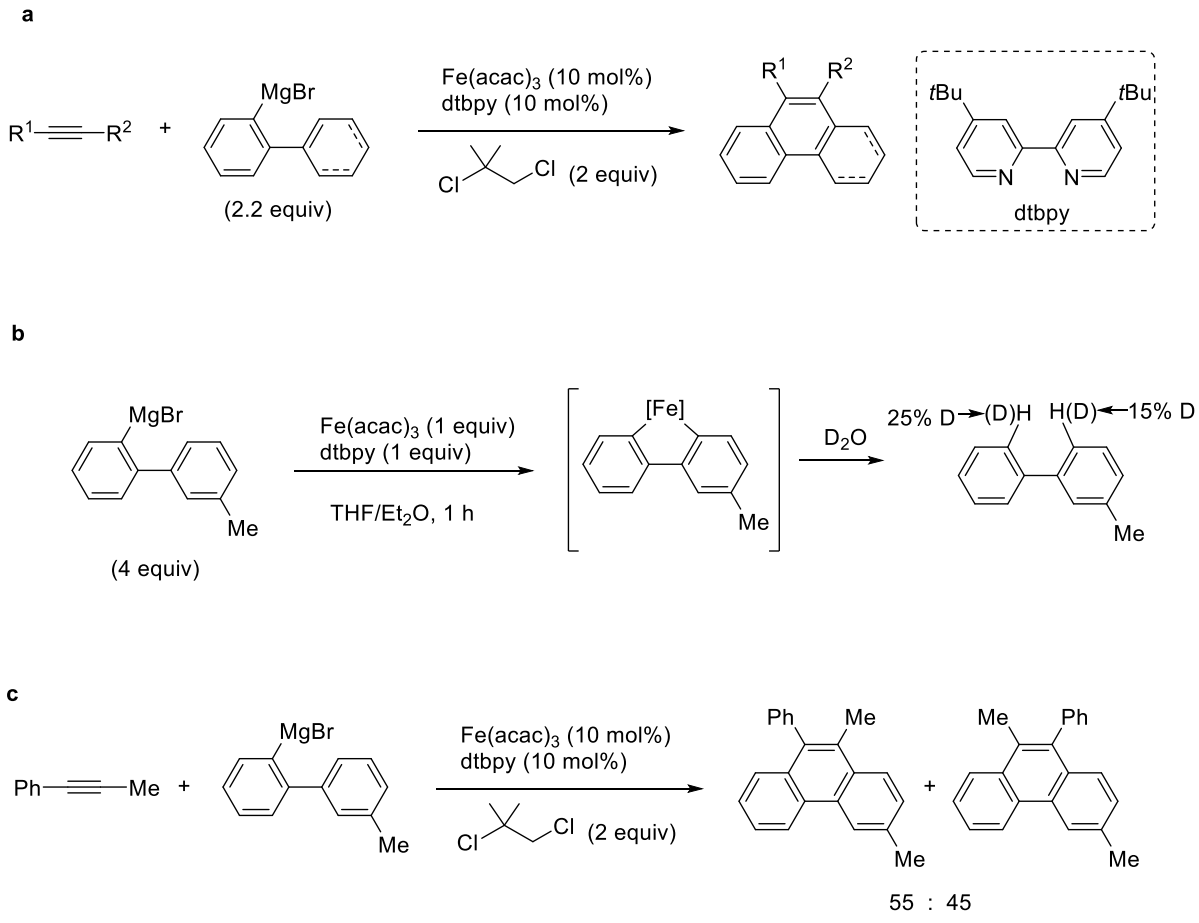


Remote C–H Activation with Iron

In 2011, Nakamura and coworkers reported an iron-catalyzed oxidative [4+2] benzannulation reaction of a 2-biaryl Grignard reagent and an alkyne to afford a phenanthrene derivative (Scheme 1.19).[38] While the exact reaction mechanism remains unclear, the reaction is proposed to involve intramolecular C–H activation of a 2-biaryliron species to generate a ferracycle species as a key intermediate. This notion was supported by a few lines of experimental observation. The reaction of excess (3'-methylbiphenyl-2-

yl)magnesium bromide (4 equiv) with the iron precatalyst (1 equiv), when quenched with D_2O, resulted in partial deuterium incorporation into 2'- and 6-positions of the recovered 3-methyl-1,1'-biphenyl (Scheme 1.19b), which suggested that a part of the 2-biaryl Grignard reagent underwent metalation of the *ortho* position of the distal aryl group. The annulation of (3'-methylbiphenyl-2-yl)magnesium bromide and 1-phenyl-propyne resulted in a near equimolar mixture of two regioisomeric products (Scheme 1.19c). Given the excellent regioselectivity observed in related iron-catalyzed carbomagnesiation of aryl(alkyl)alkyne, [39] the lack of regioselectivity would exclude a reaction pathway involving direct insertion of the alkyne into a 2-biaryliron species, but would suggest that metalation of the distal aryl group occurs prior to the insertion event.

Scheme 1.19. Iron-Catalyzed [4+2] Benzannulation Involving Remote C–H Activation

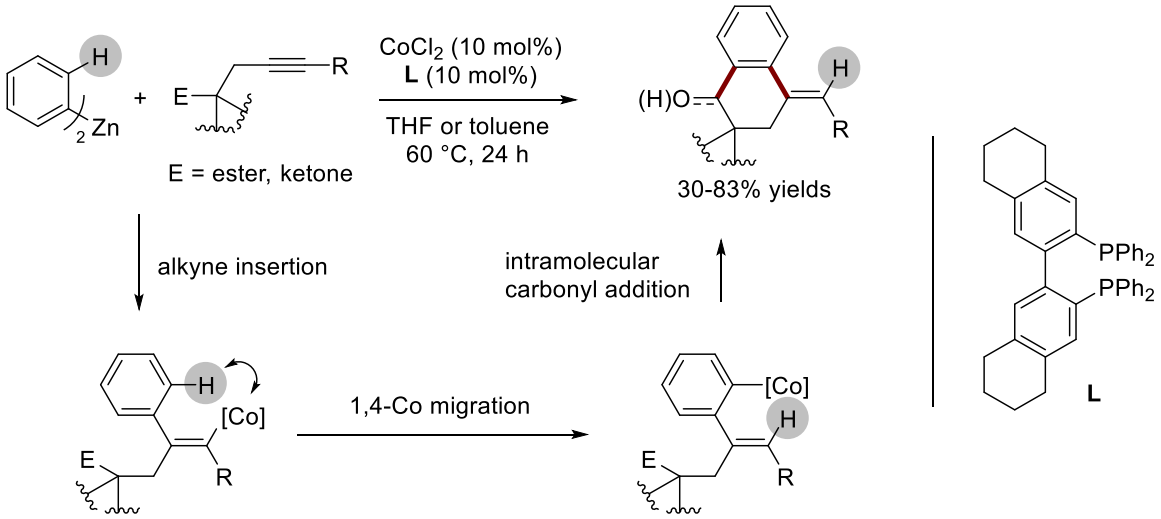


1.4 Design and Summary of Thesis Research

As discussed above, numerous catalytic and stoichiometric reactions involving remote C–H activation/1,4-metal migration of organotransition metal complexes have been reported for noble metals, palladium and rhodium in particular. By contrast, the use of earth-abundant first-row transition metals (base metals) in this type of transformations remains underdeveloped. Given the synthetic versatility of remote C–H activation/1,4-metal migration and the cost efficiency of base metal catalysis, we aimed at development of new base metal-catalyzed transformations involving this mode of C–H activation. In this respect, the present thesis research was focused on transition metal-catalyzed reactions between arylmetal reagents and alkynes, which led to an extension of the 1,4-cobalt migration to new cascade arylative cyclization reactions as well as a discovery of the ability of organochromium species to undergo remote C–H activation/1,4-migration.

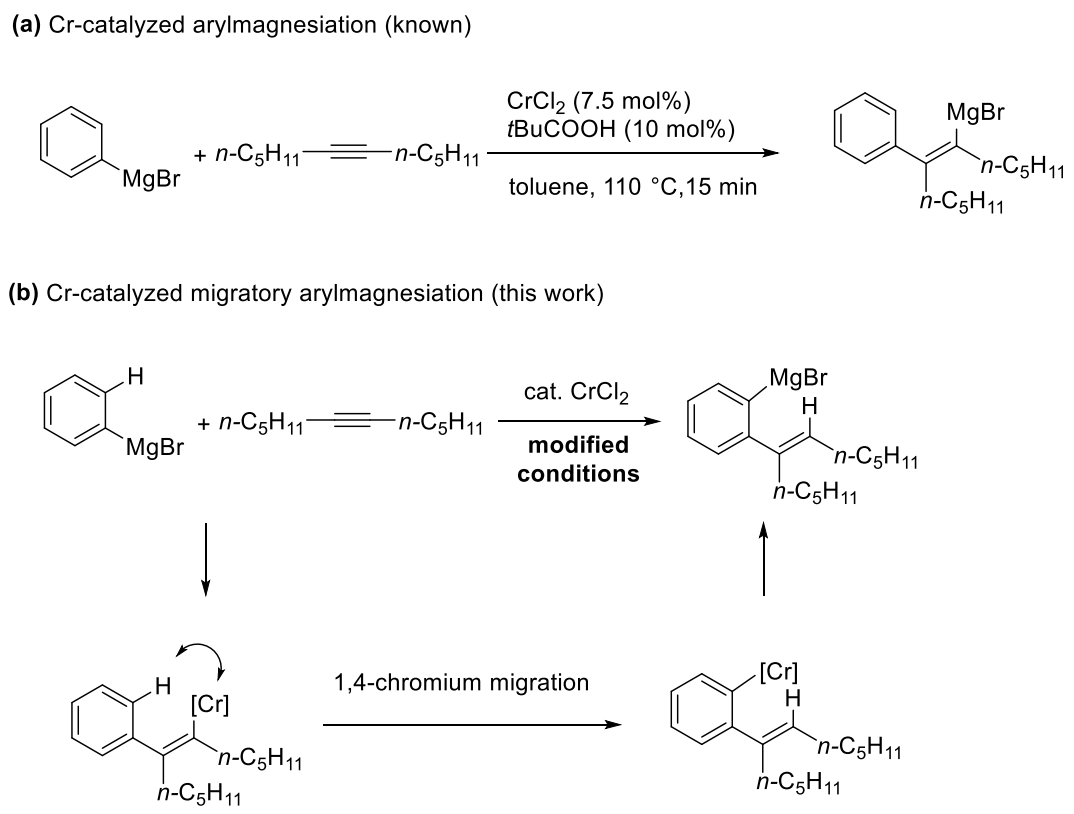
Chapter 2 describes the extension of 1,4-cobalt migration. Given the parallelism between the rhodium-catalyzed hydroarylation (Scheme 1.8) and the cobalt-catalyzed migratory arylzincation (Scheme 1.18) as well as the diverse cascade reactions involving 1,4-rhodium (or iridium) migration (e.g., Scheme 1.9 and Scheme 1.16), we became interested in the feasibility of analogous cascade reactions employing a cobalt catalyst and an arylzinc reagent. Exploration along this line allowed us to develop a series of arylative cyclization reactions between ester- or ketone-tethered alkyne substrates and arylzinc reagents catalyzed by a cobalt–biaryl-diphosphine complex (Scheme 1.20).[40] The cobalt/arylzinc reaction system not only served as an alternative to the rhodium/arylboron system in a known arylative cyclization, but also enabled the use of a new type of substrate, for which rhodium and iridium catalysts proved ineffective.

Scheme 1.20. Cobalt-Catalyzed Arylative Cyclization through 1,4-Cobalt Migration



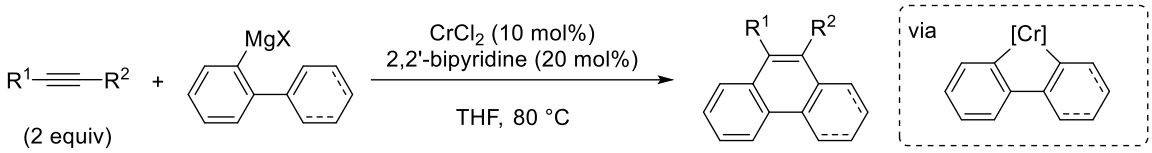
Chapter 3 reports on a chromium-catalyzed addition reaction of an aryl Grignard reagent to an internal alkyne that likely involves 1,4-chromium migration (Scheme 1.21).[41] This reaction was serendipitously discovered during attempted preparation of an alkenyl iodide for mechanistic study of the cobalt-catalyzed migratory arylzincation. Thus, a chromium-catalyzed alkyne arylmagesiation reaction [42] employed for this purpose unexpectedly indicated the feasibility of 1,4-chromium migration. Subsequent optimization studies allowed us to establish effective chromium catalyst systems for the "migratory" arylmagnesiation.

Scheme 1.21. Chromium-Catalyzed Migratory Arylmagnesiation of Alkyne



Chapter 4 describes a chromium-catalyzed [4+2] benzannulation reaction between 2-biaryl Grignard reagents and internal alkynes to afford phenanthrene derivatives (Scheme 1.22), the development of which was stimulated by the discovery of the chromium-catalyzed migratory arylmagnesiation (vide supra). Thus, given the feasibility of 1,4-chromium migration of *cis*-β-styrylchromium species, we hypothesized that 2-biarylchromium species would also undergo analogous remote C–H activation or 1,4-migration on the *ortho* position of the distal aryl group. Based on this hypothesis, a chromium–bipyridine catalyst was found to efficiently promote the desired annulation reaction. Mechanistic experiments indicated significant complexity of the reaction pathways, while providing reasonable support for the involvement of chromium-mediated remote C–H activation.

Scheme 1.22. Chromium-Catalyzed Annulation of 2-Biaryl-Grignard Reagent and Alkyne



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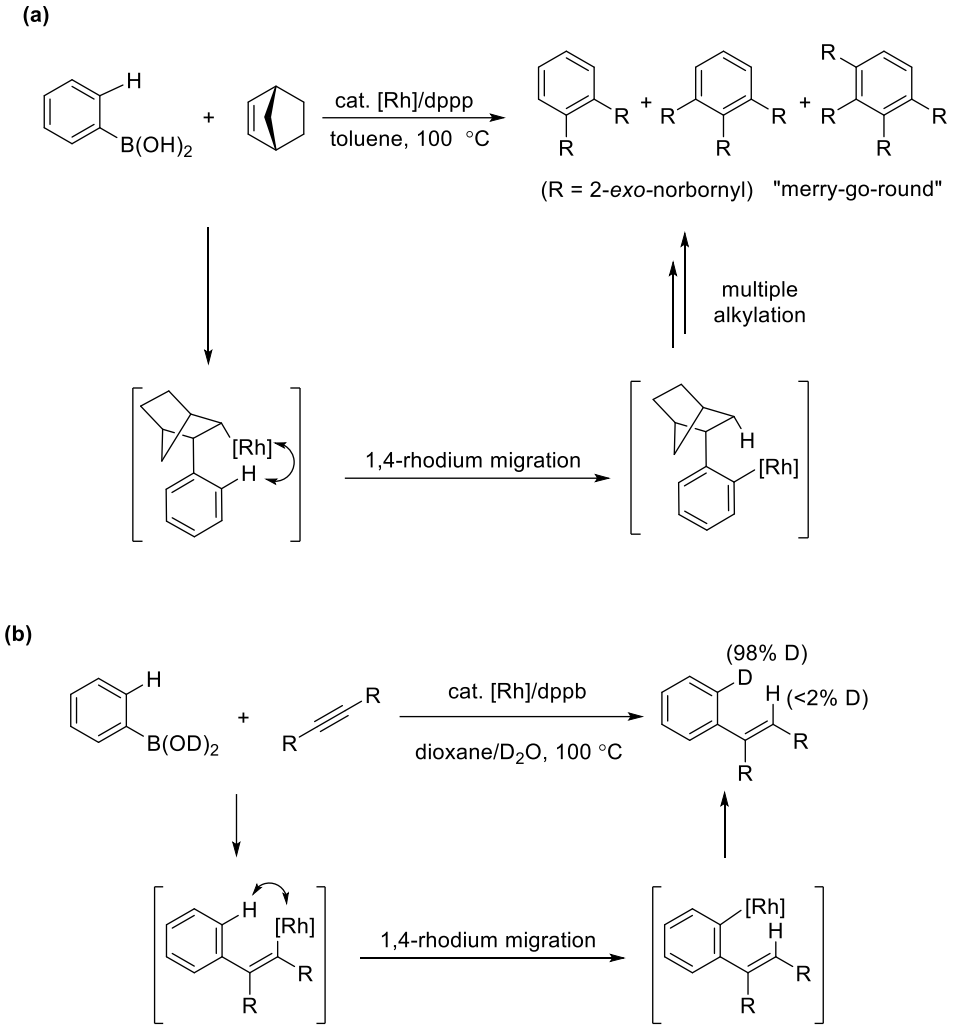
Chapter 2. Cobalt-Catalyzed Arylative Cyclization of Acetylenic Esters and Ketones with Arylzinc Reagents through 1,4-Cobalt Migration

2.1 Introduction

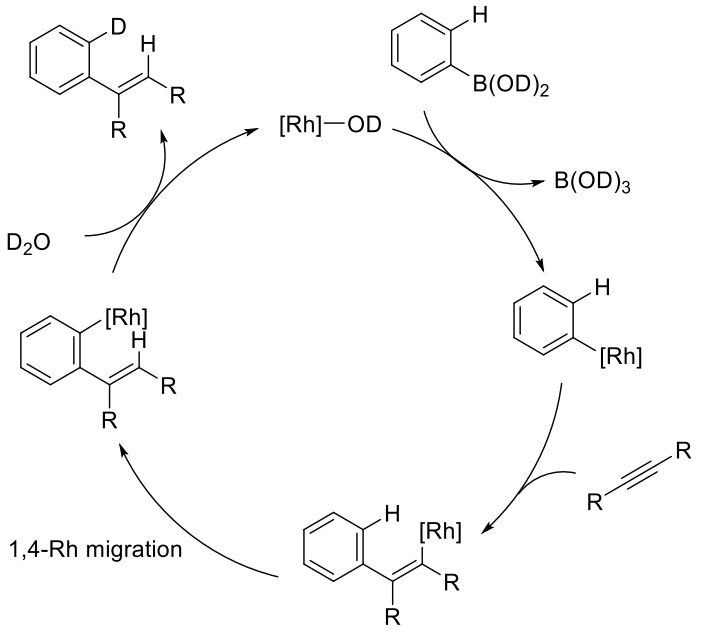
The remote 1,4-metal migration of organotransition metal species, especially organopalladium and organorhodium species, is not only a mechanistically interesting but also synthetically useful reaction. Enabling remote C−H bond activation, it has been widely employed as an elementary step to develop efficient catalytic cascade reactions.[1] While 1,4-migration of organopalladium species is involved in the Catellani reaction[2] and related reactions,[3] early examples of 1,4-migration of organorhodium(I) species were reported by Miura[4] and Hayashi[5] on the rhodium-catalyzed addition reactions of an arylboronic acid to norbornene and alkyne, respectively (Scheme 2.1). The former reaction results in "merry-go-round"-like multiple alkylation of the arylboronic acid, which can be rationalized by the alkyl-to-aryl 1,4-rhodium migration as the key step. On the other hand, the alkenyl-to-aryl 1,4-migration in the latter alkyne hydroarylation reaction in aqueous solvent was clearly demonstrated by mechanistic experiments performed in the presence of D_2O or using pentadeuteriophenylboron reagent.

Scheme 2.1. Early Examples of Rhodium-Catalyzed C−C Bond Formation Involving 1,4-Rhodium Migration



Scheme 2.2 shows a plausible catalytic cycle for the alkyne hydroarylation involving 1,4-rhodium migration. Transmetalation between a hydroxorhodium(I) species and the arylboronic acid gives rise to an arylrhodium(I) species. Migratory insertion of the alkyne into the aryl–rhodium bond results in an alkenylrhodium(I) species, which then undergoes 1,4-rhodium migration to give an *ortho*-alkenylarylrhodium(I) species. Protodemetalation of this species furnishes the hydroarylation product, while regenerating the hydroxorhodium(I) species.

Scheme 2.2. Catalytic Cycle for Rhodium-Catalyzed Alkyne Hydroarylation Involving 1,4-Rhodium Migration

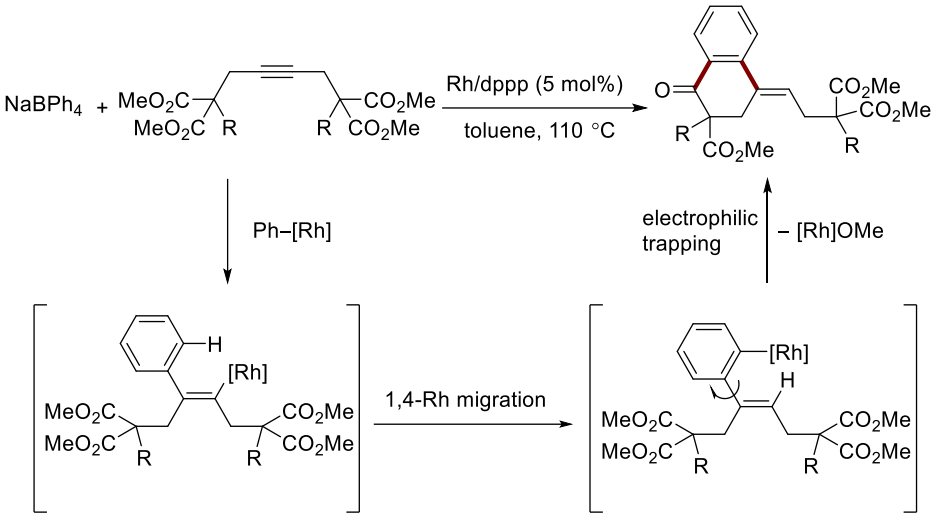


The above seminal works set the stage for further development of catalytic and stoichiometric 1,4-migration of group 9 organotransition metal species, including organorhodium(I), [6] organoiridium(I), [7] organorhodium(III), and organoiridium(III) [8] species. Capitalizing on 1,4-migration of group 9 organotransition metal species, a variety of novel cascade transformations have been developed to enable rapid access to complex molecules and polymers. Like Hayashi's hydroarylation, some of them are initiated by the insertion of an alkyne into the arylmetal species, followed by 1,4-metal migration of the resulting *cis*-β-styrylmetal species, as described below.

In 2005, Murakami and coworkers reported a rhodium-catalyzed arylative cyclization of an acetylenic tetraester substrate with sodium tetraphenylborate (Scheme 2.3).[6a] This cascade transformation is proposed to proceed via (1) insertion of the C−C triple bond into an arylrhodium(I) species, (2) vinyl-to-aryl 1,4-rhodium migration, and (3) intramolecular electrophilic trapping of the resulting arylrhodium species with the ester moiety, thus affording the tetralone product. The rhodium(I) alkoxide expelled in the last

step would undergo transmetalation with sodium tetraphenylborate to regenerate the phenylrhodium species.

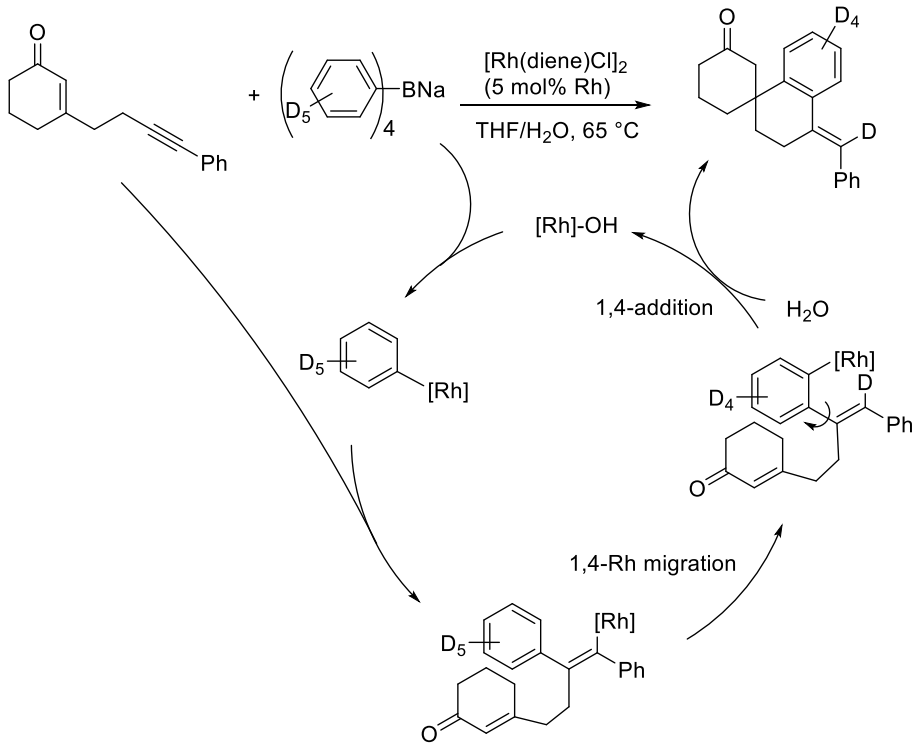
Scheme 2.3. Rh-Catalyzed Arylative Cyclization of Acetylenic Tetraester Involving 1,4-Rhodium Migration



In 2010, Hayashi and coworkers achieved a challenging spirocycle synthesis through a rhodium/diene-catalyzed arylative cyclization of alkyne-tethered 2-cycloalken-1-ones with sodium tetraarylborates (Scheme 2.4). [9] When sodium tetrakis(pentadeuteriophenyl)borate was used, quantitative deuteration at the olefin carbon of the spirocyclic product was observed. Thus, the reaction likely involves addition of an aryl–Rh complex across the C−C triple bond to generate a vinyl–Rh species and following 1,4-rhodium migration to relocate the Rh center onto the *ortho* position, affording an *ortho* alkenyl aryl–Rh species. Upon single bond rotation, this species would readily undergo subsequent intramolecular 1,4-addition to the pendant α,β-unsaturated ketone moiety to assemble the spirocyclic skeleton. Note that a primary kinetic isotope effect (k_H/k_D = 3.7) was also observed in the reaction of sodium tetrakis(2-deuteriophenyl)borate, which indicated that the 1,4-rhodium migration step could be the turnover-limiting step. In

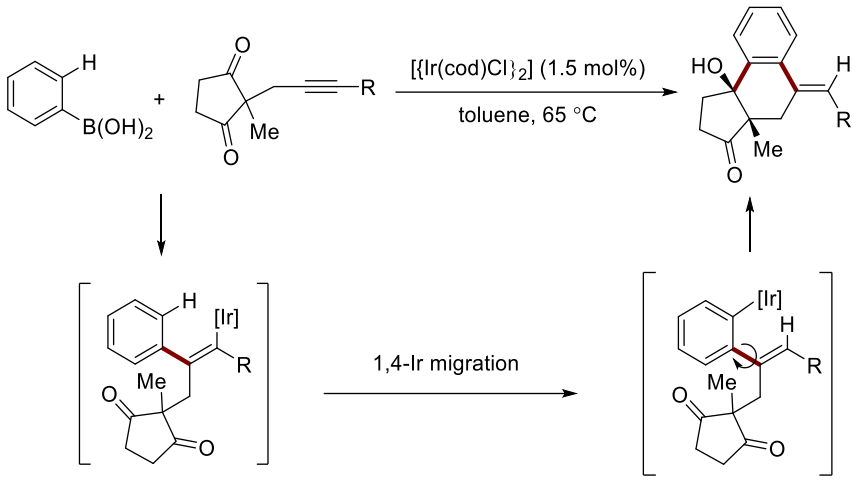
addition, an asymmetric variant of this transformation was achieved using a chiral diene ligand, creating quaternary spirocarbon stereocenters with high enantiomeric purity.

Scheme 2.4. Rhodium-Catalyzed Arylative Cyclization for Spirocycle Synthesis through Tandem 1,4-Rhodium Migration/1,4-Addition



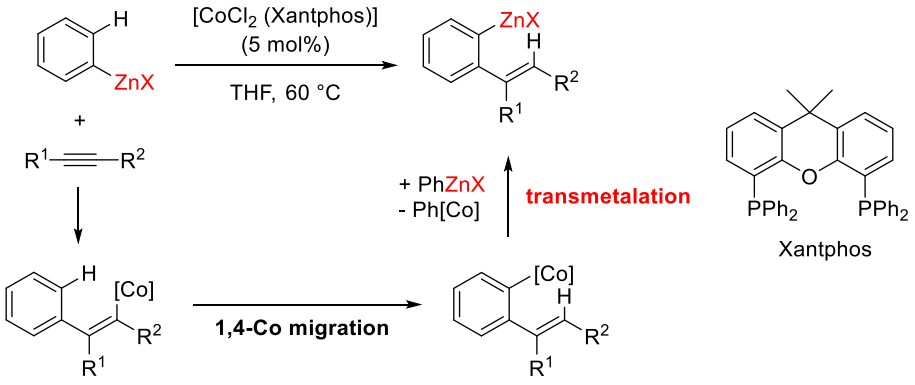
In 2014, Lam and coworkers disclosed the first example of 1,4-iridium(I) migration in a cascade arylative cyclization reaction (Scheme 2.5).[7] In the presence of a catalytic amount of $[Ir(cod)Cl]_2$, an arylboronic acid underwent arylative cylization of an alkyne bearing a cyclic 1,3-diketone moiety to afford a bicyclic product. The 1,4-iridium migration step was supported by a control experiment using pentadeuteriophenylboronic acid. Furthermore, an enantioselective variant of this reaction was achieved using a chiral diphosphine as a supporting ligand, albeit in moderate yield.

Scheme 2.5. Arylative Cyclization of Acetylenic Diketone with Arylboronic Acid Involving 1,4-Iridium Migration



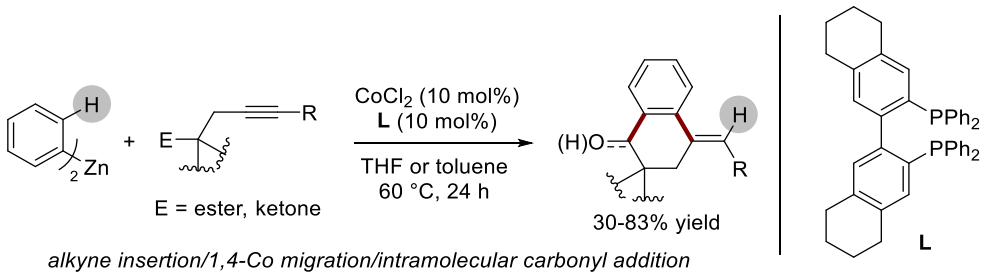
In 2012, our group disclosed a cobalt-catalyzed "migratory arylzincation" of an unfunctionalized alkyne, where the addition of an arylzinc reagent to the alkyne occurs along with concurrent transposition of the zinc atom to the *ortho* position (Scheme 2.6).[10] In analogy to the above-discussed rhodium- and iridium-catalyzed reactions, this reaction is also considered to involve insertion of the alkyne into an arylcobalt species and subsequent alkenyl-to-aryl 1,4-cobalt migration as key steps, while it features a unique catalyst turnover step. Thus, an *ortho*-alkenylarylcobalt species generated upon 1,4-cobalt migration undergoes transmetalation with the arylzinc reagent to afford an *ortho*-alkenylarylzinc species, while regenerating the arylcobalt species. As an extension, migratory arylzincation of a norbornene derivative was also demonstrated, which represents the first example of alkyl-to-aryl 1,4-cobalt migration.[11]

Scheme 2.6. Cobalt-Catalyzed Alkyne Arylzincation Involving 1,4-Cobalt Migration



On the basis of the above background, we wondered whether the synthetic utility of the 1,4-cobalt migration could further be extended to achieve cascade C–C bond forming reactions, such as those achieved with rhodium and iridium catalysts. To address this question, we explored cobalt-catalyzed reactions of arylzinc reagents with alkynes bearing pendant ester or ketone functional groups. The present study led us to demonstrate that the cobalt/arylzinc system is capable of promoting cascade arylative cyclization reactions that involve 1,4-cobalt migration and nucleophilic addition of arylcobalt species to carbonyl groups (Scheme 2.7). Furthermore, the cobalt/arylzinc system was found not only to serve as an alternative to the existing rhodium/arylboron and iridium/arylboron systems but also to exhibit unique reactivity and selectivity in some of the cascade reactions.

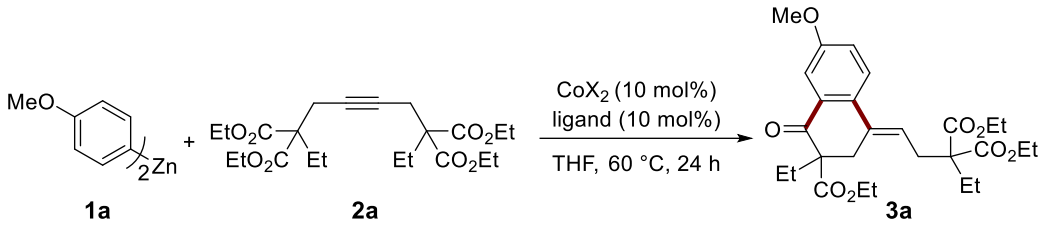
Scheme 2.7. Cobalt-Catalyzed Arylative Cyclization through 1,4-Cobalt Migration



2.2 Results and Discussion

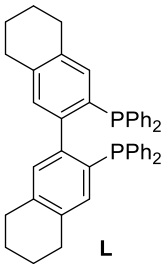
Initially, we examined the reaction of a diarylzinc reagent **1a** (prepared in-situ from 4-methoxyphenylmagnesium bromide and $ZnCl_2$·TMEDA in a 2:1 ratio) with a symmetric acetylenic tetraester **2a**, an analogue of the substrate employed by Murakami and co-workers for the rhodium-catalyzed arylative cyclization.[6a] In light of our previous work on cobalt-catalyzed migratory arylzincation,[10,11] a catalytic system comprised of a cobalt(II) salt such as $CoCl_2$ and a diphosphine ligand (10 mol% each) was employed to perform the reaction in THF at 60 °C (Table 2.1). Examination of several diphosphines clearly demonstrated a significant ligand effect on the catalytic activity. Xantphos and dppf afforded the desired cyclized product **3a** in less than 5% yield, although they were the optimum ligands for the migratory arylzincation of unfunctionalized alkyne and norbornene, respectively.[10,11] Biaryl diphosphine ligands (BINAP and BIPHEP) were found to give rise to distinct improvement in the yield of **3a** (entries 3−6). Further screening of binaphthyl- and biphenyldiphosphine ligands including chiral ones led us to identify a modified BIPHEP ligand **L** (Scheme 2.7)[12] as the optimum ligand, which afforded **3a** in 78% isolated yield (entry 7). It is noteworthy that the reaction with a monoarylzinc reagent, which was prepared in-situ by mixing 4-methoxyphenylmagnesium bromide and $ZnCl_2$·TMEDA in a 1:1 ratio, did not afford **3a** at all (entry 8). Regarding the catalyst precursor, a comparable catalytic activity could be achieved with $CoBr_2$ instead of $CoCl_2$ (entry 9), while CoF_2 turned out to be ineffective (entry 10). Note also that under otherwise identical conditions, the reaction did not occur at all employing 4-methoxyphenylboronic acid instead of the diarylzinc reagent **1a**.

Table 2.1. Screening of Reaction Conditions for Arylative Cyclization of Acetylenic Tetraester 2a[a]



1a **2a** **3a**

entry	CoX_n	ligand	GC yield (%)[b]
1	$CoCl_2$	Xantphos	1
2	$CoCl_2$	dppf	3
3	$CoCl_2$	dppe	2
4	$CoCl_2$	dppp	10
5	$CoCl_2$	(±)-BINAP	50
6	$CoCl_2$	BIPHEP	60
7	**$CoCl_2$**	**L**	**80(78)[c]**
8[d]	$CoCl_2$	**L**	0
9	$CoBr_2$	**L**	70
10	CoF_2	**L**	2



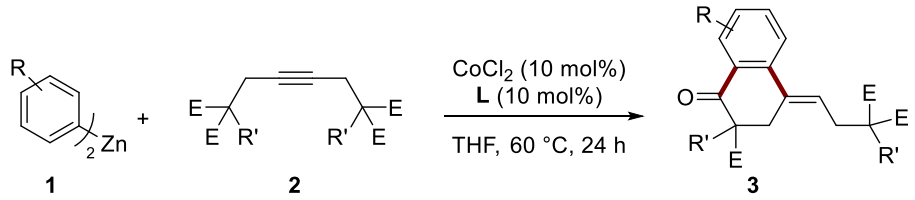
L

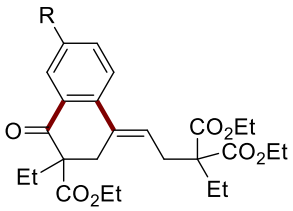
[a]Reaction conditions: Arylzinc reagent prepared from $ZnCl_2$•TMEDA (0.3 mmol) and 4-$MeOC_6H_4MgBr$ (0.6 mmol), alkyne **2a** (0.2 mmol), CoX_n (10 mol%), ligand (10 mol%), THF, 60 °C, 24 h. [b]Determined by GC. [c]Isolated yield. [d]The reaction was performed using arylzinc reagent prepared from $ZnCl_2$•TMEDA (0.3 mmol) and 4-$MeOC_6H_4MgBr$ (0.3 mmol).

With the optimized Co−**L** catalytic system in hand, the scope of diarylzinc reagents was explored for the cascade arylative cyclization reaction, employing **2a** as the model substrate (Table 2.2). Both electron-rich and electron-neutral *para*-substituents on the arylzinc reagents were well tolerated to afford the corresponding products **3a**−**3f** in moderate to good yields (60%−83%), while *para*-fluorophenylzinc reagent retarded the reaction with incomplete conversion of the tetraester **2a** over 24 h (see **3g**). The cascade arylative cyclization of **2a** with *meta*-substituted diarylzinc reagents (methyl, methoxy, and siloxy) occurred smoothly in 64%−73% yields, affording the products **3h**−**3j** with exclusive C−C bond formation at the less hindered *ortho* position distal to the substituent. This type of regioselectivity was also observed for the reaction with 3,4-methylenedioxyphenylzinc

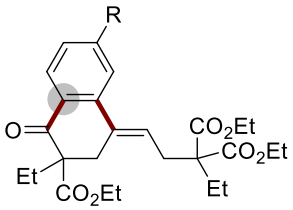
and 2-naphthylzinc reagents, which regioselectively afforded the products **3k** and **3l**, in yields of 53% and 62%, respectively. As was the case with migratory arylzincation of alkynes,[10] *ortho*-tolylzinc reagent failed to afford the desired adduct. Besides the model acetylenic tetraester **2a**, similar alkyne substrates bearing different alkyl and/or ester substituents also participated in the arylative cyclization with the diarylzinc reagent **1a**, affording the corresponding products **3m**−**3o** in respectable yields. However, unsymmetrical acetylenic substrates such as homopropargyl esters **2p** and **2q** were unproductive to undergo the present arylative cyclization reaction with the diarylzinc reagent **1a**, which only gave trace amount of desired products.

Table 2.2. Arylative Cyclization of Acetylenic Tetraester with Diarylzinc Reagent[a]

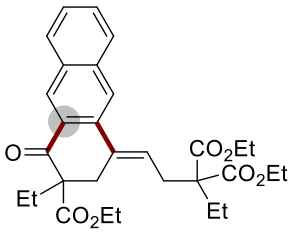




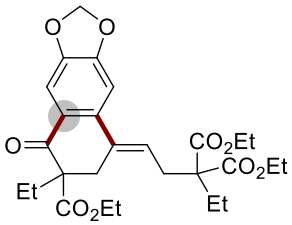
3a (R = OMe), 78%
3b (R = H), 77%
3c (R = Me), 72%
3d (R = *n*Bu), 75%
3e (R = NMe_2), 83%
3f (R = $SiMe_3$), 60%
3g (R = F), 34%



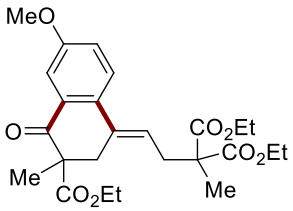
3h (R = Me), 64%
3i (R = OMe), 74%
3j (R = $OSiMe_2tBu$), 73%



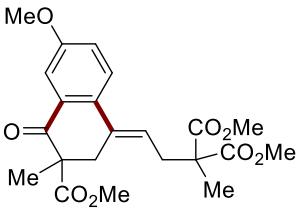
3k, 53%



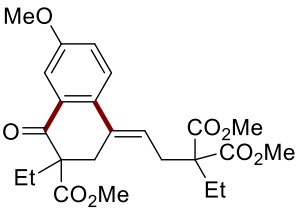
3l, 62%



3m, 70%

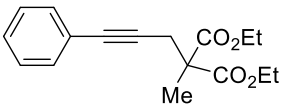


3n, 75%

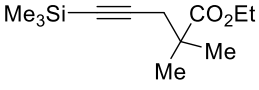


3o, 74%

Failed unsymmetrical substrates



2p



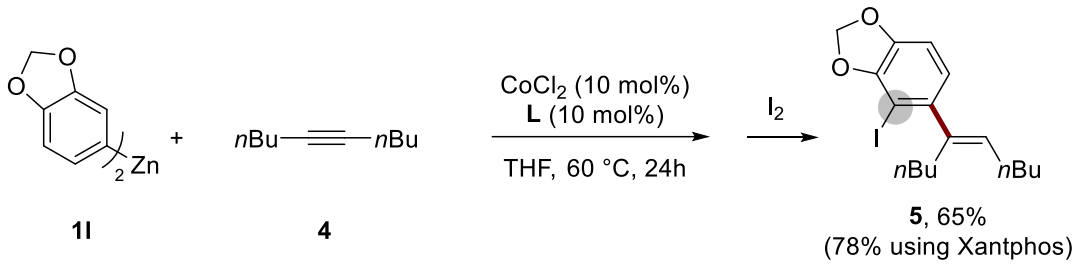
2q

[a]The reaction was performed on a 0.2 mmol scale under the reaction conditions in Table 2.1 (entry 7).

The regioselectivity with respect to the products **3h**−**3l** may be simply attributed to the preferential 1,4-cobalt migration of the initially formed alkenylcobalt species to the less hindered *ortho* position. However, the cases of 3-alkoxy, 3-siloxy and 3,4-

methylenedioxyphenylzinc reagents (**3i**, **3j** and **3l**) are intriguing since the same type of diarylzinc reagents showed opposite regioselectivity in the migratory arylzincation reaction of unfunctionalized alkynes, where 1,4-cobalt migration preferentially occurred to the proximal position of the *meta*-oxygen atom. The latter regioselectivity was explained by a secondary directing effect of the *meta*-oxygen atom in the 1,4-cobalt migration step.[10] To shed light on the origin of these contrasting regioselectivities, a reference experiment was performed using 3,4-methylenedioxyphenylzinc reagent **1l** and 5-decyne **4** under the present Co−**L** catalytic conditions (Scheme 2.8). Upon quenching with I_2, the reaction afforded the adduct **5** with exclusive iodination at the more hindered *ortho* position. This result indicates that it is not the specific nature of ligand **L** but the nature of the substrate **2a** that determined the regiochemistry of the product **3l**.

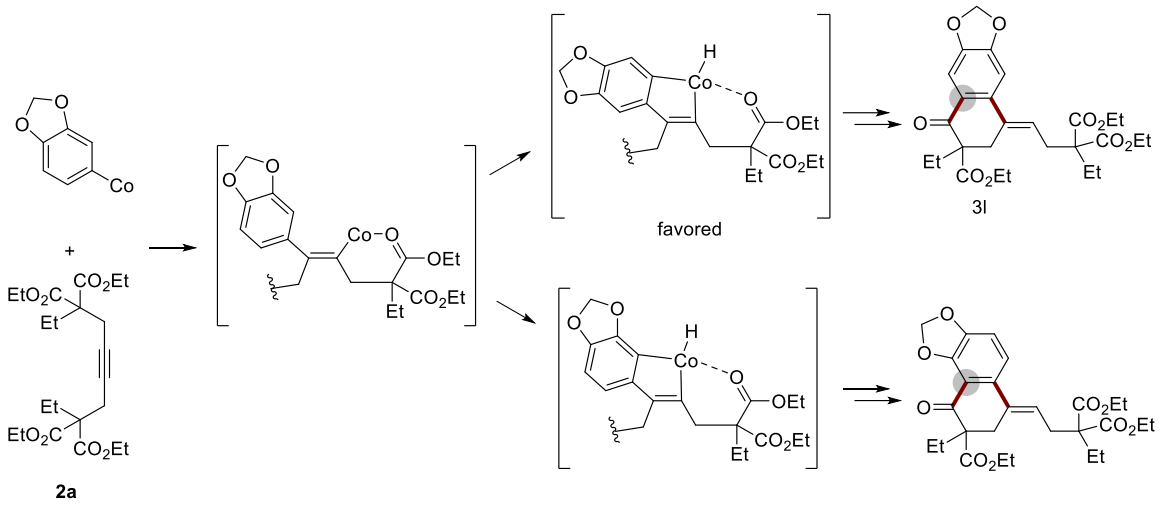
Scheme 2.8. Addition of 3,4-Methylenedioxyphenylzinc Reagent **1l** to Unfunctionalized Alkyne



1l **4** **5**, 65% (78% using Xantphos)

We speculate that the ester group of **2a** plays a critical role in the regioselective 1,4-cobalt migration during the formation of **3l** (Scheme 2.9). Thus, migratory insertion of **2a** into 3,4-methylenedixoyphenylcobalt species would produce an alkenylcobalt species, in which one of the ester carboxyl oxygens would coordinate to the cobalt center by forming a six-membered chelate structure. This coordination may interfere with the secondary directing effect of the *meta*-oxygen atom, thus favoring 1,4-migration to the less hindered *ortho* position.

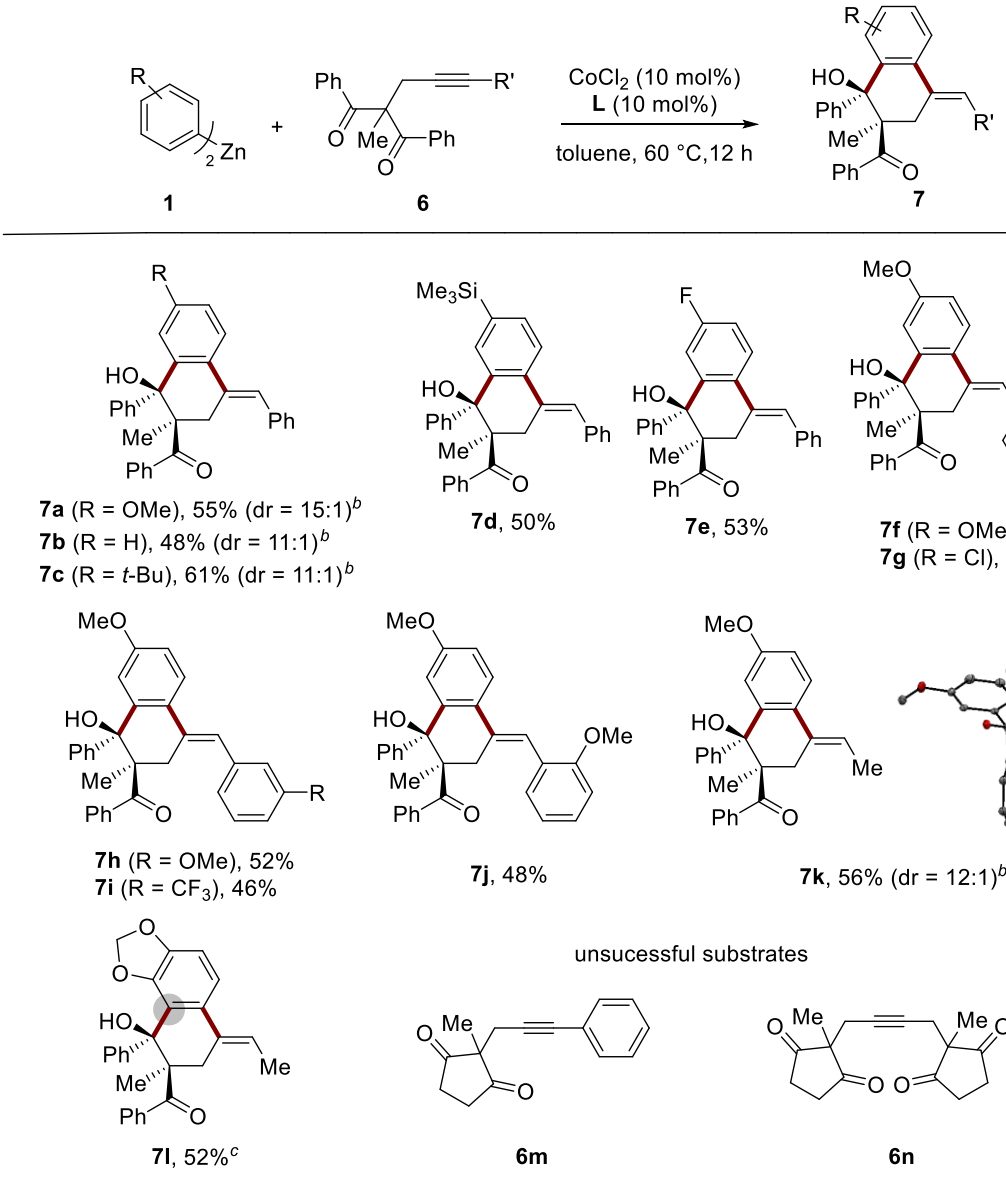
Scheme 2.9. Possible Origin of Regioselectivity for **3l**



The scope of acetylenic substrates for the arylative cyclization could be extended to homopropargyl diketones **6**, which can be readily prepared through propargylation of 1,3-diketone derivatives followed by Sonogashira coupling (Table 2.3). Thus, the Co−**L** catalytic system promoted the reaction of a diaryzinc reagent with **6** in toluene, affording a benzo-fused cyclic alcohol **7** containing adjacent quaternary carbon centers in moderate yield. Electron-donating and electron-withdrawing substituents can be introduced into the *para* position of diarylzinc reagents, affording the corresponding products **7a**−**7e**. Various modifications at the acetylenic terminus of the homopropargyl diketone were also allowed to produce a series of cyclization products **7f**−**7k**. According to GC and GCMS analysis of the crude reaction mixtures for **7a**, **7b**, and **7k**, the homopropargyl diketones were fully consumed, and the cyclization took place with high diastereoselectivity (≥10:1). On the other hand, the GC analysis of the reaction mixture excluded the formation of a hydroarylation product resulting from the addition of **1** to **6** in opposite regioselectivity, although we failed to determine any other byproducts. We managed to confirm the geometry of the C=C bond and the diastereochemistry of **7k** by X-ray crystallographic

analysis. It should be mentioned that, in our hands, the above homopropargylic diketone substrates did not participate in arylative cyclization with 4-methoxyphenylboronic acid using the iridium- or rhodium-based catalytic system, which was developed by Lam and coworkers for substrates featuring cyclic 1,3-diketone moieties (Scheme 2.5).[7] On the other hand, homopropargyl diketones **6m** and **6n** bearing cyclic 1,3-diketone moieties failed to participate in arylative cyclization under the present cobalt catalysis.

Table 2.3. Arylative Cyclization of Homopropargyl Diketone with Diarylzinc Reagent[a]

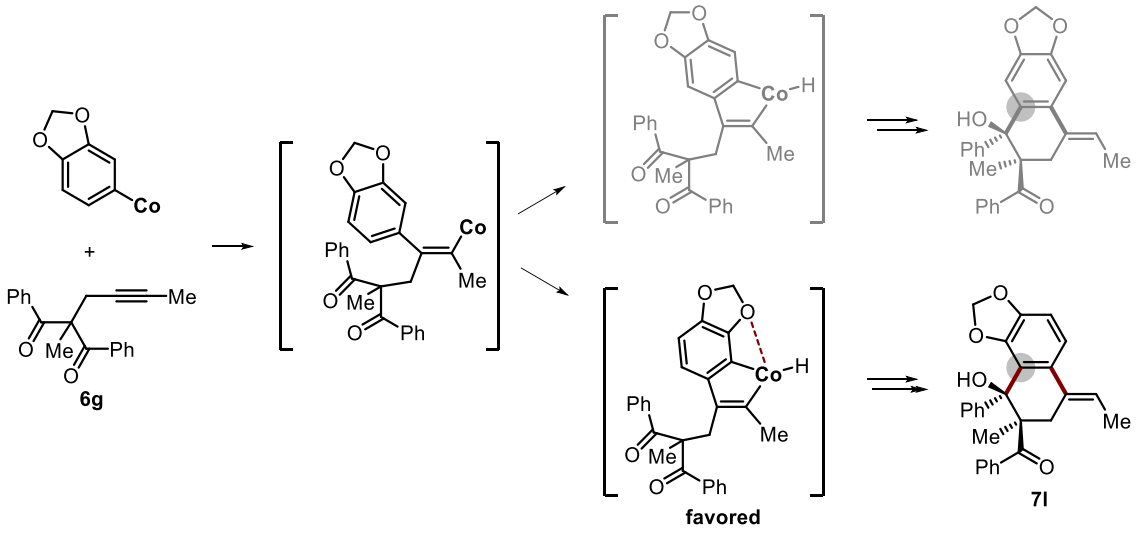


[a]The reaction was performed on a 0.2 mmol scale under the reaction conditions in Table 1 (entry 7) with a slight modification (toluene instead of THF as the solvent). [b]Diastereomer ratio was

determined for **7a**, **7b**, and **7k** by GC and GCMS analysis of the crude product. [c]Estimated yield of the product containing impurities.

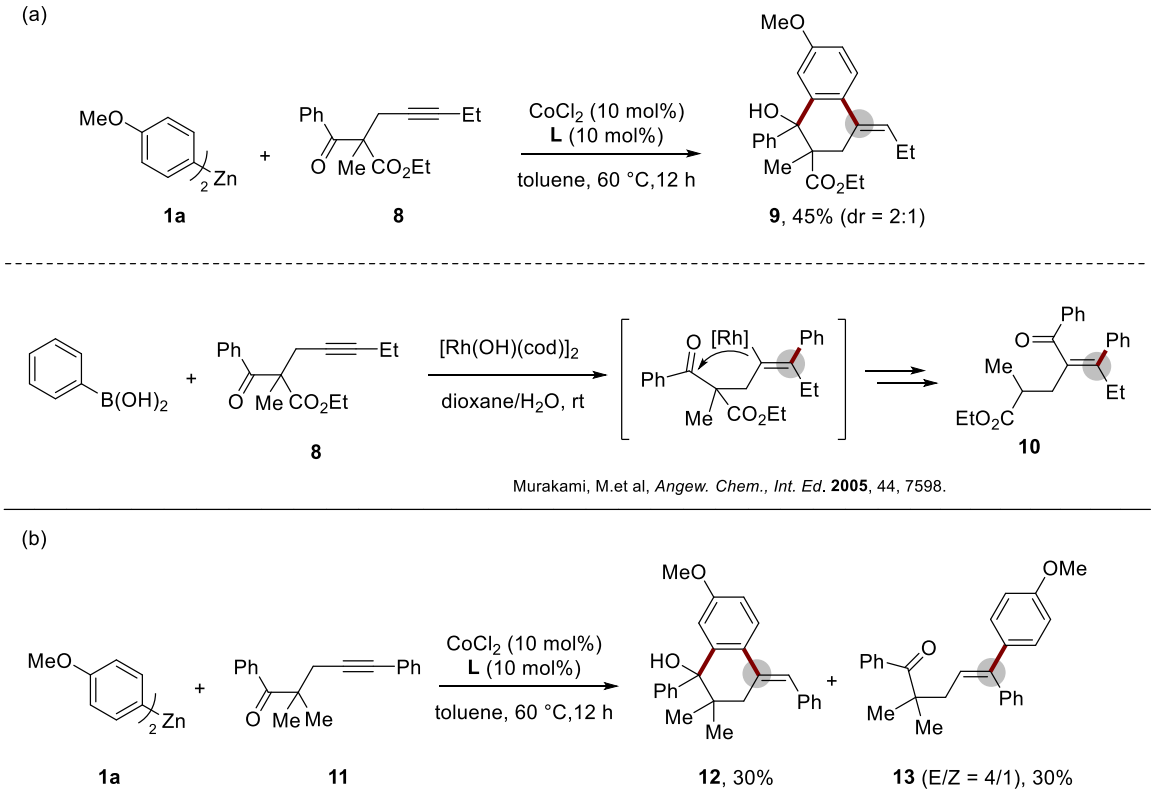
The regioselective arylation of the alkyl-substituted acetylenic carbon observed for the products **7a**–**7j** was reasonably expected from the known trend in cobalt-catalyzed (migratory) arylzincation reactions of aryl(alkyl)alkynes, where the arylation usually takes place at the acetylenic carbon distal to the aryl group.[10,13] On the contrary, the formation of the products **7k** and **7l** highlights the uniqueness of this cascade reaction, because poor regioselectivity was observed in the migratory arylzincation of unsymmetrical dialkylalkynes.[10] The product **7l** is also notable for its regioselective 1,4-migration to the proximity of the *meta*-oxygen substituent, which can be attributed to the secondary directing effect.[10] Note that this regioselectivity is opposite to the one observed in the reaction of acetylenic tetraester to produce **3l** (vide supra). Unlike the latter case, the present case should involve the formation of an alkenylcobalt intermediate without a six-membered chelate, and hence the 1,4-cobalt migration would preferentially proceed with the secondary interaction (Scheme 2.10). Further investigation would be necessary to verify these mechanistic hypotheses.

Scheme 2.10. Possible Origin of Regioselectivity for **7l**



To further explore the scope of the present catalytic system, we examined a few additional homopropargylic substrates bearing a ketoester or monoketone moiety (Scheme 2.11). The reaction of homopropargyl ketoester **8** with diarylzinc reagent **1a** resulted in chemoselective cyclization onto the keto moiety regardless of the presence of ester moiety, affording a benzo-fused cyclic alcohol product **9** in modest yield and diastereoselectivity (Scheme 2.11a). Once again, GCMS analysis excluded the formation of other types of 1:1 adducts, although no other product could be characterized despite complete consumption of **8**. The exclusive formation of the bicyclic product **9** is in a sharp contrast to the outcome of the reaction of the identical substrate **8** with phenylboronic acid under Rh catalysis, which was reported by Murakami and coworkers.[14] Thus, the Rh-catalyzed reaction produced tetrasubstituted alkene **10** through insertion of the alkyne into an arylrhodium species with opposite regioselectivity. The arylative cyclization of a homopropargyl monoketone **11** turned out to be less efficient, which resulted in a separable mixture of the desired benzo-fused product **12** and a simple hydroarylation product **13**, the latter arising from alkyne insertion with the opposite regioselectivity (Scheme 2.11b).

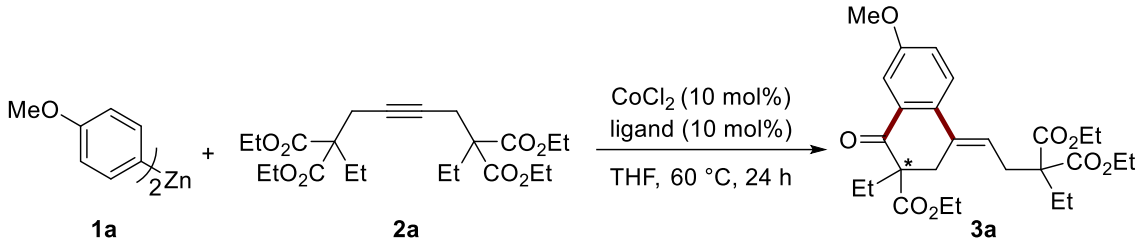
Scheme 2.11. Reactions of Homopropargylic Ketoester and Monoketone Substrates



Encouraged by the effectiveness of the biaryl-diphosphine **L** in the present cascade arylative cyclization reactions, a screening of structurally related chiral BINAP- and BIPHEP-type ligands was undertaken in order to explore asymmetric variants of the arylative cyclization. To our disappointment, such attempts only met with limited success. For example, homopropargyl diketone **6** turned out to be too reluctant to undergo arylative cyclization using typical chiral ligands with BINAP- or BIPHEP-type backbone instead of **L**, not to mention any enantioselectivity. Nevertheless, it is still noteworthy that a cobalt−(*R*)-DMM-Garphos catalyst was found to promote desymmetrizing arylative cyclization of acetylenic tetraester **2a** with diarylzinc reagent **1a**, achieving a modest enantioselectivity (Table 2.4). This preliminary result not only holds a promise for better enantioselectivity but also provides valuable mechanistic insight into the cyclization process. It supports that a diphosphine-ligated *ortho*-alkenylarylcobalt complex should be involved in the cyclization process, although a competitive pathway involving

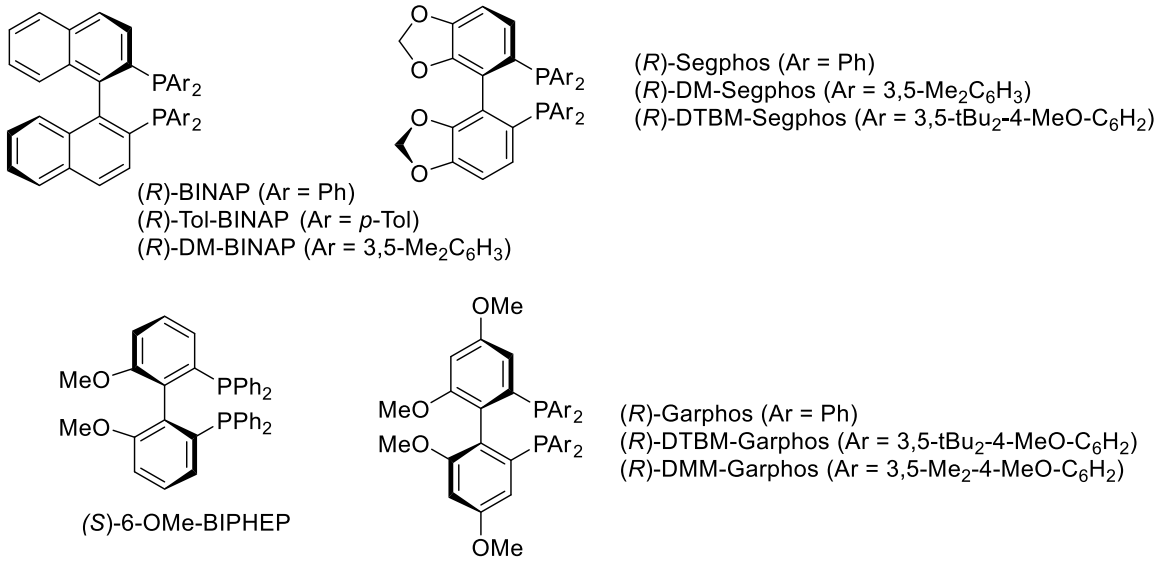
transmetalation between the *ortho*-alkenylarylcobalt species and the diarylzinc reagent **1a** prior to the intramolecular cyclization cannot be excluded.

Table 2.4. Desymmetrizing Arylation-Cyclization of Acetylenic Tetraester (**2a**)[a]



1a **2a** **3a**

entry	ligand	yield (%)[b]	ee (%)[c]
1	(*R*)-BINAP	15	26
2	(*R*)-Tol-BINAP	33	36
3	(*R*)-DM-BINAP	21	5
4	(*R*)-Segphos	30	11
5	(*R*)-DM-Segphos	18	12
6	(*R*)-DTBM-Segphos	13	25
7	(*S*)-6-OMe-BIPHEP	15	-20
8[d]	(*R*)-Garphos	22	1
9	(*R*)-DTBM- Garphos	3	-
10	(*R*)-DMM-Garphos	**42**[d]	**50**

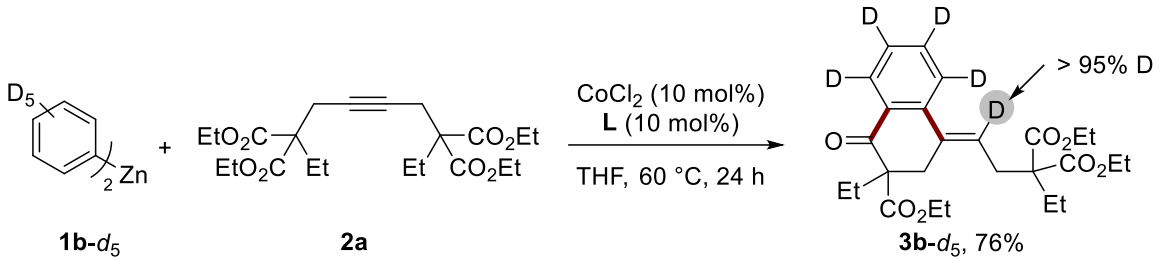


[a]The reaction was performed using diarylzinc reagent **1a** prepared from $ZnCl_2$•TMEDA (0.3 mmol) and 4-$MeOC_6H_4MgBr$ (0.6 mmol) and alkyne **2a** (0.2 mmol). [b] Determined by GC using *n*-tridecane as an internal standard. [c] Determined by chiral HPLC analysis. [d]Isolated yield.

The 1,4-cobalt migration process in the present cascade arylative cyclization reaction was unambiguously confirmed by a reaction between pentadeuteriophenylzinc

reagent **1b**-d_5 and the acetylenic tetraester **2a** (Scheme 2.12). In line with our expectation, the reaction took place with complete migration of one of the *ortho*-deuterium atoms to the vinylic position, affording the product **3b**-d_5.

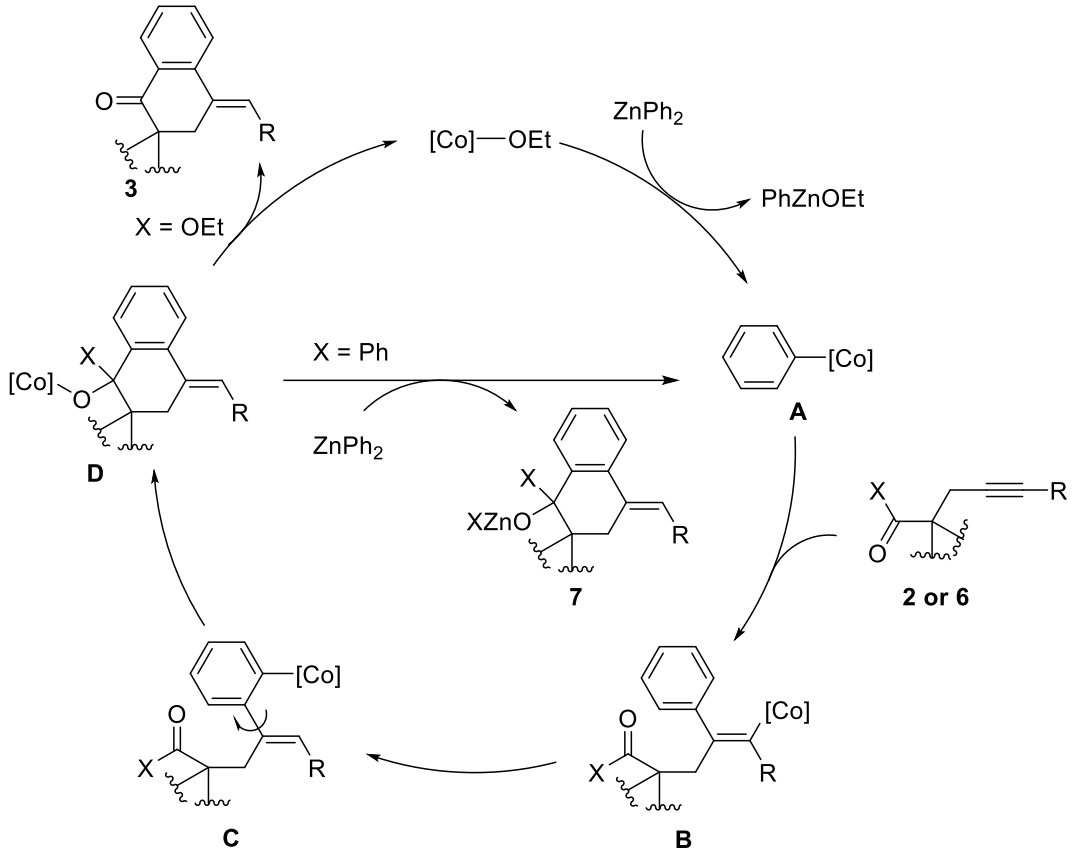
Scheme 2.12. Deuterium-Labeling Experiment



1b-d_5 **2a** **3b**-d_5, 76%

Based on the precedent rhodium- and iridium-catalyzed arylative cyclization reactions[6a,7] and our previous report on the cobalt-catalyzed migratory arylzincation reaction,[10] proposed catalytic cycles are outlined in Scheme 2.13. The catalytic cycles start with a phenylcobalt species **A** generated from the cobalt precatalyst and diphenylzinc reagent. It undergoes insertion of the acetylenic substrate **2** or **6** to produce an alkenylcobalt intermediate **B**, which is subsequently rearranged to an *ortho*-alkenylarylcobalt species **C** through 1,4-cobalt migration. Then, intramolecular cyclization via nucleophilic addition of the aryl−cobalt moiety of **C** onto the pendant carbonyl group forms a cyclized cobalt alkoxide species **D**. For the acetylenic tetraester substrate **2**, β-alkoxy elimination follows to afford the ketone product **3** along with a Co−OEt species. Transmetalation of the latter species with diphenylzinc reagent completes the catalytic cycle, regenerating the phenylcobalt species **A**. For the acetylenic ketone substrate **6**, direct transmetalation of the species **D** with diphenylzinc reagent would proceed to afford the benzo-fused alcohol product **7** in the form of zinc alkoxide with concomitant regeneration of the phenylcobalt species **A**.

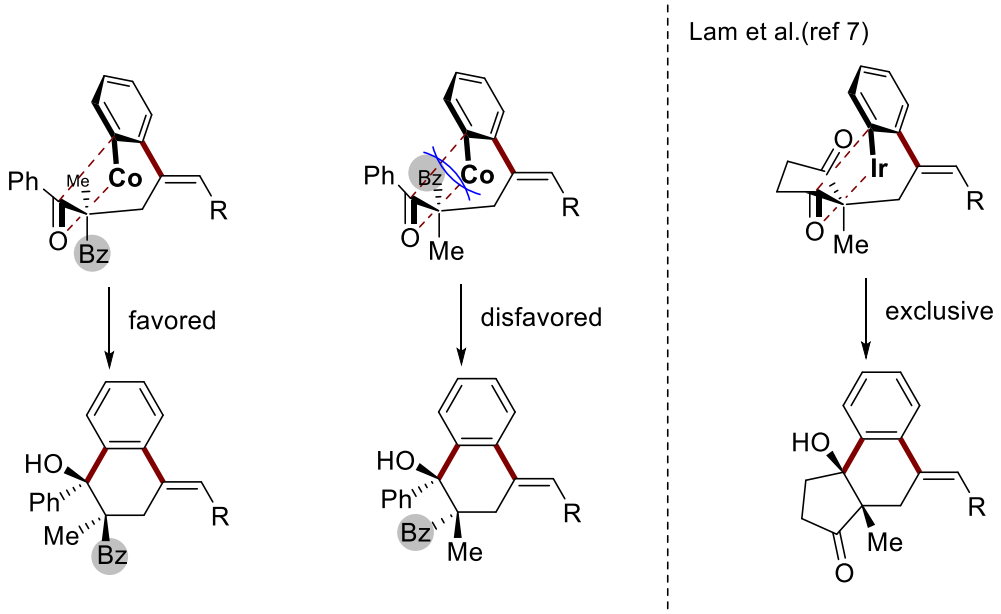
Scheme 2.13. Plausible Catalytic Cycle



The diastereoselectivity in the arylative cyclization of homopropargyl diketone substrates **6** warrants further discussion. In light of stereochemical analysis using ball-and-stick molecular models, we infer that the intermediate **C** would readily undergo the intramolecular nucleophilic addition of the aryl−cobalt moiety onto the pendant carbonyl moiety when the aryl group parallels with the C=O bond, and both of them are in a perpendicular orientation to the olefinic plane (Figure 2.1). Out of two possible transition state models complying with such structural configurations, the favored one would place the bulkier benzoyl group pointing away from the aryl−cobalt moiety to minimize steric repulsion. Such favored transition state indeed results in the observed diastereoselectivity, while possible involvement of disfavored transition state leading to the formation of the minor diastereomer cannot be excluded through present molecular model analysis. The same molecular model analysis is applicable to the cyclic diketone-bearing acetylenic

substrate employed in Lam's Ir-catalyzed arylative cyclization reaction,[7] rationalizing exclusive formation of the opposite type of diastereomer owing to the conformational rigidity of the cyclic diketone skeleton.

Figure 2.1. Plausible Models for Diastereoselective Intramolecular Cyclization.



2.3 Conclusion

In summary, we have demonstrated that 1,4-cobalt migration process can be exploited as an elementary step to achieve a cascade arylative cyclization reaction between a diarylzinc reagent and an acetylenic ester or ketone substrate for the synthesis of a benzo-fused carbocyclic product. The present study underlined the reactivity parallelism between low-valent organocobalt species and organorhodium(I)/iridium(I) species in terms of nucleophilic addition to carbonyl groups. In addition, the distinctive performance of the present cobalt catalyst on some of the substrates such as **6** and **8**, in comparison with the rhodium and iridium catalysts, illustrates the potential of cobalt catalysts to display unique and complementary reactivity and selectivity beyond that of rhodium(I) and iridium(I) catalysts. In light of the established synthetic versatility of organorhodium(I) species,[15]

further investigations into C−C bond forming reactions involving nucleophilic organocobalt species should be worthwhile.[16,17]

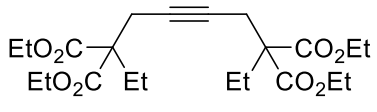
2.4 Experimental Section

General. All reactions dealing with air- or moisture-sensitive compound were performed by standard Schlenk techniques in oven-dried reaction vessels under nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on JEOL ECA-400 (400 MHz) or Bruker AV-400 (400 MHz) or Bruker AV-500 (500 MHz) NMR spectrometers. ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and $CHCl_3$ (77.0 ppm), respectively. Gas chromatographic (GC) analysis was performed on a Shimadzu GC-2010 system equipped with an FID detector and a capillary column, DB-5 (Agilent J&W, 0.25 mm i.d. x 30 m, 0.25 μm film thickness). High-resolution mass spectra (HRMS) were obtained with a Q-Tof Premier LC HR mass spectrometer.

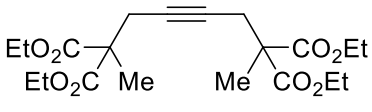
Materials. Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. Anhydrous $CoCl_2$ (97%) was purchased from Alfa Aesar and was used as received. THF was distilled over Na/benzophenone. Grignard reagents were prepared from the corresponding halides and magnesium turnings in anhydrous THF and titrated before use.

Preparation of Starting Materials

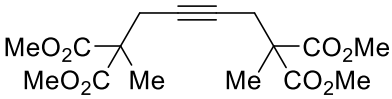
Preparation of acetylenic tetraesters: Acetylenic tetraesters **2a**–**2d** were prepared from 1,4-dibromo-2-butyne and the corresponding malonic esters according to the literature procedure.[18] **2b** and **2c** are known.



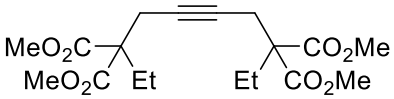
2a



2b



2c

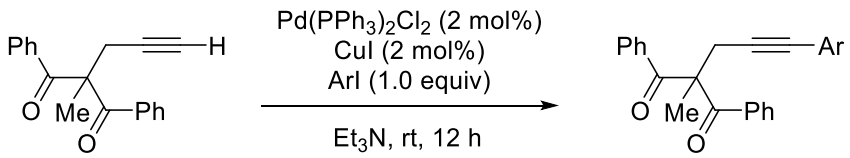


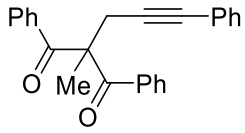
2d

tetraethyl dec-5-yne-3,3,8,8-tetracarboxylate (2a): Column chromatography (Ethyl acetate/hexane = 1/50) of the crude product afforded the title compound as colorless oil (2.90 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (q, *J* = 7.1 Hz, 8H), 2.01 (q, *J* = 7.5 Hz, 4H), 1.20 (t, *J* = 7.1 Hz, 12H), 0.78 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 77.6, 61.4, 57.5, 24.9, 22.4, 14.1, 8.4; HRMS (ESI) Calcd for $C_{22}H_{35}O_8$ $[M + H]^+$ 427.2332, found 427.2339.

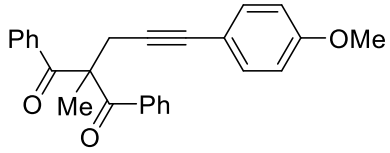
tetramethyl dec-5-yne-3,3,8,8-tetracarboxylate (2d): Column chromatography (Ethyl acetate/hexane = 1/50) of the crude product afforded the title compound as colorless oil (2.41 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 12H), 2.72 (s, 4H), 2.00 (q, *J* = 7.6 Hz, 4H), 0.77 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 77.6, 57.6, 52.6, 25.1, 22.5, 8.4; HRMS (ESI) Calcd for $C_{18}H_{27}O_8$ $[M + H]^+$ 371.1706, found 371.1703.

Preparation of homopropargyl diketone substrates bearing aryl substituents: To a triethylamine (3 mL) solution of 2-methyl-1,3-diphenyl-2-(prop-2-yn-1-yl)propane-1,3-dione[19] (4.60 mmol) and aryl iodide (4.60 mmol) was added a triethylamine (5 mL) solution of $PdCl_2(PPh_3)_2$ (63.0 mg, 0.09 mmol) and CuI (17.1 mg, 0.09 mmol). The reaction mixture was stirred at room temperature for 12 h, filtered through a pad of silica gel, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography to afford the desired arylated product.

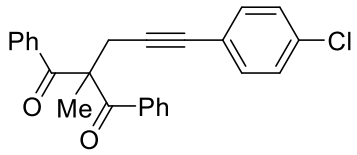




2-methyl-1,3-diphenyl-2-(3-phenylprop-2-yn-1-yl)propane-1,3-dione (6a): Column chromatography (hexane/EtOAc/CH_2Cl_2 = 7/1/1) to give **6a** as white solid (1.21 g, 75%); m.p. 75-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.4 Hz, 4H), 7.47 (t, *J* = 7.4 Hz, 2H), 7.39 – 7.30 (m, 6H), 7.29 – 7.25 (m, 3H), 3.29 (s, 2H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.6, 136.0, 133.3, 131.7, 129.1, 128.9, 128.3, 128.0, 123.4, 84.9, 84.7, 63.4, 29.1, 22.9; HRMS (ESI) Calcd for $C_{25}H_{21}O_2$ $[M + H]^+$ 353.1542, found 353.1539.

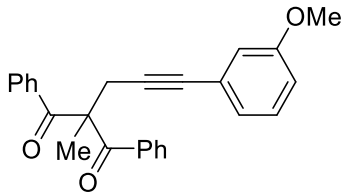


2-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-2-methyl-1,3-diphenylpropane-1,3-dione (6b): Column chromatography (hexane/EtOAc/CH_2Cl_2 = 7/1/1) to give **6b** as white solid (1.27 g, 72%); m.p. 78-79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 4H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.7 Hz, 4H), 7.26 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 3.78 (s, 3H), 3.27 (s, 2H), 1.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.6, 159.4, 136.0, 133.2, 133.1, 129.1, 128.8, 115.6, 113.9, 84.5, 83.2, 63.4, 55.3, 29.1, 22.9; HRMS (ESI) Calcd for $C_{26}H_{23}O_3$ $[M + H]^+$ 383.1647, found 383.1651.

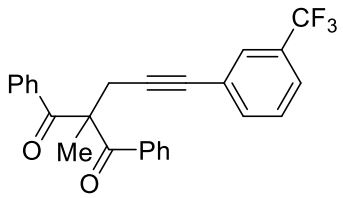


2-(3-(4-chlorophenyl)prop-2-yn-1-yl)-2-methyl-1,3-diphenylpropane-1,3-dione (6c): Column chromatography (hexane/EtOAc/CH_2Cl_2 = 7/1/1) to give **6c** as light yellow solid (1.24 g, 70%); m.p. 77-81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.7 Hz, 4H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 4H), 7.25 – 7.17 (m, 4H), 3.28 (s, 2H), 1.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.4, 135.9, 134.0, 133.3, 132.9, 129.1, 128.9, 128.6, 121.9,

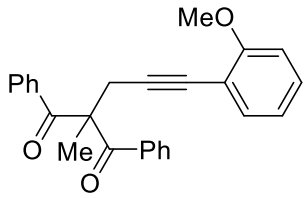
86.0, 83.7, 63.2, 29.0, 22.9; HRMS (ESI) Calcd for $C_{25}H_{20}ClO_2$ $[M + H]^+$ 387.1152, found 387.1148.



2-(3-(3-methoxyphenyl)prop-2-yn-1-yl)-2-methyl-1,3-diphenylpropane-1,3-dione (6d): Column chromatography (hexane/EtOAc/CH_2Cl_2 = 7/1/1) to give **6d** as white solid (1.34 g, 76%); m.p. 74-79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.3 Hz, 4H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.7 Hz, 4H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.88 – 6.78 (m, 2H), 3.77 (s, 3H), 3.29 (s, 2H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.5, 159.3, 136.0, 133.2, 129.3, 129.1, 128.8, 124.4, 124.3, 116.6, 114.6, 84.8, 84.6, 63.3, 55.3, 29.0, 22.9; HRMS (ESI) Calcd for $C_{26}H_{23}O_3$ $[M + H]^+$ 383.1647, found 383.1641.

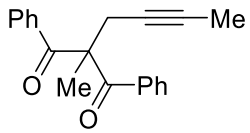


2-methyl-1,3-diphenyl-2-(3-(3-(trifluoromethyl)phenyl)prop-2-yn-1-yl)propane-1,3-dione (6e): Column chromatography (hexane/EtOAc/CH_2Cl_2 = 8/1/1) to give **6e** as white solid (1.24 g, 64%); m.p. 68-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.6 Hz, 4H), 7.56 (s, 1H), 7.49 – 7.42 (m, 4H), 7.38 – 7.30 (m, 5H), 3.32 (s, 2H), 1.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 135.8, 134.8, 133.3, 130.9 (q, $^2J_{C\text{-}F}$ = 32.7 Hz), 129.9, 129.1, 128.9, 128.8, 128.54, 128.50, 128.4 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.6 (q, $^3J_{C\text{-}F}$ = 3.9 Hz), 124.3, 123.8 (q, $^1J_{C\text{-}F}$ = 273.5 Hz), 86.9, 83.3, 63.2, 29.0, 22.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.2; HRMS (ESI) Calcd for $C_{26}H_{20}F_3O_2$ $[M + H]^+$ 421.1415, found 421.1412.

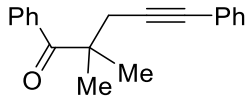


2-(3-(2-methoxyphenyl)prop-2-yn-1-yl)-2-methyl-1,3-diphenylpropane-1,3-dione (6f): Column chromatography (hexane/EtOAc/CH_2Cl_2 = 7/1/1) to give **6f** as white solid (1.28 g, 73%); m.p. 69-70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.9 Hz, 4H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.37 – 7.29 (m, 5H), 7.27 – 7.21 (m, 1H), 6.87 (t, *J* = 7.9 Hz, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 3.83 (s, 3H), 3.34 (s, 2H), 1.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.6, 160.1, 136.1, 133.9, 133.1, 129.4, 129.1, 128.8, 120.5, 112.7, 110.7, 88.9, 81.0, 63.5, 55.8, 29.3, 22.8; HRMS (ESI) Calcd for $C_{26}H_{23}O_3$ $[M + H]^+$ 383.1647, found 383.1643.

Preparation of other homopropargylic ketone substrates: Methyl-substituted homopropargylic diketone **6g**, homopropargylic ketoester **8** (known compound), and homopropargylic monoketone **11** were prepared following procedures described in the literature.[20]



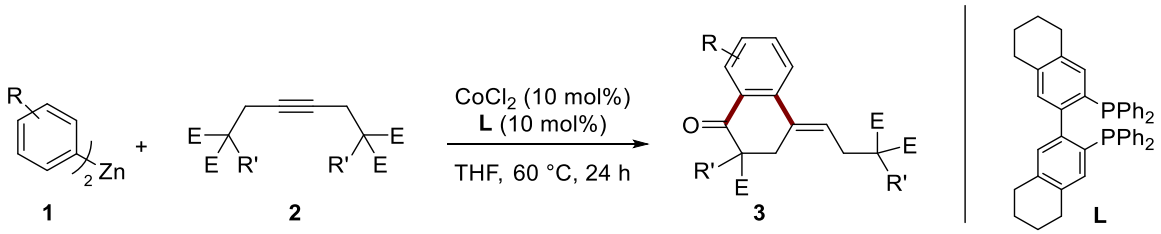
2-(but-2-yn-1-yl)-2-methyl-1,3-diphenylpropane-1,3-dione (6g): Column chromatography (hexane/EtOAc/CH_2Cl_2 = 7/1/1) to give **6g** as colorless oil (2.03 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.4 Hz, 4H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 4H), 3.04 (q, *J* = 2.6 Hz, 2H), 1.75 (s, 3H), 1.70 (t, *J* = 2.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.7, 136.0, 133.1, 129.0, 128.7, 80.0, 73.7, 63.1, 28.4, 22.7, 3.6; HRMS (ESI) Calcd for $C_{20}H_{19}O_2$ $[M + H]^+$ 291.1385, found 291.1382.



2,2-dimethyl-1,5-diphenylpent-4-yn-1-one (11): Column chromatography (hexane/EtOAc = 6/1) to give **11** as colorless oil (1.70 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$)

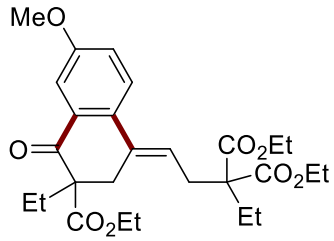
δ 7.68 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.46 (d, *J* = 7.2 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.38 – 7.34 (m, 2H), 7.29 – 7.26 (m, 3H), 2.80 (s, 2H), 1.50 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.1, 139.0, 131.7, 131.0, 128.33, 128.27, 127.9, 127.6, 123.8, 87.1, 83.2, 48.0, 31.2, 25.6; HRMS (ESI) Calcd for $C_{19}H_{19}O$ $[M + H]^+$ 263.1436, found 263.1437.

Cobalt-Catalyzed Arylative Cyclization Involving 1,4-Cobalt Migration

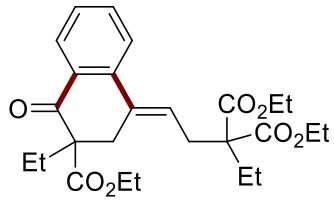


Typical procedure A: In a 10 mL Schlenk tube equipped with a stirrer bar was placed $ZnCl_2$•TMEDA (75.6 mg, 0.30 mmol). The Schlenk tube was submerged in an ice bath for 5 min, followed by dropwise addition of a THF solution of an aryl Grignard reagent (typically 0.8–1.0M, 0.60 mmol). After stirring for 1 h at 0 °C, 3,3'-bis(diphenylphosphino)-5,5',6,6',7,7',8,8'-octahydro[2,2']binaphthalene chloroform adduct (**L**, 13.8 mg, 0.020 mmol) and $CoCl_2$ (2.6 mg, 0.020 mmol) were added. After additional stirring for 5 min, acetylenic tetraester **2** (0.20 mmol) was added. The reaction mixture was stirred at 60 °C for 24 h, allowed to cool to room temperature, and quenched with saturated aqueous solution of NH_4Cl (1 mL). The resulting mixture was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography to afford the desired product. The *E*-stereochemistry of the C=C bond was confirmed for the product **3c**

by NOESY and assumed for other arylative cyclization products.

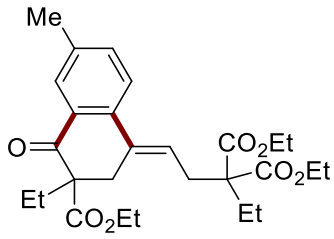


Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-6-methoxyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3a). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (76.2 mg, 78%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 2.9 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.06 (dd, *J* = 8.7, 2.9 Hz, 1H), 5.99 (t, *J* = 7.3 Hz, 1H), 4.29 – 4.16 (m, 4H), 4.15 – 4.01 (m, 2H), 3.84 (s, 3H), 3.25 (d, *J* = 14.1 Hz, 1H), 3.01 – 2.82 (m, 2H), 2.74 (d, *J* = 14.2 Hz, 1H), 2.05 – 1.90 (m, 4H), 1.25 (t, *J* = 7.1 Hz, 6H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.5, 171.6, 171.4, 159.6, 134.3, 132.5, 131.3, 125.6, 122.4, 121.8, 109.4, 61.42, 61.40, 61.36, 59.0, 58.3, 55.7, 33.8, 31.0, 26.9, 26.0, 14.27, 14.26, 14.2, 9.5, 8.7; HRMS (ESI) Calcd for $C_{27}H_{37}O_8$ $[M + H]^+$ 489.2488, found 489.2488.



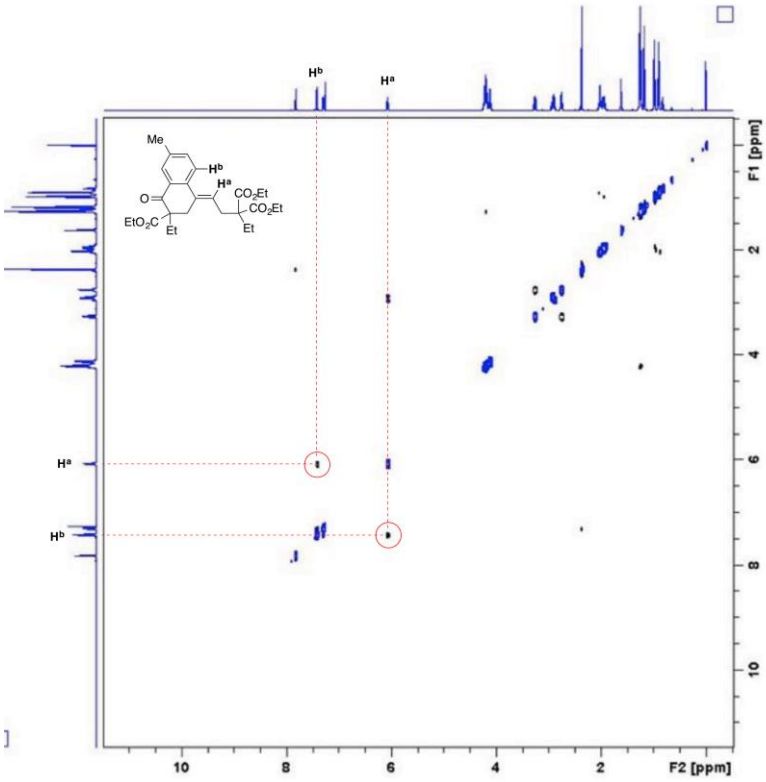
Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3b). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (70.6 mg, 77%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.60 – 7.46 (m, 2H), 7.42 – 7.28 (m, 1H), 6.12 (t, *J* = 7.4 Hz, 1H), 4.26 – 4.18 (m, 4H), 4.12 (d, *J* = 7.1 Hz, 2H), 3.28

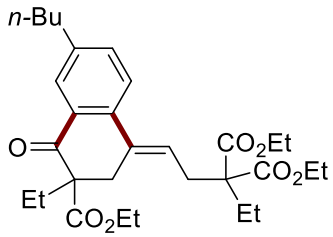
(d, *J* = 14.1 Hz, 1H), 3.04 – 2.84 (m, 2H), 2.75 (d, *J* = 14.1 Hz, 1H), 2.05 – 1.91 (m, 4H), 1.27 – 1.19 (m, 6H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.5, 171.6, 171.4, 141.1, 133.8, 133.0, 130.3, 128.1, 128.0, 124.0, 123.8, 61.5, 61.45, 61.4, 59.1, 58.2, 33.7, 31.1, 26.9, 26.0, 25.0, 14.3, 14.2, 9.5, 8.7; HRMS (ESI) Calcd for $C_{26}H_{35}O_7$ $[M + H]^+$ 459.2383, found 459.2388.



Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-6-methyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3c). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (68.0 mg, 72%). *E* geometry is arranged according to 2D-NOESY (Figure 2.2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 2.0 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.30 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.07 (t, *J* = 7.4 Hz, 1H), 4.26 – 4.17 (m, 4H), 4.15 – 4.04 (m, 2H), 3.26 (d, *J* = 14.1 Hz, 1H), 3.00 – 2.79 (m, 2H), 2.76 (d, *J* = 14.1 Hz, 1H), 2.36 (s, 3H), 2.04 – 1.89 (m, 4H), 1.29 – 1.22 (m, 6H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8, 171.7, 171.4, 138.5, 138.1, 134.8, 132.9, 130.1, 128.0, 124.0, 122.7, 61.45, 61.43, 61.3, 59.1, 58.2, 33.8, 31.0, 26.9, 26.0, 21.2, 14.3, 14.2, 9.5, 8.7; HRMS (ESI) Calcd for $C_{27}H_{37}O_7$ $[M + H]^+$ 473.2539, found 473.2533.

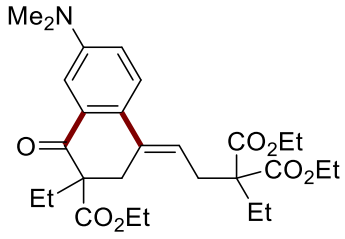
Figure 2.2. ^{1}H-^{1}H NOESY Spectrum of **3c**



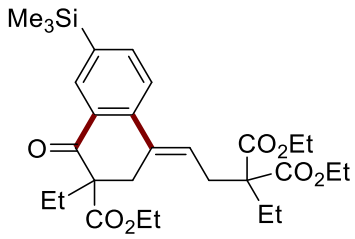


Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-6-butyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3d). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (77.1 mg, 75%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 1.9 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.30 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.07 (t, *J* = 7.4 Hz, 1H), 4.27 – 4.17 (m, 4H), 4.16 – 4.02 (m, 2H), 3.26 (d, *J* = 14.1 Hz, 1H), 2.98 – 2.82 (m, 2H), 2.76 (d, *J* = 14.1 Hz, 1H), 2.62 (t, *J* = 7.7 Hz, 2H), 2.10 – 1.87 (m, 4H), 1.61 – 1.54 (m, 2H), 1.34 (q, *J* = 7.4 Hz, 2H), 1.25 (d, *J* = 7.2 Hz, 6H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.94 – 0.85 (m, 6H); ^{13}C

NMR (101 MHz, $CDCl_3$) δ 195.7, 171.5, 171.3, 143.0, 138.5, 134.1, 132.8, 129.9, 127.3, 123.8, 122.5, 61.3, 61.25, 61.2, 59.0, 58.1, 35.1, 33.6, 33.3, 30.8, 26.7, 25.8, 22.3, 14.1, 14.0, 13.9, 9.4, 8.6; HRMS (ESI) Calcd for $C_{30}H_{43}O_7$ $[M + H]^+$ 515.3009, found 515.2999.

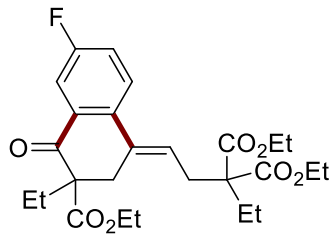


Diethyl (*E*)-2-(2-(6-(dimethylamino)-3-(ethoxycarbonyl)-3-ethyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3e). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (83.2 mg, 83%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.8 Hz, 1H), 7.27 (d, *J* = 2.9 Hz, 1H), 6.90 (dd, *J* = 8.8, 2.9 Hz, 1H), 5.90 (t, *J* = 7.4 Hz, 1H), 4.27 – 4.16 (m, 4H), 4.16 – 4.10 (m, 2H), 3.23 (d, *J* = 14.1 Hz, 1H), 2.98 (s, 6H), 2.89 (dd, *J* = 7.5, 4.2 Hz, 2H), 2.75 (d, *J* = 14.2 Hz, 1H), 2.03 – 1.89 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 6H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 171.7, 171.4, 132.6, 130.5, 124.9, 119.1, 118.4, 109.3, 61.2, 61.1, 59.0, 58.2, 40.4, 33.6, 30.7, 26.7, 25.7, 14.14, 14.1, 9.5, 8.6; HRMS (ESI) Calcd for $C_{28}H_{40}NO_7$ $[M + H]^+$ 502.2805, found 502.2801.

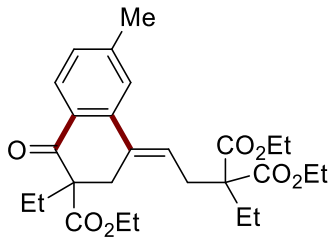


Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-6-(trimethylsilyl)-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3f). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude

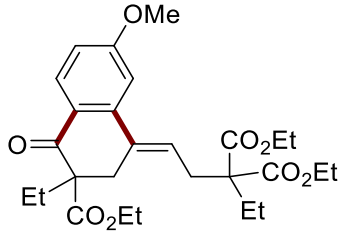
product afforded the title compound as colourless oil (63.6 mg, 60%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 1.3 Hz, 1H), 7.63 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 6.14 (t, *J* = 7.4 Hz, 1H), 4.28 – 4.17 (m, 4H), 4.15 – 4.07 (m, 2H), 3.27 (d, *J* = 14.1 Hz, 1H), 2.98 – 2.87 (m, 2H), 2.77 (d, *J* = 14.0 Hz, 1H), 2.10 – 1.88 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 6H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H), 0.27 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 171.7, 171.4, 141.3, 140.9, 138.6, 133.2, 133.1, 129.2, 123.8, 123.2, 61.5, 61.4, 59.2, 58.2, 33.6, 31.1, 26.9, 26.0, 14.3, 14.2, 9.5, 8.7, -1.1; HRMS (ESI) Calcd for $C_{29}H_{43}O_7Si$ $[M + H]^+$ 531.2778, found 531.2786.



Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-6-fluoro-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3g). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/10) of the crude product afforded the title compound as colourless oil (32.4 mg, 34%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.51 (dd, *J* = 8.8, 5.0 Hz, 1H), 7.24 – 7.14 (m, 1H), 6.05 (t, *J* = 7.4 Hz, 1H), 4.26 – 4.16 (m, 4H), 4.16 – 4.06 (m, 2H), 3.28 (d, *J* = 14.2 Hz, 1H), 2.99 – 2.84 (m, 2H), 2.75 (d, *J* = 14.1 Hz, 1H), 2.06 – 1.91 (m, 4H), 1.30 – 1.22 (m, 6H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.5, 171.4, 170.5, 162.6 (d, $J_{C\text{-}F}$ = 250.2 Hz), 137.4, 132.1, 128.6 (d, $J_{C\text{-}F}$ = 12.2 Hz), 126.3 (d, $J_{C\text{-}F}$ = 7.3 Hz), 123.8, 121.3 (d, $J_{C\text{-}F}$ = 22.8 Hz), 113.7 (d, $J_{C\text{-}F}$ = 22.3 Hz), 61.5, 61.48, 58.9, 58.2, 57.6, 33.9, 31.1, 26.9, 26.1, 14.3, 14.2, 9.5, 8.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −105.2; HRMS (ESI) Calcd for $C_{26}H_{34}FO_7$ $[M + H]^+$ 477.2289, found 477.2287.

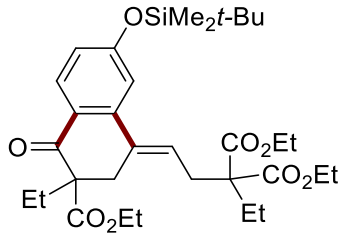


Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-7-methyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3h). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (60.4 mg, 64%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 1.6 Hz, 1H), 7.15 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.10 (t, *J* = 7.4 Hz, 1H), 4.30 – 4.17 (m, 4H), 4.17 – 4.06 (m, 2H), 3.26 (d, *J* = 14.1 Hz, 1H), 3.03 – 2.84 (m, 2H), 2.76 (d, *J* = 14.1 Hz, 1H), 2.39 (s, 3H), 2.03 (q, *J* = 7.3 Hz, 2H), 1.99 – 1.87 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 6H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 171.7, 171.4, 144.6, 141.1, 133.3, 129.3, 128.2, 128.1, 124.2, 123.3, 61.48, 61.46, 61.3, 59.1, 58.2, 33.8, 31.0, 26.9, 26.0, 22.1, 14.3, 14.2, 9.5, 8.8; HRMS (ESI) Calcd for $C_{27}H_{37}O_7$ $[M + H]^+$ 473.2539, found 473.2541.

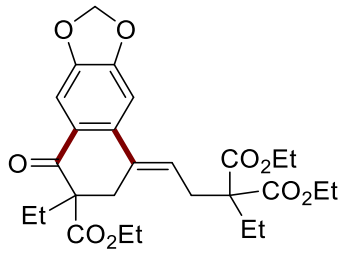


Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-7-methoxyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3i). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (72.3 mg, 74%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.7 Hz, 1H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.87 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.08 (t, *J* = 7.4 Hz, 1H), 4.27 – 4.15 (m,

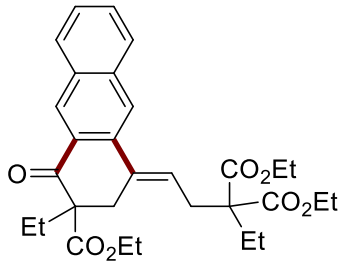
4H), 4.16 – 4.08 (m, 2H), 3.86 (s, 3H), 3.25 (d, *J* = 14.1 Hz, 1H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.75 (d, *J* = 14.0 Hz, 1H), 2.10 – 1.86 (m, 4H), 1.26 (td, *J* = 7.1, 1.2 Hz, 6H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 171.8, 171.4, 163.9, 143.3, 133.3, 130.6, 124.2, 123.8, 114.3, 108.3, 61.45, 61.43, 61.3, 58.9, 58.2, 55.6, 33.8, 31.0, 27.0, 26.0, 14.3, 14.2, 9.5, 8.7; HRMS (ESI) Calcd for $C_{27}H_{37}O_8$ $[M + H]^+$ 489.2488, found 489.2484.



Diethyl (*E*)-2-(2-(7-((*tert*-butyldimethylsilyl)oxy)-3-(ethoxycarbonyl)-3-ethyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3j). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (85.9 mg, 73%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.6 Hz, 1H), 6.88 (d, *J* = 2.3 Hz, 1H), 6.79 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.02 (t, *J* = 7.4 Hz, 1H), 4.24 – 4.17 (m, 4H), 4.16 – 4.05 (m, 2H), 3.25 (d, *J* = 14.0 Hz, 1H), 2.97 – 2.83 (m, 2H), 2.75 (d, *J* = 14.0 Hz, 1H), 2.10 – 1.85 (m, 4H), 1.26 (td, *J* = 7.1, 1.5 Hz, 6H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.99 (s, 9H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H), 0.25 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.4, 171.8, 171.4, 160.8, 143.4, 133.2, 130.5, 124.4, 123.7, 120.4, 114.1, 61.4, 61.3, 59.0, 58.3, 33.8, 31.0, 28.0, 27.0, 26.1, 25.8, 18.4, 14.3, 14.2, 9.6, 8.8, -4.1; HRMS (ESI) Calcd for $C_{32}H_{49}O_8Si$ $[M + H]^+$ 589.3197, found 589.3189.

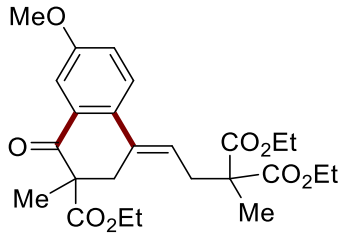


Diethyl (*E*)-2-(2-(7-(ethoxycarbonyl)-7-ethyl-8-oxo-7,8-dihydronaphtho[2,3-d][1,3]dioxol-5(6*H*)-ylidene)ethyl)-2-ethylmalonate (3k). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (62.3 mg, 62%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 6.91 (s, 1H), 6.01 (s, 2H), 5.95 (t, *J* = 7.4 Hz, 1H), 4.25 – 4.16 (m, 4H), 4.16 – 4.08 (m, 2H), 3.23 (d, *J* = 14.0 Hz, 1H), 2.96 – 2.82 (m, 2H), 2.72 (d, *J* = 14.0 Hz, 1H), 2.04 – 1.87 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 6H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 171.7, 171.4, 152.7, 148.3, 138.4, 133.1, 125.7, 122.9, 106.7, 103.3, 102.0, 61.48, 61.44, 61.4, 58.8, 58.2, 33.9, 31.0, 27.0, 26.0, 14.3, 14.2, 9.5, 8.7; HRMS (ESI) Calcd for $C_{27}H_{35}O_9$ $[M + H]^+$ 503.2281, found 503.2278.

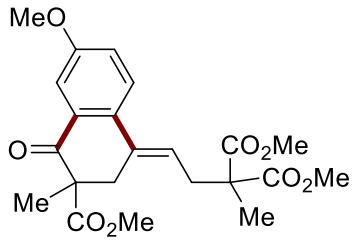


Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-4-oxo-3,4-dihydroanthracen-1(2*H*)-ylidene)ethyl)-2-ethylmalonate (3l). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (53.9 mg, 53%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.94 – 7.82 (m, 3H), 7.61 – 7.53 (m, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 6.24 (t, *J* = 7.4 Hz, 1H), 4.31 – 4.20 (m, 4H), 4.17 – 4.08 (m, 2H), 3.34 (d, *J* = 14.0 Hz, 1H), 3.04 – 2.89 (m, 2H), 2.84 (d, *J* = 14.2 Hz, 1H), 2.14 – 1.97 (m, 4H), 1.28 (t, *J* = 7.1, 2.0 Hz, 6H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.7, 171.8, 171.5, 137.0, 136.0, 133.4, 132.5, 129.9, 129.8, 128.9, 128.8, 128.0, 126.7, 123.1, 122.7, 61.49, 61.48, 61.4, 59.6, 58.3, 33.9,

31.1, 27.0, 26.1, 14.3, 14.2, 9.5, 8.8; HRMS (ESI) Calcd for $C_{30}H_{37}O_7$ $[M + H]^+$ 509.2539, found 509.2537.

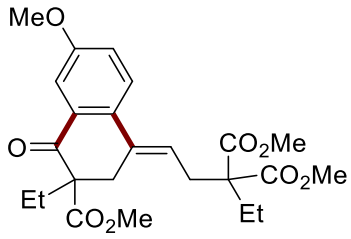


Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-6-methoxy-3-methyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-methylmalonate (3m). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (66.3 mg, 72%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 2.8 Hz, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 7.08 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.03 (t, *J* = 7.4 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 4H), 4.15 – 4.07 (m, 2H), 3.85 (s, 3H), 3.31 (d, *J* = 14.0 Hz, 1H), 2.97 – 2.76 (m, 2H), 2.67 (d, *J* = 14.1 Hz, 1H), 1.46 (s, 6H), 1.26 (t, *J* = 7.1 Hz, 6H), 1.17 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.1, 172.5, 172.0, 159.7, 134.6, 132.8, 130.8, 125.7, 122.5, 122.2, 109.4, 61.6, 61.5, 55.7, 55.0, 53.9, 37.1, 34.4, 20.4, 20.3, 14.2, 14.1; HRMS (ESI) Calcd for $C_{25}H_{33}O_8$ $[M + H]^+$ 461.2175, found 461.2173.

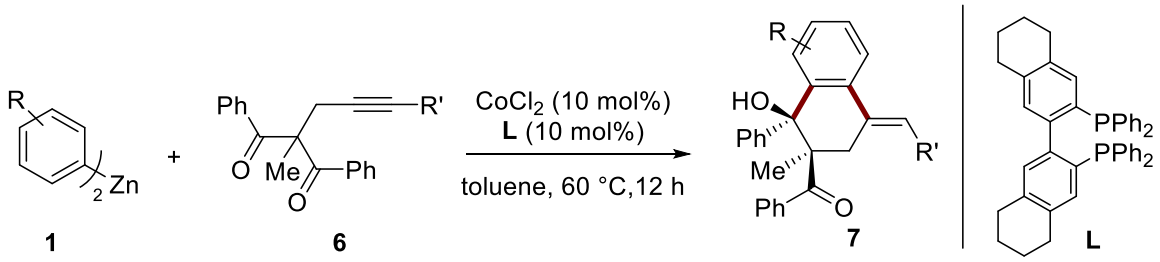


Dimethyl (*E*)-2-(2-(6-methoxy-3-(methoxycarbonyl)-3-methyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)-2-methylmalonate (3n). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (62.7 mg, 75%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 2.8 Hz, 1H), 7.46

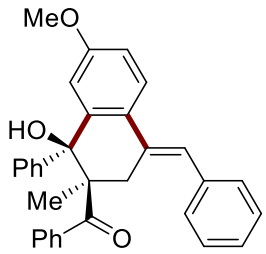
(d, *J* = 8.7 Hz, 1H), 7.09 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.01 (t, *J* = 7.5 Hz, 1H), 3.85 (s, 3H), 3.75 (s, 3H), 3.66 (s, 3H), 3.31 (d, *J* = 14.0 Hz, 1H), 2.98 – 2.77 (m, 2H), 2.67 (d, *J* = 14.0 Hz, 1H), 1.47 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 173.0, 172.4, 172.4, 159.7, 134.6, 132.8, 130.7, 125.8, 122.6, 122.1, 109.5, 55.7, 55.1, 53.9, 52.8, 52.7, 37.2, 34.5, 22.8, 20.6, 20.4; HRMS (ESI) Calcd for $C_{22}H_{27}O_8$ $[M + H]^+$ 419.1706, found 419.1708.



Dimethyl (*E*)-2-ethyl-2-(2-(3-ethyl-6-methoxy-3-(methoxycarbonyl)-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethyl)malonate (3o). Prepared according to typical procedure A. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (66.0 mg, 74%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 2.9 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 7.06 (dd, *J* = 8.7, 2.9 Hz, 1H), 5.96 (t, *J* = 7.4 Hz, 1H), 3.83 (s, 3H), 3.73 (s, 6H), 3.65 (s, 3H), 3.24 (d, *J* = 14.1 Hz, 1H), 2.90 (dd, *J* = 7.4, 5.1 Hz, 2H), 2.74 (d, *J* = 14.1 Hz, 1H), 2.07 – 1.86 (m, 4H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 172.1, 171.8, 159.6, 134.3, 132.6, 131.1, 125.7, 122.5, 121.7, 109.4, 59.1, 58.4, 55.6, 52.6, 52.5, 33.8, 31.1, 27.0, 26.2, 9.5, 8.8; HRMS (ESI) Calcd for $C_{24}H_{31}O_8$ $[M + H]^+$ 447.2019, found 447.2018.

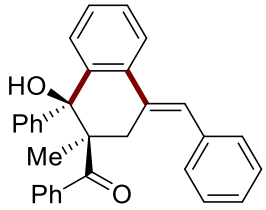


Typical procedure B: In a 10 mL Schlenk tube was placed $ZnCl_2$•TMEDA (75.6 mg, 0.30 mmol). The Schlenk tube was submerged in an ice bath for 5 min, followed by dropwise addition of a THF solution of an aryl Grignard reagent (typically 0.8–1.0 M, 0.60 mmol). After stirring for 1 h at 0 °C, the mixture was allowed to room temperature. The THF solvent was evaporated under reduced pressure, followed by the addition of toluene (0.5 mL) to afford a toluene solution of the arylzinc reagent. To this solution were added 3,3'-bis(diphenylphosphino)-5,5',6,6',7,7',8,8'-octahydro[2,2']binaphthalene chloroform adduct (**L**, 13.8 mg, 0.020 mmol) and $CoCl_2$ (2.6 mg, 0.020 mmol). After stirring for 5 min, a homopropargylic diketone substrate **6** (0.20 mmol) was added. The reaction mixture was stirred at 60 °C for 12 h, allowed to cool to room temperature, and quenched with saturated aqueous solution of NH_4Cl (1 mL). The resulting mixture was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography to afford the desired product. The *E*-stereochemistry of the C=C bond and the diastereochemistry were confirmed for the product **7k** by X-ray crystallographic analysis, and assumed for other arylative cyclization products.

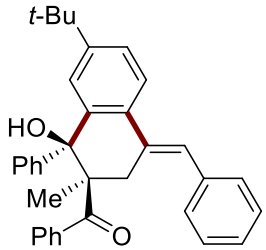


4-((*E*)-benzylidene)-1-hydroxy-7-methoxy-2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7a): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as white solid (50.6 mg, 55%); m.p. 84–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.8 Hz, 1H), 7.38 (d, *J* = 6.9 Hz, 2H), 7.33 – 7.23 (m, 5H), 7.23 – 7.12 (m, 5H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.96 – 6.84 (m, 4H), 5.98 (s, 1H), 3.44 (d, *J*

= 16.8 Hz, 1H), 2.68 (dd, *J* = 16.9, 2.8 Hz, 1H), 1.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.0, 160.4, 146.3, 142.5, 139.1, 137.4, 132.5, 130.9, 129.2, 129.17, 128.0, 127.8, 127.5, 127.4, 127.3, 127.0, 126.5, 124.4, 123.7, 115.4, 110.4, 80.8, 55.4, 55.1, 36.6, 20.2; HRMS (ESI) Calcd for $C_{32}H_{29}O_3$ $[M + H]^+$ 461.2117, found 461.2110.

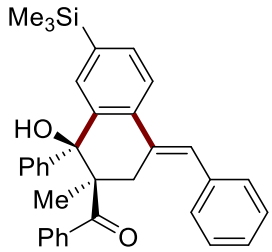


4-((*E*)-benzylidene)-1-hydroxy -2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7b): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as white solid (41.3mg, 48%); m.p. 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.67 (m, 2H), 7.37 – 7.33 (m, 2H), 7.32 – 7.25 (m, 5H), 7.25 – 7.16 (m, 6H), 7.09 – 7.03 (m, 3H), 6.92 (dd, *J* = 8.0, 1.6 Hz, 2H), 5.89 (s, 1H), 3.49 (d, *J* = 17.0 Hz, 1H), 2.75 (dd, *J* = 16.7, 2.8 Hz, 1H), 1.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.6, 144.7, 142.9, 139.0, 137.2, 134.5, 132.9, 131.0, 129.3, 129.2, 129.0, 128.1, 127.8, 127.5, 127.4, 127.2, 127.1, 126.8, 125.9, 122.8, 80.7, 55.1, 36.5, 20.2; HRMS (ESI) Calcd for $C_{31}H_{27}O_2$ $[M + H]^+$ 431.2011, found 431.2010.

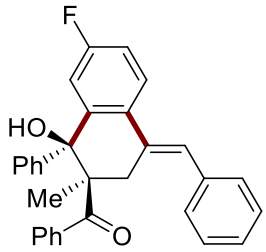


4-((*E*)-benzylidene)-1-hydroxy-7-(*tert*-butyl) -2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7c): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as white solid (59.3 mg, 61%); m.p. 80–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 2.2 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.39 – 7.35 (m, 2H),

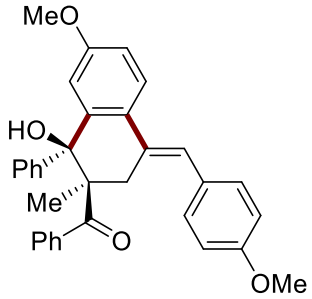
7.32 (dd, *J* = 8.6, 2.2 Hz, 2H), 7.31 – 7.23 (m, 3H), 7.22 – 7.15 (m, 5H), 7.09 – 7.04 (m, 3H), 6.96 – 6.91 (m, 2H), 5.88 (s, 1H), 3.43 (dd, *J* = 16.9, 1.1 Hz, 1H), 2.67 (dd, *J* = 16.9, 2.8 Hz, 1H), 1.46 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.1, 152.0, 144.1, 142.9, 139.3, 137.4, 133.0, 132.0, 130.8, 129.3, 129.2, 128.1, 127.8, 127.3, 127.1, 127.0, 126.7, 124.8, 124.8, 123.9, 122.6, 80.9, 55.2, 36.5, 35.0, 31.4, 20.3; HRMS (ESI) Calcd for $C_{35}H_{35}O_2$ $[M + H]^+$ 487.2637, found 487.2634.



4-((*E*)-benzylidene)-1-hydroxy -2-methyl-1-phenyl-7-(trimethylsilyl)-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7d): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as white solid (50.2 mg, 50%); m.p. 87–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 1.3 Hz, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.45 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.32 – 7.23 (m, 5H), 7.22 – 7.17 (m, 4H), 7.11 (d, *J* = 2.6 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 2H), 6.96 – 6.90 (m, 2H), 5.88 (s, 1H), 3.45 (dd, *J* = 16.9, 1.0 Hz, 1H), 2.69 (dd, *J* = 16.9, 2.8 Hz, 1H), 1.47 (s, 3H), 0.25 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.0, 143.5, 142.8, 141.3, 139.2, 137.3, 135.0, 133.2, 132.4, 132.3, 130.9, 129.3, 129.2, 128.1, 127.8, 127.3, 127.2, 127.0, 126.8, 126.0, 121.8, 80.8, 55.1, 36.5, 20.3, -0.9; HRMS (ESI) Calcd for $C_{34}H_{35}O_2Si$ $[M + H]^+$ 503.2406, found 503.2402.

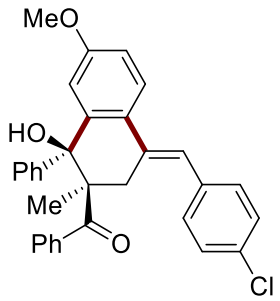


4-((*E*)-benzylidene)-7-fluoro-1-hydroxy -2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7e): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as white solid (47.5 mg, 53%); m.p. 73–76 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.72 (dd, *J* = 8.9, 5.4 Hz, 1H), 7.43 (dd, *J* = 10.0, 2.8 Hz, 1H), 7.36 – 7.33 (m, 2H), 7.32 – 7.28 (m, 2H), 7.27 – 7.25 (m, 2H), 7.24 – 7.18 (m, 4H), 7.08 – 7.04 (m, 2H), 7.02 – 6.97 (m, 2H), 6.91 – 6.88 (m, 2H), 5.94 (s, 1H), 3.49 (d, *J* = 16.8 Hz, 1H), 2.74 (dd, *J* = 16.6, 2.9 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.3, 163.5 (d, $^{1}J_{C\text{-}F}$ = 247.3 Hz), 142.3, 138.7, 137.0, 133.1, 131.9, 131.2, 130.8, 129.21, 129.19, 129.1, 128.7, 128.1, 127.9, 127.5, 127.2, 126.9, 125.7 (d, $^{4}J_{C\text{-}F}$ = 2.4 Hz), 124.9 (d, $^{3}J_{C\text{-}F}$ = 7.8 Hz), 115.2 (d, $^{2}J_{C\text{-}F}$ = 22.1 Hz), 114.0 (d, $^{2}J_{C\text{-}F}$ = 22.5 Hz), 80.5, 55.0, 36.4, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.2; HRMS (ESI) Calcd for $C_{31}H_{26}FO_2$ $[M + H]^+$ 449.1917, found 449.1914.

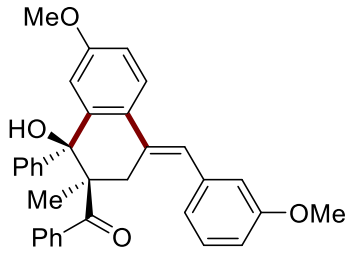


(1-hydroxy-7-methoxy-4-((*E*)-4-methoxybenzylidene)-2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7f): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/30) of the crude product afforded the title compound as white solid (41.2 mg, 42%); m.p. 82–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.9 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.31 – 7.23 (m, 5H), 7.22 – 7.18 (m, 2H), 7.07 (t, *J* = 7.7 Hz, 2H), 6.89 – 6.78 (m, 4H), 6.77 – 6.63 (m, 2H), 5.96 (s, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.42 (d, *J* = 16.8 Hz, 1H), 2.65 (dd, *J* = 16.8, 2.7 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.2, 160.2, 158.3, 146.0, 142.6, 139.2, 131.2,

130.8, 130.4, 130.1, 129.2, 127.8, 127.76, 127.4, 127.3, 127.0, 124.3, 123.4, 115.3, 113.5, 110.4, 80.8, 55.44, 55.4, 55.1, 36.6, 20.2; HRMS (ESI) Calcd for $C_{33}H_{31}O_4$ $[M + H]^+$ 491.2222, found 491.2219.

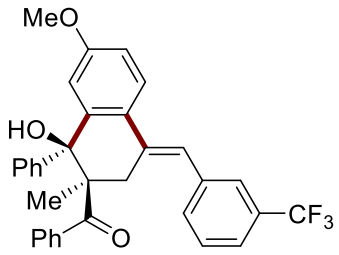


(1-hydroxy-7-methoxy-4-((*E*)-4-chlorobenzylidene)-2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7g): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/30) of the crude product afforded the title compound as light yellow solid (39.5 mg, 40%); m.p. 86–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.33 (m, 2H), 7.32 – 7.23 (m, 5H), 7.23 – 7.19 (m, 2H), 7.17 – 7.12 (m, 2H), 7.08 (dd, *J* = 8.3, 7.3 Hz, 2H), 6.85 (dd, *J* = 8.9, 2.8 Hz, 1H), 6.83 (d, *J* = 2.6 Hz, 1H), 6.80 – 6.71 (m, 2H), 6.00 (s, 1H), 3.79 (s, 3H), 3.36 (d, *J* = 16.7 Hz, 1H), 2.66 (dd, *J* = 16.7, 2.8 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.7, 160.6, 146.4, 142.4, 139.0, 135.9, 133.2, 132.2, 131.1, 130.4, 129.2, 128.2, 127.8, 127.4, 127.36, 127.2, 127.1, 124.4, 122.3, 115.4, 110.5, 110.1, 80.9, 55.5, 54.9, 36.6, 20.1; HRMS (ESI) Calcd for $C_{32}H_{28}ClO_3$ $[M + H]^+$ 495.1727, found 495.1722.

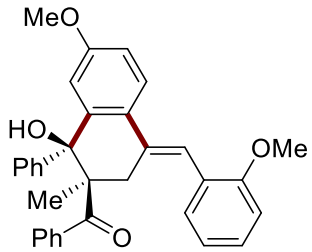


(1-hydroxy-7-methoxy-4-((*E*)-3-methoxybenzylidene)-2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7h): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/30) of the crude product

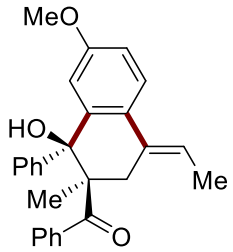
afforded the title compound as white solid (51.1 mg, 52%); m.p. 78–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.9 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.31 – 7.18 (m, 7H), 7.13 – 7.04 (m, 3H), 6.87 (d, *J* = 2.6 Hz, 1H), 6.84 (dd, *J* = 8.9, 2.8 Hz, 1H), 6.70 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.50 (d, *J* = 7.6 Hz, 1H), 6.38 (t, *J* = 2.0 Hz, 1H), 5.97 (s, 1H), 3.78 (s, 3H), 3.73 (s, 3H), 3.46 (d, *J* = 16.7 Hz, 1H), 2.66 (dd, *J* = 16.8, 2.8 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.8, 160.4, 159.3, 146.4, 142.5, 139.0, 138.8, 132.9, 130.9, 129.2, 129.0, 127.8, 127.5, 127.4, 127.3, 127.1, 124.5, 123.6, 121.7, 115.4, 114.8, 112.0, 110.4, 80.8, 55.4, 55.3, 55.1, 36.6, 20.2; HRMS (ESI) Calcd for $C_{33}H_{31}O_4$ $[M + H]^+$ 491.2222, found 491.2217.



1-hydroxy-7-methoxy-2-methyl-1-phenyl-4-((*E*)-3-(trifluoromethyl)benzylidene)-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7i): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/25) of the crude product afforded the title compound as white solid (48.6 mg, 46%); m.p. 73–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.9 Hz, 1H), 7.42 – 7.34 (m, 3H), 7.34 – 7.22 (m, 7H), 7.20 (s, 1H), 7.10 – 7.01 (m, 3H), 6.97 (s, 1H), 6.87 (dd, *J* = 9.0, 2.8 Hz, 2H), 6.06 (s, 1H), 3.79 (s, 3H), 3.35 (d, *J* = 16.5 Hz, 1H), 2.70 (dd, *J* = 16.6, 2.8 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.4, 160.8, 146.6, 142.5, 138.8, 138.1, 134.2, 132.1, 131.3, 130.4 (q, $^{2}J_{C\text{-}F}$ = 32.1 Hz), 129.3, 128.4, 127.8, 127.5, 127.4, 127.1, 126.9, 126.0 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 124.5, 123.1 (q, $^{3}J_{C\text{-}F}$ = 3.4 Hz), 122.1, 115.5, 110.6, 106.0 (q, $^{1}J_{C\text{-}F}$ = 276.5 Hz), 80.9, 55.5, 54.8, 36.5, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.4; HRMS (ESI) Calcd for $C_{33}H_{28}F_3O_3$ $[M + H]^+$ 529.1991, found 529.1984.



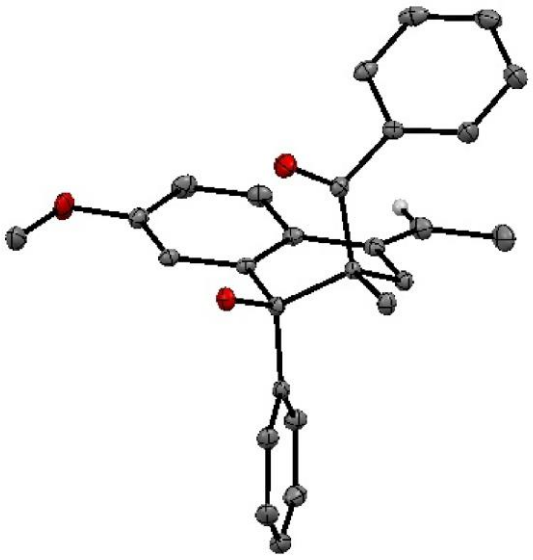
(1-hydroxy-7-methoxy-4-((*E*)-2-methoxybenzylidene)-2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7j): Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/25) of the crude product afforded the title compound as white solid (47.1 mg, 48%); m.p. 74–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.8 Hz, 1H), 7.39 (d, *J* = 7.1 Hz, 2H), 7.32 – 7.21 (m, 7H), 7.16 (t, *J* = 6.8 Hz, 1H), 7.07 (t, *J* = 7.7 Hz, 2H), 7.03 (d, *J* = 2.7 Hz, 1H), 6.90 – 6.83 (m, 2H), 6.79 (t, *J* = 7.3 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 5.92 (s, 1H), 3.79 (s, 3H), 3.65 (s, 3H), 3.31 (d, *J* = 16.9 Hz, 1H), 2.67 (dd, *J* = 16.9, 2.8 Hz, 1H), 1.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.9, 160.2, 157.5, 146.1, 142.7, 139.0, 132.1, 130.6, 130.1, 129.3, 128.2, 127.8, 127.6, 127.3, 127.2, 126.4, 124.8, 119.8, 119.6, 115.2, 110.3, 110.26, 80.8, 55.4, 55.3, 55.2, 36.5, 20.2; HRMS (ESI) Calcd for $C_{33}H_{31}O_4$ $[M + H]^+$ 491.2222, found 491.2218.

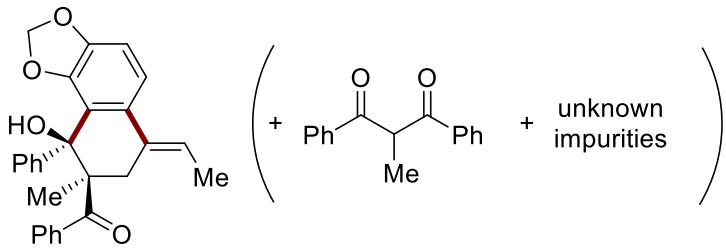


((*E*)-4-ethylidene-1-hydroxy-7-methoxy-2-methyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methanone (7k). Prepared according to typical procedure B. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as white solid (44.6 mg, 56%); m.p. 88–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.8 Hz, 1H), 7.45 – 7.39 (m, 1H), 7.37 – 7.31 (m, 6H), 7.31 – 7.22 (m, 4H), 6.82 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.05 (q, *J* = 7.1 Hz, 1H), 6.02 (s, 1H), 3.79 (s,

3H), 3.07 (d, *J* = 17.3 Hz, 1H), 2.25 (d, *J* = 17.5 Hz, 1H), 1.56 (s, 3H), 1.38 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.6, 159.6, 145.1, 142.3, 139.9, 131.2, 130.6, 129.0, 127.9, 127.8, 127.4, 127.2, 126.7, 123.8, 118.3, 115.2, 109.9, 80.7, 55.4, 54.4, 35.0, 20.2, 13.4; HRMS (ESI) Calcd for $C_{27}H_{27}O_3$ $[M + H]^+$ 399.1960, found 399.1951. Recrystallization from ethyl acetate afforded single crystals of **7k** suitable for X-ray diffraction analysis, which unambiguously confirmed the diastereochemistry and the C=C bond geometry of **7k** (Figure 2.3).[21]

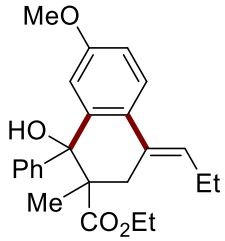
Figure 2.3. ORTEP Diagram of **7k** (thermal ellipsoids drawn at 50% probability)





(*E*)-(6-Ethylidene-9-hydroxy-8-methyl-9-phenyl-6,7,8,9-tetrahydronaphtho[1,2-d][1,3]dioxol-8-yl)(phenyl)methanone (7l): The title compound could not be isolated in a pure form due to the presence of 2-methyl-1,3-diphenylpropane-1,3-dione (formed

presumably via propargylic C–C bond cleavage)[22] and other unknown impurities. However, a series of characteristic ^{1}H NMR peaks and GCMS analysis supported its identity. The regiochemistry of 1,4-migration was assigned on the basis of a characteristic doublet signal at 6.82 ppm (J = 8.4 Hz), which should correspond to the aromatic proton next to the methylenedioxy group. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–7.11 (complex, 11H), 6.82 (d, J = 8.4 Hz, 1H), 6.05 (q, J = 7.1 Hz, 1H), 6.30 (q, J = 4.4 Hz, 1H), 5.91 (d, J = 1.2 Hz, 1H), 5.76 (d, J = 1.2 Hz, 1H), 4.60 (s, 1H), 2.87 (d, J = 15.6 Hz, 1H), 1.75 (d, J = 5.2 Hz, 3H), 1.47 (s, 3H).

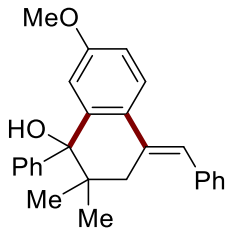


Ethyl-(*E*)-1-hydroxy-7-methoxy-2-methyl-1-phenyl-4-propylidene-1,2,3,4-tetrahydronaphthalene-2-carboxylate (9): The reaction of diarylzinc reagent **1a** and homopropargylic ketoester **8** was performed according to the procedure B. Column chromatography (hexane/EtOAc = 20/1) of the crude product afforded major and minor diastereomers of the title compound in 30% and 15% yield, respectively.

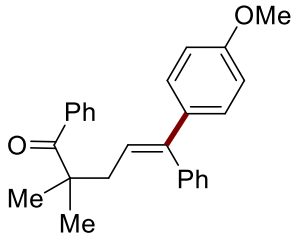
Major diastereomer: Colorless oil (22.8 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.9 Hz, 1H), 7.29 (dd, J = 8.0, 1.9 Hz, 2H), 7.25 – 7.18 (m, 3H), 7.15 (d, J = 2.8 Hz, 1H), 6.79 (dd, J = 8.8, 2.8 Hz, 1H), 6.06 (t, J = 6.8 Hz, 1H), 5.61 (s, 1H), 4.00 (m, 2H), 3.73 (s, 3H), 3.01 (dd, J = 16.4, 1.3 Hz, 1H), 2.25 – 2.11 (m, 2H), 2.10 – 2.02 (m, 1H), 1.27 (s, 3H), 1.09-1.04 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.6, 159.4, 144.5, 141.9, 130.4, 128.8, 128.2, 127.3, 127.2, 125.7, 123.9, 115.2, 109.9, 78.9, 61.3, 55.3, 50.3, 34.3, 21.4, 20.6, 14.0, 13.9; HRMS (ESI) Calcd for $C_{24}H_{29}O_4$ $[M + H]^+$ 381.2066, found 381.2062.

Minor diastereomer: Colorless oil (11.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.9 Hz, 1H), 7.21 – 7.14 (m, 3H), 7.09 (dd, J = 7.9, 1.8 Hz, 2H), 7.00 (d, J = 2.8 Hz, 1H),

6.83 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.20 (t, *J* = 7.1 Hz, 1H), 5.01 (s, 1H), 4.02 (q, *J* = 7.1 Hz, 2H), 3.85 – 3.78 (m, 1H), 3.73 (s, 3H), 2.69 – 2.66 (m, 1H), 2.31 – 2.15 (m, 2H), 1.31 (s, 3H), 1.11 – 1.06 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 159.5, 144.7, 140.2, 129.2, 127.48, 127.46, 127.3, 127.1, 127.0, 123.4, 115.2, 110.9, 78.5, 61.3, 55.3, 50.0, 31.6, 21.6, 21.0, 14.3, 14.0; HRMS (ESI) Calcd for $C_{24}H_{29}O_4$ $[M + H]^+$ 381.2066, found 381.2062.



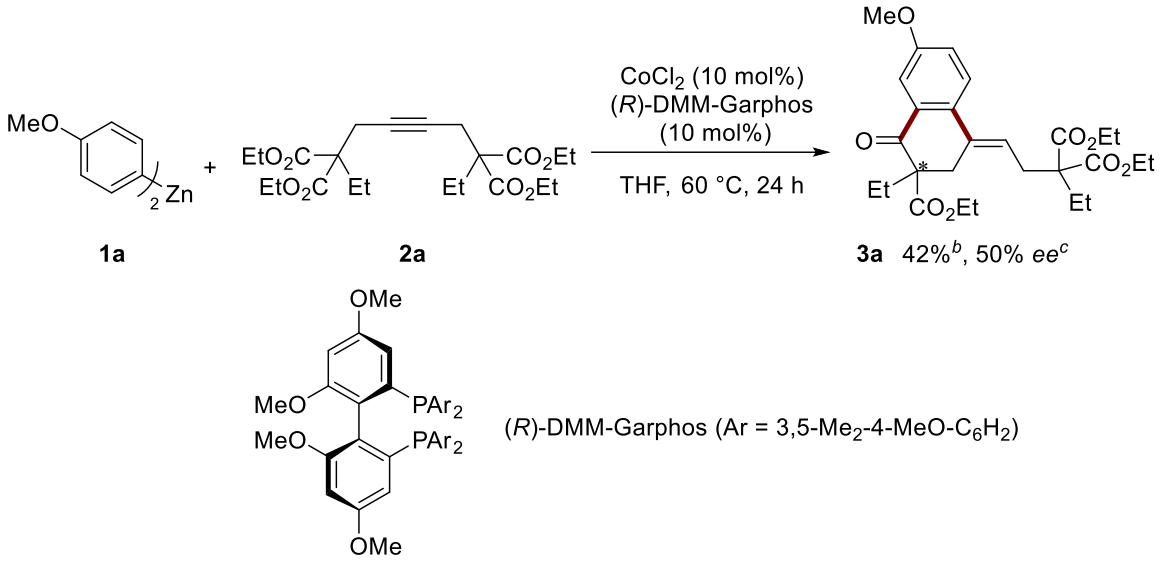
(*E*)-4-benzylidene-7-methoxy-2,2-dimethyl-1-phenyl-1,2,3,4-tetrahydronaphthalen-1-ol (12): The reaction of arylzinc **1a** and homopropargylic ketone **11** was performed according to the procedure B. Column chromatography (hexane/EtOAc = 30/1) of the crude product afforded the title compound as a colorless solid (22.2 mg, 30%). m.p. 111–112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.7 Hz, 1H), 7.38 – 7.32 (m, 4H), 7.31 – 7.28 (m, 2H), 7.27 – 7.26 (m, 2H), 7.25 – 7.21 (m, 2H), 7.19 (s, 1H), 6.89 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.86 (d, *J* = 2.7 Hz, 1H), 3.72 (s, 3H), 2.73 (dd, *J* = 15.1, 1.3 Hz, 1H), 2.62 (dd, *J* = 15.1, 2.1 Hz, 1H), 2.16 (s, 1H), 0.97 (s, 3H), 0.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 144.2, 143.9, 138.3, 134.6, 129.5, 128.8, 128.6, 128.3, 127.0, 126.8, 126.5, 124.9, 123.7, 114.6, 112.6, 80.8, 55.4, 39.5, 38.7, 25.2, 23.7; HRMS (ESI) Calcd for $C_{26}H_{27}O_2$ $[M + H]^+$ 371.2011, found 371.2004.



5-(4-methoxyphenyl)-2,2-dimethyl-1,5-diphenylpent-4-en-1-one (13): The title compound was obtained (22.2 mg, 30%, *E*/*Z* = 4/1 as determined by ^{1}H NMR) as a colorless

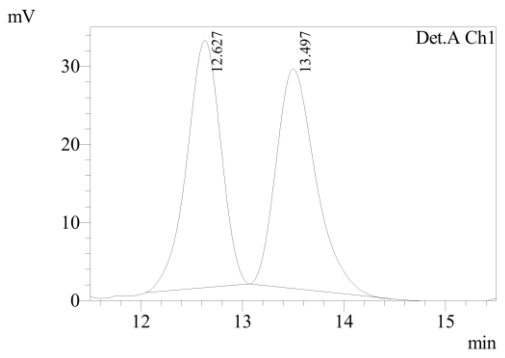
oil from the reaction of **1a** and **11**, along with the above compound **12**. ^{1}H NMR (400 MHz, $CDCl_3$, major isomer) δ 7.60 – 7.53 (m, 2H), 7.46 – 7.39 (m, 1H), 7.38 – 7.28 (m, 6H), 7.08 (d, *J* = 9.0 Hz, 4H), 6.77 (d, *J* = 8.8 Hz, 2H), 5.92 (t, *J* = 7.4 Hz, 1H), 3.77 (s, 3H), 2.60 (d, *J* = 7.3 Hz, 2H), 1.31 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$, major isomer) δ 208.5, 159.0, 143.6, 140.3, 138.8, 135.4, 131.3, 131.0, 130.1, 128.5, 128.3, 128.2, 127.9, 127.5, 127.1, 123.2, 113.6, 55.4, 48.5, 40.3, 26.2; HRMS (ESI) Calcd for $C_{26}H_{27}O_2$ $[M + H]^+$ 371.2011, found 371.2008.

Enantioselective Arylative Cyclization of 2a[a]



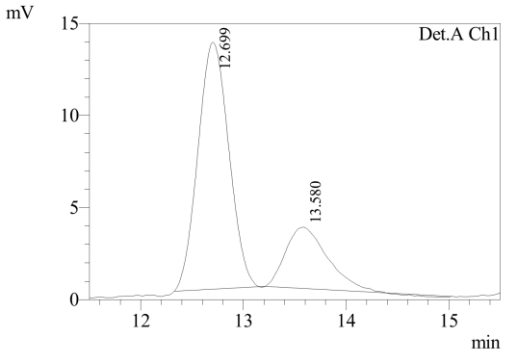
[a] The reaction was performed using arylzinc reagent **1a** prepared from $ZnCl_2$•TMEDA (0.3 mmol) and 4-$MeOC_6H_4MgBr$ (0.6 mmol) and alkyne **2a** (0.2 mmol). [b] Isolated yield. [c] Determined by chiral HPLC analysis.

Figure 2.4. HPLC Traces for Enantioselective Arylative Cyclization of **2a**



UV Detector Ch1 254nm

Peak#	Ret. Time	Area %
1	12.627	49.236
2	13.497	50.764
Total		100.000

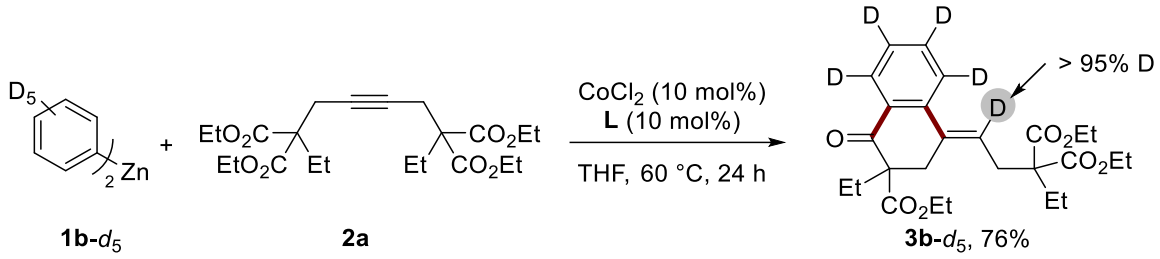


UV Detector Ch1 254nm

Peak#	Ret. Time	Area %
1	12.699	75.022
2	13.580	24.978
Total		100.000

HPLC traces for a racemic sample of **3a** (left) and an enantioenriched sample of **3a** obtained by the Co–(*R*)-DMM-Garphos catalyzed reaction (right). HPLC conditions: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 95:5; detection wavelength = 254 nm; flow rate = 1.0 mL/min. t_R = 12.7 min (major) and 13.6 min (minor).

Deuterium-labeling experiment



1b-d_5 **2a** **3b-d_5**, 76%

Diethyl (*E*)-2-(2-(3-(ethoxycarbonyl)-3-ethyl-4-oxo-3,4-dihydronaphthalen-1(2*H*)-ylidene-5,6,7,8-d_4)ethyl-2-*d*)-2-ethylmalonate (3b-d_5). Prepared according to typical procedure A using pentadeuteriophenylzinc reagent **1b-d_5** and alkyne **2a**. Column chromatography (Ethyl acetate/hexane = 1/20) of the crude product afforded the title compound as colourless oil (70.4 mg, 76%). *E* geometry is arranged in analogue with **3c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 – 4.17 (m, 4H), 4.16 – 4.04 (m, 2H), 3.28 (d, *J* = 14.2 Hz, 1H), 2.98 – 2.82 (m, 2H), 2.76 (d, *J* = 14.2 Hz, 1H), 2.08 – 1.87 (m, 4H), 1.25 (t, *J* = 7.1 Hz, 6H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.5, 171.6, 171.38, 171.37, 141.0, 132.9, 130.2, 61.44, 61.4, 61.3, 59.0, 58.2, 33.7, 31.0, 26.9, 26.0, 14.3, 14.2, 14.16, 9.5, 8.7; HRMS (ESI) Calcd for $C_{26}H_{30}D_5O_7$ $[M + H]^+$ 464.2697, found 464.2694.

2.5 References

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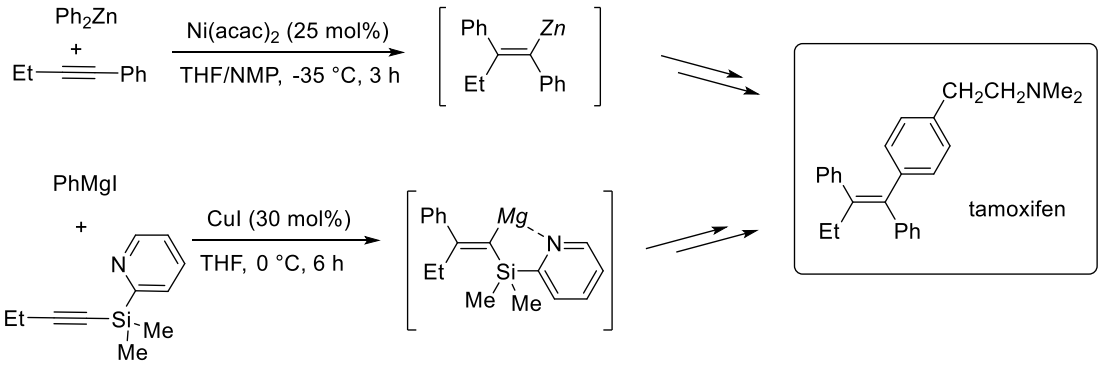
Chapter 3. Chromium-Catalyzed Migratory Arylmagnesiation of Unactivated Alkynes

3.1 Introduction

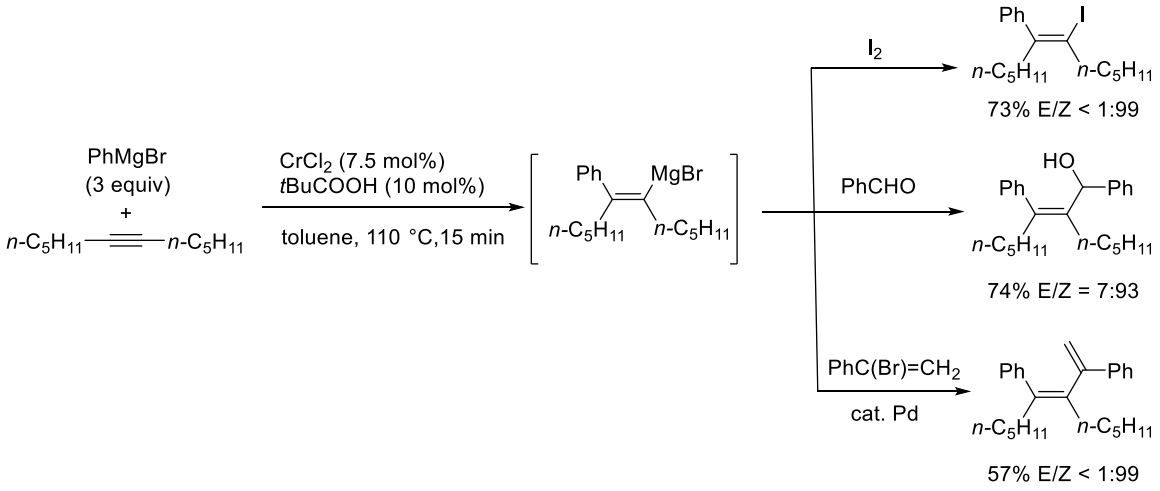
Carbometalation reaction through the addition of organometallic reagents to alkynes plays an indispensable role in modern organic synthesis, providing straightforward synthetic approaches to stereochemically well-defined multisubstituted alkenes.[1] For example, expedient and stereoselective synthesis of pharmaceutically active tetrasubstituted alkenes such as tamoxifen (for treatment of breast cancer) has been achieved by alkyne carbozincation[2] and carbomagnesiation[3] reactions, owing to the high *syn*-selectivity of the carbometalation process (Scheme 3.1). Among such alkyne carbometalation reactions, the addition of aryl Grignard reagents, i.e., arymagnesiation, is particularly attractive and has been extensively studied for the ready availability of Grignard reagents as well as for the value of the resulting vinylarene derivatives. Thus, various transition metals such as copper,[4] manganese,[5] iron,[6] chromium,[7] and nickel[8] have been successfully employed for the catalytic arylmagnesiation of alkynes.

Scheme 3.1. Nickel-Catalyzed Carbozincation and Copper-Catalyzed Carbomagnesiation of Alkyne to Synthesize Tamoxifen



As an example of alkyne arylmagnesiation reactions, in 2007, a chromium-catalyzed arylmagnesiation reaction of unactivated internal alkynes was reported by the group of Yorimitsu and Oshima (Scheme 3.2).[7] A simple catalytic system comprising $CrCl_2$ and pivalic acid was effective to promote the *syn*-selective addition of an aryl Grignard reagent to a dialkylacetylene in a short reaction time albeit at an elevated temperature. The resulting stereochemically well-defined alkenylmagnesium bromide could be employed for a series of electrophilic trappings and coupling reactions.

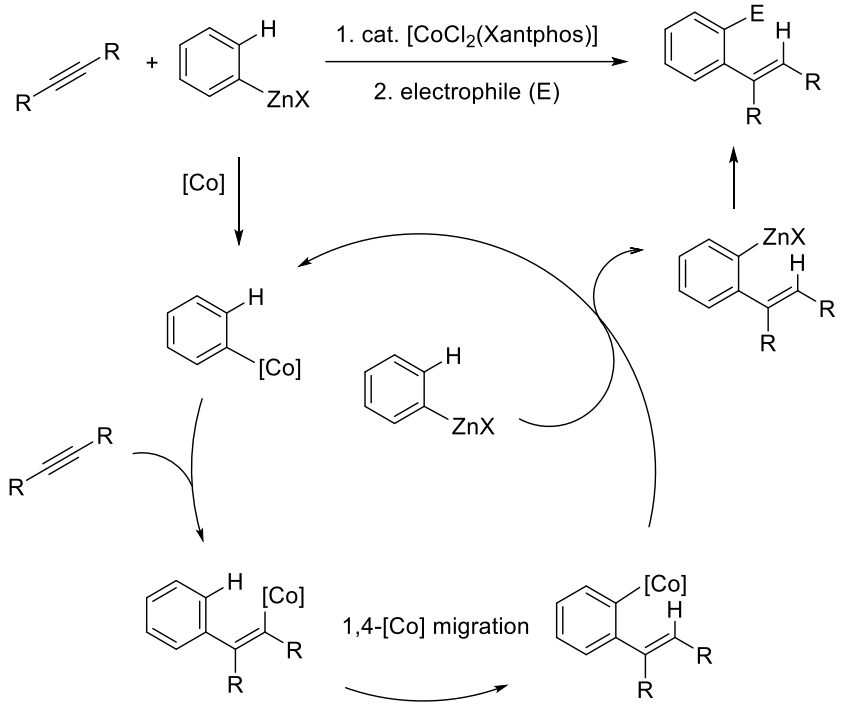
Scheme 3.2. Chromium-Catalyzed Arylmagnesiation of an Internal Alkyne



In 2012, our group disclosed a cobalt-catalyzed migratory arylzincation reaction of unactivated internal alkynes, which involves 1,4-cobalt migration as a key elementary step (Scheme 3.3).[9] Compared to the typical alkyne arylmetalation, the reaction is unique as it offers an access to *ortho*-alkenylarylzinc species, which can be captured by an external electrophile to afford 1,2-difunctionalized arenes. The reaction represents the first example of 1,4-cobalt migration, and is notable since no such "migratory arylmetalation" has been achieved before, regardless of extensive studies on 1,4-metal migration of transition metals other than cobalt.[10,11] It is worthwhile to note that cobalt-catalyzed "normal" arylzincation

of alkynes was achieved earlier by Yorimitsu and Oshima using ligand-free $CoBr_2$,[12] and also recently by Gosmini using $CoBr_2$(bpy) (bpy = bipyridine) as a precatalyst.[13] Thus, the diphosphine ligand (Xantphos) apparently plays a crucial role in the 1,4-cobalt migration process.

Scheme 3.3. Cobalt-Catalyzed Migratory Arylzincation of Alkynes

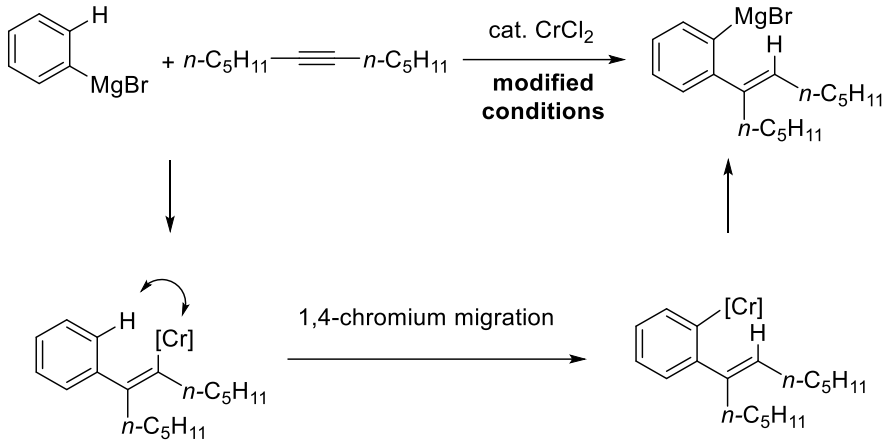


The above-mentioned migratory arylzincation and typical transition metal-catalyzed arylmetalation reactions are both initiated by migratory insertion of an alkyne into an aryl–transition metal species. The resulting β-styrylmetal species undergoes 1,4-metal migration followed by transmetalation with the arylmetal reagent in the former reaction, while it directly takes part in transmetalation in the latter. Thus, these arylmetalation reactions share the migratory insertion and transmetalation steps as common elementary steps. Given this mechanistic consideration, one may hypothesize that a typical arylmetalation reaction, catalyzed by a transition metal other than cobalt, could potentially

be converted to a "migratory" arylmetalation reaction, if the transition metal had an ability to undergo 1,4-metal migration depending on the ligand and other reaction conditions.

In this chapter, we have reported on discovery and development of a chromium-catalyzed migratory arylmagnesiation reaction of internal alkynes (Scheme 3.4),[14] which would serve as a proof of the above hypothesis. By modifying the reaction conditions of the chromium-catalyzed arylmagnesiation developed by Yorimitsu and Oshima (Scheme 3.2), the addition of an arylmagnesium bromide to a dialkylacetylene was found to afford an *ortho*-alkenylarylmagnesium bromide as a major product rather than the normal arylmagnesiation product. According to our mechanistic understanding of (migratory) arylmetalation reactions, the present reaction likely proceeds via insertion of the alkyne into an arylchromium species, alkenyl-to-aryl 1,4-chromium migration, and transmetalation between the resulting arylchromium species and the starting aryl Grignard reagent to regenerate catalytically active arylchromium species. The resulting *ortho*-alkenylarylmagnesium bromide is amenable to subsequent electrophilic trapping reactions.

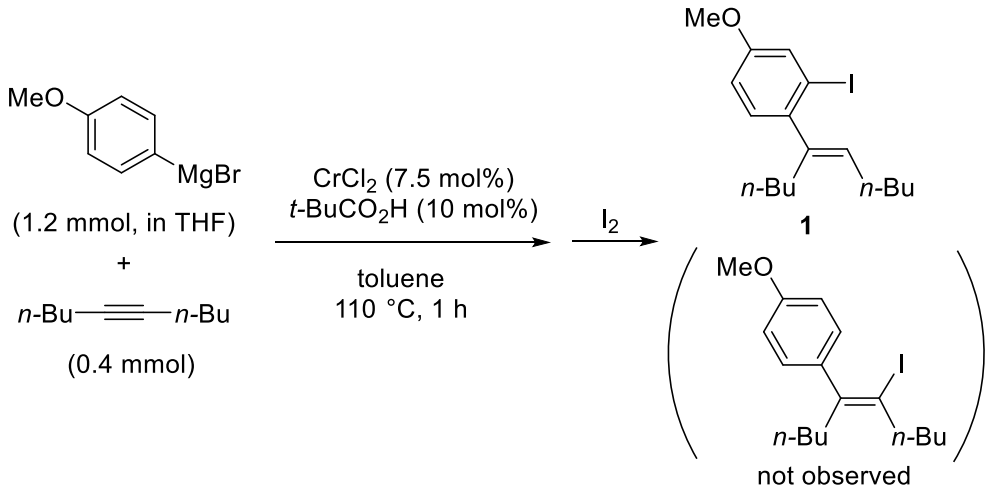
Scheme 3.4. Chromium-Catalyzed Migratory Arylmagnesiation of Internal Alkyne



3.2 Results and Discussion

The present reaction was serendipitously discovered in the course of our attempt on preparation of an alkenyl iodide using the Yorimitsu–Oshima arylmagnesiation (Scheme 3.5). While the original protocol employed Grignard reagents prepared in Et_2O and rather short reaction times (< 1 h), and also 4-methoxyphenylmagnesium bromide was not among the reported examples, we performed the reaction of this Grignard reagent prepared in THF with 5-decyne for a reaction time of 1 h followed by the addition of iodine. Contrary to our expectation, the ^{1}H NMR spectrum of the crude product did not show any sign of the desired alkenyl iodide. Instead, we observed characteristic signals that could be assigned to *ortho*-alkenylaryl iodide **1**, which was supported by comparison with the authentic sample of **1** prepared by the cobalt-catalyzed migratory arylzincation. [9]

Scheme 3.5. Unexpected Observation of Migratory Arylmagnesiation of Alkyne

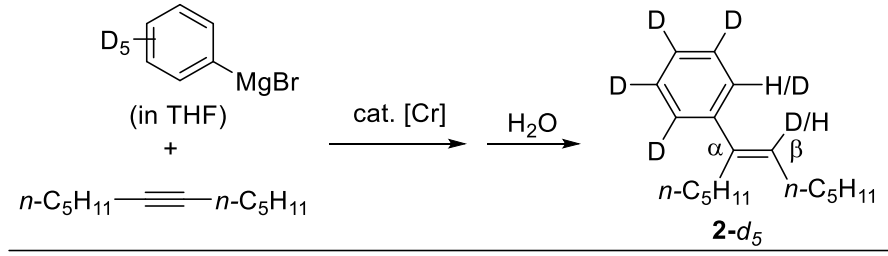


To further examine the feasibility of the chromium-catalyzed migratory arylmagnesiation, the addition reaction of pentadeuterated phenylmagnesium bromide to 6-dodecyne was explored (Table 3.1). First, we performed a series of screening experiments under ligand-free conditions. As a result, the reaction using $CrCl_2$ (10 mol%) proceeded in

i-Pr_2O at 110 °C and afforded, on quenching with H_2O after 12 h, the addition product **2**-d_5 in 50% yield with 72% deuterium incorporation into the β-position (entry 1, conditions A). In addition to this major product, we also detected 1,2,3,4-tetrapentylnaphthalene-5,6,7,8-d_4 (ca. 10%) and hexapentylbenzene (< 5%) by GCMS analysis. The former byproduct would form through the annulative coupling of the Grignard reagent and two molecules of the alkyne, while the latter should be derived from cyclotrimerization of the alkyne. Although the yield of **2**-d_5 was found to reach near 50% at a shorter reaction time such as 1 h and 6 h, the degree of deuterium incorporation into the β-position was apparently lower (entries 2 and 3). Although comparable yields of **2**-d_5 were obtained at reaction times of 1 h and 6 h, the deuteration ratios at the β-position were apparently lower (entries 2 and 3). Further extension of the reaction time or addition of *t*-$BuCO_2H$ did not improve the deuteration rate. The reaction performed in toluene as the solvent instead of *i*-Pr_2O led to a lower deuteration rate (entry 4).

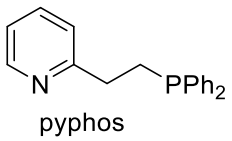
Next, we performed a set of screening experiments on ligand effects to observe significant acceleration of the migratory arylmagnesiation enabled by 2-(2-diphenylphosphino)ethyl)pyridine (pyphos). Thus, using $CrCl_2$ (10 mol%) and pyphos (20 mol%), the reaction took place in THF at 80 °C to afford **2**-d_5 in 63% yield with a β-deuteration rate of 71% after 18 h (entry 5, conditions B). As was observed for the reaction under ligand-free conditions, a shorter reaction time resulted in a comparable yield and a lower β-deuteration rate (entry 6). At 80 °C, the reaction was shut down in the absence of ligand, while other ligands such as 1,10-phenanthroline (phen) and 1,2-diphenylphosphinoethane (dppe) promoted the addition less efficiently with much lower β-deuteration rates (entries 7–9). Unlike the ligand-free conditions, *i*-Pr_2O proved to be an ineffective solvent for the Cr/pyphos system.

Table 3.1. Addition of Pentadeuterated Phenylmagnesium Bromide to 6-Dodecyne[a]



Condition A
$CrCl_2$ (10 mol%)
i-Pr_2O, 110 °C,12 h

Condition B
$CrCl_2$ (10 mol%)
pyphos (20 mol%)
THF, 80 °C,18 h



Entry	Conditions	Yield (%)[b]	% D at Cβ[c]
1	A	50	72
2	A, reaction time = 1 h	47	26
3	A, reaction time = 6 h	48	59
4	A, toluene instead of *i*-Pr_2O	43	21
5	B	68 (63)[d]	71
6	B, reaction time = 6 h	59	41
7	B, without pyphos	0	–
8	B, phen instead of pyphos	44	23
9	B, dppe instead of pyphos	31	25

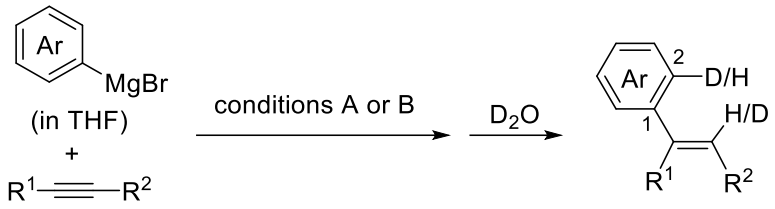
[a] The reaction was performed using 0.2 mmol of 6-dodecyne and 0.6 mmol of C_6D_5MgBr (in THF). [b] Determined by GC using *n*-tridecane as an internal standard. [c] Determined by ^1H NMR analysis. [d] Isolated yield.

Having established the two sets of reaction conditions, we investigated the scope of the chromium-catalyzed migratory arylmagnesiation (Table 3.2). Thus, reactions using different arylmagnesium bromides and alkynes were carried out under conditions A or B, and quenched with D_2O to probe the extent of 1,4-migration. Under conditions A, phenyl-, 4-methoxyphenyl-, and 4-fluorophenylmagnesium bromides participated in the reaction with 6-dodecyne to afford the desired adducts in moderate yields with high level of 1,4-migration (> 80% D at the C2 position, entries 1–3). By contrast, the reactions of 4-tolyl-

and 4-dimethylaminophenylmagnesium bromides were accompanied by limited 1,4-migration, as indicated from much lower C2-deuteration rates, i.e., 20% and 45%, respectively (entries 4 and 5). Interestingly, the C2-deuteration rates for these reactions were considerably improved by the addition of 10 mol% of CuBr (entries 6 and 7), which might facilitate transmetalation between organochromium species and Grignard reagents.

Under conditions B, a series of *para*- and *meta*-substituted arylmagnesium bromides reacted with 6-dodecyne to afford the corresponding adducts in moderate yields (50–80%) with moderate to good degrees of 1,4-migration (60–90%, entries 8–16). The reaction of 3-tolylmagnesium bromide took place with exclusive 1,4-migration to the less hindered *ortho*-position (entry 15). Meanwhile, the reaction of 3-methoxyphenylmagnesium bromide was accompanied by a competitive 1,4-migration to the less hindered and more hindered *ortho* positions in a ratio of 81:19 (entry 16). The addition of 2-tolylmagnesium bromide to 6-dodecyne took place smoothly, but with only a small degree of 1,4-migration (entry 17). Unfortunately, the scope of alkynes of the present migratory arylmagnesiation was found to be rather narrow. Although the addition of 4-methoxyphenylmagnesium bromide to 5-decyne, not unexpectedly, proceeded smoothly to afford the desired migratory adduct in a moderate yield (entry 18), the reaction of an unsymmetrical dialkylalkyne, 2,2-dimethyl-3-decyne, was rather sluggish despite a high degree (85%) of 1,4-migration (entry 19). Other alkynes such as 1-phenyl-1-propyne, 1-phenyl-1-butyne and 1-trimethylsilyl-1-propyne were sluggish to participate in the present reaction, resulting in no or limited degree of 1,4-migrations (entries 20–22).

Table 3.2. Chromium-Catalyzed Migratory Arylmagnesiation of Alkynes[a]

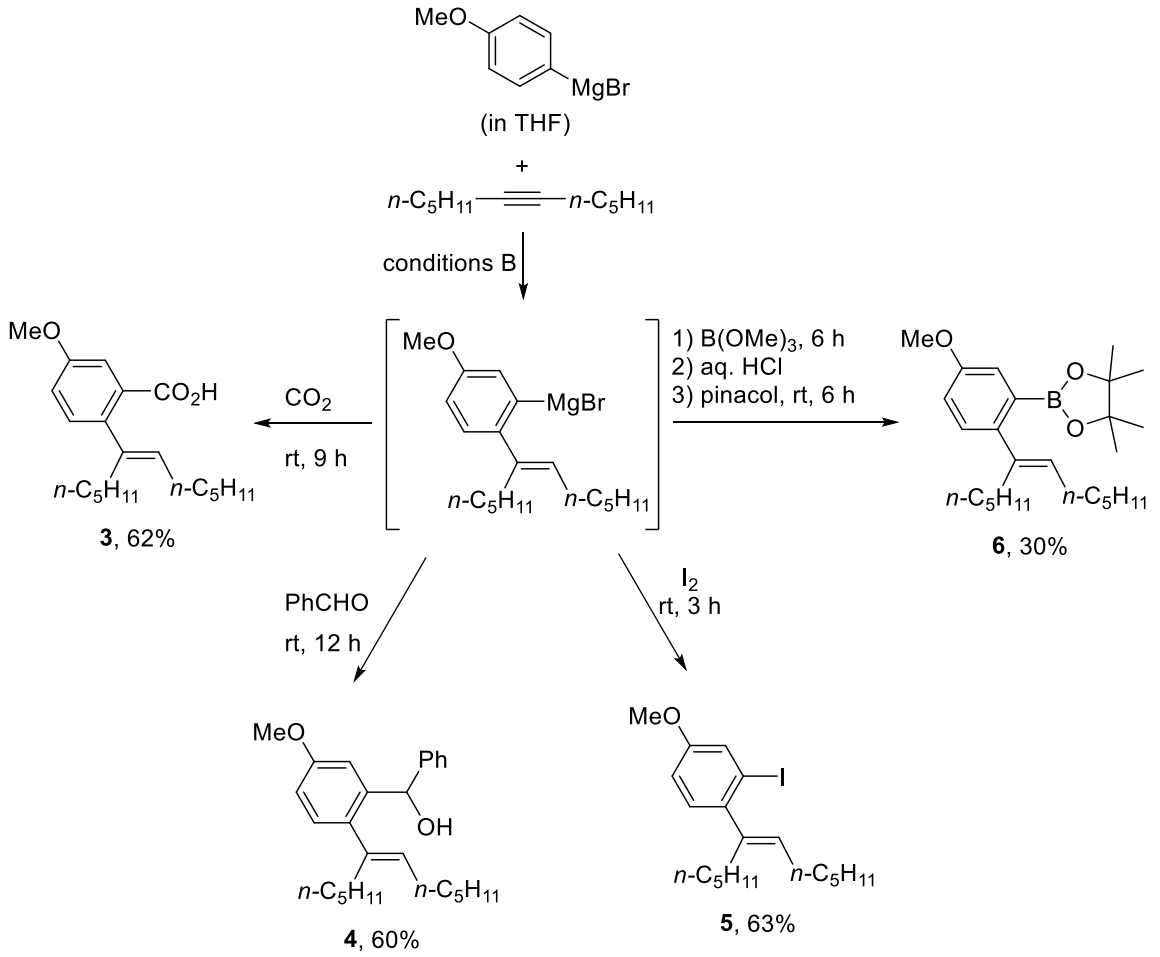


Entry	Conditions	Ar	R^1	R^2	Yield (%)[b]	% D at C2[c]
1	A	Ph	*n*-C_5H_{11}	*n*-C_5H_{11}	74	86
2	A	4-$MeOC_6H_4$	*n*-C_5H_{11}	*n*-C_5H_{11}	65	91
3	A	4-FC_6H_4	*n*-C_5H_{11}	*n*-C_5H_{11}	32	83
4	A	4-MeC_6H_4	*n*-C_5H_{11}	*n*-C_5H_{11}	79	20
5	A	4-$Me_2NC_6H_4$	*n*-C_5H_{11}	*n*-C_5H_{11}	56	45
6	A[d]	4-MeC_6H_4	*n*-C_5H_{11}	*n*-C_5H_{11}	56	50
7	A[e]	4-$Me_2NC_6H_4$	*n*-C_5H_{11}	*n*-C_5H_{11}	64	82
8	B	Ph	*n*-C_5H_{11}	*n*-C_5H_{11}	52	77
9	B	4-$MeOC_6H_4$	*n*-C_5H_{11}	*n*-C_5H_{11}	74	84[f]
10	B	4-FC_6H_4	*n*-C_5H_{11}	*n*-C_5H_{11}	60	91[f]
11	B	4-MeC_6H_4	*n*-C_5H_{11}	*n*-C_5H_{11}	50	78
12	B	4-$Me_2NC_6H_4$	*n*-C_5H_{11}	*n*-C_5H_{11}	61	65[f]
13	B	4-$Me_3SiC_6H_4$	*n*-C_5H_{11}	*n*-C_5H_{11}	60	66
14	B	4-*t*-BuC_6H_4	*n*-C_5H_{11}	*n*-C_5H_{11}	59	62
15	B	3-MeC_6H_4	*n*-C_5H_{11}	*n*-C_5H_{11}	64	70[g]
16	B	3-$MeOC_6H_4$	*n*-C_5H_{11}	*n*-C_5H_{11}	76	80[h]
17	B	2-MeC_6H_4	*n*-C_5H_{11}	*n*-C_5H_{11}	81	16
18	B	4-$MeOC_6H_4$	*n*-Bu	*n*-Bu	64	76
19	B	4-$MeOC_6H_4$	*n*-C_6H_{13}	*t*-Bu	14	85
20	B	4-$MeOC_6H_4$	Me	Ph	25	0
21	B	4-$MeOC_6H_4$	Et	Ph	18	0
22	B	4-$MeOC_6H_4$	Me	$SiMe_3$	26	34

[a] The reaction was performed under either conditions A or B described in Table 1. [b] Isolated yield. [c] Determined by ^{1}H NMR analysis. [d] CuBr (10 mol%) was added. [e] CuBr (10 mol%) was added, and the reaction was performed in *t*-BuOMe. [f] Refers to %H at the β-position. [g] Less hindered ortho position was exclusively deuterated. [h] Less hindered and more hindered *ortho* positions were deuterated in a ratio of 81:19.

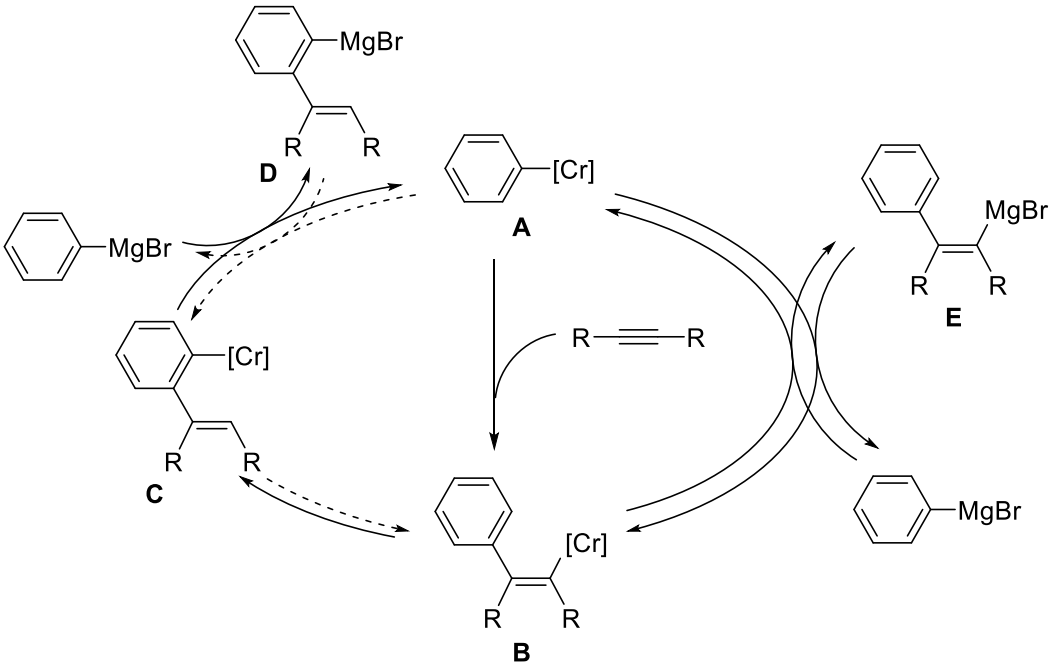
The *ortho*-alkenylarylmagnesium bromide formed by the present reaction could readily be captured by electrophiles, as demonstrated by several specific transformations (Scheme 3.6). Thus, the reaction between 4-methoxyphenylmagnesium bromide and 6-dodecyne (under conditions B) and subsequent treatment of the reaction mixture with CO_2 (balloon), benzaldehyde or iodine at ambient temperature afforded the desired trapping products, i.e., a benzoic acid derivative **3**, a diarylmethanol **4** or an *ortho*-alkenylaryliodine **5**, respectively, in moderate yields (60–63%). The same *ortho*-alkenylarylmagnesium bromide could also be intercepted by trimethyl borate, and treatment of the reaction mixture with aqueous HCl and pinacol furnished the pinacol boronate ester **6**, albeit in a low yield (30%).

Scheme 3.6. Electrophilic Trapping of *ortho*-Alkenylarylmagnesium Species.



A proposed reaction mechanism of the present reaction is shown in Scheme 3.7. An arylchromium species **A** generated from the chromium precatalyst and the arylmagnesium bromide would undergo insertion of the alkyne to give an alkenylchromium species **B**. Subsequent 1,4-chromium migration would proceed to form an *ortho*-alkenylarylchromium species **C**. Finally, chromium-to-magnesium transmetalation between the species **C** and the arylmagnesium bromide would afford the *ortho*-alkenylarylmagnesium bromide **D** and regenerate the species **A**. Given the incomplete 1,4-migrations observed, direct transmetalation between the alkenylchromium species **B** and the starting arylmagnesium bromide would also take place competitively to form the normal arylmagnesiation product **E**. At the same time, in light of the increase of the 1,4-migration rate over the reaction time (Table 3.1, entries 1–3, 5, and 6), this transmetalation step would be reversible, thus converting a part of the initially formed arylmagnesiation product **E** into the migratory arylmagnesiation product **D**. The lower 1,4-migration rates obtained for pentadeuterated phenylmagnesium bromide (72% and 71%, Table 3.1) compared with those for phenylmagnesium bromide (86% and 77%, Table 3.2) likely originate from the H/D kinetic isotope effect of in the 1,4-migration step.

Scheme 3.7. Proposed Reaction Mechanism.



3.3 Conclusions

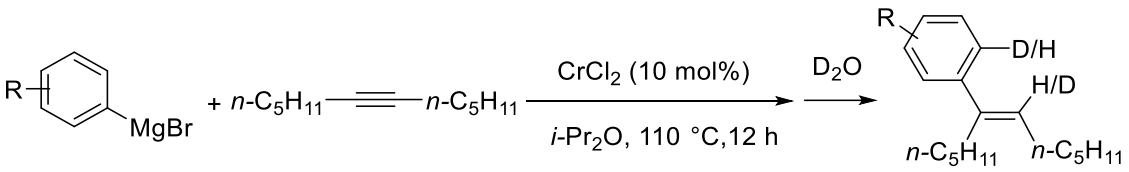
In conclusion, the present study has demonstrated the ability of chromium to take part in a 1,4-metal migration process. Chromium-based catalytic systems modified by appropriate solvent or ligand promote the addition of aryl Grignard reagents to unactivated dialkylalkynes to afford *ortho*-alkenylarylmagnesium species. The present migratory arylmagnesiation reaction represents the first example of remote metal migration involving organochromium species, and also a new example of chromium-catalyzed C–H functionalization.[15,16,17] While the substrate scope is rather narrow, the reaction may complement some of the limitations of the cobalt-catalyzed migratory arylzincation of alkynes owing to the increased nucleophilicity of the resultant organomagnesium species. Remote migrations mediated by chromium and other inexpensive transition metals deserve further investigations.

3.4 Experimental Section

General. All reactions dealing with air- or moisture-sensitive compound were performed by standard Schlenk techniques in oven-dried reaction vessels under nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on JEOL ECA-400 (400 MHz) or Bruker AV-400 (400 MHz) or Bruker AV-500 (500 MHz) NMR spectrometers. ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and $CHCl_3$ (77.0 ppm), respectively. Gas chromatographic (GC) analysis was performed on a Shimadzu GC-2010 system equipped with an FID detector and a capillary column, DB-5 (Agilent J&W, 0.25 mm i.d. x 30 m, 0.25 μm film thickness). High-resolution mass spectra (HRMS) were obtained with a Q-Tof Premier LC HR mass spectrometer.

Materials. Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. Anhydrous $CrCl_2$ (99.99%) was purchased from Aldrich and was used as received. THF, *i*Pr_2O (diisopropyl ether), *t*BuOMe (tert-butyl methyl ether) was distilled over Na/benzophenone. Grignard reagents were prepared from the corresponding halides and magnesium turnings in anhydrous THF (with a typical concentration of 1 M) and titratiod before use. 2,2-Dimethyl-3-decyne was prepared according to known procedures.[18]

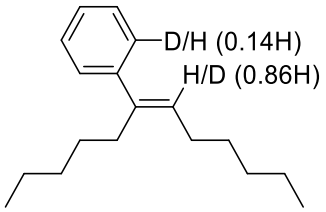
Chromium-Catalyzed Migratory Arylmagnesiation of Unactivated Alkynes



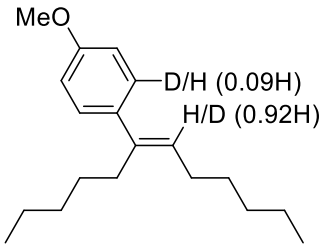
Typical procedure A (conditions A): Inside a glovebox, a 10 mL Schlenk tube was charged with $CrCl_2$ (2.4 mg, 0.020 mmol). The Schlenk tube was taken out from the glovebox and submerged in an ice bath for 5 min prior to the addition of a Grignard reagent (0.60 mmol in THF). After stirring for 10 min at 0 °C, the resulting mixture was allowed to warm to room temperature and concentrated under reduced pressure, followed by the addition of *i*-Pr_2O (0.5 mL). After stirring for 5 min, 6-dodecyne (33.2 mg, 0.20 mmol) was added. The reaction mixture was stirred at 110 °C for 12 h, and then allowed to cool to room temperature, quenched by the addition of D_2O (0.5 mL), and diluted with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford the desired product.

According to GCMS analysis of the crude product, the reaction was typically accompanied by two minor byproducts, i.e., (1) a naphthalene derivative formed via annulation of the Grignard reagent and two molecules of the alkyne (ca. 10%), and (2) a cyclotrimerization product of the alkyne (< 5%). These byproducts are not always readily removable, and

would account for (at least partially) impurities observed in ^{1}H and ^{13}C NMR spectra of some of the products. Additionally, the splitting ^{13}C signals arising from C–D coupling in deuterated products are not readily resolved probably due to limited accumulation time for ^{13}C NMR spectra. We managed to obtain the expected splitting pattern for the product of Table 2, Entry 9 as a representative case, after a quite long accumulation time (18 h).

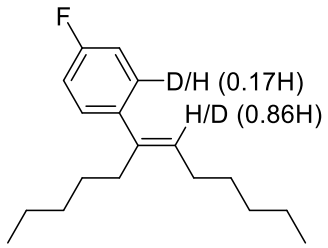


(*E*)-1-(Dodec-6-en-6-yl) benzene-2-*d* (Table 2, entry 1): Prepared according to typical procedure A. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (36.3 mg, 74%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 – 7.24 (m, 3.14H), 7.26 – 7.16 (m, 1H), 5.63 (t, J = 7.3 Hz, 0.86H), 2.46 (t, J = 7.0 Hz, 2H), 2.16 (q, J = 7.2 Hz, 2H), 1.46 – 1.38 (m, 2H), 1.37 – 1.27 (m, 4H), 1.26 – 1.17 (m, 6H), 0.87 (t, J = 6.8 Hz, 3H), 0.80 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 142.4, 139.5, 128.5, 128.2, 128.1, 126.4, 125.8, 31.02, 31.01, 29.0, 28.7, 27.9, 27.8, 22.0, 21.9, 13.9, 13.8; HRMS (ESI) Calcd for $C_{18}H_{28}D$ $[M + H]^+$ 246.2332, found 246.2333. The ^{1}H and ^{13}C NMR spectral patterns, except for the deuterated positions, are in good agreement with the literature data for the non-deuterated derivative.[12,19]

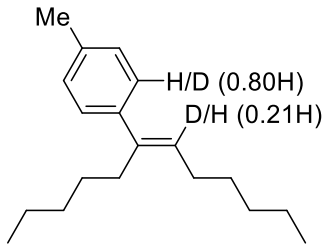


(*E*)-1-(Dodec-6-en-6-yl)-4-methoxybenzene-2-*d* (Table 2, entry 2): Prepared according to typical procedure A. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded the title compound as a colorless oil (35.8 mg, 65%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.26 (d, J = 9.2 Hz, 1.09H), 6.91 – 6.77 (m, 2H), 5.55 (t, J = 7.3 Hz,

0.92H), 3.73 (s, 3H), 2.42 (t, *J* = 7.0 Hz, 2H), 2.13 (q, *J* = 7.3 Hz, 2H), 1.43 – 1.35 (m, 2H), 1.33 – 1.26 (m, 4H), 1.25 – 1.19 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.81 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 158.0, 138.8, 134.7, 126.87, 126.86, 113.6, 113.5, 55.0, 31.02, 31.00, 29.1, 28.7, 27.9, 27.8, 22.0, 21.9, 13.9, 13.8; HRMS (ESI) Calcd for $C_{19}H_{30}DO$ $[M + H]^+$ 276.2438, found 276.2443.

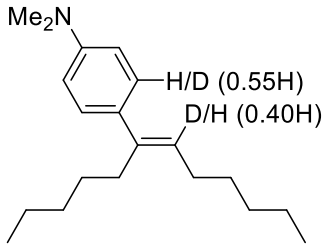


(*E*)-1-(Dodec-6-en-6-yl)-4-fluorobenzene-2-*d* (Table 2, entry 3): Prepared according to typical procedure A. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (16.8 mg, 32%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.36 (dd, *J* = 9.3, 5.5 Hz, 1.17H), 7.21 – 7.07 (m, 2H), 5.61 (t, *J* = 7.3 Hz, 0.86H), 2.44 (t, *J* = 6.8 Hz, 2H), 2.15 (q, *J* = 7.2 Hz, 2H), 1.46 – 1.35 (m, 2H), 1.34 – 1.27 (m, 4H), 1.25 – 1.20 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.7 (d, $^1J_{C\text{-}F}$ = 250.2 Hz),, 140.0, 139.3, 138.9, 129.1, 128.2 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 115.4 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 115.3 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 31.5, 31.4, 29.4, 29.2, 28.4, 28.2, 22.5, 22.4, 14.4, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.8; HRMS (ESI) Calcd for $C_{18}H_{27}DF$ $[M + H]^+$ 264.2238, found 264.2235.

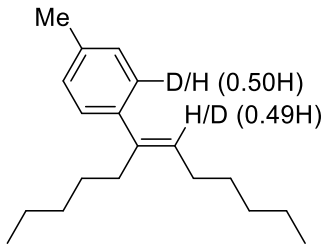


(*E*)-1-(Dodec-6-en-6-yl-7-*d*)-4-methylbenzene (Table 2, entry 4): Prepared according to typical procedure A. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (41.1 mg, 79%); ^{1}H NMR (400 MHz, DMSO-

d_6) δ 7.21 (d, *J* = 8.2 Hz, 1.80H), 7.10 (d, *J* = 7.9 Hz, 2H), 5.59 (t, *J* = 7.3 Hz, 0.21H), 2.43 (t, *J* = 7.0 Hz, 2H), 2.27 (s, 3H), 2.14 (t, *J* = 7.1 Hz, 2H), 1.45 – 1.38 (m, 2H), 1.36 – 1.26 (m, 4H), 1.25 – 1.19 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H), 0.81 (t, *J* = 6.8 Hz, 3H); HRMS (ESI) Calcd for $C_{19}H_{30}D$ $[M + H]^+$ 260.2489, found 260.2483. The ^1H and ^{13}C NMR spectral patterns, except for the deuterated positions, are in good agreement with the literature data for the non-deuterated derivative.[12]

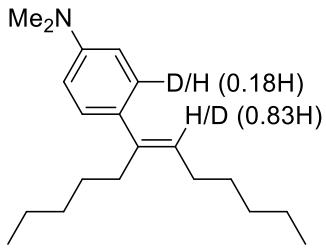


(*E*)-4-(Dodec-6-en-6-yl-7-*d*)-*N*,*N*-dimethylaniline (Table 2, entry 5): Prepared according to typical procedure A. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded the title compound as a colorless oil (32.3 mg, 56%); ^1H NMR (400 MHz, Methylene Chloride-d_2) δ 7.23 (d, *J* = 8.0 Hz, 1.55H), 6.69 (d, *J* = 7.8 Hz, 2H), 5.57 (t, *J* = 7.3 Hz, 0.40H), 2.92 (s, 6H), 2.45 (t, *J* = 7.3 Hz, 2H), 2.16 (td, *J* = 7.2, 1.7 Hz, 2H), 1.48 – 1.41 (m, 2H), 1.38 – 1.32 (m, 4H), 1.31 – 1.25 (m, 6H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); HRMS (ESI) Calcd for $C_{20}H_{33}DN$ $[M + H]^+$ 289.2754, found 289.2755.

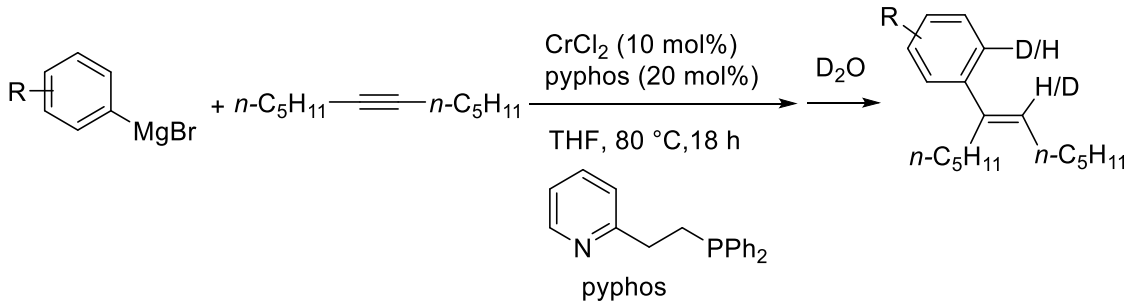


(*E*)-1-(Dodec-6-en-6-yl)-4-methylbenzene-2-*d* (Table 2, entry 6): Prepared according to typical procedure A with a modification, that is, addition of CuBr (2.9 mg, 0.020 mmol) together with $CrCl_2$. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (29.0 mg, 56%); ^1H NMR (400 MHz, DMSO-

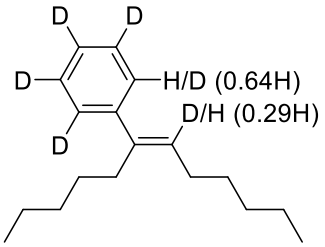
d_6) δ 7.22 (d, *J* = 8.0 Hz, 1.50H), 7.10 (d, *J* = 7.8 Hz, 2H), 5.59 (t, *J* = 7.2 Hz, 0.49H), 2.43 (t, *J* = 6.8 Hz, 2H), 2.27 (s, 3H), 2.14 (t, *J* = 7.4 Hz, 2H), 1.49 – 1.37 (m, 2H), 1.31 – 1.26 (m, 4H), 1.27 – 1.17 (m, 6H), 0.86 (t, *J* = 7.0 Hz, 3H), 0.80 (t, *J* = 6.8 Hz, 3H); HRMS (ESI) Calcd for $C_{19}H_{30}D$ $[M + H]^+$ 260.2489, found 260.2485. The ^1H NMR spectral patterns, except for the deuterated positions, are in good agreement with the literature data for the non-deuterated derivative. [12] The ^{13}C NMR spectrum is reported for the product with higher deuterium incorporation into the ortho position (Table 2, entry 11).



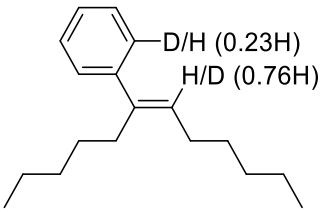
(*E*)-4-(Dodec-6-en-6-yl)-*N*,*N*-dimethylaniline-3-*d* (Table 2, entry 7): Prepared according to typical procedure A with a modification, that is, addition of CuBr (2.9 mg, 0.020 mmol) together with $CrCl_2$ and use of *t*BuOMe instead of *i*-Pr_2O. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded the title compound as a colorless oil (36.8 mg, 64%); ^1H NMR (400 MHz, CD_2Cl_2) δ 7.23 (d, *J* = 9.1 Hz, 1.13H), 6.81 – 6.57 (m, 2H), 5.56 (t, *J* = 7.2 Hz, 0.87H), 2.92 (s, 6H), 2.44 (t, *J* = 7.3 Hz, 2H), 2.16 (q, *J* = 7.3 Hz, 2H), 1.48 – 1.39 (m, 2H), 1.36 – 1.32 (m, 4H), 1.30 – 1.25 (m, 6H), 0.91 (t, *J* = 7.0 Hz, 3H), 0.85 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ 139.4, 139.3, 129.1, 126.7, 126.5, 126.2, 112.5, 40.8, 31.9, 31.7, 29.8, 29.3, 28.6, 28.5, 22.6, 22.5, 13.85, 13.83; HRMS (ESI) Calcd for $C_{20}H_{33}DN$ $[M + H]^+$ 289.2754, found 289.2753.



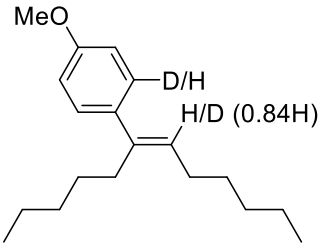
Typical procedure B (conditions B): Inside a glovebox, a 10 mL Schlenk tube was charged with $CrCl_2$ (2.4 mg, 0.020 mmol) and pyphos (11.7 mg, 0.040 mmol). The Schlenk tube was taken out from the glovebox and submerged in an ice bath for 5 min prior to the addition of an aryl Grignard reagent (0.60 mmol in THF). After stirring at 0 °C for 10 min, 6-dodecyne (33.2 mg, 0.20 mmol) was added. The reaction mixture was stirred at 80 °C for 18 h, and then allowed to cool to room temperature, quenched by the addition of D_2O (0.5 mL), and diluted with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford the desired product.



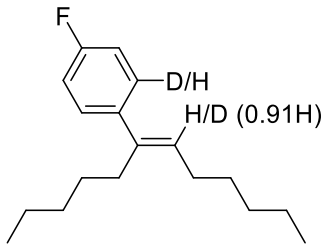
(*E*)-1-(Dodec-6-en-6-yl-7-*d*) benzene-2,3,4,5-d_4 (Table 1, entry 5): Prepared according to typical procedure B with pentadeuteratiod phenylmagnesium bromide. The reaction was quenched with H_2O. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (31.4 mg, 63%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (s, 0.64H), 5.65 (t, *J* = 7.3 Hz, 0.29H), 2.48 (t, *J* = 7.4 Hz, 2H), 2.18 (t, *J* = 7.4 Hz, 2H), 1.48 – 1.41 (m, 2H), 1.37 – 1.32 (m, 6H), 1.30 – 1.24 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 143.5, 140.2, 140.1, 129.3, 126.3, 32.0, 31.8, 29.84, 29.81, 29.7, 28.6, 22.8, 22.7, 14.24, 14.21; HRMS (ESI) Calcd for $C_{18}H_{24}D_5$ $[M + H]^+$ 250.2583, found 250.2586.



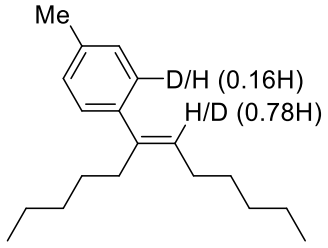
(*E*)-1-(Dodec-6-en-6-yl) benzene-2-*d* (Table 2, entry 8): Prepared according to typical procedure B. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (25.5 mg, 52%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 3.23H), 7.21 (t, *J* = 6.5 Hz, 1H), 5.65 (t, *J* = 7.3 Hz, 0.76H), 2.48 (t, *J* = 7.4 Hz, 2H), 2.19 (q, *J* = 7.2 Hz, 2H), 1.49 – 1.38 (m, 2H), 1.39 – 1.32 (m, 6H), 1.31 – 1.24 (m, 4H), 0.92 (t, *J* = 6.9 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 140.0, 136.7, 129.1, 128.1, 128.0, 126.3, 31.9, 31.7, 29.7, 29.6, 28.5, 28.4, 22.6, 22.5, 14.08, 14.05; HRMS (ESI) Calcd for $C_{18}H_{28}D$ $[M + H]^+$ 246.2332, found 246.2329. The ^{1}H and ^{13}C NMR spectral patterns, except for the deuterated positions, are in good agreement with the literature data for the non-deuterated derivative.[12,19]



(*E*)-1-(Dodec-6-en-6-yl)-4-methoxybenzene-2-*d* (Table 2, entry 9): Prepared according to typical procedure B. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded the title compound as a colorless oil (40.7 mg, 74%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 9.2 Hz, ~1H; overlapped with $CHCl_3$), 6.84 (d, *J* = 9.4 Hz, 2H), 5.58 (t, *J* = 7.3 Hz, 0.84H), 3.81 (s, 3H), 2.45 (t, *J* = 7.3 Hz, 2H), 2.17 (q, *J* = 7.3 Hz, 2H), 1.49 – 1.42 (m, 2H), 1.39 – 1.31 (m, 6H), 1.30 – 1.25 (m, 4H), 0.92 (t, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 139.5, 136.1, 127.9, 127.4, 127.0 (t, $^{1}J_{C\text{-}D}$ = 23.2 Hz), 113.6, 113.5, 55.4, 32.0, 31.8, 29.9, 29.8, 28.7, 28.6, 22.8, 22.7, 14.24, 14.22; HRMS (ESI) Calcd for $C_{19}H_{30}DO$ $[M + H]^+$ 276.2438, found 276.2434.

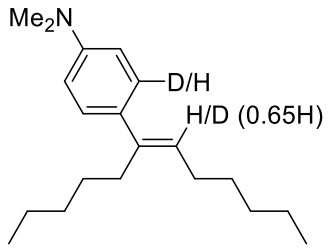


(*E*)-1-(Dodec-6-en-6-yl)-4-fluorobenzene-2-*d* (Table 2, entry 10): Prepared according to typical procedure B. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (31.6 mg, 60%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.24 (m, ~1H; overlapped with $CHCl_3$), 7.00 – 6.94 (m, 2H), 5.58 (t, *J* = 7.3 Hz, 0.91H), 2.44 (t, *J* = 7.3 Hz, 2H), 2.16 (q, *J* = 7.3 Hz, 2H), 1.46 – 1.39 (m, 2H), 1.36 – 1.30 (m, 6H), 1.30 – 1.24 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H), 0.85 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7 (d, $^{1}J_{C\text{-}F}$ = 245.4 Hz), 139.4(d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 139.1, 136.7, 129.1, 127.7 ($^{3}J_{C\text{-}F}$ = 7.8 Hz), 114.8 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 114.7 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 31.8, 31.6, 29.8, 29.6, 28.5, 28.3, 22.6, 22.5, 14.1, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.5; HRMS (ESI) Calcd for $C_{18}H_{27}DF$ $[M + H]^+$ 264.2238, found 249.2233.

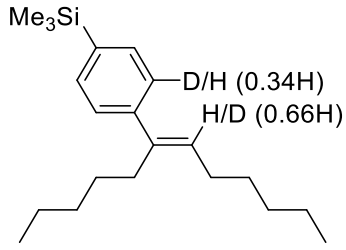


(*E*)-1-(Dodec-6-en-6-yl)-4-methylbenzene-2-*d* (Table 2, entry 11): Prepared according to typical procedure B. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (25.9 mg, 50%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.4 Hz, 1.16H), 7.13 – 7.09 (m, 2H), 5.61 (t, *J* = 7.3 Hz, 0.78H), 2.46 (t, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 2.17 (q, *J* = 7.3 Hz, 2H), 1.48 – 1.41 (m, 2H), 1.39 – 1.31 (m, 6H), 1.29 – 1.20 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.5, 139.8, 135.9, 128.8, 128.7, 128.4, 126.1, 31.9, 31.7, 29.7, 29.6, 28.52, 28.45, 22.6, 22.5, 21.0, 14.09, 14.08; HRMS (ESI) Calcd for $C_{19}H_{30}D$ $[M + H]^+$

260.2489, found 260.2484. The ^{1}H and ^{13}C NMR spectral patterns, except for the deuterated positions, are in good agreement with the literature data for the non-deuterated derivative.[12]

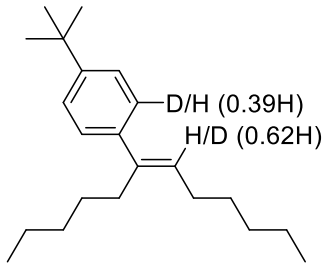


(*E*)-4-(Dodec-6-en-6-yl)-*N*,*N*-dimethylaniline-3-*d* (Table 2, entry 12): Prepared according to typical procedure B. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded the title compound as a colorless oil (35.2 mg, 61%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, ~1H; overlapped with $CHCl_3$), 6.69 (d, *J* = 8.3 Hz, 2H), 5.56 (t, *J* = 7.2 Hz, 0.65H), 2.94 (s, 6H), 2.44 (t, *J* = 7.6 Hz, 2H), 2.16 (q, *J* = 7.1 Hz, 2H), 1.47 – 1.39 (m, 2H), 1.36 – 1.31 (m, 6H), 1.29 – 1.26 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H), 0.85 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.35, 139.29, 129.2, 126.9, 126.5, 112.7, 40.9, 31.9, 31.7, 29.8, 29.5, 28.6, 28.5, 22.64, 22.55, 14.09, 14.06; HRMS (ESI) Calcd for $C_{20}H_{33}DN$ $[M + H]^+$ 289.2754, found 289.2751.

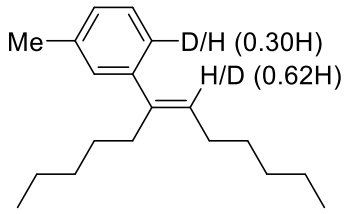


(*E*)-4-(Dodec-6-en-6-yl)phenyl-3-*d*)trimethylsilane (Table 2, entry 13): Prepared according to typical procedure B. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (38.1 mg, 60%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.8 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1.34H), 5.68 (t, *J* = 7.3 Hz, 0.66H), 2.48 (t, *J* = 7.5 Hz, 2H), 2.19 (q, *J* = 7.2 Hz, 2H), 1.47 – 1.42 (m, 2H), 1.38 – 1.32 (m, 6H), 1.30 – 1.23 (m, 4H), 0.90 (t, *J* = 6.8 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 3H), 0.27 (s, 9H); ^{13}C

NMR (101 MHz, $CDCl_3$) δ 143.8, 139.9, 138.0, 133.2, 133.1, 129.3, 125.6, 31.9, 31.6, 29.7, 29.6, 28.6, 28.5, 22.6, 22.5, 14.12, 14.08, -1.1; HRMS (ESI) Calcd for $C_{21}H_{36}DSi$ $[M + H]^+$ 318.2727, found 318.2722.

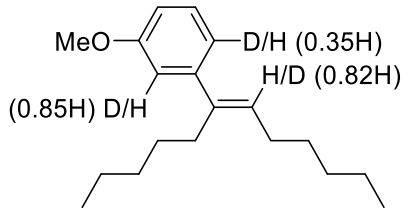


(*E*)-1-(*tert*-Butyl)-4-(dodec-6-en-6-yl)benzene-3-*d* (Table 2, entry 14): Prepared according to typical procedure B. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (35.6 mg, 59%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.28 (m, 3.39H), 5.65 (t, *J* = 7.3 Hz, 0.62H), 2.47 (d, *J* = 7.6 Hz, 2H), 2.18 (q, *J* = 7.2 Hz, 2H), 1.48 – 1.40 (m, 2H), 1.34 – 1.32 (m, 15H), 1.29 – 1.27 (m, 4H), 0.90 (t, *J* = 6.8 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.1, 140.3, 139.6, 136.7, 128.4, 125.7, 125.0, 124.9, 34.4, 32.9, 32.0, 31.7, 31.4, 29.6, 28.6, 28.5, 22.6, 22.5, 14.1(2C); HRMS (ESI) Calcd for $C_{22}H_{36}D$ $[M + H]^+$ 302.2958, found 302.2954.

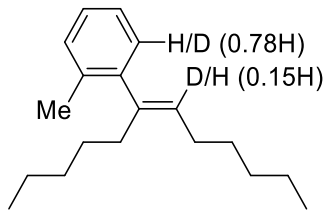


(*E*)-1-(Dodec-6-en-6-yl)-3-methylbenzene-6-*d* (Table 2, entry 15): Prepared according to typical procedure B. Silica gel chromatography (eluent: pentane) of the crude product afforded the title compound as a colorless oil (33.2 mg, 64%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.12 (m, 2.30H), 7.03 (d, *J* = 7.4 Hz, 1H), 5.63 (t, *J* = 7.3 Hz, 0.62H), 2.47 (t, *J* = 7.4 Hz, 2H), 2.35 (s, 3H), 2.18 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 2H), 1.38 – 1.30 (m, 6H), 1.30 – 1.25 (m, 4H), 0.92 (t, *J* = 6.8 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 137.5, 128.9, 128.0, 127.9, 127.1, 123.4, 31.9, 31.7, 29.7, 29.6,

28.54, 28.46, 22.6, 22.5, 21.5, 14.09, 14.07; HRMS (ESI) Calcd for $C_{19}H_{30}D$ $[M + H]^+$ 260.2489, found 260.2484. The ^1H and ^{13}C NMR spectral patterns, except for the deuterated positions, are in good agreement with the literature data for the non-deuterated derivative.[12]

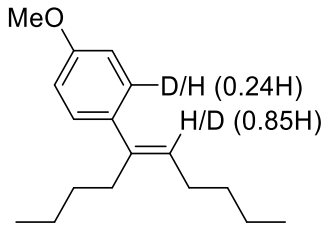


(*E*)-1-(Dodec-6-en-6-yl)-3-methoxylbenzene-6-*d* (Table 2, entry 16): Prepared according to typical procedure B. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded the title compound as a colorless oil (41.8 mg, 76%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 1H), 6.94 (d, *J* = 8.0 Hz, 0.35H), 6.88 (d, *J* = 2.6 Hz, 0.85H), 6.77 (dd, *J* = 8.2, 2.5 Hz, 1H), 5.65 (t, *J* = 7.3 Hz, 0.82H), 3.82 (s, 3H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.17 (q, *J* = 7.2 Hz, 2H), 1.48 – 1.41 (m, 2H), 1.37 – 1.32 (m, 6H), 1.29 – 1.25 (m, 4H), 0.91 (t, *J* = 6.9 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 145.1, 139.9, 129.3, 129.0, 128.9, 112.3, 111.4, 55.2, 31.9, 31.7, 29.8, 29.6, 28.5, 28.4, 22.6, 22.5, 14.07, 14.06; HRMS (ESI) Calcd for $C_{19}H_{30}DO$ $[M + H]^+$ 276.2438, found 276.2433. The ^1H and ^{13}C NMR spectral patterns, except for the deuterated positions, are in good agreement with the literature data for the non-deuterated derivative.[12]

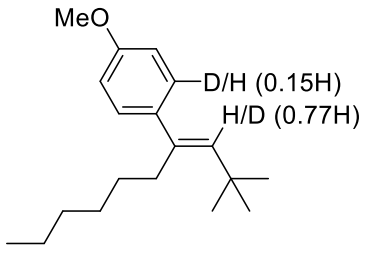


(*E*)-1-(Dodec-6-en-6-yl-7-*d*)-2-methylbenzene (Table 2, entry 17): Prepared according to typical procedure B. Silica gel chromatography (eluent:pentane) of the crude product afforded the title compound as a colorless oil (42.0 mg, 81%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.10 (m, 2.78H), 7.07 – 7.00 (m, 1H), 5.24 (t, *J* = 7.3 Hz, 0.15H), 2.33 (t, *J* = 7.0

Hz, 2H), 2.27 (s, 3H), 2.17 (t, *J* = 7.0 Hz, 2H), 1.46 – 1.39 (m, 2H), 1.38 – 1.31 (m, 4H), 1.28 – 1.21 (m, 6H), 0.92 (t, *J* = 7.0 Hz, 3H), 0.85 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 140.4, 135.2, 129.9, 129.8, 129.0, 126.2, 125.1, 32.0, 31.7, 31.6, 29.6, 29.5, 27.9, 22.6, 22.5, 19.9, 14.1, 14.06; HRMS (ESI) Calcd for $C_{19}H_{30}D$ $[M + H]^+$ 260.2489, found 260.2485. The ^{1}H and ^{13}C NMR spectral patterns, except for the deuterated positions, are in good agreement with the literature data for the non-deuterated derivative.[7]

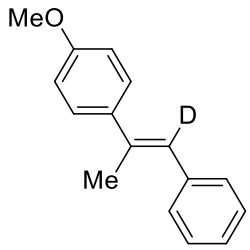


(*E*)-1-(Dec-5-en-5-yl)-4-methoxybenzene-2-*d* (Table 2, entry 18): Prepared according to typical procedure B. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded the title compound as a colorless oil (31.6 mg, 64%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.26 (d, *J* = 9.0 Hz, 1.24H), 6.97 – 6.62 (m, 2H), 5.55 (t, *J* = 7.3 Hz, 0.85H), 3.73 (s, 3H), 2.43 (t, *J* = 7.2 Hz, 2H), 2.14 (q, *J* = 7.2 Hz, 2H), 1.44 – 1.32 (m, 4H), 1.27 – 1.17 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.82 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.5, 139.3, 135.2, 127.4, 127.3, 114.1, 114.0, 55.5, 32.1, 31.0, 29.0, 28.1, 22.4, 22.3, 14.34, 14.29; HRMS (ESI) Calcd for $C_{17}H_{26}DO$ $[M + H]^+$ 248.2125, found 248.2122.

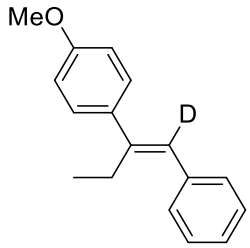


(*E*)-1-(2,2-dimethyldec-3-en-4-yl)-4-methoxybenzene-2-*d* (Table 2, entry 19): Prepared according to typical procedure B. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded a mixture of the title compound and minor unknown impurities as a colorless oil (7.7 mg, 14%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 9.1

Hz, 1.15H), 6.95 – 6.66 (m, 2H), 5.50 (s, 0.77H), 3.80 (s, 3H), 2.56 (t, *J* = 7.4 Hz, 2H), 1.50 – 1.22 (m, 8H), 1.19 (s, 9H), 0.84 (d, *J* = 7.8 Hz, 3H); HRMS (ESI) Calcd for $C_{19}H_{30}DO$ $[M + H]^+$ 276.2438, found 276.2434.

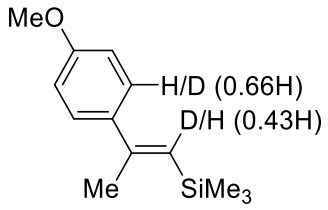


(*E*)-1-Methoxy-4-(1-phenylprop-1-en-2-yl-1-*d*)benzene (Table 2, entry 20): Prepared according to typical procedure B. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded a mixture of the title compound and minor unknown impurities as a colorless oil (11.3 mg, 25%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.8 Hz, 2H), 7.40 – 7.35 (m, 4H), 7.27 – 7.22 (m, 1H), 6.92 (d, *J* = 8.6 Hz, 2H), 3.85 (s, 3H), 2.27 (s, 3H); HRMS (ESI) Calcd for $C_{16}H_{16}DO$ $[M + H]^+$ 226.1342, found 226.1340. The ^1H NMR spectral patterns, except for the olefinic position, are in good agreement with the literature data for the non-deuterated derivative.[20]



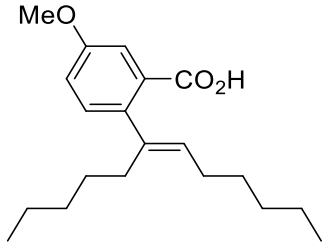
(*E*)-1-Methoxy-4-(1-phenylbut-1-en-2-yl-1-*d*)benzene (Table 2, entry 21): Prepared according to typical procedure B. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded a mixture of the title compound and minor unknown impurities as a colorless oil (8.6 mg, 18%); ^1H NMR (400 MHz, acetone-d_6) δ 7.45 – 7.34 (m, 4H), 7.34 – 7.27 (m, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.98 (d, *J* = 8.6 Hz, 2H), 3.84 (s, 3H), 2.33 (q, *J* = 7.4 Hz, 2H), 0.82 (t, *J* = 7.4 Hz, 3H); HRMS (ESI) Calcd for $C_{17}H_{18}DO$

$[M + H]^+$ 240.1499, found 240.1494. The ^1H NMR spectral patterns, except for the olefinic position, are in good agreement with the literature data for the non-deuterated derivative.[21]



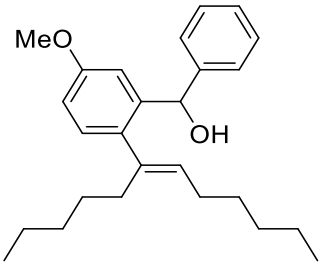
(*E*)-(2-(4-Methoxyphenyl)prop-1-en-1-yl-1-*d*)trimethylsilane (Table 2, entry 22): Prepared according to typical procedure B. Silica gel chromatography (eluent: hexane/Et_2O = 200/1) of the crude product afforded a mixture of the title compound and minor unknown impurities as a colorless oil (11.5 mg, 26%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.8 Hz, 1.66H), 6.85 (d, *J* = 8.5 Hz, 2H), 5.84 (s, 0.43H), 3.81 (s, 3H), 2.19 (s, 3H), 0.18 (s, 9H); HRMS (ESI) Calcd for $C_{13}H_{20}DOSi$ $[M + H]^+$ 222.1424, found 222.1420. The ^1H NMR spectral patterns, except for the olefinic position, are in good agreement with the literature data for the non-deuterated derivative.[22]

Electrophilic Trapping of *ortho*-Alkenylarylmagnesium Bromide

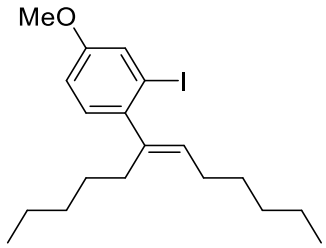


(*E*)-2-(Dodec-6-en-6-yl)-5-methoxybenzoic acid (3): After the reaction of 4-methoxyphenylmagnesium bromide and 6-dodecyne under conditions B, a CO_2-filled balloon was attached to the Schlenk tube. The reaction mixture was stirred at room temperature for 9 h, followed by the addition of saturated aqueous NH_4Cl (2 mL) and ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ethyl acetate = 5/1) of the crude product afforded the title compound as a colorless oil (39.6 mg, 62%); ^1H NMR (400 MHz, $CDCl_3$)

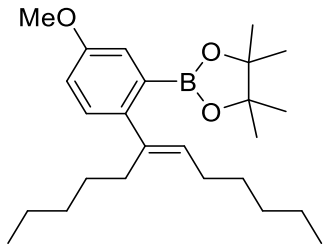
δ 7.45 (d, *J* = 2.8 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 1H), 7.01 (dd, *J* = 8.5, 2.8 Hz, 1H), 5.29 (t, *J* = 7.3 Hz, 1H), 3.84 (s, 3H), 2.37 (t, *J* = 7.1 Hz, 2H), 2.15 (q, *J* = 7.2 Hz, 2H), 1.45 – 1.38 (m, 2H), 1.36 – 1.30 (m, 4H), 1.27 – 1.18 (m, 6H), 0.90 (t, *J* = 6.8 Hz, 3H), 0.84 (t, *J* = 6.8 Hz, 3H)); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 157.9, 140.9, 139.2, 131.9, 129.6, 129.4, 118.5, 114.8, 55.5, 32.4, 31.9, 31.5, 29.3, 28.22, 28.15, 22.6, 22.5, 14.1, 14.0; HRMS (ESI) Calcd for $C_{20}H_{31}O_3$ $[M + H]^+$ 319.2273, found 319.2270.



(*E*)-(2-(Dodec-6-en-6-yl)-5-methoxyphenyl)(phenyl)methanol (4): The reaction of 4-methoxyphenylmagnesium bromide and 6-dodecyne under conditions B was quenched by the addition of benzaldehyde (64 mg, 0.60 mmol) at room temperature. After stirring for 12 h, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (2 mL) and then diluted with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/ethyl acetate = 20/1) of the crude product afforded the title compound as a colorless oil (45.6 mg, 60%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 4H), 7.25 – 7.20 (m, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.93 (d, *J* = 2.7 Hz, 1H), 6.78 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.02 (d, *J* = 3.8 Hz, 1H), 5.19 (t, *J* = 7.2 Hz, 1H), 3.75 (s, 3H), 2.45 – 2.18 (m, 2H), 2.13 (t, *J* = 7.0 Hz, 2H), 2.10 (d, *J* = 3.8 Hz, 1H), 1.38 – 1.33 (m, 2H), 1.30 – 1.23 (m, 10H), 0.88 (t, *J* = 6.9 Hz, 3H), 0.84 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 143.9, 142.3, 139.0, 136.4, 131.5, 130.4, 128.2, 127.2, 126.7, 112.9, 112.3, 110.0, 72.6, 55.2, 32.8, 32.0, 31.6, 29.4, 28.1, 27.9, 22.6, 22.5, 14.1 (2C).; HRMS (ESI) Calcd for $C_{26}H_{37}O_2$ $[M + H]^+$ 381.2794, found 381.2792.



(*E*)-1-(Dodec-6-en-6-yl)-2-iodo-4-methoxybenzene (5): The reaction of 4-methoxyphenylmagnesium bromide and 6-dodecyne under conditions B was quenched by the addition of iodine (305 mg, 1.2 mmol) at room temperature. After stirring for 3 h, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (2 mL) and then diluted with ethyl acetate (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography (eluent: hexane/Et_2O = 250/1) of the crude product afforded the title compound as a colorless oil (50.4 mg, 63%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 2.6 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.83 (dd, *J* = 8.4, 2.6 Hz, 1H), 5.25 (t, *J* = 7.3 Hz, 1H), 3.78 (s, 3H), 2.34 (t, *J* = 7.0 Hz, 2H), 2.15 (q, *J* = 7.2 Hz, 2H), 1.52 – 1.49 (m, 2H), 1.47 – 1.33 (m, 10H), 0.91 (t, *J* = 6.7 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 142.7, 141.7, 136.7, 131.6, 129.7, 124.0, 113.8, 55.5, 32.9, 31.9, 31.6, 29.2, 28.0, 27.7, 22.6, 22.6, 14.1, 14.1; HRMS (ESI) Calcd for $C_{19}H_{30}IO$ $[M + H]^+$ 401.1341, found 401.1338.



(*E*)-2-(2-(Dodec-6-en-6-yl)-5-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6): The reaction of 4-methoxyphenylmagnesium bromide and 6-dodecyne under conditions B was quenched by the addition of trimethyl borate (104 mg, 1.0 mmol) at 0 °C. After stirring at room temperature for 6 h, the reaction mixture was hydrolyzed by

the addition of aqueous HCl (1.0 M, 4 mL) and additional stirring for 3 h. The resulting mixture was extracted with dichloromethane (3 x 10 mL), and the combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was dissolved in Et_2O (5 mL) and treated with pinacol (118 mg, 1.0 mmol) in the presence of 4Å molecular sieves (200 mg) at room temperature for 6 h. The mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography (eluent: hexane/Et_2O = 30/1) to afford the title compound as a colorless oil (24.0 mg, 30%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 2.9 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.86 (dd, *J* = 8.4, 2.9 Hz, 1H), 5.20 (t, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 2.37 (t, *J* = 7.0 Hz, 2H), 2.11 (q, *J* = 7.2 Hz, 2H), 1.45 – 1.39 (m, 2H), 1.35 – 1.32 (m, 4H), 1.30 (s, 12H), 1.26 – 1.22 (m, 6H), 0.90 (t, *J* = 7.0 Hz, 3H), 0.83 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 143.5, 142.1, 129.2, 128.9, 118.8, 115.6, 110.0 (borylated carbon), 83.4 (2C), 55.3, 32.8, 31.9, 31.7, 29.5, 28.4, 28.0, 24.8 (4C), 22.65, 22.6, 14.1 (2C); HRMS (ESI) Calcd for $C_{25}H_{42}BO_3$ $[M + H]^+$ 401.3227, found 401.3223.

3.5 References

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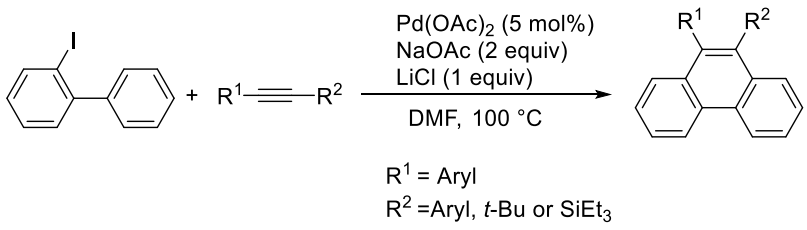
Chapter 4. Phenanthrene Synthesis via Chromium-Catalyzed Annulation of Biaryl-2-Magnesium Reagents and Alkynes

4.1 Introduction

Polycyclic aromatic hydrocarbons (PAHs) have received considerable attention as common structural elements in organic materials.[1] They are incorporated as core structural motifs in various semiconducting or luminescent molecules for applications in organic field-effect transistors (OFETs) and organic light-emitting diodes (OLEDs).[2] Among such polycyclic aromatics, phenanthrene represents a small but versatile elementary skeleton, as its modification by different functional groups offers an opportunity to achieve attractive properties.[3] As such, a number of phenanthrene derivatives have been synthesized to explore their optical and electronic properties.[4]

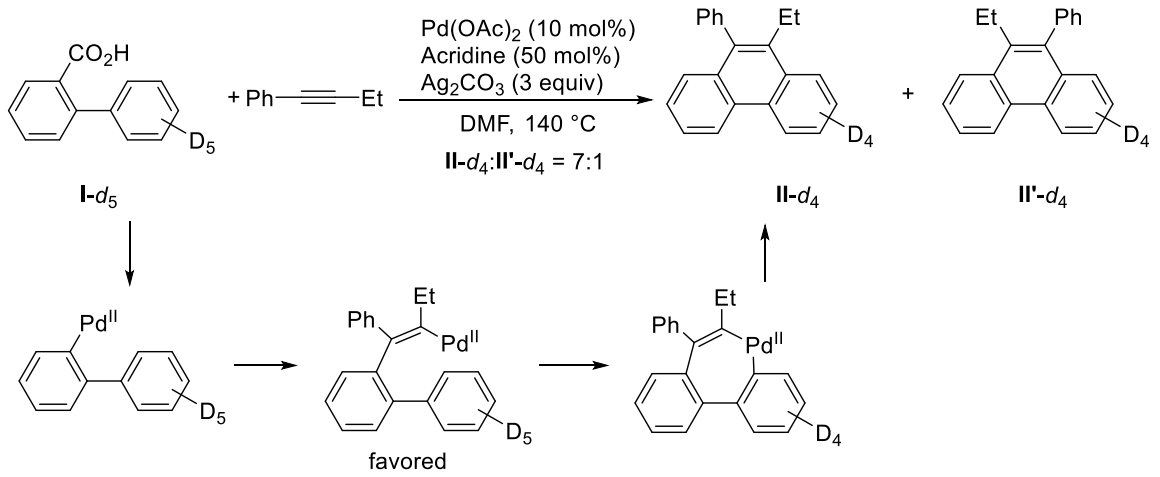
Thus far, various synthetic approaches for the construction of the phenanthrene frameworks from readily available building blocks have been developed. Among them, the intermolecular [4 + 2] benzannulation between 2-functionalized 1,1'-biaryls and alkynes is highly attractive from the viewpoint of step- and atom-efficiency. Early examples were developed by Heck[5] and Larock[6], using Pd-catalyzed annulation of internal acetylenes and 2-iodide-1,1'-biaryls (Scheme 4.1). The reaction was general for aryl acetylenes.

Scheme 4.1. Phenanthrene Synthesis through Pd-Catalyzed Annulation of 2-Iodide-1,1'-Biaryl and Internal Acetylene



In 2010, Glorius and coworkers reported the Pd-catalyzed formal [4 + 2] annulation of 2-arylbenzoic acids with alkynes via successive cleavage of both C−H and C−C bonds (Scheme 4.2).[7] The reaction of 2-pentadeuteriophenylbenzoic acid **I**-d_5 and 1-phenyl-1-butyne could provide phenanthrene product in high regioselectivity (**II**-d_4:**II'**-d_4 = 7:1) owing to the proposed selective insertion of alkyne into biarylpalladium species.

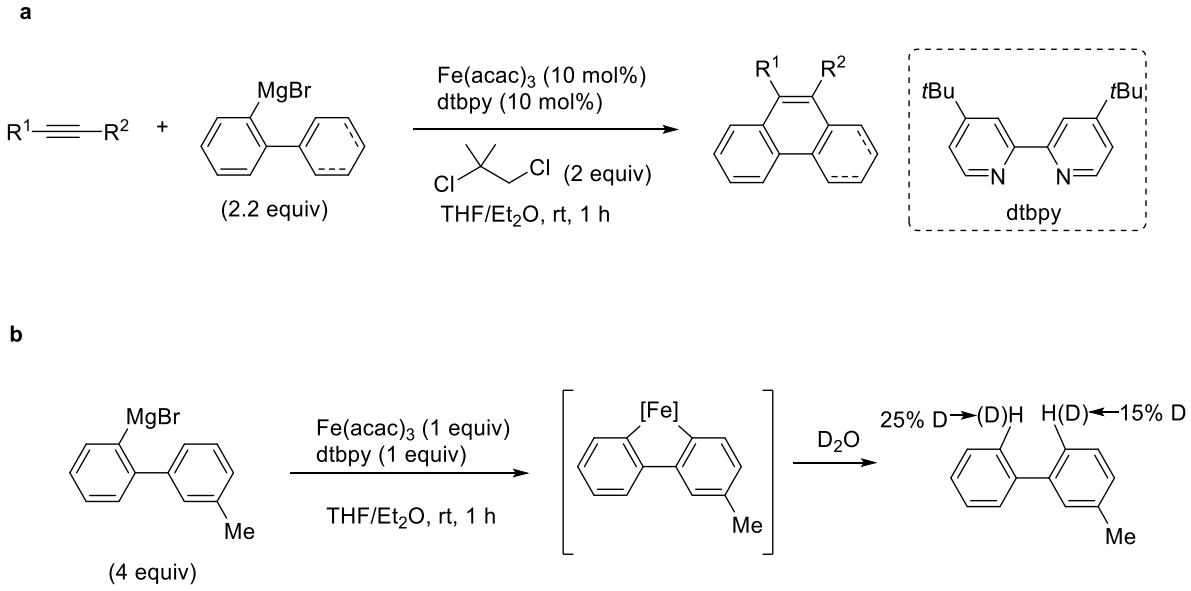
Scheme 4.2. Phenanthrene Synthesis through Pd-Catalyzed Annulation of 2-Arylbenzoic Acids and Internal Alkynes



In 2011, Nakamura and coworkers reported the Fe-catalyzed formal [4+2] annulation of biaryl-2-Grignard reagent and alkynes in the presence of a catalytic system comprising $Fe(acac)_3$, 4, 4'-di-*tert*-butyl-2, 2'-bipyridyl, and 1,2-dichloro-2-methylpropane (Scheme 4.3a).[8] The reaction took place at room temperature and tolerated sensitive functional groups such as bromide and olefin. A five-membered ferrocycle intermediate was proposed to mediate the activation of the *ortho* C–H bond prior to insertion of alkyne according to the following control experiment (Scheme 4.3b). (3'-Methylbiphenyl-2-yl)magnesium bromide (0.4 mmol) reacted with $Fe(acac)_3$ (35 mg, 0.1 mmol) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (27 mg, 0.1 mmol) in the absence of alkyne and 1,2-dichloro-2-methylpropane. Upon quenching with D_2O, the reaction gave 3-methyl-1,1'-biphenyl with

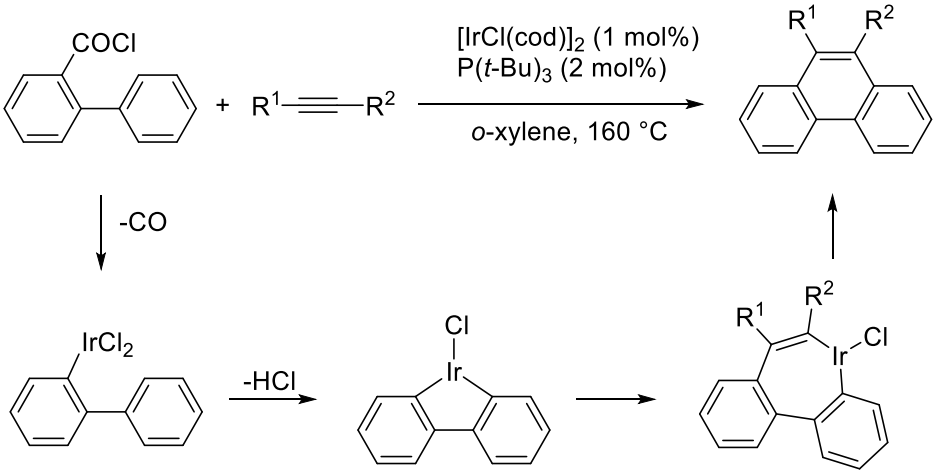
deuterium incorporation into both 2'- and 6-position (25% and 15% respectively) as indicated by ^{1}H-NMR and GCMS analysis.

Scheme 4.3. Phenanthrene Synthesis through Fe-Catalyzed Annulation of Biaryl-2-Grignard Reagent and Alkynes



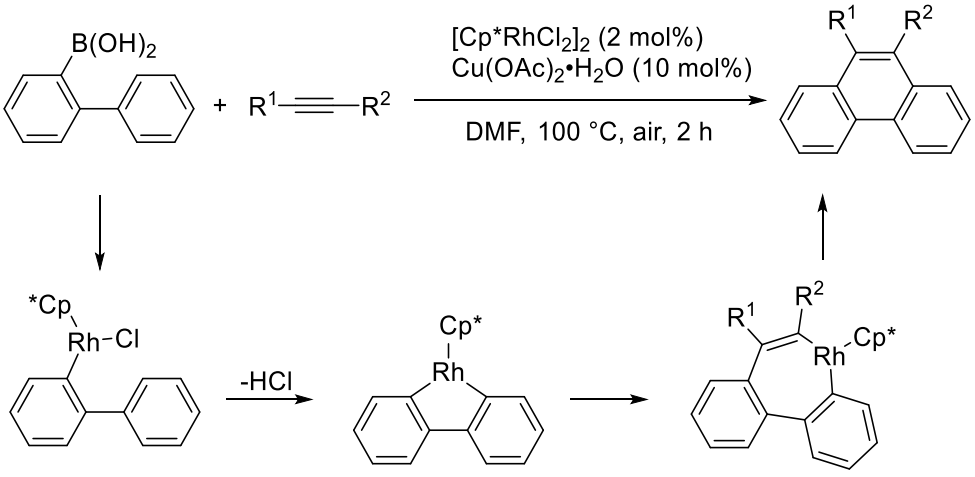
In 2014, Miura and coworkers reported the annulation of 2-arylbenzoyl chlorides and alkynes to synthesize phenanthrene derivatives in the presence of a catalyst system of $[IrCl(cod)]_2$/P(*t*-Bu)$_3$ (Scheme 4.4).[9] The reaction occured without any base and was general for both aliphatic and aromatic alkynes. A five-membered iridacycle was proposed to mediate the facile intramolecular iridation via C−H bond cleavage.

Scheme 4.4. Phenanthrene Synthesis through Ir-Catalyzed Annulation of 2-Arylbenzoyl Chlorides and Internal Alkynes



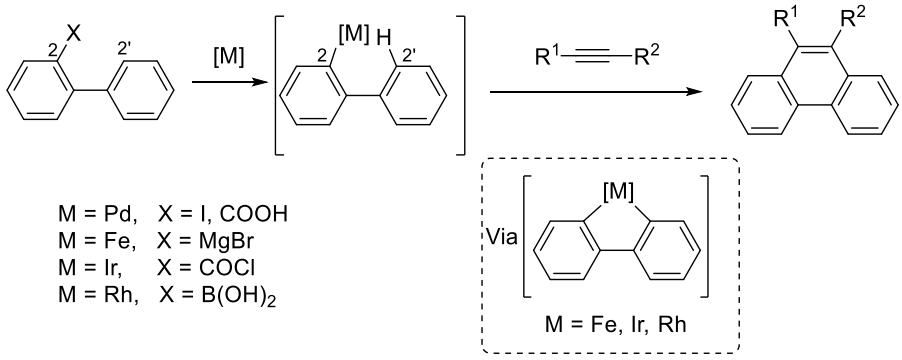
In 2016, Miura and coworkers also reported the oxidative annulation of (2-arylphenyl)boronic acids and alkynes to construct phenanthrene derivatives in the presence of a rhodium catalyst with dioxygen as a terminal oxidant (Scheme 4.5).[10] The reaction occurred without external base and was proposed to proceed via a five-membered rhodacycle via intramolecular C−H bond cleavage.

Scheme 4.5. Phenanthrene Synthesis through Rh-Catalyzed Oxidative Annulation of 2-Arylphenylboronic Acids and Internal Alkynes



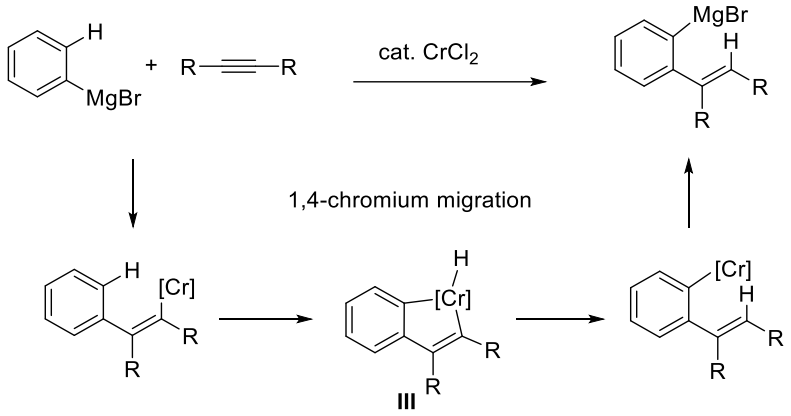
In general, the above annulation strategy involves the intramolecular C2'−H bond activation of 2-biaryl−transition metal species as a key step, where the transition metal is palladium,[5,6,7] iron,[8] iridium,[9] or rhodium[10] (Scheme 4.6). In addition, except for those catalyzed by palladium, these annulative coupling reactions favor the pathway via formation of the five-membered biaryl metalacycle prior to insertion of alkynes.

Scheme 4.6. Phenanthrene Synthesis through Annulative Coupling of 2-Functionalized Biaryl and Alkyne



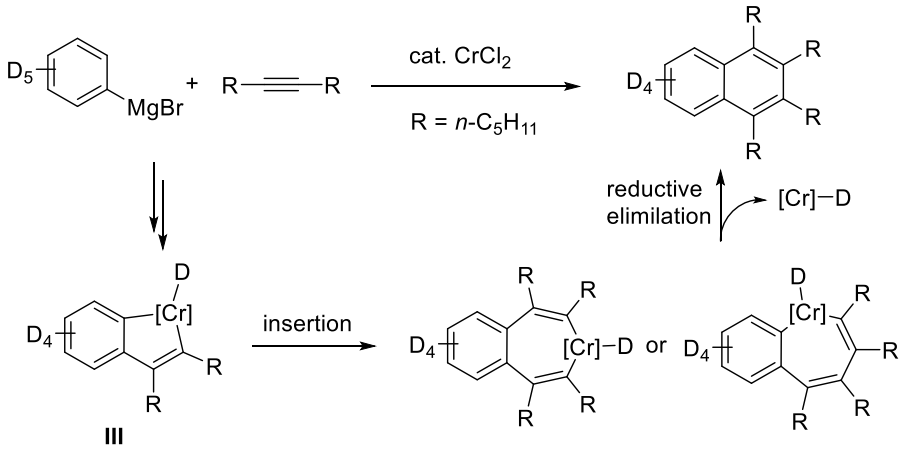
Recently, we discovered a chromium-catalyzed addition reaction of an aryl Grignard reagent to a dialkylalkyne to afford an *ortho*-alkenylarylmagnesium species, which likely involves 1,4-chromium migration as the key step (Scheme 4.7).[11] The reaction is proposed to proceed through insertion of the alkyne into an arylchromium species, 1,4-chromium migration, and transmetalation between the resulting *ortho*-alkenylarylchromium species and the Grignard reagent. In light of a mechanistic study on related 1,4-rhodium migration, one may also propose that the key 1,4-chromium migration is initiated by oxidative addition of the *ortho* C–H bond to chromium to form a 5-membered chromacycle **III**, which then undergoes reductive elimination to give the *ortho*-alkenylarylchromium species.[12]

Scheme 4.7. Chromium-Catalyzed Migratory Arylmagnesiation of Alkyne



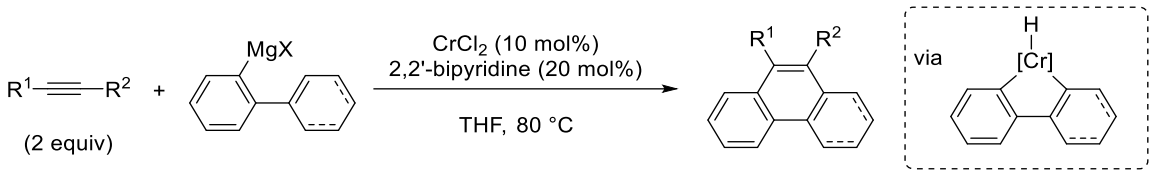
During the development of the above migratory arylmagnesiation reaction using pentadeuteriophenylmagnesium bromide and 6-dodecyne, we detected a byproduct assignable to 1,2,3,4-tetrapentylnaphthalene-5,6,7,8-d_4 by GCMS analysis. The formation of this byproduct may be explained by reaction pathways shown in Scheme 4.8, while alternative pathways would also be conceivable. Thus, the chromacycle **III** would undergo insertion of the alkyne into the alkenyl–Cr or aryl–Cr bond to generate the respective seven-membered chromacycle intermediates. These intermediates would then undergo reductive elimination to afford the naphthalene product, while the fate of the accompanying D–Cr species would not be obvious.

Scheme 4.8. Reaction Pathways for the Formation of Naphthalene Derivative as A Byproduct



Based on our own findings on the chromium catalysis (Scheme 4.7) and the general mechanistic aspect of the annulative phenanthrene synthesis (Scheme 4.6), we envisioned that a 2-biarylchromium species, generated by transmetalation from the corresponding Grignard reagent, would undergo annulation with an internal alkyne via intramolecular C–H activation,[13] thus affording a phenanthrene derivative. On the basis of this hypothesis, we have successfully developed a chromium-catalyzed annulation reaction of 2-biaryl Grignard reagents and alkynes to afford a series of 9,10-disubstituted phenanthrenes, which is reported in this chapter (Scheme 4.9). The reaction features a simple catalytic system comprising inexpensive $CrCl_2$ and bidentate nitrogen ligand such as bipyridine. Unlike the iron-catalyzed variant reported earlier by Nakamura et al.,[8] the present reaction does not necessitate an external oxidant, which is also mechanistically interesting. Analysis of byproducts of the reaction, together with deuterium-labeling experiments, shed light on mechanistic complexity of the reaction.

Scheme 4.9. Chromium-Catalyzed Annulation of Biaryl-2-Magnesium Reagent with Alkyne

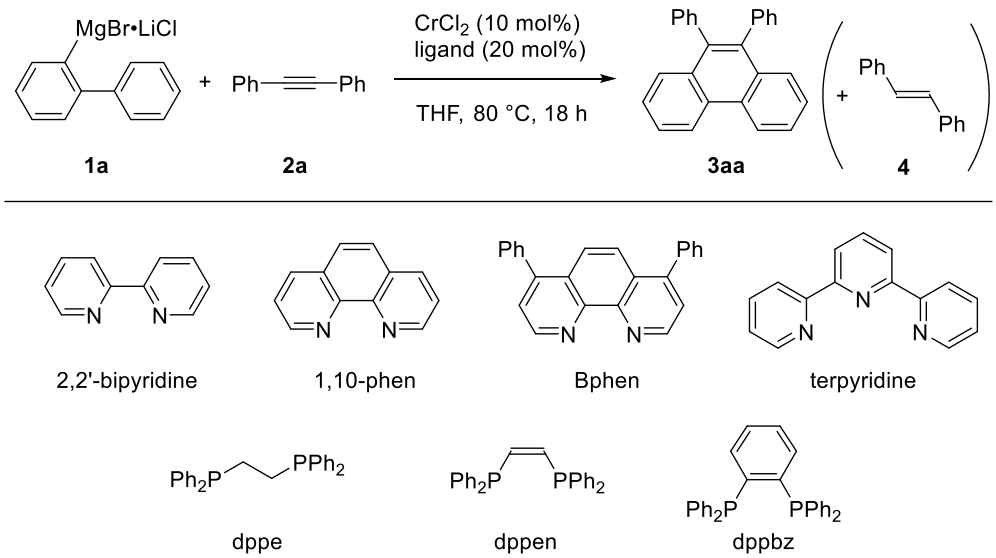


4.2 Results and Discussion

At the beginning of the present work, we examined the annulation reaction of [1,1′-biphenyl]-2-ylmagnesium reagent **1a** with diphenylacetylene (**2a**, 2 equiv) in the presence of $CrCl_2$ in THF at 80 °C (Table 4.1). To our delight, the desired phenanthrene **3aa** was detected by GC/MS analysis, albeit in low yield (entry 1). No homocoupling product of Grignard reagent **1a** was detected. Subsequently, various ligands were screened to improve the reaction efficiency. As a result, 2,2'-bipyridine was identified as the optimal ligand, achieving 78% isolated yield of **3aa** (entry 2). Another N,N'-bidentate ligands such as 1,10-phenanthroline and bathophenanthroline afforded somewhat lower yields (entries 3 and 4), while N,N',N"-tridentate ligand terpyridine and bidentate phosphine ligands (dppe, dppen, dppbz) turned out to be far less ineffective (entries 5-8). The addition of 2,3-dichlorobutane (DCB) as an oxidant[14] was detrimental, leading to significant amount of side-product generated from homocoupling of the Grignard reagent **1a** (entry 9). Importantly, (*E*)-stilbene **4** was detected as a byproduct by GC/MS analysis, suggesting that diphenylacetylene **2a** acted as a hydrogen acceptor. This observation prompted us to examine norbornene as a possible hydrogen acceptor to minimize consumption of **2a**, which unfortunately resulted in a diminished yield of **3aa** (entry 10). Note that the reaction became rather sluggish by using $FeCl_2$ or $NiCl_2$ instead of $CrCl_2$ under otherwise identical

conditions (entries 11 and 12). It is also notable that the present reaction took place at room temperature, albeit with lower conversion and yield (entry 13).

Table 4.1. Optimization of Reaction Conditions for Chromium-Catalyzed Annulation of 1,1'-Biphenyl-2-Magnesium Reagent with Diphenylacetylene[a]



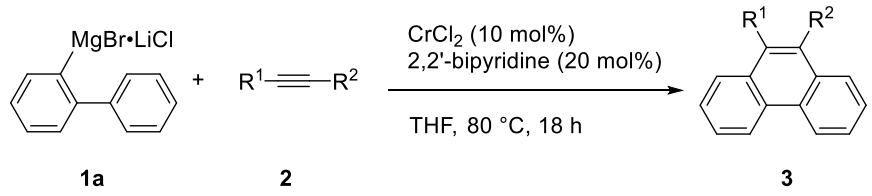
Entry	ligand	Conv. of alkyne (%)[b]	**3aa** yield (%)[b]
1	-	100	19
2	**2,2'-bipyridine**	**100**	**80 (78)**[c]
3	1,10-phen	100	67
4	Bphen	100	57
5	terpyridine	51	15
6	dppe	85	30
7	dppen	47	12
8	dppbz	94	20
9[d]	2,2'-bipyridine	9	16
10[e]	2,2'-bipyridine	100	21
11[f]	2,2'-bipyridine	94	7
12[g]	2,2'-bipyridine	100	14
13[h]	2,2'-bipyridine	76	56

[a] Reactions Conditions: $CrCl_2$ (10 mol%), ligand (20 mol%), **1a** (0.2 mmol, in THF), **2a** (0.4 mmol), THF, 80 °C, 18 h. [b] Determined by GC using *n*-tridecane as an internal standard. [c] The yield of isolated product is shown in parentheses. [d] DCB (2,3-dichlorobutane, 0.50 mmol) was added. [e] Norbornene (0.40 mmol) was added. [f] $FeCl_2$ (10 mol%)was used instead of $CrCl_2$. [g] $NiCl_2$ (10 mol%)was used instead of $CrCl_2$. [h] The reaction was performed at room temperature.

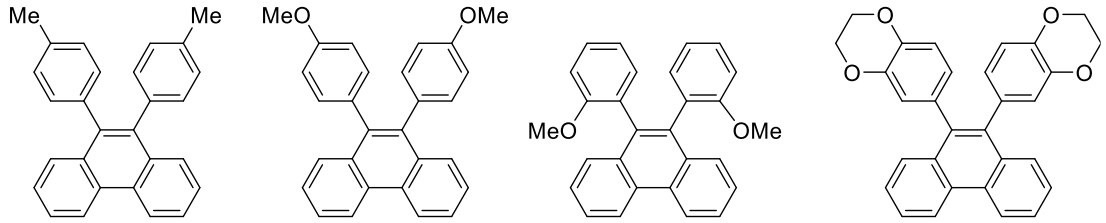
With the optimized conditions in hand (Table 4.1, entry 2), we began to investigate the scope of alkynes for the present annulation reaction (Table 4.2). A series of diarylacetylenes participated in the annulation reaction with **1a** to afford the corresponding 9,10-disubstiuted phenanthrenes **3ab**−**3ah** in moderate yields. Electron-donating substituents were tolerated on the phenyl group of symmetrical diarylacetylenes (**2b**−**2e**), regardless of their presence at the *ortho*-, *meta*- or *para* position. The reaction became somewhat sluggish with diarylacetylenes bearing trifluoromethyl groups (see the products **3ag** and **3ah**), where incomplete conversion of the alkyne was observed. The use of 1,2-di(thiophen-2-yl)ethyne **2i** also led to the formation of the desired heteroaryl-substituted phenanthrene in a modest yield. Besides the diarylalkynes, a series of aryl(alkyl)alkynes

proved suitable to take part in the present transformation, affording the corresponding phenanthrene derivatives **3aj–3ao**. For these alkynes, higher yields were achieved employing bathophenanthroline as the ligand instead of 2,2'-bipyridine. Once again, the reaction was compatible with functional groups including Cl and OMe (**3al** and **3am**), as well as sterically hindered *ortho*-methyl substituent (**3an**). Interestingly, the reaction of phenyl(cyclopropyl)acetylene (**2o**) resulted in the expected product **3ao** in 50% yield, accompanied by a small amount (10%) of another phenanthrene derivative **3ao'** as a result of the ring-opening of the cyclopropyl group. The present annulation reaction was also applicable to unsymmetrical or symmetrical dialkylalkynes, affording the desired products **3ap** and **3aq** in good yields. However, the reaction of a terminal alkyne such as phenylacetylene resulted in partial dimerization of the alkyne rather than the desired annulation.

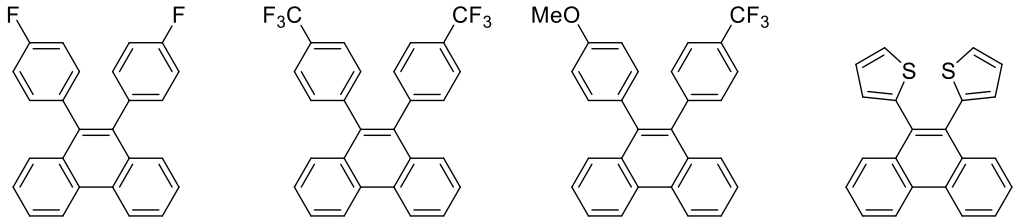
Table 4.2. Scope of Alkynes for the Phenanthrene Synthesis[a]



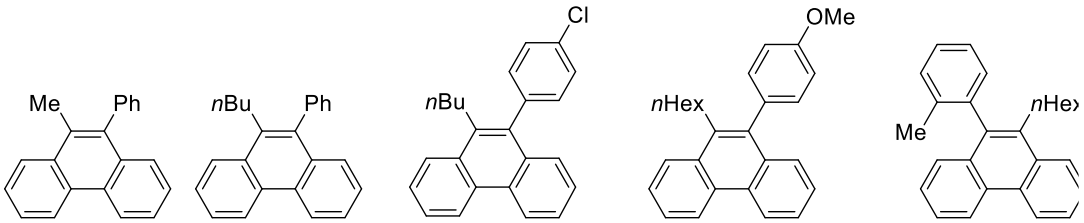
1a **2** **3**



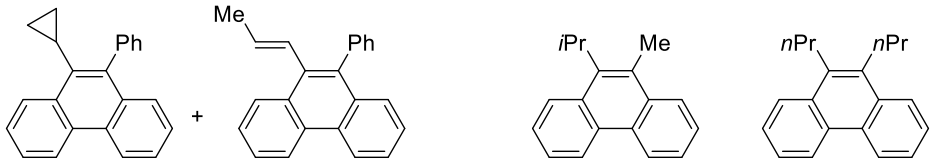
3ab, 57% **3ac**,66% **3ad**,65% **3ae**,51%



3af,54% **3ag**,41%[b] **3ah**,48%[c] **3ai**,49%



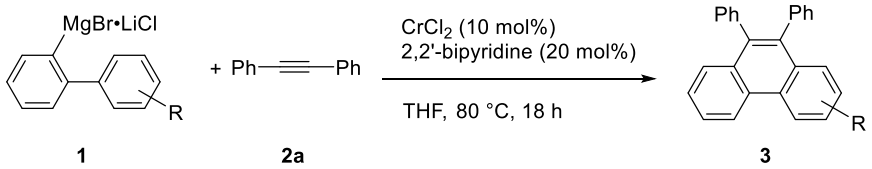
3aj, 88%[d] **3ak**, 88%[d] **3al**, 52%[d] **3am**, 78%[d] **3an**, 73%[d]



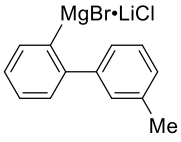
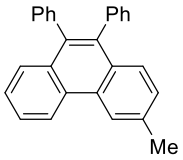
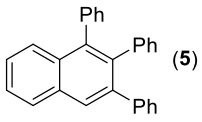
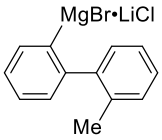
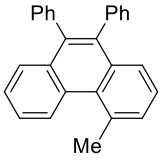
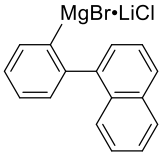
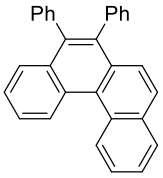
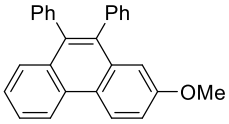
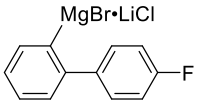
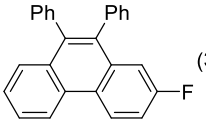
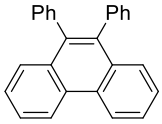
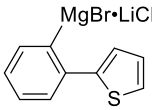
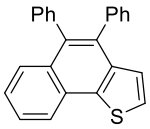
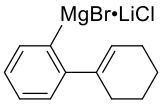
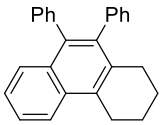
[a] The reaction was performed on a 0.2 mmol scale under the reaction conditions in Table 4.1, entry 2. [b] 80% Conversion of **2g** as determined by GC using *n*-tridecane as an internal standard. [c] 86% Conversion of **2h** as determined by GC using *n*-tridecane as an internal standard. [d] Using bathophenanthroline as the ligand instead of 2,2'-bipyridine. [e] Inseparable mixture of **3ao** and **3ao'** was obtained, yields were determined by ^{1}H-NMR analysis.

This present reaction annulation protocol was successfully applied to a range of substituted biaryl Grignard reagents **1b**−**1h** using diphenylacetylene **2a** as the reaction partner (Table 4.3). The Grignard reagents were readily prepared in small scale (2 mmol) through magnesium insertion into the starting aryl bromides in the presence of LiCl, according to Knochel's procedure (see Experimental section for detail).[15] Biaryl Grignard reagent bearing a *meta*-methyl substituent, **1b** underwent regioselective annulation at the less hindered *ortho* position to afford the corresponding 3-substituted phenanthrene **3ba** in 54% yield (entry 1). As a byproduct of this reaction, we managed to isolate 1,2-3-triphenylnaphthalene (**5**) in 23% yield, which appeared to result from dimerization of **2a**. The structure of **5** was unambiguously characterized by X-ray crystallographic analysis (Figure 4.1, Experimental Section). In fact, the naphthalene derivative **5** was consistently detected (in a varying quantity) in the crude product of the rest of the entries in Table 4.2. Regardless of the steric hindrance, biaryl Grignard reagents bearing 2-tolyl or1-naphthyl group took part in the reaction to give the desired phenanthrenes **3ca** and **3da** in moderate yields (entries 2 and 3). Grignard reagents bearing 4-methoxyphenyl or 4-fluorophenyl group were also tolerated to afford the products **3ea** and **3fa** (entries 4 and 5), while the latter case was accompanied by a partially defluorinated product, i.e., **3aa**. Notably, 2-(2-thienyl)phenyl Grignard reagent **1g** could also be employed in the annulation with **2a**, furnishing 4,5-diphenylnaphtho[1,2-*b*]thiophene **3ga** (entry 6). In addition, the reaction using 2-(cyclohexen-1-yl)phenyl Grignard reagent **1h** resulted in naphthalene derivative **3ha** in a high yield of 83% (entry 7).

Table 4.3. Scope of Biaryl Grignard Reagents for the Phenanthrene Synthesis[a]



1 **2a** **3**

entry	**1** (ArMgX)	product	yield[b]
1	 (**1b**)	 (**3ba**) +  (**5**)	54% (**3ba**) + 23% (**5**)
2	 (**1c**)	 (**3ca**)	39%
3	 (**1d**)	 (**3da**)	54%
4	 (**1e**)	 (**3ea**)	62%
5	 (**1f**)	 (**3fa**) +  (**3aa**)	55% (**3fa**)[c] + 11% (**3aa**)[c]
6	 (**1g**)	 (**3ga**)	50%
7	 (**1h**)	 (**3ha**)	83%

[a] The reaction was performed on a 0.2 mmol scale under the reaction conditions in Table 4.1, entry 2. [b] Isolated yield. [c] Inseparable mixture of **3fa** and **3aa** was obtained, yields were estimated by ^{1}H-NMR analysis.

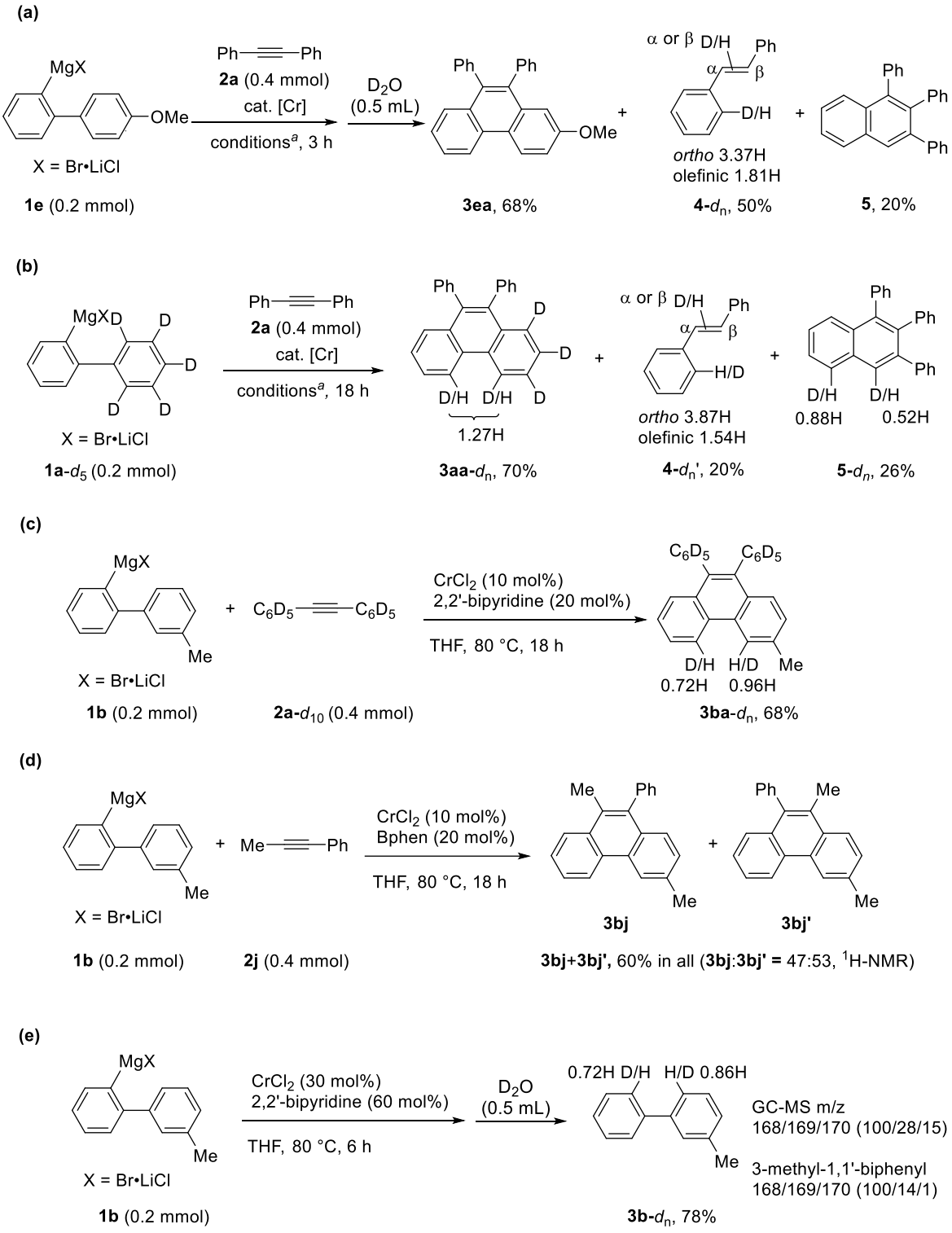
A series of mechanistic experiments were performed to gain insight into the reaction pathway of the present annulation reaction (Scheme 4.10). The annulation of the biaryl Grignard reagent **1e** and **2a**, upon quenching with D_2O after 3 h, afforded the phenanthrene product **3ea** along with partially deuterated (*E*)-stilbene **4**-d_n and 1,2,3-triphenylnaphthalene **5** (Scheme 4.10a). For **4**, deuteration was observed substantially at the *ortho* position (0.63D) and slightly at the olefinic position (0.19D), which implied the presence of metalated stilbene species in the reaction mixture. The reaction of pentadeuterated biaryl Grignard reagent **1a**-d_5 with **2a** also afforded a mixture of phenanthrene **3aa**-d_n, (*E*)-stilbene **4**-d_n', and triphenylnaphthalene **5**-d_n, the deuterium distribution among which was intriguing (Scheme 4.10b). For **3aa**-d_n, the deuterium content at the inner rim positions (4- and 5-positions) was apparently lower than unity (0.73D). This indicates that the *ortho* position of **1a**-d_5 not involved in the C–C bond formation undergoes partial C–D bond cleavage/C–H bond formation during the reaction. For **4**-d_n', deuteration of the olefinic position was more substantial than that of the *ortho* position, which would reflect the role of **2a** to accept *ortho*-deuterium atom of **1a**-d_5. Finally, **5**-d_n displayed substantial and slight deuterations of the 4- and 5-positions, respectively, which appeared to be consistent with the deuteration pattern in **4**-d_n'. Interestingly, GC/MS analysis of **4**-d_n' and **5**-d_n indicated the presence of certain amounts of doubly deuterated molecules, as the peak intensity of [M+2] species was apparently greater than expected from natural abundance (see Experimental section).

On the basis of the analysis of the reaction of **1a**-d_5, we speculated that the *ortho* deuterium atom of **1a**-d_5 not only migrates to the C–C triple bond of **2a**, but also undergoes partial, and possibly reversible exchange with the *ortho*-hydrogen atom of **2a**. We also suspected that not only the *ortho*-deuterated positions (i.e., 2'- and 6'-positions) but also the 6-position of **1a**-d_5 are involved in such exchange process. This conjecture was supported by the reaction of unsymmetrical biaryl Grignard reagent **1b** and fully deuterated

diphenylacetylene **2a**-d_{10} (Scheme 4.10c). Thus, the product **3ba**-d_n showed apparent deuterium incorporation into the 5-position (0.72H). Deuteration of the 4-position was almost negligible, which is reasonable in light of the steric hindrance of the neighboring methyl substituent.

The reaction of **1b** with unsymmetrical 1-phenyl-1-proyne **2j** resulted in a mixture of regioisomers **3bj** and **3bj'** in near 1:1 ratio (Scheme 4.10d). This regiochemistry is similar to the one observed in the iron-catalyzed benzannulation[8] but is distinct from the excellent regioselectivity observed in chromium-catalyzed arylmagnesiaton of aryl(alkyl) alkyne.[16] In the absence of alkyne, the reaction of **1b** with $CrCl_2$ (30 mol%) and 2,2'-bipyridine (60 mol%), upon quenching with D_2O after 6 h, afforded 3-methyl-biphenyl **3b**-d_n partially deuterated at the 2'- and 6-positions (Scheme 4.10e and Experimental section). Note that a nonnegligible part of **3b**-d_n was doubly deuterated, as indicated from the GCMS analysis. These results suggest that (1) a biarylchromium species, formed by transmetalation from the Grignard reagent, would undergo intramolecular C–H activation to form a chromacycle intermediate, (2) the chromacycle would undergo insertion of the alkyne into either of the aryl–Cr bonds, (3) the chromacycle may also rearrange into another biarylchromium species, and (4) this transposition would occur reversibly. (Scheme 4.11, **C**).

Scheme 4.10. Mechanistic Experiments



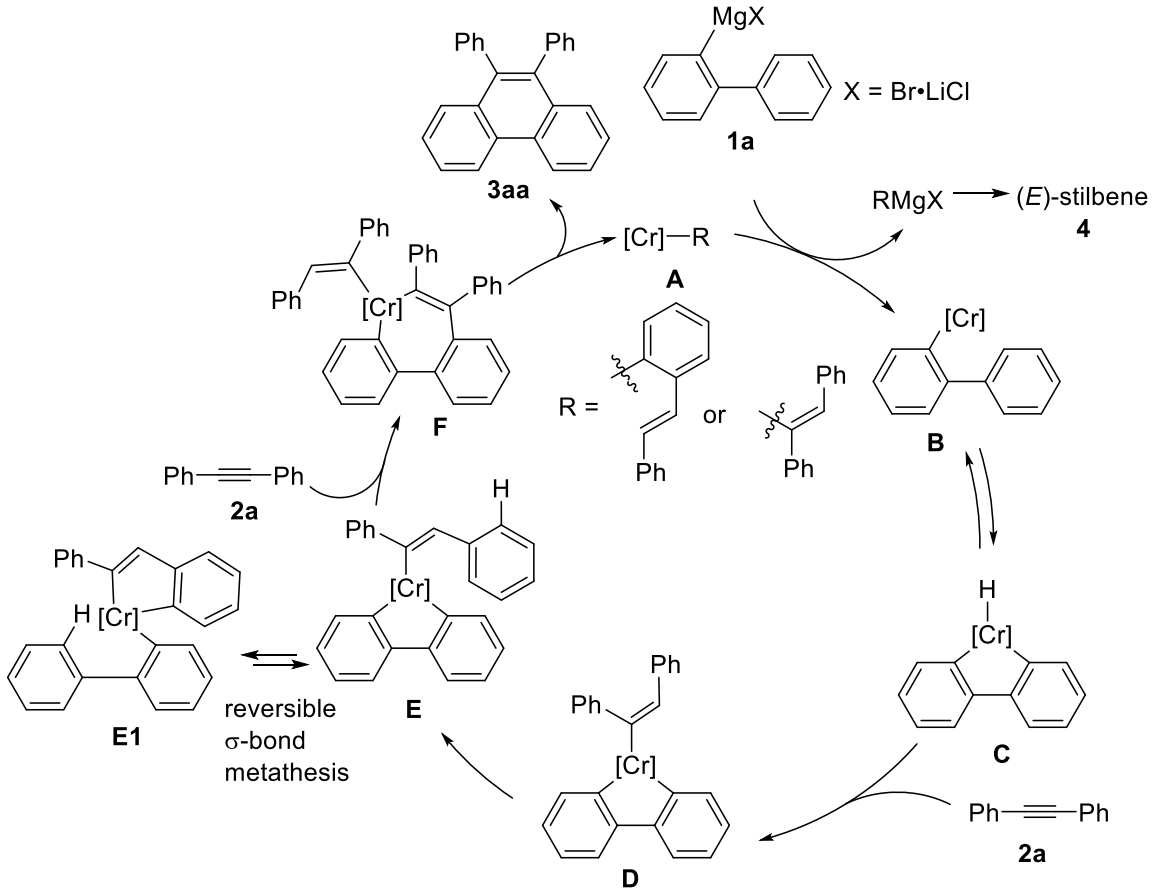
[a] The reaction was carried out under standard conditions in Table 4.1, entry 2.

On the basis of the above observations, we would propose a possible reaction mechanism outlined in Scheme 4.11. Transmetalation between biaryl Grignard reagnent **1a**

and the chromium precatalyst generates a biaryl-2-chromium species **B**,[17] which undergoes reversible C−H activation to give a five-membered chromacycle **C**. This process would cause reversible C–H activation of not only the 2'- and 6'-position but also the 6-position. Subsequent insertion of **2a** into the Cr−H bond of the species **C** leads to an alkenyl–chromacycle species **D**. The species **D** then undergoes *E*/*Z* isomerization of the double bond to afford another alkenyl–chromacycle species **E**. The species **E** then undergoes insertion of **2a** into the aryl–Cr bond to form a 7-membered chromacycle **F**, followed by reductive elimination to furnish the phenanthrene product **3aa** along with stilbenylchromium species **A**. Transmetalation of **A** with **1a** regenerates the species **B** and releases stilbenyl Grignard reagent, which is responsible for the formation of (*E*)-stilbene **4**.

While the main reaction pathway described above provides a superficial explanation for the formation of **3aa** and **4**, additional pathways need to be invoked to rationalize some of the key experimental observations (see Experimental section). First, the stilbenylchromium species **A**, like the biarylchromium species **B**, would undergo reversible C–H activation via a chromacycle intermediate to generate an *ortho*-stilbenylchromium species **A'** (Scheme 4.12). Transmetalation of the species **A'** with **1a** to form *ortho*-stilbenyl Grignard reagent would account for the deuterium incorporation into the *ortho* position of **4**-d_n (Scheme 4.10a). Second, we are also tempted to propose a σ-bond metathesis process involving the species **E**. Thus, σ-bond metathesis between the aryl–Cr bond and the *ortho* C–H bond of the stilbenyl ligand would reversibly generate an isomer **E1**. This reversible process would be responsible for the partial exchange between the biaryl *ortho*-hydrogens and the diphenylacetylene *ortho*-hydrogens, which was indicated in the labeling experiments shown Scheme 4.10b and Scheme 4.10c. Finally, the formation of 1,2,3-triphenylnaphthalene **5** and its deuteration pattern in the labeling experiment could be explained by the reaction of the species **A** or **A'** with **2a**.

Scheme 4.11. Proposed Mechanism



4.3 Conclusions

In summary, we have developed a [4+2] benzannulation reaction between biaryl-2-Grignard reagents and internal alkynes under a simple chromium–bipyridine catalytic system. The reaction is applicable to a variety of diaryl-, arylalkyl-, and dialkylalkynes and different biaryl Grignard reagents, affording various 9,10-disubstituted phenanthrene derivatives. Compared with the previously reported iron-catalyzed variant, no external oxidant is necessary because the excess alkyne acts as a hydrogen acceptor. Deuterium labeling experiments revealed that rather complex main- and side reaction pathways are involved in the present annulation, where the chromium center is capable of undergoing facile intramolecular C–H activation via oxidative addition or σ-bond metathesis mechanism. The present findings would stimulate further exploration of C–H bond functionalization using earth-abundant chromium catalysts.[18,19,20]

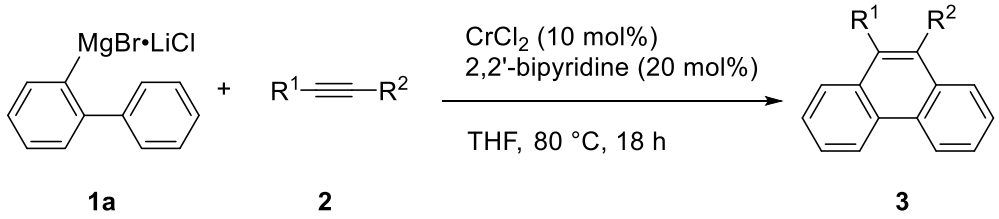
4.4 Experimental Section

General. All reactions dealing with air- or moisture-sensitive compound were performed by standard Schlenk techniques in oven-dried reaction vessels under nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on JEOL ECA-400 (400 MHz) or Bruker AV-400 (400 MHz) or Bruker AV-500 (500 MHz) NMR spectrometers. 1H and ^{13}C NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and $CHCl_3$ (77.0 ppm), respectively. Gas chromatographic (GC) analysis was performed on a Shimadzu GC-2010 system equipped with an FID detector and a capillary column, DB-5 (Agilent J&W, 0.25 mm i.d. x 30 m, 0.25 μm film thickness). High-resolution mass spectra (HRMS) were obtained with

a Q-Tof Premier LC HR mass spectrometer. Melting points were determined using a capillary melting point apparatus and are uncorrected.

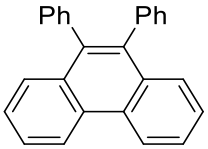
Materials. Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. Anhydrous $CrCl_2$ (99.99%) was purchased from STREM and was used as received. THF was distilled over Na/benzophenone. Biaryl-2-bromides used for preparation of Grignard reagents were synthesized according to literature procedure.[21] Grignard reagents were prepared from the corresponding halides and magnesium turnings in anhydrous THF with the presence of LiCl and titrated before use.[15] Alkyne substrates are known in literature, 1,2-bis(4-methoxyphenyl)ethyne (**2b**), [22] 1,2-bis(4-fluorophenyl)ethyne (**2c**),[22] 1,2-bis(4-trifluoromethylphenyl)ethyne (**2d**),[22] 1,2-di(thiophen-2-yl)ethyne (**2i**),[22] 1,2-Bis(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)ethyne **(2f)**,[23] 1-chloro-4-(hex-1-yn-1-yl)benzene (**2l**),[24] were prepared according the reported procedures. For all the known substrates, their ^{1}H NMR and ^{13}C NMR spectra showed good agreement with the literature data.

Chromium-Catalyzed Annulation of 1,1'-Biphenyl-2-Magnesium Reagent with Alkynes

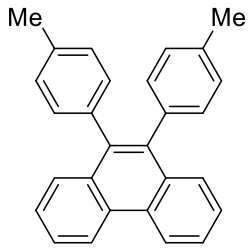


Typical procedure (standard condition): Inside glovebox, $CrCl_2$ (2.4 mg, 0.02 mmol) and 2,2'-bipyridine (6.3 mg, 0.04 mmol) were placed in a 10 mL Schlenk tube (for arylalkylalkynes **2j**–**2o**, 0.04 mmol of Bphen ligand was used instead of 2,2'-bipyridine). The Schlenk tube was then moved out to fume hood. The corresponding alkyne (**2**, 0.4 mmol) and Grignard reagent (**1a**, 0.2 mmol in THF) were added to the above mixture under Schlenk line. After stirring for 10 mins at room temperature, the reaction temperature was

raised to 80 °C and the resultant dark solution was kept stirring for 18 h. Then, the reaction mixture was cooled down to room temperature and quenched by saturated NH_4Cl aqueous solution (1 mL) before diluted with dichloromethane (2 mL). The aqueous layer was extracted with dichloromethane (3 x 5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford the desired product.

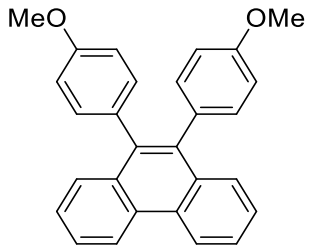


9,10-diphenylphenanthrene (3aa): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 30/1) of the crude product afforded the title compound as white solid (51.5 mg, 78%), the compound data were in good accordance with the literature;[9] m.p. 236 – 237 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, *J* = 8.3 Hz, 2H), 7.81 – 7.64 (m, 2H), 7.61 – 7.53 (m, 2H), 7.53 – 7.46 (m, 2H), 7.29 – 7.13 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6, 137.2, 131.9, 131.0, 130.0, 127.8, 127.6, 126.6, 126.5, 126.4, 122.5; HRMS (ESI) Calcd for $C_{26}H_{19}$ $[M + H]^+$ 331.1487, found 331.1483.

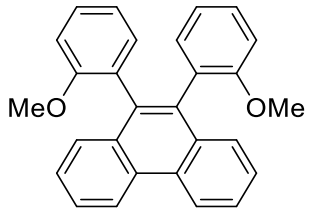


9,10-di-*p*-tolylphenanthrene (3ab): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (40.8 mg, 57%), the compound data were in good accordance with the literature;[9] m.p. 245 – 246 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 8.0 Hz, 2H), 7.74 – 7.60 (m, 2H), 7.60 – 7.53 (m, 2H), 7.50 – 7.42 (m, 2H), 7.16 – 6.96 (m, 8H), 2.33 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2, 136.6, 135.8, 132.2, 130.9, 129.9, 128.3,

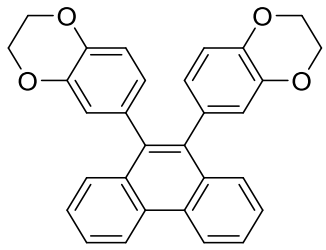
127.9, 126.5, 126.2, 122.4, 21.3; HRMS (ESI) Calcd for $C_{18}H_{23}$ $[M + H]^+$ 359.1800, found 359.1812.



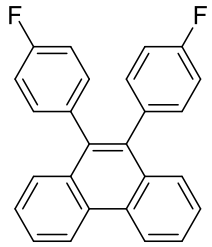
9,10-bis(4-methoxyphenyl)phenanthrene (3ac): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 20/1) of the crude product afforded the title compound as white solid (51.5 mg, 66%), the compound data were in good accordance with the literature;[9] m.p. 263 – 264 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 8.3 Hz, 2H), 7.66 (t, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.07 (d, *J* = 8.6 Hz, 4H), 6.81 (d, *J* = 8.6 Hz, 4H), 3.81 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 137.1, 132.3, 132.0, 132.0, 130.0, 127.8, 126.5, 126.3, 122.5, 113.1, 55.1; HRMS (ESI) Calcd for $C_{28}H_{23}O_2$ $[M + H]^+$ 391.1698, found 391.1701.



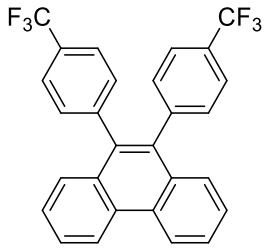
9,10-bis(2-methoxyphenyl)phenanthrene (3ad): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 20/1) of the crude product afforded the title compound as white solid (50.7 mg, 65%); m.p. 177 – 178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 8.3 Hz, 2H), 7.73 – 7.58 (m, 2H), 7.52 – 7.41 (m, 4H), 7.23 – 7.18 (m, 2H), 7.13 (dd, *J* = 7.4, 1.8 Hz, 2H), 6.88 – 6.78 (m, 4H), 3.61 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 134.4, 132.0, 131.1, 130.1, 128.9, 128.5, 127.2, 126.4, 126.0, 122.6, 119.8, 110.1, 55.2.; HRMS (ESI) Calcd for $C_{28}H_{23}O_2$ $[M + H]^+$ 391.1698, found 391.1702.



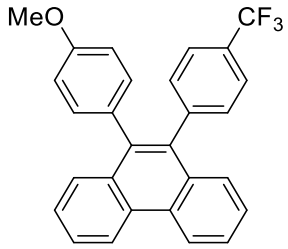
9,10-bis(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)phenanthrene (3ae): White solid (45.5 mg, 51%, eluent: hexane/CH_2Cl_2 = 20/1),which is obtained as a mixture of two rotamers as indicated by ^{13}C NMR spectrum;[25] m.p. 173–174 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 8.3 Hz, 2H), 7.74–7.58 (m, 4H), 7.57–7.44 (m, 2H), 6.77 (dd, *J* = 8.2, 2.8 Hz, 2H), 6.71 (dd, *J* = 7.9, 2.0 Hz, 2H), 6.67–6.55 (m, 2H), 4.30–4.21 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.8, 142.7, 142.1, 142.0, 136.72, 136.67, 132.92, 132.9, 132.13, 132.09, 129.9, 127.9 (2C), 126.5 (2C), 126.3 (2C), 124.35, 124.33, 122.4 (2C), 119.8, 119.77, 116.5, 116.4, 64.4 (2C), 64.33, 64.29 (one peak for aromatic ^{13}C signal is overlapped);HRMS (ESI) Calcd for $C_{30}H_{23}O_4$ $[M + H]^+$ 447.1596, found 447.1592.



9,10-bis(4-fluorophenyl)phenanthrene (3af): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 30/1) of the crude product afforded the title compound as white solid (39.5 mg, 54%); m.p. 170 – 171 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, *J* = 8.3 Hz, 2H), 7.69 (ddd, *J* = 8.3, 5.9, 2.4 Hz, 2H), 7.60 – 7.46 (m, 4H), 7.16 – 7.04 (m, 4H), 7.00 – 6.92 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6 (d, $^1J_{CF}$ = 239.4 Hz), 136.5, 135.3(d, $^4J_{CF}$ = 3.3 Hz), 132.5 (d, $^3J_{CF}$ = 7.9 Hz), 131.7, 130.1, 127.6, 126.8, 126.7, 122.6, 114.8 (d, $^2J_{CF}$ = 21.2 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ −114.2; HRMS (ESI) Calcd for $C_{26}H_{17}F_2$ $[M + H]^+$ 367.1298, found 367.1307.

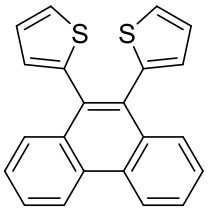


9,10-bis(4-(trifluoromethyl)phenyl)phenanthrene (3ag): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 20/1) of the crude product afforded the title compound as white solid (38.2 mg, 41%), the compound data were in good accordance with the literature; [9] m.p. 286 – 288 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 8.3 Hz, 2H), 7.72 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 2H), 7.61 – 7.50 (m, 6H), 7.44 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 136.1, 131.4, 131.2, 130.4, 129.3 (q, $^{2}J_{CF}$ = 32.8 Hz), 127.6, 127.2, 125.0 (q, $^{3}J_{CF}$ = 3.8 Hz), 124.2 (q, $^{1}J_{CF}$ = 269.1 Hz), 122.9 (one peak for aromatic ^{13}C signal is overlapped); ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8; HRMS (ESI) Calcd for $C_{28}H_{17}F_6$ $[M + H]^+$ 467.1234, found 467.1254.

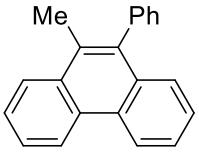


9-(4-methoxyphenyl)-10-(4-(trifluoromethyl)phenyl)phenanthrene (3ah): Prepared according to typical procedure. Column chromatography (hexane/toluene = 20/1) of the crude product afforded the title compound as white solid (41.1 mg, 48%); m.p. 185 – 186 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (dd, *J* = 8.3, 4.2 Hz, 2H), 7.69 (dddd, *J* = 8.3, 6.8, 4.5, 1.4 Hz, 2H), 7.61 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.55 – 7.48 (m, 4H), 7.43 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 143.8, 137.1, 136.0, 132.0, 131.9 (2C), 131.4 (2C), 131.3, 131.1, 130.2, 130.0, 128.6 (q, $^{2}J_{CF}$ = 32.4 Hz), 127.9, 127.3, 126.8, 126.76,

126.72, 126.6, 124.6 (q, $^{3}J_{CF}$ = 3.8 Hz, 2C), 124.3 (q, $^{1}J_{CF}$ = 273.0 Hz), 122.6, 122.5, 113.3 (2C), 55.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.2; HRMS (ESI) Calcd for $C_{28}H_{20}F_3O$ $[M + H]^+$ 429.1466, found 429.1461.

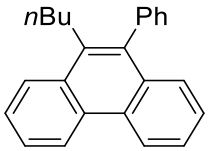


9,10-di(thiophen-2-yl)phenanthrene (3ai): Prepared according to typical procedure. Column chromatography (hexane/toluene = 20/1) of the crude product afforded the title compound as white solid (33.5 mg, 49%), the compound data were in good accordance with the literature; [9] m.p. 244 – 245 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 8.4 Hz, 2H), 7.81 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.70 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 2H), 7.55 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 2H), 7.34 (dd, *J* = 5.1, 1.2 Hz, 2H), 7.02 (dd, *J* = 5.1, 3.4 Hz, 2H), 6.95 (dd, *J* = 3.5, 1.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.7, 132.3, 132.2, 130.3, 129.3, 127.9, 127.1, 126.9, 126.3, 126.1, 122.4; HRMS (ESI) Calcd for $C_{22}H_{15}S_2$ $[M + H]^+$ 343.0615, found 343.0614.

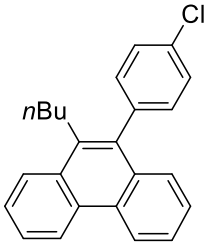


9-methyl-10-phenylphenanthrene (3aj): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (47.2 mg, 88%), the compound data were in good accordance with the literature;[26] m.p. 99 – 100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 – 8.77 (m, 1H), 8.75 (d, *J* = 7.8 Hz, 1H), 8.23 – 8.12 (m, 1H), 7.77 – 7.64 (m, 2H), 7.59 (ddd, *J* = 8.3, 6.7, 1.6 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.50 – 7.47 (m, 1H), 7.44 (ddd, *J* = 8.0, 6.7, 1.2 Hz, 1H), 7.39 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.34 – 7.30 (m, 2H), 2.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7, 137.1, 132.3, 131.9, 130.4, 130.0, 129.8, 129.4, 128.4, 127.4,

127.0, 126.8, 126.4, 126.2, 125.6, 125.1, 122.9, 122.3, 17.4; HRMS (ESI) Calcd for $C_{21}H_{17}$ $[M + H]^+$ 269.1330, found 269.1333.

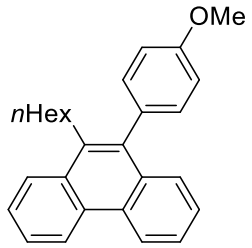


9-butyl-10-phenylphenanthrene (3ak): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (58.1 mg, 88%), the compound data were in good accordance with the literature;[9] m.p. 118 – 119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 – 8.78 (m, 1H), 8.74 (dd, *J* = 8.5, 1.2 Hz, 1H), 8.19 – 8.13 (m, 1H), 7.72 – 7.65 (m, 2H), 7.58 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.49 – 7.44 (m, 1H), 7.44 – 7.40 (m, 1H), 7.35 – 7.30 (m, 3H), 3.04 – 2.77 (m, 2H), 1.60 (tt, *J* = 8.0, 6.3 Hz, 2H), 1.31 (h, *J* = 7.4 Hz, 2H), 0.82 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 136.8, 134.9, 132.4, 130.9, 130.4, 130.2, 129.3, 128.3, 127.6, 127.0, 126.7, 126.3, 126.1, 125.6, 125.2, 123.1, 122.3, 33.0, 30.2, 23.2, 13.8; HRMS (ESI) Calcd for $C_{24}H_{23}$ $[M + H]^+$ 331.1800, found 331.1788.

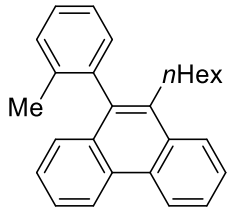


9-butyl-10-(4-chlorophenyl)phenanthrene (3al): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (35.8 mg, 52%); m.p. 217 – 218 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85 – 8.80 (m, 1H), 8.76 (dd, *J* = 8.4, 1.1 Hz, 1H), 8.23 – 8.16 (m, 1H), 7.79 – 7.67 (m, 2H), 7.62 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.46 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.36 – 7.25 (m, 3H), 2.94 – 2.78 (m, 2H), 1.62 (tt, *J* = 8.1, 6.2 Hz, 2H), 1.36 (h, *J* = 7.3 Hz, 2H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 135.4, 135.1, 133.1, 132.1, 131.7, 130.8, 130.5, 129.4, 128.6, 127.3, 126.9, 126.4,

126.3, 125.8, 125.2, 123.1, 122.4, 33.1, 30.3, 23.2, 13.8; HRMS (ESI) Calcd for $C_{24}H_{22}Cl$ $[M + H]^+$ 345.1410, found 345.1405.

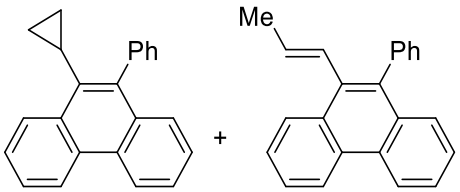


9-hexyl-10--(4-methoxyphenyl)phenanthrene (3am): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (57.4 mg, 78%); m.p. 149 – 150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 – 8.77 (m, 1H), 8.73 (d, *J* = 8.3 Hz, 1H), 8.20 – 8.12 (m, 1H), 7.72 – 7.64 (m, 2H), 7.58 (ddd, *J* = 8.3, 6.6, 1.5 Hz, 1H), 7.49 – 7.40 (m, 1H), 7.38 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H), 3.94 (s, 3H), 3.18 – 2.52 (m, 2H), 1.69 – 1.56 (m, 2H), 1.37 – 1.18 (m, 6H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 136.5, 135.3, 132.8, 132.7, 131.2, 131.0, 130.4, 129.3, 127.6, 126.7, 126.3, 126.0, 125.6, 125.2, 123.1, 122.3, 113.8, 55.3, 31.4, 30.8, 30.6, 29.8, 22.6, 14.1; HRMS (ESI) Calcd for $C_{27}H_{29}O$ $[M + H]^+$ 369.2218, found 369.2202.



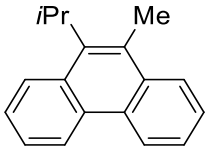
9-hexyl-10-(*o*-tolyl)phenanthrene (3an): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (51.4 mg, 73%); m.p. 218 – 219 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (dt, *J* = 6.8, 2.9 Hz, 1H), 8.75 (dd, *J* = 8.3, 1.2 Hz, 1H), 8.20 – 8.14 (m, 1H), 7.73 – 7.63 (m, 2H), 7.59 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), 7.45 – 7.31 (m, 4H), 7.28 – 7.18 (m, 2H), 2.96 (ddd, *J* = 13.4, 11.6, 4.8 Hz, 1H), 2.63 (ddd, *J* = 13.4, 11.6, 5.3 Hz, 1H), 1.96 (s, 3H), 1.73 – 1.48 (m, 2H), 1.35 – 1.14 (m, 6H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101

MHz, $CDCl_3$) δ 139.7, 136.8, 136.0, 134.7, 131.8, 131.2, 130.5, 130.0, 129.5, 127.5, 126.9, 126.7, 126.6, 126.0, 125.8, 125.7, 125.2, 123.1, 122.4, 31.3, 30.5, 30.1, 29.9, 22.5, 19.8, 14.1; HRMS (ESI) Calcd for $C_{27}H_{29}$ $[M + H]^+$ 353.2269, found 353.2271.



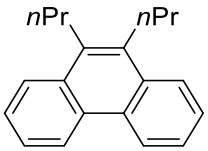
3ao **3ao'**

9-cyclopropyl-10-phenylphenanthrene (3ao) + (*E*)-9-phenyl-10-(prop-1-en-1-yl)phenanthrene (3ao'): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compounds as inseparable white solid mixture (35.3 mg, **3ao**, 50% + **3ao'**, 10%), the compound data of **3ao**[27] and **3ao'**[28] were in good accordance with the literature; **3ao:** ^1H NMR (400 MHz, $CDCl_3$) δ 9.27 – 8.62 (m, 3H), 7.69 (dq, *J* = 6.8, 3.5 Hz, 2H), 7.64 – 7.58 (m, 2H), 7.56 – 7.50 (m, 2H), 7.49 – 7.44 (m, 2H), 7.42 – 7.36 (m, 2H), 2.09 (tt, *J* = 8.5, 5.8 Hz, 1H), 0.93 – 0.73 (m, 2H), 0.35 (td, *J* = 6.1, 4.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 138.9, 134.0, 132.9, 131.9, 131.1, 130.1, 129.8, 127.9, 127.2, 126.8, 126.42, 126.44, 126.3, 126.1, 126.0, 122.7, 122.3, 13.3, 9.6; HRMS (ESI) Calcd for $C_{23}H_{19}$ $[M + H]^+$ 295.1487, found 295.1482.



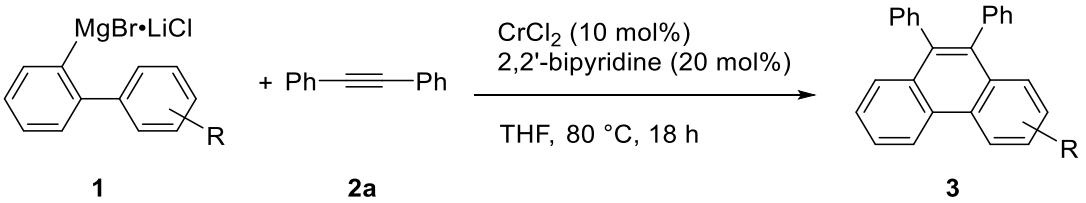
9-isopropyl-10-methylphenanthrene (3ap): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (27.2 mg, 58%); m.p. 98 – 99 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 – 8.57 (m, 2H), 8.34 (dd, *J* = 6.3, 3.5 Hz, 1H), 8.24 – 8.04 (m, 1H), 7.68 – 7.46 (m, 4H), 4.12 (p, *J* = 7.3 Hz, 1H), 2.80 (s, 3H), 1.63 (d, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 132.6, 131.1, 130.3, 129.5, 129.1, 128.8, 126.6, 125.8, 125.5,

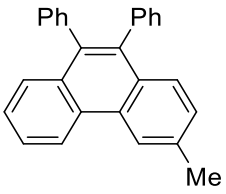
125.1, 124.6, 123.2, 122.7, 29.4, 22.0, 16.6; HRMS (ESI) Calcd for $C_{18}H_{19}$ $[M + H]^+$ 235.1487, found 235.1477.



9,10-dipropylphenanthrene (3aq): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (35.7 mg, 68%), the compound data were in good accordance with the literature;[8] m.p. 94 – 95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 – 8.61 (m, 2H), 8.35 – 7.98 (m, 2H), 7.86 – 7.50 (m, 4H), 3.38 – 3.00 (m, 4H), 2.25 – 1.64 (m, 4H), 1.17 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.9, 131.3, 129.8, 126.5, 125.4, 124.7, 122.9, 31.5, 24.0, 14.8; HRMS (ESI) Calcd for $C_{20}H_{23}$ $[M + H]^+$ 263.1800, found 263.1803.

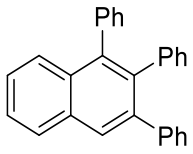
Chromium-Catalyzed Annulation of 1,1'-Biaryl-2-Magnesium Reagents with Diphenylacetylene





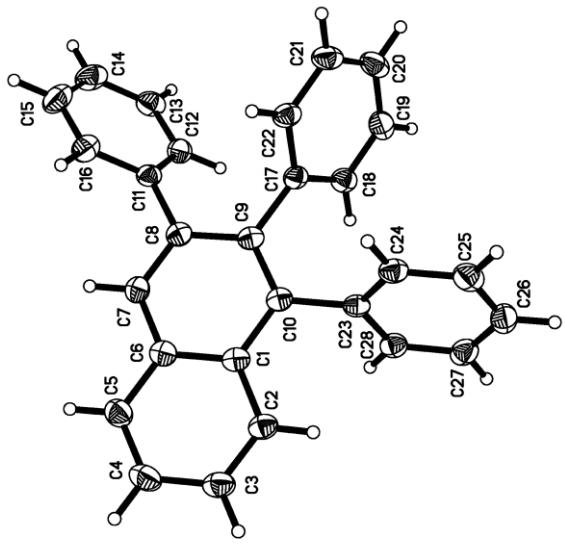
3-methyl-9,10-diphenylphenanthrene (3ba): Prepared according to typical procedure. Column chromatography (hexane/toluene = 40/1) of the crude product afforded the title compound as white solid (37.2 mg, 54%), the compound data were in good accordance with the literature;[29] m.p. 207 – 209 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 8.3 Hz, 1H), 8.63 (s, 1H), 7.68 (ddd, *J* = 8.3, 6.8, 1.5 Hz, 1H), 7.58 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.55 – 7.44 (m, 2H), 7.35 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.32 – 7.09 (m, 10H), 2.67 (s, 3H); ^{13}C NMR

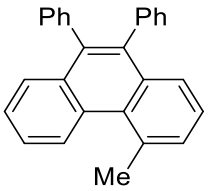
(101 MHz, $CDCl_3$) δ 139.7, 139.7, 137.1, 136.2, 136.1, 132.0, 131.1, 131.0, 130.0, 129.8, 129.7, 128.3, 127.8, 127.7, 127.5, 127.5, 126.5, 126.4, 126.2, 122.5, 122.3, 22.0; HRMS (ESI) Calcd for $C_{27}H_{21}$ $[M + H]^+$ 345.1643, found 345.1640.



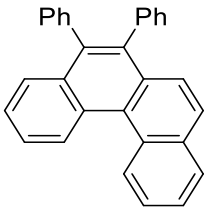
1,2,3-triphenylnaphthalene (5): obtained together with **3ba** according to typical procedure. Column chromatography (hexane/toluene = 20/1) of the crude product afforded the title compound as white solid (16.4 mg, 23%), the compound data were in good accordance with the literature;[30] m.p. 152 – 153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 2H), 7.58 (dt, *J* = 8.5, 1.0 Hz, 1H), 7.52 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.40 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.29 – 7.21 (m, 3H), 7.20 – 7.14 (m, 7H), 6.98 – 6.91 (m, 3H), 6.90 – 6.83 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.0, 140.0, 139.9, 139.4, 139.2, 138.1, 132.7, 132.0, 131.5, 131.2, 130.0, 128.7, 127.9, 127.5, 126.9, 126.9, 126.4, 126.2, 126.1, 126.1, 125.6; HRMS (ESI) Calcd for $C_{28}H_{21}$ $[M + H]^+$ 357.1643, found 357.1638.

Figure 4.1. ORTEP Diagram of **5** (Thermal ellipsoids drawn at 50% probability)

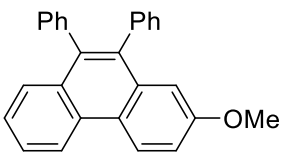




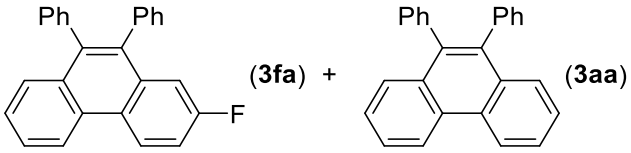
4-methyl-9,10-diphenylphenanthrene (3ca): Prepared according to typical procedure. Column chromatography (hexane/toluene = 40/1) of the crude product afforded the title compound as white solid (26.8 mg, 39%); m.p. 135 – 136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 8.5 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.53 (d, *J* = 7.3 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.40 – 7.33 (m, 1H), 7.26 – 7.10 (m, 10H), 3.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 139.8, 137.7, 137.1, 135.0, 133.5, 133.1, 131.1, 131.0, 131.0, 130.2, 127.6, 127.6, 127.5, 127.5, 127.5, 126.4, 126.4, 125.9, 125.7, 125.0, 27.4; HRMS (ESI) Calcd for $C_{27}H_{21}$ $[M + H]^+$ 345.1643, found 345.1633.



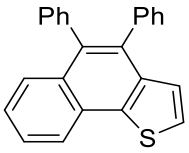
5,6-diphenylbenzo[*c*]phenanthrene (3da): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 20/1) and subsequent GPC purification afforded the title compound as white solid (41.1 mg, 54%), the compound data were in good accordance with the literature;[29] m.p. 181 – 182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (d, *J* = 8.4 Hz, 2H), 8.03 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.80 (d, *J* = 8.9 Hz, 1H), 7.76 – 7.65 (m, 4H), 7.59 – 7.53 (m, 2H), 7.38 – 7.12 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.7, 139.5, 137.5, 137.2, 133.1, 132.8, 131.2, 131.1, 130.1, 129.9, 129.7, 128.5, 128.3, 128.2, 127.6, 127.6, 127.5, 127.4, 127.1, 126.5, 126.5, 126.1, 126.0, 126.0, 125.6, 125.3; HRMS (ESI) Calcd for $C_{30}H_{21}$ $[M + H]^+$ 381.1643, found 381.1645.



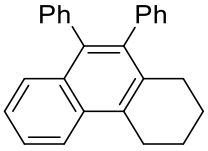
2-methoxy-9,10-diphenylphenanthrene (3ea): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 10/1) of the crude product afforded the title compound as white solid (44.7 mg, 62%), the compound data were in good accordance with the literature;[29] m.p. 205 – 206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (dd, *J* = 8.8, 6.0 Hz, 2H), 7.66 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.55 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.45 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.33 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.30 – 7.15 (m, 10H), 6.97 (d, *J* = 2.7 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 139.7, 139.6, 137.8, 136.8, 133.4, 131.0, 130.9, 130.9, 130.1, 127.9, 127.7, 127.5, 126.5, 126.5, 126.4, 125.6, 124.4, 124.1, 122.0, 116.2, 108.9, 55.2; HRMS (ESI) Calcd for $C_{27}H_{21}O$ $[M + H]^+$ 361.1592, found 361.1601.



2-fluoro-9,10-diphenylphenanthrene (3fa) + 9,10-diphenylphenanthrene (3aa): Prepared according to typical procedure using 4'-fluoro-1,1'-biphenyl-2-magnesium reagent **1f**. Column chromatography (hexane/dichloromethane = 20/1) of the crude product afforded the title compounds as white solid mixture (45.6 mg; **3fa**, 55% + **3aa**, 11%), the data of **3fa** were in good accordance with the literature;[31] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (dd, *J* = 9.2, 5.6 Hz, 1H), 8.74 (d, *J* = 8.3 Hz, 1H), 7.68 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.58 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.41 (td, *J* = 8.5, 2.8 Hz, 1H), 7.30 – 7.10 (m, 11H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4 (d, $^{1}J_{CF}$ = 246.3 Hz), 139.3, 139.0, 138.4, 136.6 (d, $^{4}J_{CF}$ = 3.8 Hz), 133.6 (d, $^{3}J_{CF}$ = 8.3 Hz), 131.4, 130.9, 129.8, 128.0, 127.8, 127.6, 126.8, 126.6, 126.4, 124.8 (d, $^{3}J_{CF}$ = 8.8 Hz), 122.3, 115.3 (d, $^{2}J_{CF}$ = 23.8 Hz), 112.3 (d, $^{2}J_{CF}$ = 22.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.4; HRMS (ESI) Calcd for $C_{26}H_{18}F$ $[M + H]^+$ 349.1393, found 349.1390.

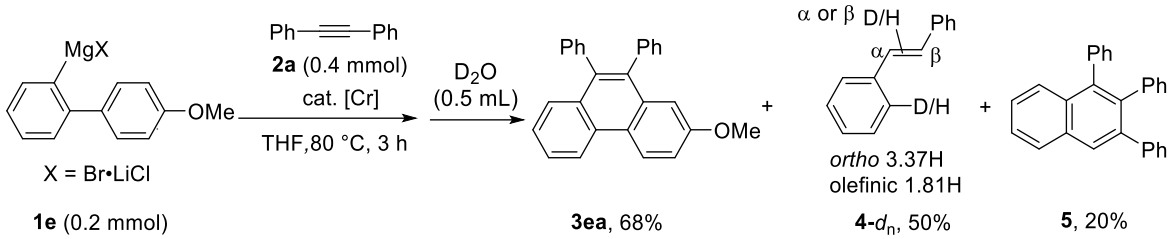


4,5-diphenylnaphtho[1,2-*b*]thiophene (3ga): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 20/1) of the crude product afforded the title compound as white solid (33.6 mg, 50%), the compound data were in good accordance with the literature;[8] m.p. 213 – 215 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.61 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.49 – 7.41 (m, 2H), 7.34 – 7.20 (m, 10H), 7.18 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 139.0, 137.6, 137.0, 135.5, 134.9, 131.5, 130.7, 130.5, 128.4, 128.1, 127.6, 126.6, 126.6, 126.4, 125.8, 124.6, 123.7; HRMS (ESI) Calcd for $C_{24}H_{17}S$ $[M + H]^+$ 337.1051, found 337.1036.



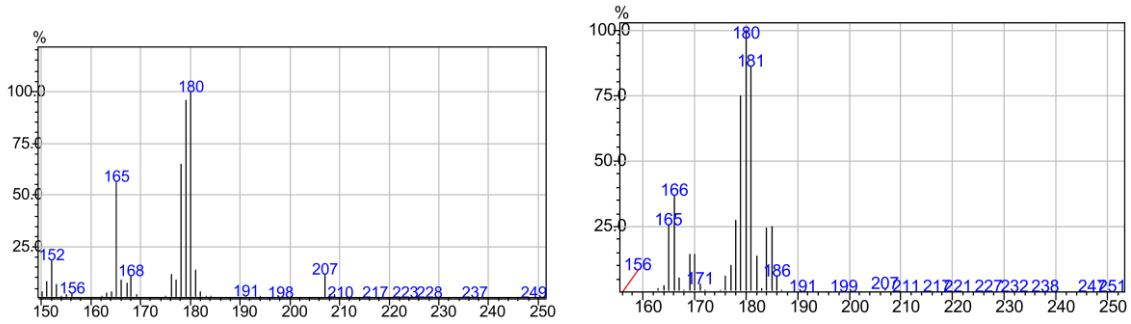
9,10-diphenyl-1,2,3,4-tetrahydrophenanthrene (3ha): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 40 /1) of the crude product afforded the title compound as white solid (55.5 mg, 83%), the compound data were in good accordance with the literature;[8] m.p. 190 – 191 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.4 Hz, 1H), 7.60 – 7.53 (m, 2H), 7.38 (ddd, *J* = 8.3, 6.6, 1.2 Hz, 1H), 7.27 – 7.19 (m, 5H), 7.18 – 7.12 (m, 3H), 7.10 – 7.05 (m, 2H), 3.32 (t, *J* = 6.5 Hz, 2H), 2.55 (t, *J* = 6.3 Hz, 2H), 2.07 – 1.96 (m, 2H), 1.91 – 1.77 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 139.8, 139.7, 136.7, 133.2, 131.8, 131.4, 131.2, 131.1, 130.2, 127.5, 127.5, 127.4, 126.2, 126.0, 125.7, 125.0, 122.7, 30.1, 26.6, 23.3, 23.0; HRMS (ESI) Calcd for $C_{26}H_{23}$ $[M + H]^+$ 335.1800, found 335.1809.

Preliminary Mechanistic Study

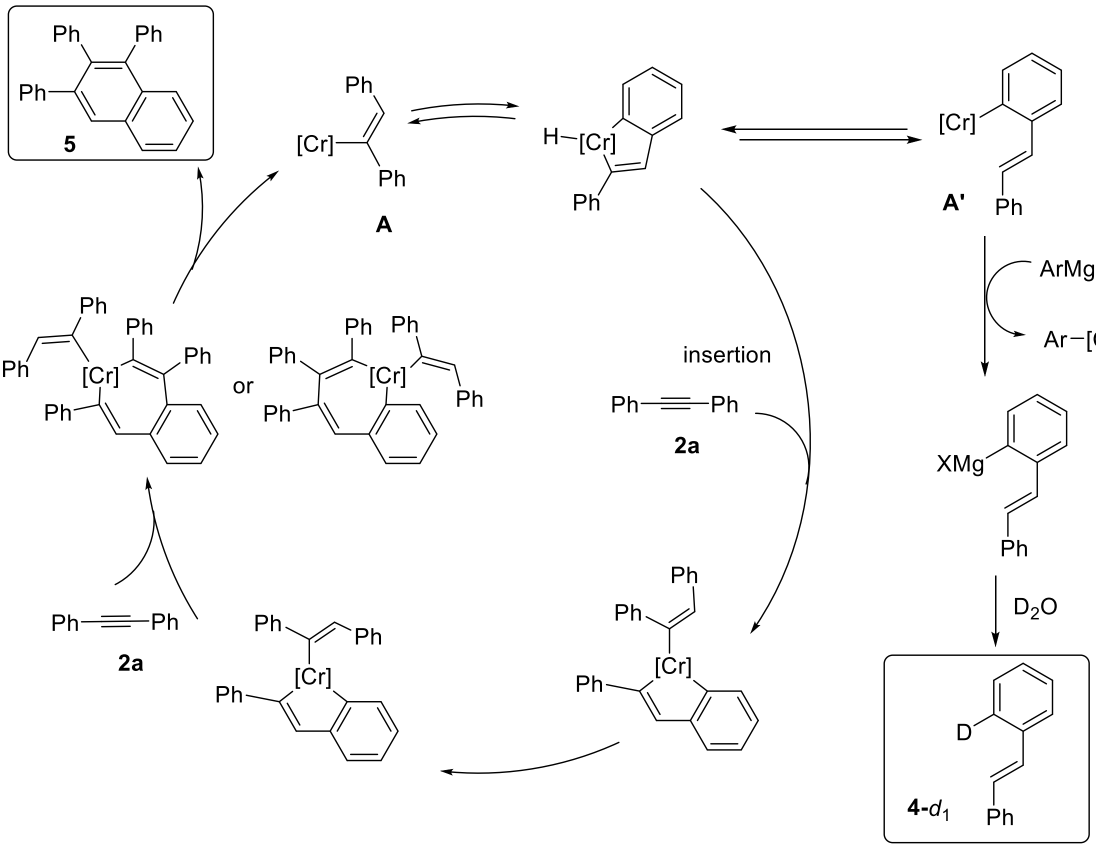


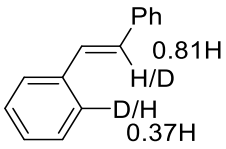
The annulation of biaryl Grignard reagent **1e** (0.2 mmol) and alkyne **2a** (0.4 mmol) under standard conditions, after 3 h, was quenched by D_2O (0.5 mL) at ambient temperature. The expected **3ea** was obtained, accompanied by the formation of **4**-d_n and **5**. **4**-d_n was deuterated at either olefinic or *ortho* position (1.81H and 3.37H respectively). GC/MS analysis of **4**-d_n (m/z: 180/181/182 = 100/78/14) also suggested that the deuterium atom was incorporated (substantial increase of m/z181, [M+1]; Figure 4.2).

Figure 4.2. Mass Spectra of Standard (*E*)-Stilbene (left) and Deuterated (*E*)-Stilbene **4**-d_n (right)

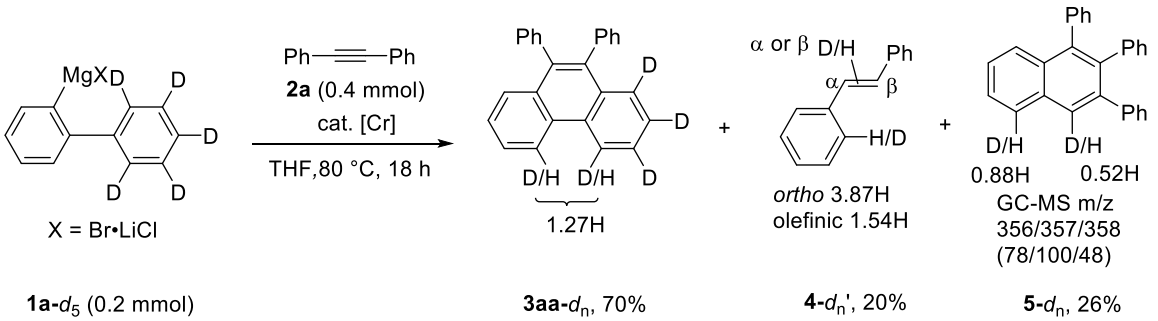


Scheme 4.12. Possible Explanation for Formation of *ortho*-D-(*E*)-stilbene **4**-d_1 and **5**





Deuterated (*E*)-stilbene (4-d_n): Obtained in above experiment according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (18.0 mg, 50%); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.58 (d, *J* = 7.5 Hz, 3.37H), 7.42 (t, *J* = 7.5 Hz, 4H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.19 (s, 1.81H); HRMS (ESI) Calcd for $C_{14}H_{12}D$ $[M + H]^+$ 182.1080, found 182.1074.



Deuterium-labeled Grignard reagent **1a**-d_5 reacted with **2a** to afford deuterated products **3aa**-d_n, **4**-d_n' and **5**-d_n under standard conditions. Deuterium loss was observed for **3aa**-d_n (1.27H in all for 4- and 5-position). **4**-d_n' was deuterated at either olefinic or *ortho* position (1.54H and 3.87H respectively). GC/MS analysis of **4**-d_n' (m/z: 180/181/182 = 100/75/40) and **5**-d_n (m/z: 356/357/358 = 78/100/48) indicated that two deuterium atoms were incorporated into **4**-d_n' (substantial increase of m/z 182, [M+2]; Figure 4.3), as well as **5**-d_n (substantial increase of m/z 358, [M+2]; Figure 4.4).

Figure 4.3. Mass Spectra of Standard (*E*)-Stilbene (left) and Deuterated (*E*)-Stilbene **4**-d_n' (right)

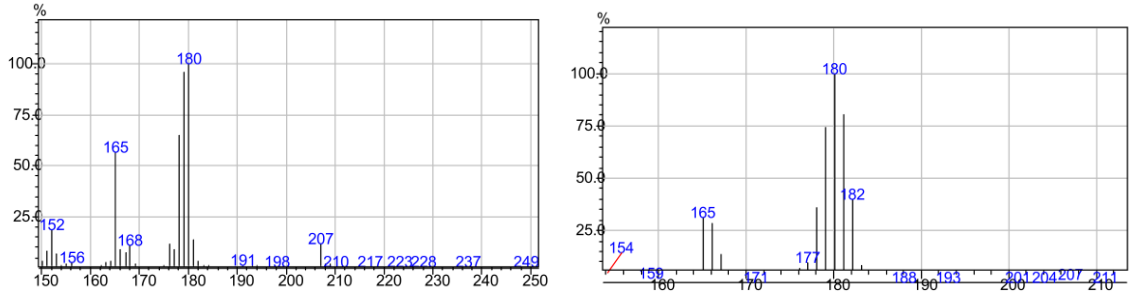
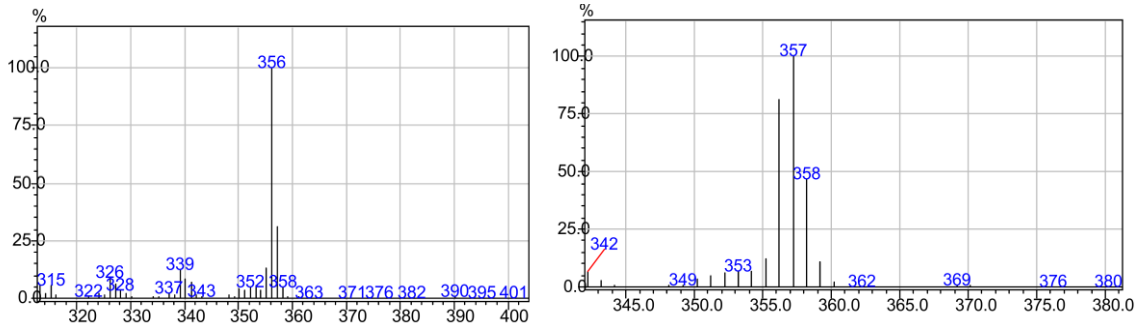
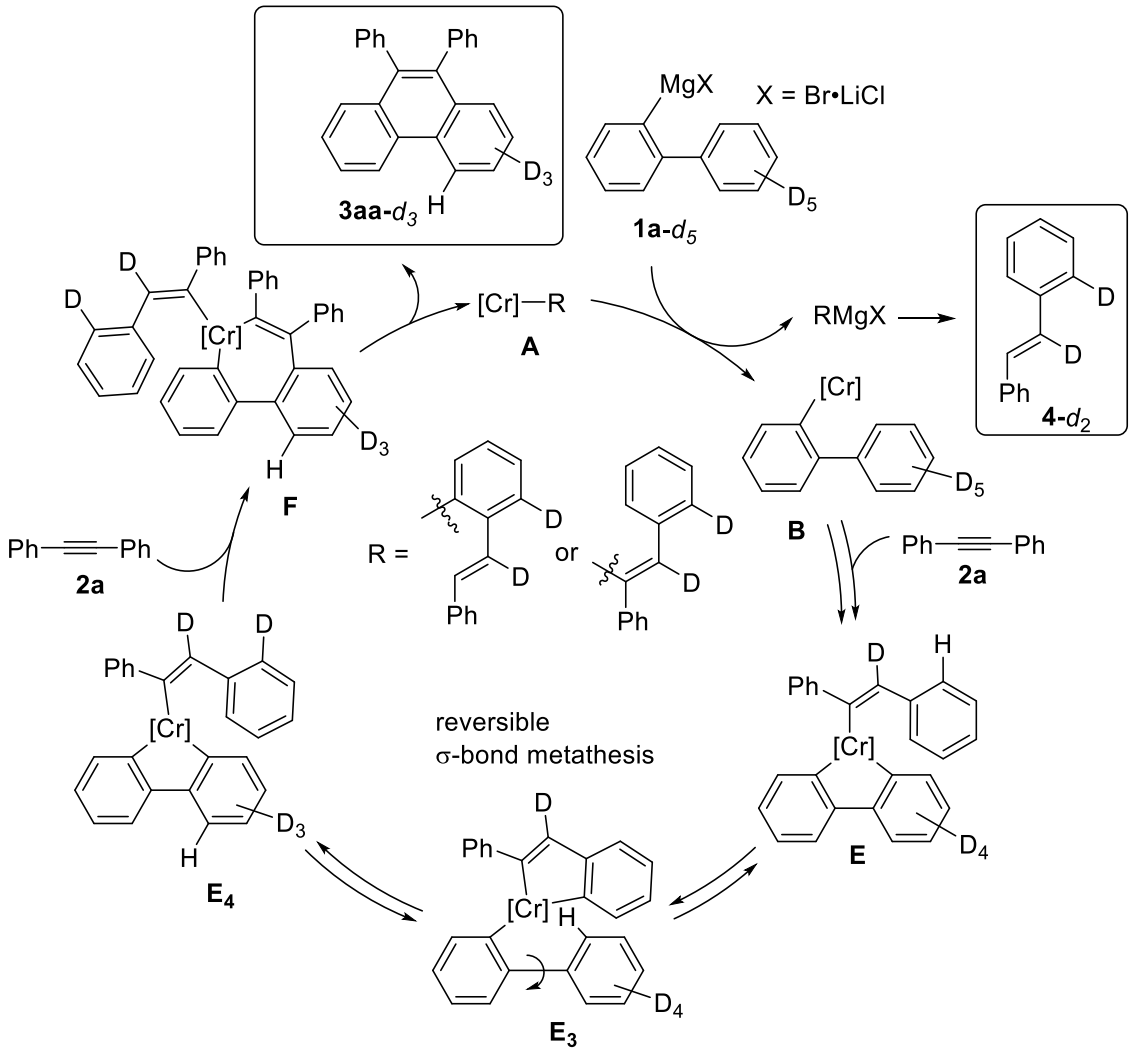
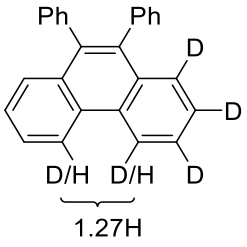


Figure 4.4. Mass Spectra of Standard **5** (left) and Deuterated **5**-d_n (right)



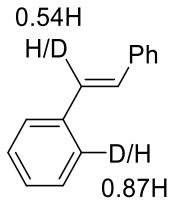
Scheme 4.13. Possible Explanation for Deuterium Loss of **3aa**-d_3 and Incorporations of Two D Atoms into **4**-d_2



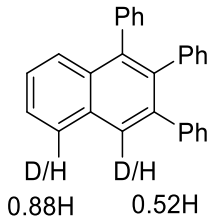


Deuterated 9,10-diphenylphenanthrene (3aa-d_n): Prepared according to typical procedure. Column chromatography (hexane/dichloromethane = 30/1) of the crude product afforded the title compound as white solid (46.8 mg, 70%), the compound data were in good accordance with the literature except the deuterated position;[29] ^{1}H NMR (400 MHz,

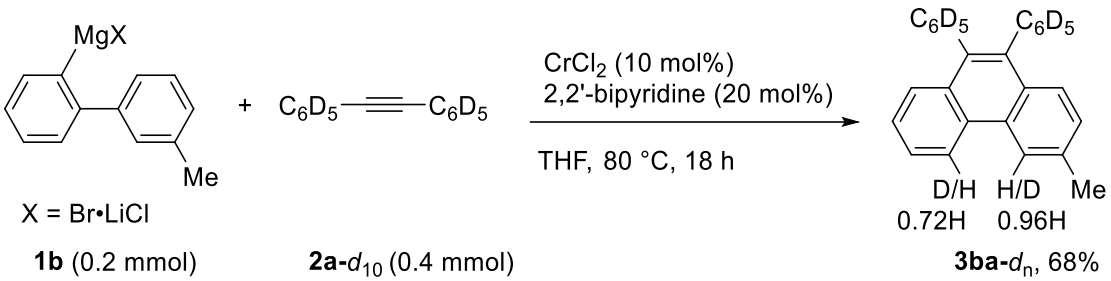
$CDCl_3$) δ 8.97 – 8.75 (m, 1.27H), 7.70 (ddd, *J* = 8.3, 5.3, 1.4 Hz, 1H), 7.60 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.52 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 7.37 – 7.12 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 137.2, 131.9, 131.1, 131.0, 130.0, 127.8, 127.6, 126.6, 126.5, 126.4, 122.5, 122.4; HRMS (ESI) Calcd for $C_{26}H_{15}D_4$ $[M + H]^+$ 335.1738, found 335.1749.



Deuterated (*E*)-stilbene (4-d_n'): Obtained in above deuterium-labeling experiment according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (7.2 mg, 20%), the deuterium distribution is arranged in line with **5**-d_n (vide infra); ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.80 – 7.56 (m, 3.87H), 7.39 (t, *J* = 7.6 Hz, 4H), 7.33 – 7.24 (m, 3.54H); HRMS (ESI) Calcd for $C_{14}H_{11}D_2$ $[M + H]^+$ 183.1143, found 183.1138.

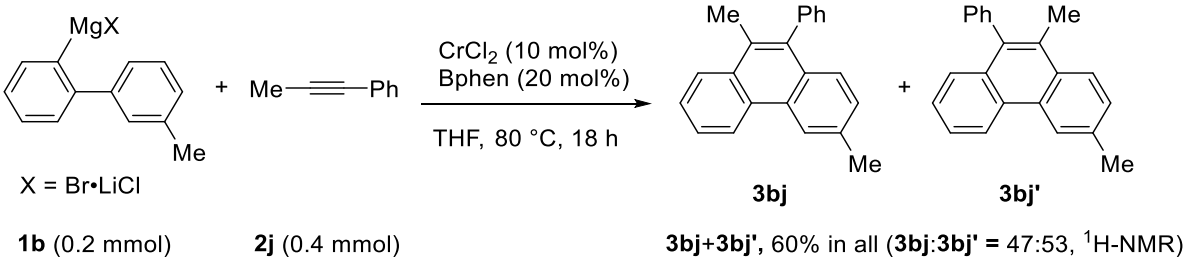


Deuterated 1,2,3-triphenylnaphthalene (5-d_n): Obtained in above deuterium-labeling experiment according to typical procedure. Column chromatography (hexane/dichloromethane = 40/1) of the crude product afforded the title compound as white solid (18.6 mg, 26%); ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.07 (d, *J* = 8.2 Hz, 0.88H), 7.99 (s, 0.52H), 7.58 (ddd, *J* = 8.1, 6.1, 1.9 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.31 – 7.14 (m, 10H), 6.99 – 6.89 (m, 5H); ^{13}C NMR (101 MHz, Acetone-d_6) δ 142.0, 142.0, 140.2, 139.9, 139.8, 139.4, 139.1, 138.1, 132.9, 132.8, 132.0, 131.4, 131.1, 129.9, 128.6, 128.0, 128.0, 127.5, 127.5, 126.8, 126.5, 126.5, 126.2, 126.2, 126.1, 125.6; HRMS (ESI) Calcd for $C_{28}H_{19}D_2$ $[M + H]^+$ 359.1769, found 359.1760.

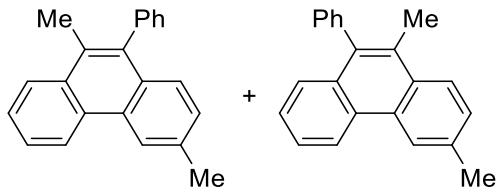


Reaction of **1b** and dectadeuterated diphenylacetylene **2a**-d_{10} under standard conditions afforded **3ba**-d_n in 68% yield, which is at least deuterated at 5-position (0.72H).

Deuterated 3-methyl-9,10-diphenylphenanthrene (3ba-d_n): Prepared according to typical procedure. Column chromatography (hexane/toluene = 40/1) of the crude product afforded the title compound as white solid (56.9 mg, 68%), the compound data were in good accordance with the literature except for deuterated positions;[32] m.p. 217 – 219 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, J = 8.4 Hz, 0.72H), 8.62 (s, 0.96H), 7.69 – 7.62 (m, 1H), 7.58 (d, J = 8.3 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 7.34 (d, J = 8.4 Hz, 1H), 2.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6, 139.5, 137.1, 136.2, 136.1, 132.0, 130.1, 129.8, 129.7, 128.3, 127.81, 127.75, 127.0 (t, $^1J_{C\text{-}D}$ = 23.3 Hz), 126.5, 126.2, 126.1, 122.5, 122.3, 22.0; HRMS (ESI) Calcd for $C_{27}H_{10}D_{11}$ $[M + H]^+$ 356.2334, found 356.2340.

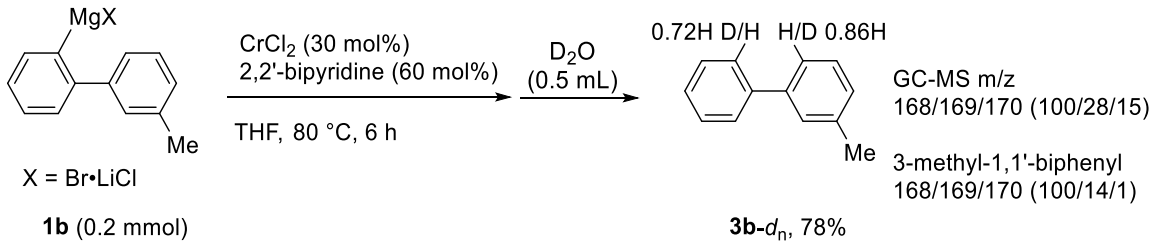


3'-Methyl-1,1'-biphenyl-2-magnesium reagent **1b** reacted with unsymmetrical alkyne **2j** to afford **3bj** and **3bj'** as a white solid mixture (33.9 mg) under standard condition, using Bphen as the ligand, in 60% overall yield. The ratio is assigned as 47:53 (**3bj**:**3bj'**) according to ^{1}H-NMR analysis of corresponding inseparable mixture after silica gel column chromatography (hexane/dichloromethane = 50/1), and shows good accordance with the related literature. [8]



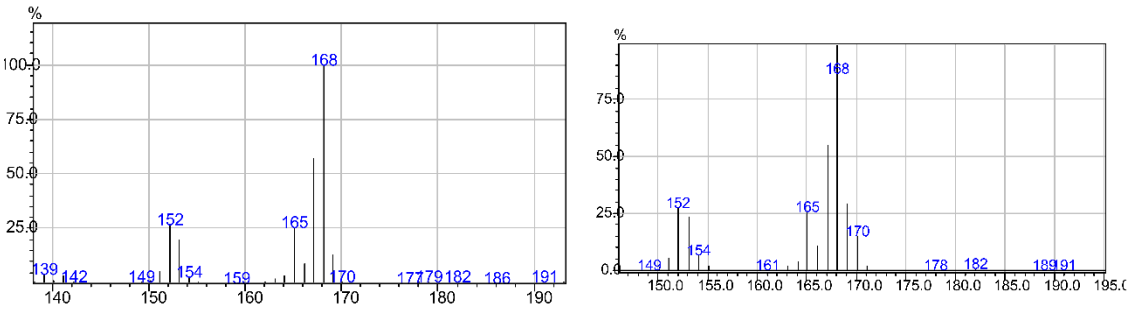
3bj **3bj'**

3,9-dimethyl-10-phenylphenanthrene (3bj) + 3,10-dimethyl-9-phenylphenanthrene (3bj'): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 – 8.77 (m, 1H), 8.73 (d, *J* = 8.3 Hz, 1.14H), 8.58 (s, 1.14H), 8.53 (s, 1H), 8.19 – 8.12 (m, 1H), 8.05 (d, *J* = 8.4 Hz, 1.14H), 7.72 – 7.65 (m, 2H), 7.60 – 7.49 (m, 6.56H), 7.48 – 7.44 (m, 2.14H), 7.42 – 7.39 (m, 1.14H), 7.38 – 7.35 (m, 1.14H), 7.32– 7.28 (m, 4.48H), 7.28 – 7.25 (m, 2H), 2.66 (s, 3.42H), 2.60 (s, 3H), 2.45 (s, 6.42H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 140.8, 137.0, 136.1, 135.8, 135.2, 132.5, 132.1, 130.5, 130.4, 130.3, 130.0, 129.8, 129.74, 129.71, 129.4, 129.1, 128.7, 128.5, 128.37, 128.35, 128.0, 127.4, 127.3, 127.0, 126.7, 126.2, 126.0, 125.4, 125.1, 125.0, 122.8, 122.7, 122.3, 122.1, 22.0, 21.9, 17.3, 17.2; HRMS (ESI) Calcd for $C_{22}H_{19}$ $[M + H]^+$ 283.1487, found 283.1481.



In the absence of alkyne, the reaction of **1b** with $CrCl_2$ (30 mol%) and 2,2'-bipyridine (60 mol%), upon quenching with D_2O after 6 h, afforded deuterated 3-methyl-biphenyl **3b**-d_n with incorporation of two deuterium atoms into both 2'- and 6-position (substantial increase of m/z170, [M+2]; Figure 4.5).

Figure 4.5. Mass Spectra of Standard 3-Methyl-Biphenyl (left) and Deuterated 3-Methyl-Biphenyl **3b**-d_n (right)



Deuterated 3-methyl-biphenyl (3b-d_n): Obtained in above control experiment in the absence of alkyne, in 78% GC yield. ^{1}H NMR analysis of the crude product indicated deuterium incorporation into both 2'- and 6-position; the spectra data were in good accordance with the literature;[8] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.58 (m, 1.72H), 7.51 – 7.41 (m, 3.86H), 7.36 (t, J = 7.4 Hz, 2H), 7.20 (d, J = 7.3 Hz, 1H), 2.46 (s, 3H).

4.5 References

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List of Publications

1, Cobalt-Catalyzed Arylative Cyclization of Acetylenic Esters and Ketones with Arylzinc Reagents through 1,4-Cobalt Migration. Yan, J.; Yoshikai, N. *ACS Catal*. **2016**, *6*, 3738.

2, Chromium-Catalyzed Migratory Arylmagnesiation of Unactivated Alkynes. Yan, J.; Yoshikai, N. *Org. Chem. Front.* **2017**, Advance Article. DOI: 10.1039/C7QO00427C

3, Gold-Catalyzed Cycloisomerization and Diels–Alder Reaction of 1,6-Diyne Esters with Alkenes and Diazenes to Hydronaphthalenes and –cinnolines. Yan, J.; Tay, G. L.; Neo, C.; Lee, B. R.; Chan, P. W. H. *Org. Lett.* **2015**, 17, 4176.