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Phenanthrene Synthesis via Chromium-Catalyzed Annulation of 2-Biaryl Grignard Reagents and Alkynes

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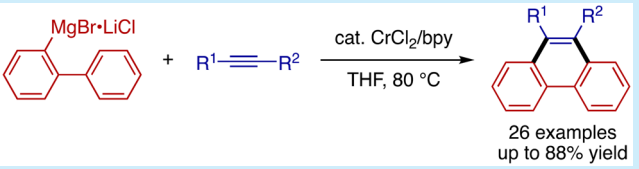
Supporting Information

ABSTRACT: A chromium/2,2′-bipyridine-catalyzed annulation reaction of 2-biarylmagnesium reagents with alkynes is reported. The reaction is applicable to a variety of aryl- and/or alkyl-substituted internal alkynes as well as 2-biaryl and related Grignard reagents, thus affording phenanthrene derivatives in moderate to good yields. The reaction proceeds at the expense of excess alkyne as a hydrogen acceptor and thus does not need an external oxidant. Deuterium-labeling experiments shed light on the reaction mechanism, which likely involves multiple intramolecular C−H activation processes on chromium.



Phenanthrene represents one of the simplest structural elements in materials science based on polycyclic aromatic hydrocarbons (PAHs).[1] The selective synthesis of substituted phenanthrenes would be not only useful for the preparation of phenanthrene-based materials[2] but also promising, when combined with other C−C coupling methods such as the Scholl reaction, for the bottom-up construction of extended polyaromatic systems.[3] Among various approaches to phenanthrene synthesis, transition-metal-catalyzed annulation of a 2-functionalized biaryl and an alkyne via C−H activation is attractive in terms of atom and step economy (Scheme 1a).[4−6] Since the seminal works of Heck and Larock on the palladium-catalyzed annulation of 2-iodobiaryl,[4a,b] annulation reactions employing different biaryl substrates have been achieved under palladium,[4c] iron,[4d] iridium,[4e] or rhodium[4f] catalysis. Among them, Nakamura's iron-catalyzed annulation of 2-biaryl Grignard reagents using 1,2-dichloroisobutane as an oxidant

Scheme 1. Annulation of 2-Functionalized Biaryl and Alkyne to Phenanthrene via C−H Activation

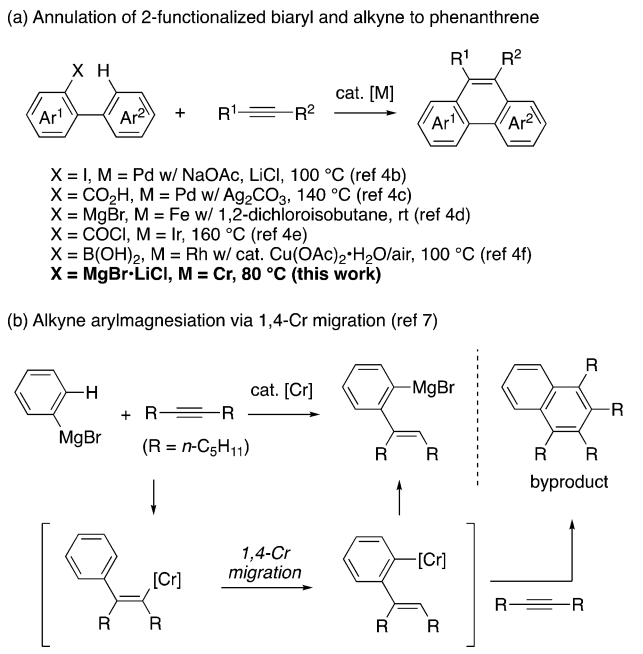
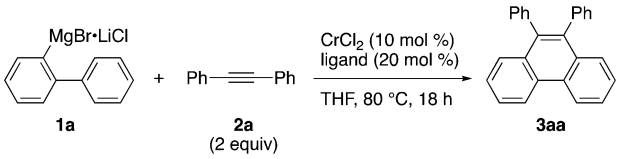


Table 1. Optimization of Reaction Conditions[a]



entry	ligand	conv of **2a** (%)[b]	yield of **3aa** (%)[b]
1	none	100	19
2	2,2′-bipyridine (bpy)	100	80 (78)
3	1,10-phenanthroline	100	67
4	bathophenanthroline	100	57
5	terpyridine	51	15
6	dppe	85	30
7[c]	bpy	100	21
8[d]	bpy	9	16
9[e]	bpy	76	56

[a]Reaction conditions: **1a** (prepared from 2-bromobiphenyl and Mg/LiCl; 0.2 mmol in THF), **2a** (0.4 mmol), $CrCl_2$ (10 mol %), ligand (20 mol %), THF, 80 °C, 18 h. [b]Determined by GC using *n*-tridecane as an internal standard. Isolated yield is shown in parentheses. [c]Norbornene (0.4 mmol) was added. [d]2,3-Dichlorobutane (0.5 mmol) was added. [e]The reaction was performed at room temperature.

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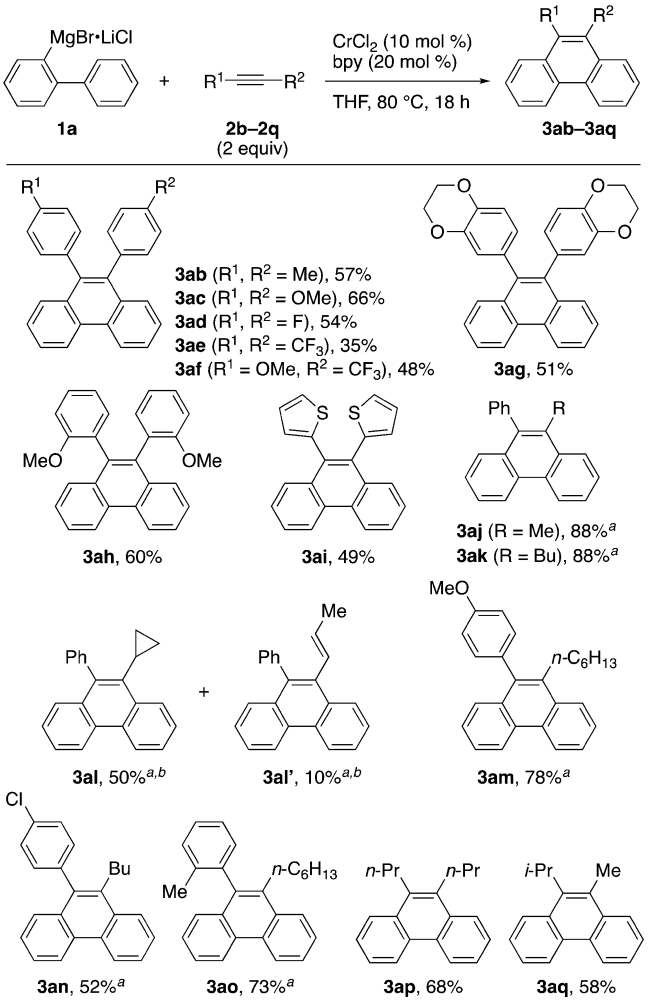
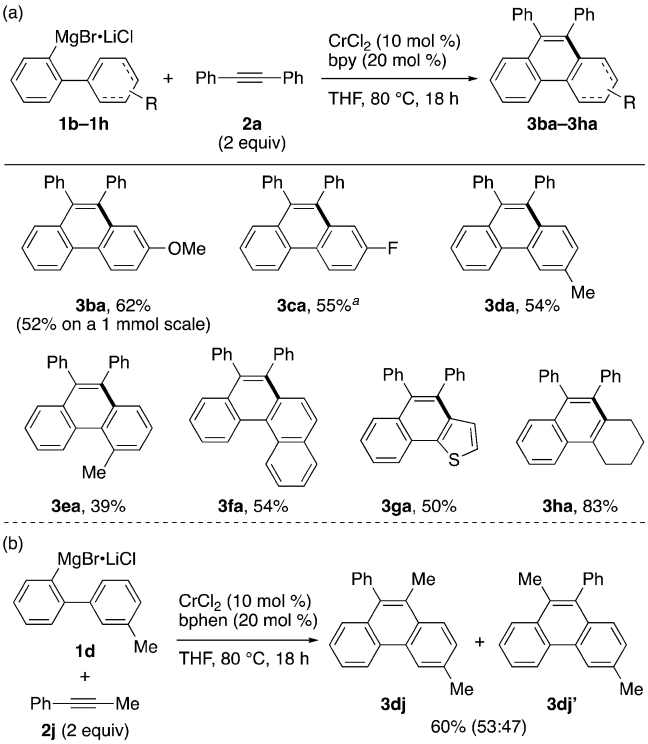
Scheme 2. Scope of Alkynes



[a]Bphen was used instead of bpy. [b]Phenyl(cyclopropyl)acetylene was used as the reactant, and an inseparable mixture of **3al** and **3al'** was obtained.

Scheme 3. Reaction of Different Grignard Reagents[a]



[a]Obtained as a mixture with the defluorinated product (i.e., **3aa**; 11%).

is notable for the low cost of the catalyst and the mild reaction temperature.[4d] This reaction, however, requires 2 equiv of the Grignard reagent, which can be more precious than the alkyne, because 1 equiv is sacrificially consumed as a hydrogen acceptor. Here, we report on a chromium-catalyzed annulation reaction of a 2-biaryl Grignard reagent and an alkyne to form a phenanthrene derivative. In contrast to iron catalysis, the present reaction proceeds at the expense of excess alkyne as a hydrogen acceptor.

The present study was prompted by our recent finding of a chromium-catalyzed addition reaction of an aryl Grignard reagent to a dialkylalkyne to afford an *ortho*-alkenylarylmagnesium species via a 1,4-chromium migration (Scheme 1b).[7−10] During this study, we observed a small amount of 1,2,3,4-tetraalkylnaphthalene, which appeared to be formed via dehydrogenative annulation of the styrenylchromium or *ortho*-alkenylarylchromium species with another molecule of the alkyne via C(sp^2)−H activation. Building on this observation, and in light of recent progress in chromium catalysis,[11−13] we envisioned that the 2-biaryl Grignard reagent could undergo annulation with an alkyne to form a phenanthrene derivative.

At the outset, we explored the reaction between the 2-biphenylmagnesium bromide−lithium chloride complex (**1a**), prepared from 2-bromobiphenyl and Mg·LiCl,[14] and diphenylacetylene (**2a**, 2 equiv) (Table 1). In the presence of $CrCl_2$ (10 mol %) in THF at 80 °C, the reaction afforded 9,10-diphenylphenanthrene (**3aa**) in 19% GC yield (entry 1). Upon ligand screening, 2,2′-bipyridine (bpy) was found to dramatically improve the yield of **3aa** to 80% (78% isolated yield; entry 2). 1,10-Phenanthroline and bathophenanthroline (bphen) also promoted the reaction in somewhat lower yields (entries 3 and 4), while terpyridine and diphosphine ligands such as dppe were much less effective (entries 5 and 6).

GCMS analysis of the $CrCl_2$/bpy-catalyzed reaction indicated the formation of (*E*)-stilbene (**4**) and 1,2,3-triphenylnapthalene (**5**) as byproducts. While their origin was probed later (vide infra), **4** and **5** appeared to be formed by reduction of **2a** and dimerization of **2a**, respectively. The consumption of **2a** could not be suppressed by the addition of norbornene as a hydrogen acceptor (entry 7). Unlike the iron-catalyzed annulation,[4d] a dichloroalkane oxidant was only detrimental (entry 8), causing substantial homocoupling of **1a**. Note that the present reaction took place even at room temperature, albeit with lower conversion and yield (entry 9).

With the $CrCl_2$/bpy system, the reaction of **1a** with different alkynes was explored (Scheme 2). A variety of diarylalkynes participated in the annulation to afford 9,10-diarylphenanthrenes **3ab**−**3ah** in moderate to good yields. The reaction became somewhat sluggish with CF_3 groups on the *para*-position (see **3ae** and **3af**). Di(2-thienyl)acetylene also afforded the desired product **3ai** in 49% yield. Aryl(alkyl)alkynes also proved to be competent substrates, for which better yields were achieved using bphen instead of bpy. Interestingly, the reaction of phenyl(cyclopropyl)acetylene was accompanied by a partial

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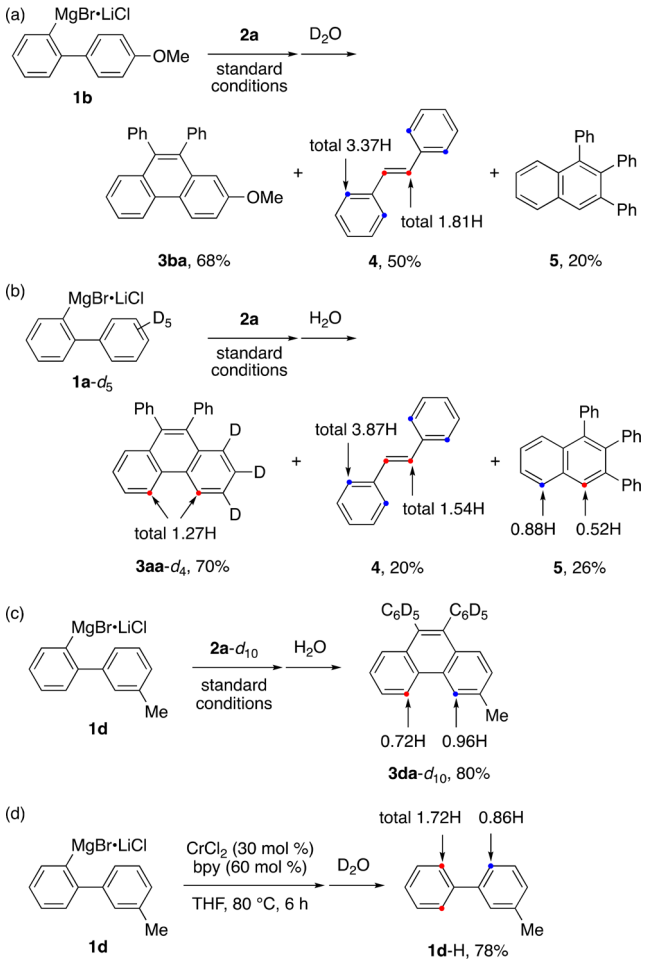
Scheme 4. Deuterium-Labeling Experiments[a]



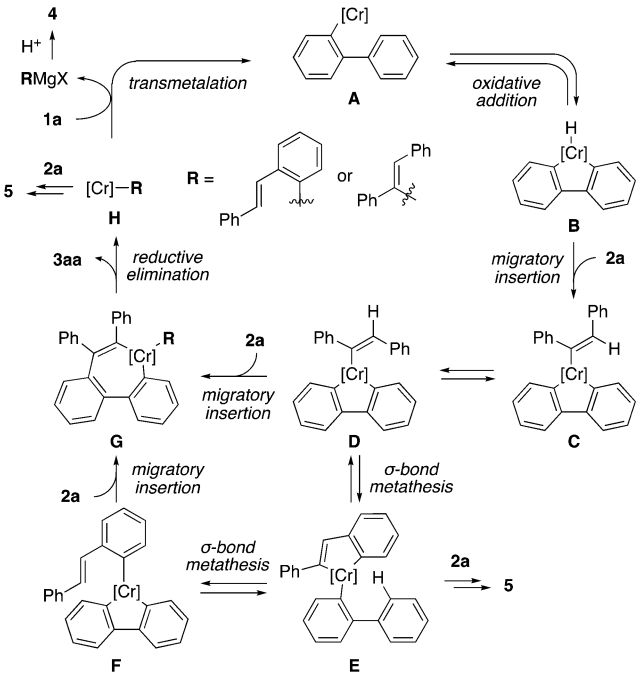
[a]The yield was determined by GC for Scheme 5d. ^{1}H NMR integrations lower than that expected for nondeuterated compounds are indicated.

cleavage of the cyclopropyl ring, affording a small amount of 9-phenyl-10-propenylphenanthrene **3al′** along with the expected product **3al**. Dialkylalkynes such as 4-octyne and 4-methylpent-2-yne also afforded the corresponding phenanthrene products **3ap** and **3aq**. Phenylacetylene failed to give the desired phenanthrene but underwent dimerization, as judged from GCMS analysis of the crude product.

Next, we subjected different 2-biaryl- and related Grignard reagents to the annulation with **2a** (Scheme 3a). 4-Methoxyphenyl- and 4-fluorophenyl-substituted Grignard reagents afforded the products **3ba** and **3ca**, respectively, while the latter was accompanied by partial hydrodefluorination. 3-Tolyl-substituted Grignard reagent underwent regioselective annulation at the less hindered *ortho* position (**3da**). The steric hindrance of 2-tolyl- and 1-naphthyl-substituted Grignard reagents could be tolerated (**3ea** and **3fa**). 2-Thienyl- and 2-alkenyl-substituted Grignard reagents also afforded the desired products **3ga** and **3ha** in moderate to good yields. The reaction between unsymmetrical Grignard reagent **1d** and 1-phenyl-1-propyne (**2j**) afforded regioisomers **3dj** and **3dj′** in a ca. 1:1 ratio, demonstrating the lack of regioselectivity in the alkyne insertion process (Scheme 3b).

To gain insight into the reaction mechanism and the origin of the byproducts **4** and **5**, we performed a series of deuterium-

Scheme 5. Proposed Reaction Pathways



labeling experiments. First, the reaction between Grignard reagent **1b** and **2a**, when quenched with D_2O, afforded phenanthrene **3ba**, **4**, and **5**, with partial deuteration of the *ortho* and olefinic positions of **4** (Scheme 4a). Second, the reaction using pentadeuterated Grignard reagent **1a**-d_5 demonstrated partial deuterium transfer to the *ortho* and olefinic positions of **4** and the 4- and 5-positions of **5** (Scheme 4b). Third, the reaction between Grignard reagent **1d** and decadeuterated diphenylacetylene (**2a**-d_{10}) furnished the phenanthrene **3da**-d_{10} with slight deuteration of the less hindered bay region (Scheme 4c). Finally, the treatment of **1d** with a mixture of $CrCl_2$ (30 mol %) and bpy (60 mol %), upon quenching with D_2O, resulted in partial deuteration of the *ortho* positions of both the aryl rings (Scheme 4d).

To rationalize the lack of the regioselectivity in alkyne insertion (Scheme 3b) and the results of the deuterium-labeling experiments (Scheme 4), we propose reaction pathways (for **1a** and **2a**) shown in Scheme 5 (see the Supporting Information for further details). A 2-biarylchromium species **A** would undergo intramolecular C−H oxidative addition to give a metallafluorene hydride **B**. Migratory insertion of **2a** into the Cr−H bond of **B** would generate an alkenyl−metallafluorene **C**, followed by isomerization to the *trans* isomer **D** presumably via a zwitterionic carbene intermediate.[15] The intermediate **D** may undergo insertion of another molecule of **2a** into the biaryl−Cr bond (**G**), followed by reductive elimination to afford **3aa** along with a stilbenyl−Cr species **H**.[6a] Transmetalation between **H** and **1a** would regenerate **A** and afford stilbenyl−Mg species (**R**MgX). As judged from the H/D scrambling results, **D** may also undergo sequential *σ*-bond metathesis via a metallaindene species **E**, causing migration of the chromium atom on the stilbenyl ligand. The resulting intermediate **F** would also lead to **3aa** via alkyne insertion/reductive elimination. The annulation of metallaindene species **E** or the stilbenyl−Cr species **H** with **2a** would be responsible for the formation of **5**. The role of the bipyridine ligand

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remains unclear, while we suspect that it facilitates the reductive elimination toward selective formation of **3aa**.

In summary, we have developed a chromium-catalyzed annulation reaction of 2-biarylmagnesium bromides and related Grignard reagents with internal alkynes to form phenanthrene derivatives. The reaction is mechanistically unique for the role of excess alkyne as a hydrogen acceptor and the involvement of multiple C−H activation processes. Further investigation into chromium-catalyzed C−H activation/C−C bond formation is underway.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b03342.

Detailed experimental procedures and spectral data (PDF)

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Notes

The authors declare no competing financial interest.

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