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

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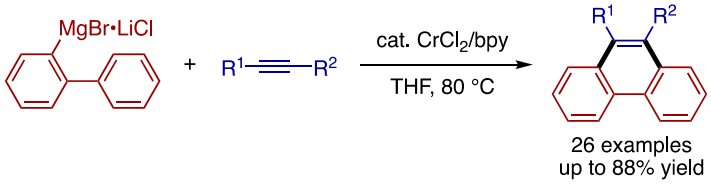
Supporting Information Placeholder



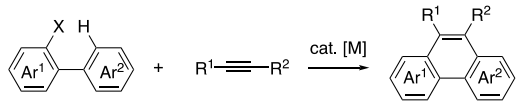
ABSTRACT: A chromium/2,2'-bipyridine-catalyzed annulation reaction of 2-biarylmagnesium reagents with alkynes is reported. The reaction is applicable to a variety of aryl- and/or alkyl-substituted internal alkynes as well as 2-biaryl and related Grignard reagents, thus affording phenanthrene derivatives 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 not only be 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 is notable for the low cost of the catalyst and the mild reaction temperature.[4d] This reaction, however, requires two equivalents of the Grignard reagent, which can be more precious than the alkyne, because one equivalent 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.

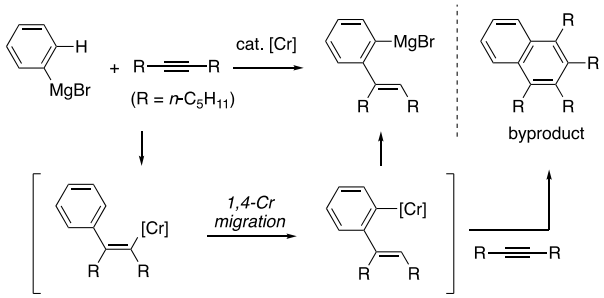
Scheme 1. Annulation of 2-Functionalized Biaryl and Alkyne to Phenanthrene via C–H Activation

(a) Annulation of 2-functionalized biaryl and alkyne to phenanthrene



X = I, M = Pd w/ NaOAc, LiCl, 100 °C (ref 4b)
X = CO_2H, M = Pd w/ Ag_2CO_3, 140 °C (ref 4c)
X = MgBr, M = Fe w/ 1,2-dichloroisobutane, rt (ref 4d)
X = COCl, M = Ir, 160 °C (ref 4e)
X = $B(OH)_2$, M = Rh w/ cat. $Cu(OAc)_2 \cdot H_2O$/air, 100 °C (ref 4f)
X = MgBr·LiCl, M = Cr, 80 °C (this work)

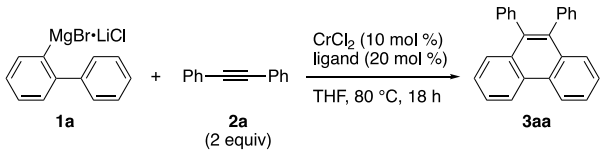
(b) Alkyne arylmagnesiation via 1,4-Cr migration (ref 7)



At the outset, we explored the reaction between 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).

Table 1. Optimization of Reaction Conditions[a]

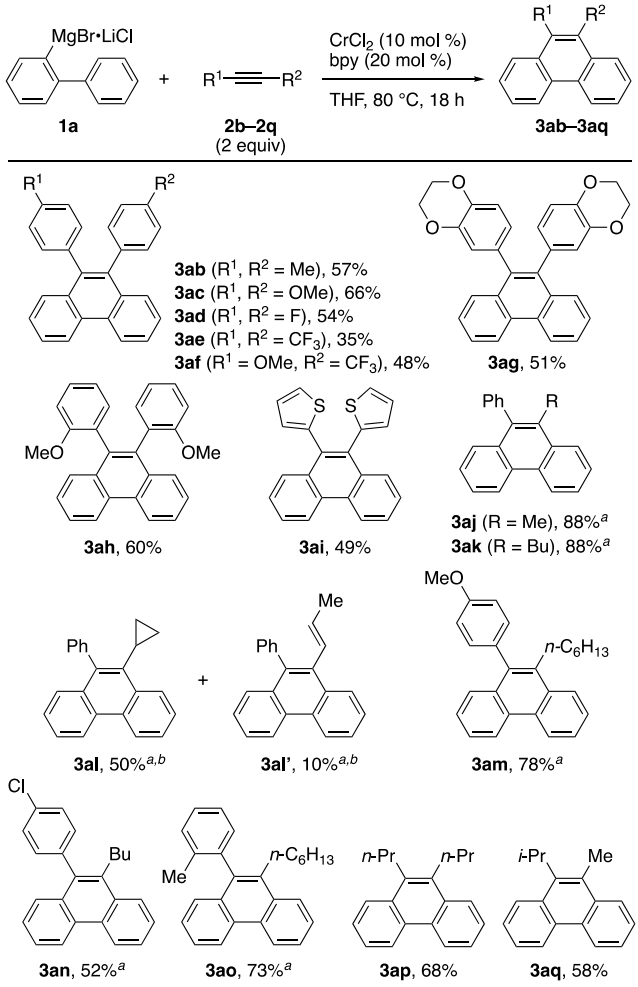


entry	ligand	conv of **2a** (%)[b]	yield of **3aa** (%)[b]
1	none	100	19
2	2,2'-bipyridine (bpy)	100	80 (78)
3	1,10-phenanthroline	100	67
4	bathophenanthroline	100	57
5	terpyridine	51	15
6	dppe	85	30
7[c]	bpy	100	21
8[d]	bpy	9	16
9[e]	bpy	76	56

[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.

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 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.

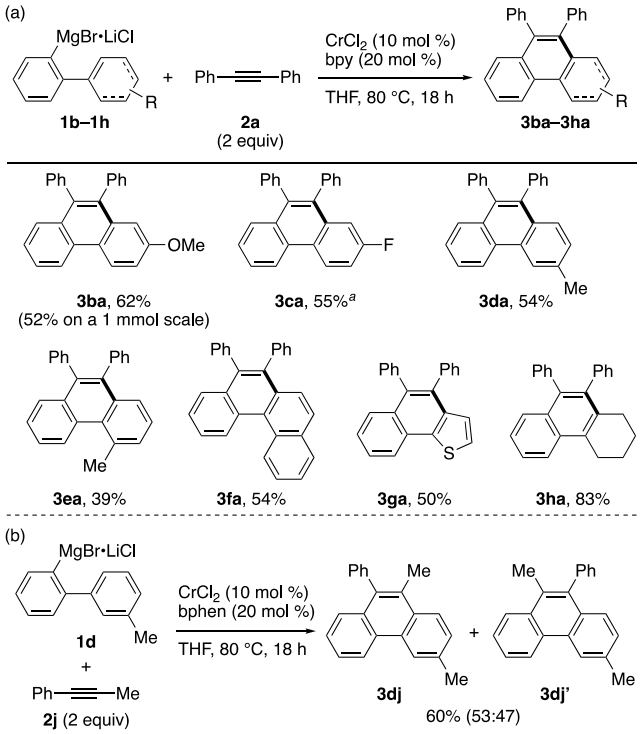
Scheme 2. Scope of Alkynes



[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.

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).

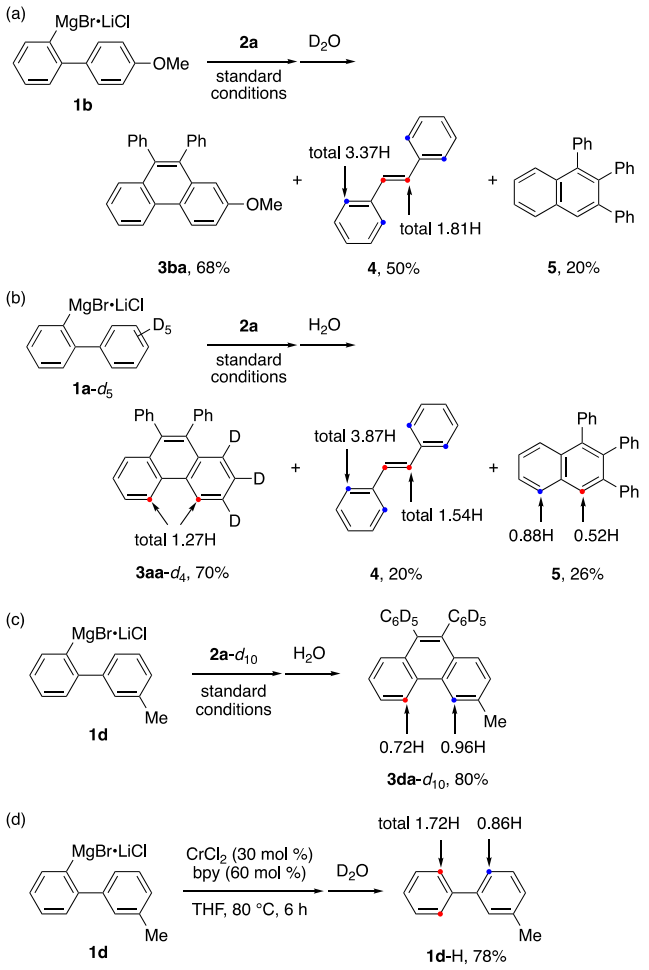
Scheme 3. Reaction of Different Grignard Reagents[a]



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

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

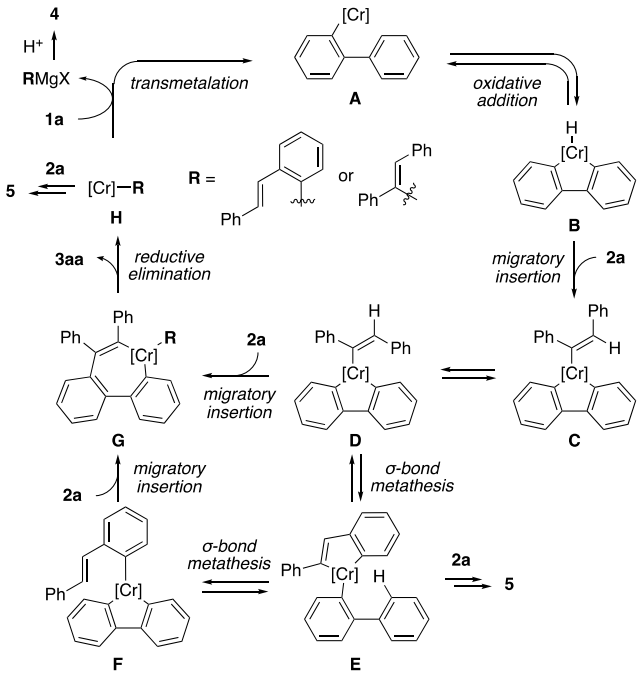
Scheme 4. Deuterium-Labeling Experiments[a]



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

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

Scheme 5. Proposed Reaction Pathways



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

This material is available free of charge via the Internet at http://pubs.acs.org.

Detailed experimental procedures and spectral data (PDF)

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Notes

The authors declare no competing financial interest.

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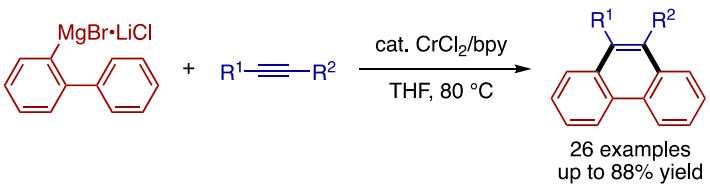

26 examples
up to 88% yield