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Chromium-Mediated Synthesis of Polycyclic Aromatic Compounds from Halobiaryls

Ken-ichiro Kanno, Yuanhong Liu, Atsushi Iesato, Kiyohiko Nakajima,[†] and Tamotsu Takahashi*

Catalysis Research Center, and Graduate School of Pharmaceutical Sciences, Hokkaido University, and SORST, Japan Science and Technology Agency (JST), Sapporo 001-0021, Japan, and Department of Chemistry, Aichi University of Education, Igaya, Kariya, Aichi 448-8542, Japan

tamotsu@cat.hokudai.ac.jp

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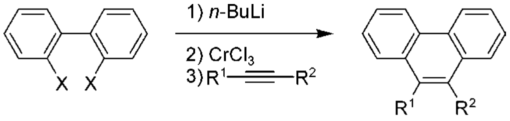
ABSTRACT



R^1, R^2= H, alkyl, aryl, alkynyl, TMS, CO_2R etc.

Reaction of 2,2′-dihalobiphenyl with butyllithium followed by the addition of chromium(III) chloride and alkynes afforded the corresponding phenanthrene derivatives via formal [4 + 2] cycloaddition. A variety of alkynes could be used for this reaction, such as alkyl, aryl, silyl, and alkoxycarbonyl alkynes. Repetitive process of the reaction gave more extended polycyclic compounds such as benzo[*g*]chrysene and azacyclopentaphenalene derivatives.

Construction of polycyclic aromatic ring skeletons has attracted considerable attention in recent years due to their increasing importance in organic material science.[1] Among several synthetic methods for polycyclic aromatics,[2,3] intermolecular [4 + 2] cycloadditions between functionalized biaryls and alkynes seem the simplest and straightforward for the formation of phenanthrene derivatives. Although several examples of such strategy with a series of late transition metals are known,[4] there are still some limitations for availability of substituents of alkynes. In this paper we would like to report chromium-mediated phenanthrene formation from 2,2′-dihalobiphenyl and various alkynes and its application to synthesis of polycyclic aromatic compounds.

In the late of 1950s, Zeiss and co-workers reported that triphenylchromium(III) could catalyze the cyclization of 2-butyne or diphenylacetylene to afford the corresponding hexasubstituted benzene along with 1,2,3,4-tetrasubstituted naphthalene.[5] Later, Ehmann and co-workers investigated that the reaction of 2-biphenylylmagnesium halide with chro-

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[†] Aichi University of Education.

(1) (a) Katz, H. E.; Bao, Z.; Gilat, S. L. *Acc. Chem. Res.* **2001**, *34*, 359. (b) Dimitrakopoulos, C. D.; Malenfant, P. R. L. *Adv. Mater.* **2002**, *14*, 99.

(2) (a) Watson, M. D.; Fechtenkötter, A.; Müllen, K. *Chem. Rev.* **2001**, *101*, 1267. (b) Harvey, R. G.; Fu, P. P. *Chem. Rev.* **1978**, *78*, 317. (c) Floyd, A. J.; Dyke, S. F.; Ward, S. E. *Chem. Rev.* **1976**, *76*, 6, 509.

(3) Selected examples of intramolecular cyclizations: (a) Tovar, J. D.; Swager, T. M. *J. Organomet. Chem.* **2002**, *653*, 215. (b) Yamaguchi, S.; Swager, T. M. *J. Am. Chem. Soc.* **2001**, *123*, 12087. (c) Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. *J. Am. Chem. Soc.* **1997**, *119*, 4578. (d) Fürstner, A.; Mamane, V. *Chem. Commun.* **2003**, 2112. (e) Fürstner, A.; Mamane, V. *J. Org. Chem.* **2002**, *67*, 6264. (f) Yao, T.; Campo, M. A.; Larock, R. C. *Org. Lett.* **2004**, *6*, 2677.

(4) (a) Edelbach, B. L. Lachicotte R. J.; Jones, W. D. *Organometallics* **1999**, *18*, 4040. (b) Edelbach, B. L. Lachicotte R. J.; Jones, W. D. *Organometallics* **1999**, *18*, 4660. (c) Müller, C.; Lachicotte, R. J.; Jones, W. D. *Organometallics* **2002**, *21*, 1975. (d) Iverson, C. N.; Jones, W. D. *Organometallics* **2001**, *20*, 5745. (e) Larock, R. C.; Dory, M. J.; Tian, Q.; Zenner, J. M. *J. Org. Chem.* **1997**, *62*, 7536. (f) Campo M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2002**, *124*, 14326. (g) Campo, M. A.; Huang, Q.; Yao, T.; Tian, Q.; Larock, R. C. *J. Am. Chem. Soc.* **2003**, *125*, 11506. (h) Dyker, G.; Kellner, A. *Tetrahedron Lett.* **1994**, *35*, 7633. (i) Wu, G.; Rheingold, A.; Geib, S. J.; Heck, R. F. *Organometallics* **1987**, *6*, 1941. (j) Dougherty, T. K.; Lau, K. S. Y.; Hedberg, F. L. *J. Org. Chem.* **1983**, *48*, 5273. (k) Mandal, A. B.; Lee, G.-H.; Liu, Y.-H.; Peng, S.-M.; Leung M.-k. *J. Org. Chem.* **2000**, *65*, 332.

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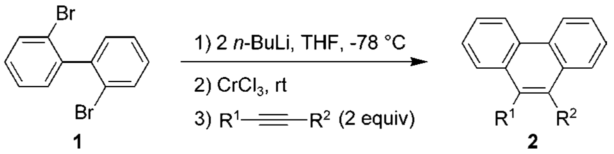
mium(III) chloride followed by 2-butyne produced 9,10-dimethyl-phenanthrene via dibenzochromacyclopentadiene as an intermediate.[6] Although these results have suggested the usefulness of organochromium complex for construction of polycyclic aromatic compounds with alkynes, their investigations were concentrated on the mechanism of these reactions, and efficiency and applicability of the reactions had not been examined sufficiently.[7]

Until now our group has reported zirconium-mediated synthesis of highly substituted polycyclic aromatic compounds.[8] Furthermore, we found that the combination of these zirconium-mediated reactions with chromium(III) chloride have shown unique reactivity toward a series of unsaturated compounds.[9] During the course of our investigation in such direction, we found efficient synthesis of polycyclic compounds from halobiaryls and alkynes mediated by chromium as described below.

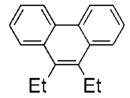
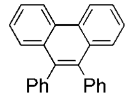
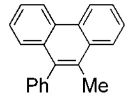
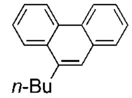
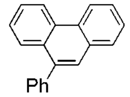
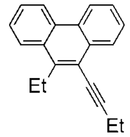
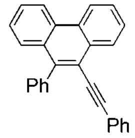
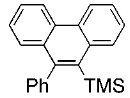
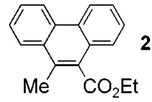
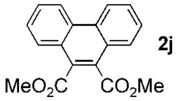
A typical experimental procedure is as follows (Scheme 1). To a THF solution of 2,2′-dibromobiphenyl **1** was added *n*-butyllithium at −78 °C, and the mixture was stirred for 1 h. After addition of 1 equiv of chromium(III) chloride, the mixture was warmed to room temperature. After stirring for 1 h, 2 equiv of an alkyne was added, and the mixture was heated to 50 °C for 6−12 h to afford the corresponding phenanthrene derivatives **2** in good to excellent yields.[10]

Scheme 1



As summarized in Table 1, the chromium-mediated reaction was applicable for a wider variety of alkynes compared with the precedent methods,[4] and the desired phenanthrenes were obtained in good to excellent yields. Arylalkynes can be used for this benzannulation as well as aliphatic alkynes (entries 2 and 3). With terminal alkynes, the desired phenanthrenes were formed without significant loss of efficiency (entries 4 and 5). When conjugated diynes were subjected to the reaction, the corresponding alkynylphenanthrenes were formed, and no biphenanthryl derivatives, the doubly annulated products, were obtained (entries 6 and 7). As functionalized alkynes, silylated alkynes and alkynes with one or two ester groups can be used for this reaction to produce the corresponding phenanthrene derivatives **2h−j** in good yields. For the reactions using alkynes with ethoxy- or methoxycarbonyl groups (entries 9 and 10), addition of TMEDA was effective to increase the product yields by ca. 10%.

Table 1. Synthesis of Phenanthrenes Using $CrCl_3$

entry	alkyne	time / h	product		yield / %[a]
1	Et—≡—Et	12		**2a**	95 (75)
2	Ph—≡—Ph	6		**2b**	- (48)
3	Ph—≡—Me	36		**2c**	75 (58)
4	*n*-Bu—≡	12		**2d**	75 (58)
5	Ph—≡	12		**2e**	63 (45)
6	Et—≡—≡—Et	24		**2f**	67 (47)
7	Ph—≡—≡—Ph	24		**2g**	- (45)
8	Ph—≡—TMS	24		**2h**	88 (75)
9[b]	Me—≡—CO_2Et	24		**2i**	46 (31)
10[b]	MeO_2C—≡—CO_2Me	6		**2j**	54 (43)

[a] GC yields. Isolated yields are shown in parentheses. [b] The reaction was carried out in the presence of 2 equiv of TMEDA.

The chromium-mediated reaction can be applied for the other dilithium compounds. As shown in Scheme 2, it is well-known that a reaction of diphenylacetylene with 2 equiv of butyllithium affords dilithiated stilbene derivative in high yield.[11] When the dilithiated stilbene derivative was treated with chromium(III) chloride followed by the addition of

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(5) (a) Zeiss, H. H.; Herwig, W. *J. Am. Chem. Soc.* **1958**, *80*, 2913. (b) Zeiss, H. H.; Tsutsui, M. *J. Am. Chem. Soc.* **1959**, *81*, 6090. (c) Herwig, W.; Metlesics, W.; Zeiss, H. H. *J. Am. Chem. Soc.* **1959**, *81*, 6203.

(6) (a) Whitesides, G. M.; Ehmann, W. J. *J. Am. Chem. Soc.* **1968**, *90*, 804. (b) Whitesides, G. M.; Ehmann, W. J. *J. Am. Chem. Soc.* **1970**, *92*, 5625.

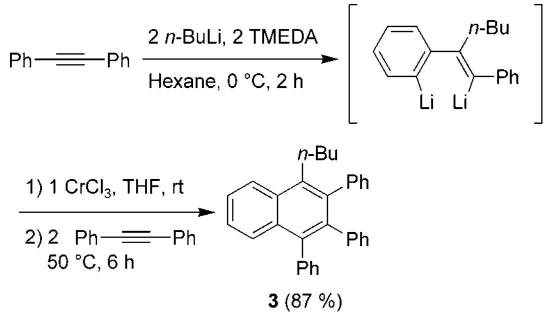
(7) Recent example of chromium-mediated cyclization: Nishikawa, T.; Kakiya, H.; Shinokubo, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, *123*, 4629.

(8) (a) Takahashi, T.; Li, Y.; Stepnicka, P.; Kitamura, M.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **2002**, *124*, 576. (b) Takahashi, T.; Kitamura, M.; Shen, B.; Nakajima, K. *J. Am. Chem. Soc.* **2000**, *122*, 12876. (c) Takahashi, T.; Hara, R.; Nishihara, Y.; Kotora, M. *J. Am. Chem. Soc.* **1996**, *118*, 5154.

(9) Takahashi, T.; Liu, Y.; Iesato, A.; Chaki, S.; Nakajima, K.; Kanno, K. *J. Am. Chem. Soc.* **2005**, *127*, 11928.

(10) Although the reaction mechanism is still unclear yet, it seems to proceed *via* formation of dibenzochromacyclopentadiene as key intermediate followed by cycloaddition with alkynes.

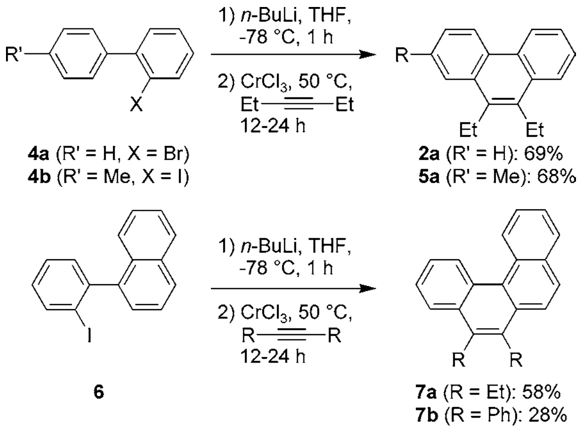
Scheme 2



diphenylacetylene, 1-butyl-2,3,4-triphenylnaphthalene **3** was obtained in 87% isolated yield.

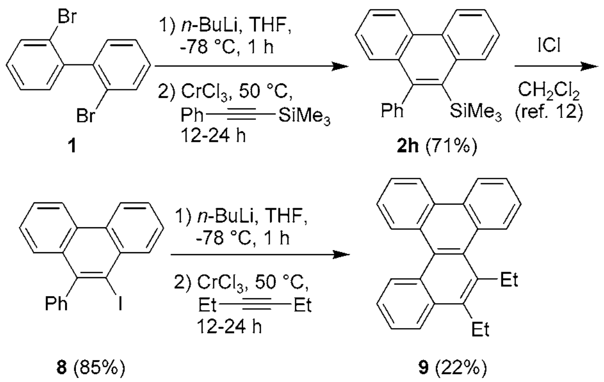
2,2′-Dilithiobiphenyl derivatives were prepared from not only 2,2′-dihalogenated biphenyls but 2-monohalogenated ones. When 2 equiv of *n*-butyllithium was added to 2-bromobiphenyl **4a**, the same dilithiated biphenyl was generated as that from dibromobiphenyl. After treatment with chromium(III) chloride and 3-hexyne, 9,10-diethylphenanthrene **2a** was obtained in a comparable yield. Similarly, 2-iodo-4′-methylbiphenyl **4b** was converted into the corresponding phenanthrene **5a** in the same way in 58% yield (Scheme 3).

Scheme 3



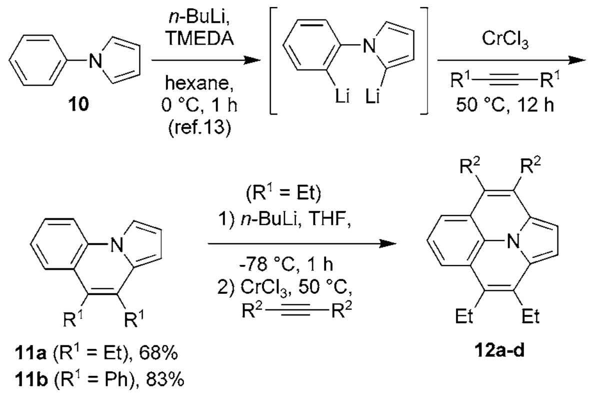
The use of monohalogenated biaryl enabled us to produce more extended polycyclic aromatic compounds. As shown in Scheme 3, 1-(2-lithiophenyl)-2-lithionaphthalene was generated by the addition of 2 equiv of *n*-butyllithium into the THF solution of 1-(2-iodophenyl)naphthalene **6**. After the reaction with chromium(III) chloride and an alkyne, the corresponding benzo[*c*]phenanthrenes **7** were formed.

Scheme 4



Furthermore, stepwise benzannulation is also possible by appropriate selection of the substituents on the starting alkynes as shown in Scheme 4. The reaction with 2,2′-dibromobiphenyl **1** and 1-phenyl-2-trimethylsilylacetylene afforded 9-phenyl-10-trimethylsilylphenanthrene **2h**, which could be converted into 9-iodo-10-phenylphenanthrene **8** by the treatment with iodine monochloride in high yield.[12] When the iodophenanthrene **8** was subjected again to the chromium-mediated reaction with 3-hexyne, the corresponding benzo[*g*]chrysene **9** was obtained.

Scheme 5



1-Phenylpyrrole **10** was dilithiated by the addition of 2 equiv of *n*-butyllithium in hexane in the presence of TMEDA.[13] This dilithiated 1-phenylpyrrole was converted to the pyrroloquinoline derivative **11** by the same way as above in good yield (Scheme 5). Moreover, the bay region of the pyrroloquinoline **11** could also be dilithiated and transformed into the corresponding 9b-azacyclopenta[*cd*]phenalenes **12** (Scheme 5 and Table 2). It is worth noting that the chromium-mediated reaction enables us to construct these polycyclic systems in short steps.

Table 2. Synthesis of Azacyclopentaphenalene **12**

entry	R	time/h	product	yield/%
1	Et	12	**12a**	39
2	Ph	3	**12b**	55
3	*p*-tol	12	**12c**	49
4	2-thienyl	24	**12d**	38

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(11) (a) Mulvaney, J. E.; Carr, L. J. *J. Org. Chem.* **1968**, *33*, 3286. (b) Mulvaney, J. E.; Garlund, Z. G.; Garlund, S. L.; Newton, D. J. *J. Am. Chem. Soc.* **1966**, *88*, 476.

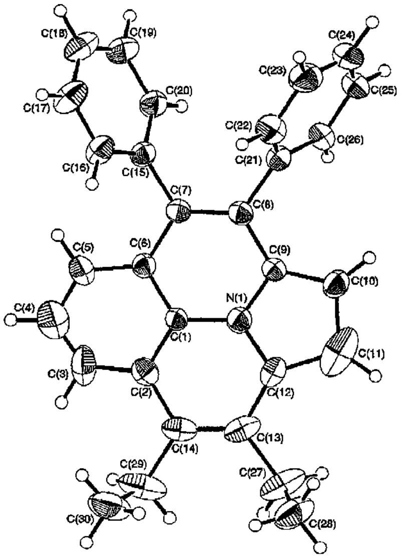

Figure 1. Molecular structure of 9b-azacyclopentaphenalene **12b**.

Azacyclopentaphenalene **12b** was characterized by X-ray crystallographical analysis (Figure 1), which shows **12b** has highly planar structure in the solid state. All of the atoms that constitute the fused polycyclic skeleton are located on the same plane.

In summary, the chromium-mediated benzannulation reaction allows us to construct a variety of polycyclic aromatic compounds starting from halogenated biaryls and a series of alkynes. A wide availability of alkynes is the most remarkable advantage of this benzannulation reaction compared to the palladium-catalyzed ones. Also, the present reaction provides a convenient method to build up the complex polycyclic skeletons compared with the known methods. Further investigation especially for the synthesis of heterocyclic compounds is now in progress.

Supporting Information Available: Experimental details and spectroscopic characterization of new compounds and X-ray crystallographical data of **12b** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) (a) Campo, M. A.; Larock, R. C. *Org. Lett.* **2000**, *23*, 3675−3677. (b) Miller, R. B.; McGarvey, G. *Synth. Commun.* **1978**, *8*, 291.

(13) Faigl, F.; Schlosser, M. *Tetrahedron* **1993**, *49*, 10271.