ORGANIC LETTERS

2009
Vol. 11, No. 22
5198−5201

Synthesis of Highly Substituted Naphthalene and Anthracene Derivatives by Rhodium-Catalyzed Oxidative Coupling of Arylboronic Acids with Alkynes

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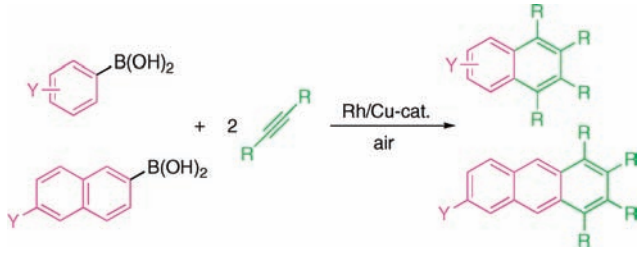
Received September 13, 2009

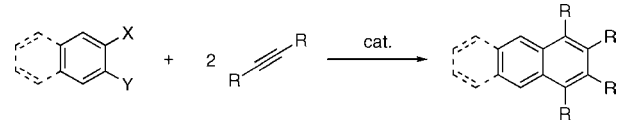
ABSTRACT



The rhodium-catalyzed oxidative 1:2 coupling reactions of arylboronic acids with alkynes effectively proceeds in the presence of a copper−air oxidant to produce the corresponding annulated products. Of special note, anthracene derivatives can be obtained selectively from 2-naphthylboronic acids.

Linearly fused aromatic ring systems can be seen in various π-conjugated functional materials such as organic semiconductors and luminescent materials.[1] Highly substituted derivatives around fused aromatic cores are of particular interest because of their stability, solubility, enhanced ability to transport charge, and fluorescent properties in the solid state.[2] Among modern potential strategies to prepare polysubstituted and fused aromatics is transition metal-catalyzed homologation, such as benzene to naphthalene and naphthalene to anthracene, by the coupling of a given aromatic substrate with two alkyne molecules (Scheme 1).[3] Thus, the

Scheme 1



catalytic transformations of various di- ($X \neq H$, $Y \neq H$)[3,4] and monofunctionalized aromatic substrates ($X \neq H$, $Y = H$)[5] have been developed. The latter reaction involving regioselective C−H bond cleavage is attractive from an atom-economic point of view.[6]

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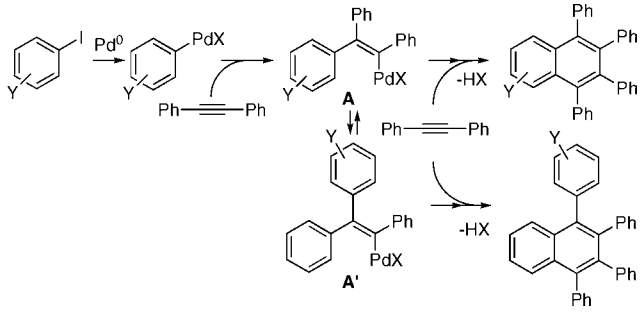
(2) For example, see: (a) Kaur, I.; Stein, N. N.; Kopreski, R. P.; Miller, G. P. *J. Am. Chem. Soc.* **2009**, *131*, 3424. (b) Ahmed, E.; Briseno, A. L.; Xia, Y.; Jenekhe, S. A. *J. Am. Chem. Soc.* **2008**, *130*, 1118. (c) Paraskar, A. S.; Reddy, A. R.; Patra, A.; Wijsboom, Y. H.; Gidron, O.; Shimon, L. J. W.; Leitus, G.; Bendikov, M. *Chem.—Eur. J.* **2008**, *14*, 10639. (d) Cicoira, F.; Santato, C. *Adv. Funct. Mater.* **2007**, *17*, 3421. (e) Qiao, X.; Padula, M. A.; Ho, D. M.; Vogelaar, N. J.; Scutt, C. E.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1996**, *118*, 741.

10.1021/ol9021172 CCC: $40.75
Published on Web 10/15/2009

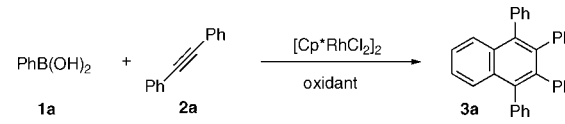
The palladium-catalyzed reaction of aryl iodides (X = I, Y = H)[5c−e] seems to be of considerable synthetic utility because of the wide availability of simple substrates as aryl sources. It has been proposed that the reaction involves the formation of a vinylpalladium intermediate (**A**) via the oxidative addition of ArI toward Pd(0) species and sebsequent alkyne insertion (Scheme 2).[5c] Then cyclopalladation,

Scheme 2



the second alkyne insertion, and final reductive elimination may occur to form a 1,2,3,4-tetrasubstituted naphthalene. However, the vinylpalladium intermediate tends to undergo *E*/*Z* isomerization (**A** to **A′**).[7] Therefore, the reaction of substituted aryl iodides with diphenylacetylene gives the corresponding naphthalene as a mixture of its isomers.

Table 1. Reaction of Phenylboronic Acid (**1a**) with Diphenylacetylene (**2a**)[a]



entry	oxidant (mmol)	solvent	temp (°C)	% yield of **3a**[b]
1	$Cu(OAc)_2{\cdot}H_2O$ (0.5)	DMF	100	56
2	$Cu(OAc)_2{\cdot}H_2O$ (0.5)	DMSO	100	3
3	$Cu(OAc)_2{\cdot}H_2O$ (0.5)	*o*-xylene	100	3
4	$Cu(OAc)_2{\cdot}H_2O$ (0.5)	dioxane	100	22
5	$Cu(OAc)_2{\cdot}H_2O$ (0.5)	NMP	100	50
6	$Cu(OAc)_2{\cdot}H_2O$ (0.5)	DMF	80	53
7	$Cu(OAc)_2{\cdot}H_2O$ (0.5)	DMF	60	53
8	AgOAc (0.5)	DMF	100	74
9	AgOAc (0.5)	DMF	80	66
10	AgOAc (0.5)	DMF	60	67
11	AgOAc (0.5)	DMF	rt	67
12	Ag_2CO_3 (0.25)	DMF	100	32
13	$AgOCOCF_3$ (0.5)	DMF	100	87
14[c]	$Cu(OAc)_2{\cdot}H_2O$ (0.025)	DMF	100	86 (78)

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), $[(Cp^*RhCl_2)_2]$ (0.005 mmol), solvent (3 mL) under N_2 for 2 h. [b] GC yield based on the amount of **2a** used. Value in parentheses indicate the yield after purification. [c] Under air.

Arylboronic acids are also widely used and commercially available as arylation reagents. The catalytic homologation of arylboron reagents with alkynes has, however, been less explored, and only two examples with *o*-bromophenylboronic acids (X = $B(OH)_2$, Y = Br) have been reported.[8] During our study of the homologations via the rhodium-catalyzed oxidative coupling of aromatic substrates with alkynes,[5g−i] it has been revealed that even ortho-unfunctionalized, simple phenylboronic acids (X = $B(OH)_2$, Y = H) undergo the coupling effectively to give 1,2,3,4-tetrasubstituted naphthalenes selectively.[9] Fortunately, the isomer formation has been found not to occur in this Rh-based system. Furthermore, the reaction of 2-naphthylboronic acids also proceeds smoothly to afford the desired anthracene derivatives selectively. These new findings are described herein.

In an initial attempt, phenylboronic acid (**1a**) (0.5 mmol) was treated with diphenylacetylene (**2a**) (0.5 mmol) in the presence of $[Cp^*RhCl_2]_2$ (0.005 mmol) and $Cu(OAc)_2{\cdot}H_2O$ (0.5 mmol) as catalyst and oxidant, respectively, in DMF (3 mL) at 100 °C under N_2 for 2 h. As a result, 1,2,3,4-tetraphenylnaphthalene (**3a**) was formed in 56% yield (entry 1 in Table 1, Cp* = pentamethylcyclopentadienyl). While the reaction was sluggish in DMSO, *o*-xylene, and dioxane, a comparable result was obtained in NMP (entries 2−5). The reaction was not sensitive to the temperature between 60 and

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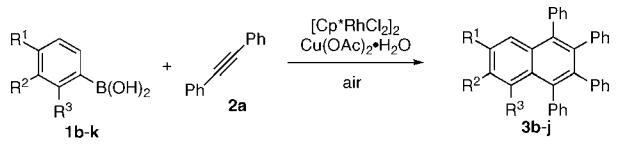
Table 2. Reaction of Arylboronic Acids **1** with Diphenylacetylene (**2a**)[a]



entry	**1**	R^1	R^2	R^3	product, % yield[b]
1	**1b**	Me	H	H	**3b**, 73 (66)
2	**1c**	OMe	H	H	**3c**, 72 (72)
3	**1d**	Cl	H	H	**3d**, 89 (83)
4	**1e**	F	H	H	**3e**, 82 (82)
5	**1f**	Br	H	H	**3f**, 79 (79)
6	**1g**	CF_3	H	H	**3g**, 22
7[c]	**1g**	CF_3	H	H	**3g**, 82 (82)
8[c]	**1h**	CO_2Me	H	H	**3h**, 64
9[d]	**1h**	CO_2Me	H	H	**3h**, 91 (87)
10[c]	**1i**	CHO	H	H	**3i**, 59
11[d]	**1i**	CHO	H	H	**3i**, 79 (79)
12	**1j**	H	Me	H	**3b**, 51 (51)
13	**1k**	H	H	Me	**3j**, 35 (34)

[a] Reaction conditions: **1** (0.5 mmol), **2a** (0.5 mmol), $[(Cp^*RhCl_2)_2]$ (0.005 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol), DMF (3 mL) at 100 °C under air for 2 h. [b] GC yield based on the amount of **2a** used. Value in parentheses indicate the yield after purification. [c] $Cu(OCOCF_3)_2 \cdot nH_2O$ (0.025 mmol) was used in place of $Cu(OAc)_2 \cdot H_2O$. [d] $AgOCOCF_3$ (0.5 mmol) was used under N_2 in place of $Cu(OAc)_2 \cdot H_2O$.

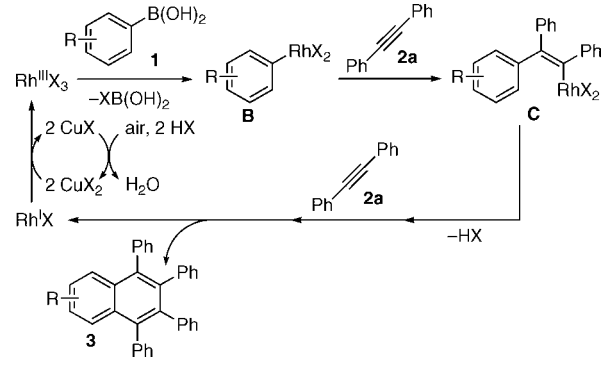
100 °C (entries 6 and 7). AgOAc could also be used as oxidant (entires 8−11). Thus, with AgOAc, the reaction proceeded smoothly even at room temperature to form **3a** in 67% yield within 2 h (entry 11). $AgOCOCF_3$ gave a better yield (87%, entry 13). To our delight, a comparably good yield was obtained when the reaction was conducted with a catalytic amount of $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol) under air (entry 14). Thus, the aerobic oxidative coupling proceeded efficiently to give **3a** in 86% yield.

Table 2 summarizes the results for the coupling of a series of substituted phenylboronic acids **1b**−**k** with **2a**. 4-Methyl-, methoxy-, chloro-, fluoro-, and bromophenylboronic acids **1b**−**f** reacted with **2a** smoothly under the aerobic conditions to form 6-substituted 1,2,3,4-tetraphenylnaphthalenes **3b**−**f** in 72−89% yields (entries 1−5). It was found that electron-deficient phenylboronic acids were less reactive in the present reaction. Thus, the reaction of 4-(trifluoromethyl)phenylboronic acid (**1g**) with **2a** under the standard conditions gave the corresponding naphthalene **3g** in only 22% yield (entry 6). In this case, the use of $Cu(OCOCF_3)_2$ (0.025 mmol) in place of $Cu(OAc)_2$ improved the yield to 82% (entry 7). Even under the modified condition with $Cu(OCOCF_3)_2$, the reactions of 4-(methoxycarbonyl)- (**1h**) and 4-formyl- (**1i**) phenylboronic acids were sluggish (entries 8 and 10). In these reactions, $AgOCOCF_3$ was found to be more effective as oxidant. Thus, in the presence of the Ag salt (0.5 mmol) under N_2, naphthalenes **3h** and **3i** were obtained in 91% and 79% yields, respectively (entries 9 and 11). Treatment of 3-methyl- (**1j**) and 2-methyl- (**1k**) phenylboronic acids with **2a** under the standard conditions with $Cu(OAc)_2$ gave **3b** and **3j** in moderate yields (entries 12 and 13).

The reactions of **1a** with various internal alkynes **2b**−**f** in place of **2a** were next examined. Under the optimized conditions in Table 1 (entry 14), methyl- (**2b**), methoxy- (**2c**), and chloro- (**2d**) substituted diphenylacetylenes underwent the coupling with **1a** to afford the corresponding 1,2,3,4-tetraarylnaphthalenes **3k**−**m** selectively (entries 1−3 in Table 3). 1-Phenylpropyne (**2e**) reacted with **1a** smoothly to give 1,4-dimethyl-2,3-diphenylnaphthalene (**3n**) in 70% yield along with a small amount (7%) of a separable unidentified isomer (entry 4). In contrast, the reaction of 4-octyne (**2f**) was sluggish under the standard aerobic conditions to form 1,2,3,4-tetrapropylnaphthalene (**3o**) in only 10% yield (entry 5). The reaction efficiency was improved by using a stoichiometric amount of $Cu(OAc)_2 \cdot H_2O$ (0.5 mmol) at room temperature (entry 7). 1-Phenyl-2-(trimethylsilyl)acetylene did not couple with **1a** at all under the standard conditions.

A plausible mechanism for the reaction of **1** with **2a** is illustrated in Scheme 3, in which neutral ligands are omitted.

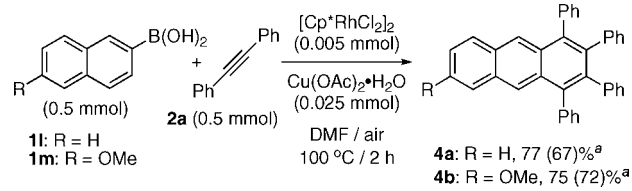
Scheme 3



Initial transmetalation of the added $Rh(III)X_3$ species with **1** gives an arylrhodium intermediate **B**. Then, alkyne insertion occurs to form a vinylrhodium species **C**. Subsequent cyclorhodation, the second alkyne insertion, and reductive elimination afford naphthalene **3**. The resulting RhX(I) species seems to be oxidized in the presence of the copper cocatalyst under air to regenerate $Rh(III)X_3$.

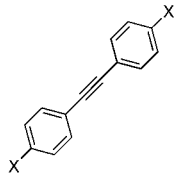
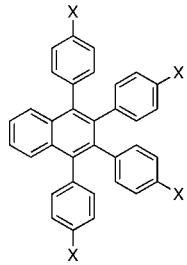
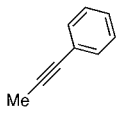
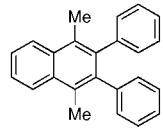
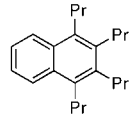
The homologation from naphthalene substrates to anthracene derivatives could be achieved by the present procedure (Scheme 4). Thus, treatment of 2-naphthylboronic acid (**1*l***) with **2a** under the standard aerobic conditions gave

Scheme 4



[a] GC yield based on the amount of **2a** used. Value in parentheses indicate the yield after purification.

Table 3. Reaction of Phenylboronic Acid (**1a**) with Alkynes **2**[a]

entry	2	temp (°C)	product, % yield[b]
			
1	**2b**: X = Me	100	**3k**: X = Me, 80 (80)
2	**2c**: X = OMe	100	**3l**: X = OMe, 53 (48)
3	**2d**: X = Cl	100	**3m**: X = Cl, 90 (83)
			
4	**2e**	100	**3n**, 70 (70)[c]
			
5	**2f**	60	**3o**, 10
6[d]		60	**3o**, 42
7[d]		rt	**3o**, 47 (46)

[a] Reaction conditions: **1a** (0.5 mmol), **2** (0.5 mmol), $[(Cp^*RhCl_2)_2]$ (0.005 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol), DMF (3 mL) under air for 2 h. [b] GC yield based on the amount of **2** used. Value in parentheses indicate the yield after purification. [c] A small amount (7%) of a regioisomer was also formed. [d] $Cu(OAc)_2 \cdot H_2O$ (0.5 mmol) was used under N_2.

1,2,3,4-tetraphenylanthracene (**4a**) in 77% yield as a single coupling product. 6-Methoxy-2-naphthylboronic acid (**1m**) also underwent the reaction in a similar manner to afford the corresponding anthracene **4b**.

It should be noted that the corresponding phenanthrenes were not formed at all, while the mixtures of anthracene and phenanthrene derivatives were usually formed in the previous homologations of iodides[5c] and acid chlorides.[5f] Various arylboron compounds,[10] including 2-naphthylboronates,[11] are now preparable via the direct borylation of their parent arenes under Ir-catalysis. Combining our homologation with borylation, a wide range of fused aromatic compounds including acenes appear to be readily available.

In summary, we have demonstrated that the rhodium-catalyzed oxidative coupling of substituted phenyl- and naphthylboronic acids with alkynes proceeds efficiently to give the corresponding 1,2,3,4-tetrasubstituted naphthalene and anthracene derivatives, respectively. Particularly, the latter is the first example, to our knowledge, of the selective construction of anthracene frameworks by homologations with monofunctionalized naphthyl substrates ($X \neq H$, $Y = H$ in Scheme 1). Work is underway toward further development of the synthetic methods.

Acknowledgment. This work was partly supported by Grants-in-Aid from the Ministry of Education, Culture, Sports, Science and Technology, Japan and the Kurata Memorial Hitachi Science and Technology Foundation.

Supporting Information Available: Standard experimental procedure and characterization data of products. This material is available free of charge via the Internet at http://pubs.acs.org.

OL9021172

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