ORGANIC LETTERS

2010
Vol. 12, No. 8
1864−1867

Rhodium-Catalyzed Alkenylation of Nitriles via Silicon-Assisted C−CN Bond Cleavage

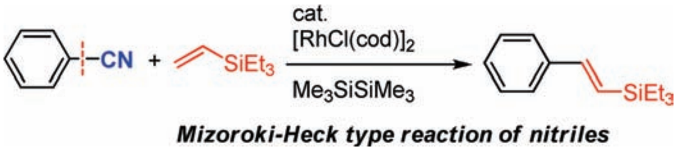
Yusuke Kita,[†] Mamoru Tobisu,[*,‡] and Naoto Chatani[*,†]

*Frontier Research Base for Global Young Researchers, Graduate School of Engineering,
Osaka University, Suita, Osaka 565-0871, Japan, and Department of Applied Chemistry,
Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan*

tobisu@chem.eng.osaka-u.ac.jp; chatani@chem.eng.osaka-u.ac.jp

Received February 25, 2010

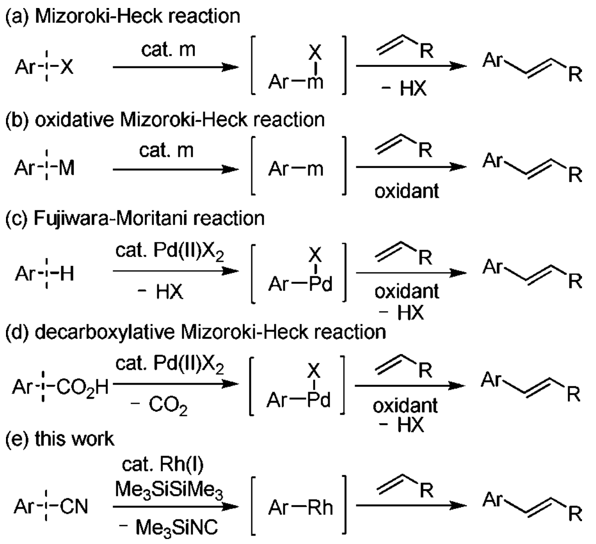
ABSTRACT



Rhodium-catalyzed Mizoroki−Heck type reaction of nitriles via the cleavage of C−C bonds is described. Orthogonal and iterative functionalizations of arenes were also demonstrated by combining the present and conventional halide-based cross-coupling reactions.

The Mizoroki−Heck reaction has been recognized as a powerful tool for the arylation of alkenes.[1] In addition to the standard Mizoroki−Heck reaction using aryl halides or their equivalents[2] (Scheme 1a), several variants have been developed. They can be classified based on the method used to generate the key aryl-metal species: transmetalation from organometallic reagents (oxidative Mizoroki−Heck reaction, Scheme 1b),[3] electrophilic subsitution of arenes (Fujiwara−Moritani reaction, Scheme 1c),[4] and decarboxylation of aryl carboxylic acids (Scheme 1d).[5] Herein, we report a new variant of the Mizoroki−Heck process, in which an aryl−metal

Scheme 1. Catalytic Arylation of Alkenes



[†] Department of Applied Chemistry, Faculty of Engineering.

[‡] Frontier Research Base for Global Young Researchers, Graduate School of Engineering.

(1) For reviews of the Mizoroki−Heck reaction, see: (a) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (b) Whitcombe, N. J.; Hii, K. K. M.; Gibson, S. E. *Tetrahedron* **2001**, *57*, 7449. (c) Knowles, J. P.; Whiting, A. *Org. Biomol. Chem.* **2007**, *5*, 31. (d) *The Mizoroki-Heck Reactione*; Oestreich, M., Ed.; Wiley-VCH: Weinheim, 2009.

(2) Selected recent examples; aroyl chloride: (a) Sugihara, T.; Satoh, T.; Miura, M. *Tetrahedron Lett.* **2005**, *46*, 8269. Diazonium salt: (b) Kikukawa, K.; Ikenaga, K.; Kono, K.; Toritani, K.; Wada, F.; Matsuda, T. *J. Organomet. Chem.* **1984**, *270*, 277. Arylsulfonyl chloride: (c) Dubbaka, S. R.; Vogel, P. *Chem.*−*Eur. J.* **2005**, *11*, 2633. *N*-nitroso-*N*-arylacetamide: (d) Kikukawa, K.; Naritomi, M.; He, G. X.; Wada, F.; Matsuda, T. *J. Org. Chem.* **1985**, *50*, 299. Aryl phoshonium salt: (e) Hwang, L. K.; Na, Y.; Lee, J.; Do, Y.; Chang, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 6166. Hypervalent iodo compound: (f) Aydin, J.; Larsson, J. M.; Selander, N.; Szabo, K. J. *Org. Lett.* **2009**, *11*, 2852–2854.

(3) Selected recent examples; M = B: (a) Xiong, D.-C.; Zhang, L.-H.; Ye, X.-S. *Org. Lett.* **2009**, *11*, 170. M = Sn: (b) Parrish, J. P.; Jung, Y. C.; Shin, S. I.; Jung, K. W. *J. Org. Chem.* **2002**, *67*, 7127. M = Si: (c) Koike, T.; Du, X.; Sanada, T.; Danda, Y.; Mori, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 89. M = $P(O)(OH)_2$: (d) Inoue, A.; Shinokubo, H.; Oshima, K. *J. Am. Chem. Soc.* **2003**, *125*, 1484. M = Bi: (e) Asano, R.; Moritani, I.; Fujiwara, Y.; Teranishi, S. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2910. M = Sb: (f) Matoba, K.; Motofusa, S.-i.; Sik Cho, C.; Ohe, K.; Uemura, S. *J. Organomet. Chem.* **1999**, *574*, 3.

(4) A review: (a) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633. A recent report: (b) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072.

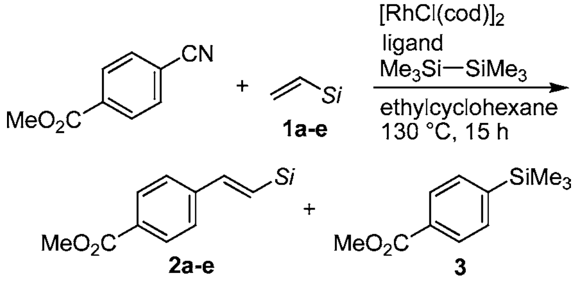
10.1021/ol100481h

species is generated from aryl cyanides via the cleavage of a carbon−carbon bond. Synthetic applications of this decyanative Mizoroki−Heck reaction, including orthogonal and iterative functionalization of arenes, are also demonstrated.

Previously, we reported rhodium-catalyzed silylation[6a,b] and decyanation[6c] reactions of aryl cyanides via the cleavage of C−CN bonds. In these reactions, an arylrhodium species generated from aryl cyanides and organosilicon reagents is postulated to be a key intermediate. Indeed, we also reported that tethered electrophiles can intercept the arylrhodium intermediate to afford cyclized products.[6b] On the basis of these results, we envisioned that an arylrhodium complex generated in our catalytic system should react with external alkenes to furnish an alkenylated product, especially in consideration of the number of catalytic reactions involving the addition of arylrhodium intermediates to alkenes.[7] One isolated example of a Mizoroki−Heck-type alkenylation of nitrile (34% yield), in which a C−CN bond is cleaved via oxidative addition to a nickel catalyst, was reported.[8]

First, we examined the reaction of methyl 4-cyanobenzoate with several alkenes, including terminal alkenes, cyclic alkenes, α,β-unsaturated carbonyl compounds, vinyl acetate, vinyl ethers, and vinylsilanes, under the conditions we identified as being suitable for the intramolecular arylation reaction.[6b] As a result, the desired Mizoroki−Heck-type product **2a** was obtained in 46% yield, along with the undesired silylated byproduct **3**,[6a,b] when triethylvinylsilane (**1a**) was used as an alkene component (entry 1 in Table 1).

Table 1. Reaction Optimization[a]



			yields (%)[b]	
entry	*Si*	ligand	**2**	**3**
1[c]	$SiEt_3$ (**a**)	$P(4\text{-}CF_3C_6H_4)_3$	46	22
2	$SiEt_3$ (**a**)	$P(4\text{-}CF_3C_6H_4)_3$	60	28
3	$SiEt_3$ (**a**)	$P(4\text{-}FC_6H_4)_3$	65	18
4	$SiMe_3$ (**b**)	$P(4\text{-}FC_6H_4)_3$	25	25
5	Si^tBuMe_2 (**c**)	$P(4\text{-}FC_6H_4)_3$	36	14
6	Si^iPr_3 (**d**)	$P(4\text{-}FC_6H_4)_3$	11	79
7	$Si(O^iPr)_3$ (**e**)	$P(4\text{-}FC_6H_4)_3$	68[d]	0

[a] Reaction conditions: methyl 4-cyanobenzoate (0.5 mmol), vinylsilane (2 mmol), hexamethyldisilane (1 mmol), $[RhCl(cod)]_2$ (0.025 mmol), ligand (0.05 mmol), ethylcyclohexane (0.5 mL), 130 °C, 15 h. [b] Isolated yields based on nitrile. [c] Run using **1a** (1 mmol). [d] NMR yield.

One possible reason for the inapplicability of other alkenes may be the side reactions initiated by silylrhodation of alkenes, such as dehydrogenative silylation and oligomerization of alkenes.[9] Inspired by the promising result using **1a**, we next optimized the reaction conditions to improve the selectivity (Table 1). By increasing the amount of **1a** (4 equiv to nitrile), the yield of alkenylated product was improved (entry 2). The choice of the ligand also proved to affect the selectivity significantly. Among the ligands examined, $P(4\text{-}FC_6H_4)_3$ proved to be the most effective.[10] The effect of the substituents on the silicon atom of vinylsilanes was also examined (entries 4−7). The use of vinylsilanes bearing trimethyl-, *tert*-butyldimethyl-, and triisopropylsilyl groups, as in **1b**−**d**, lowered the yields of the corresponding alkenylated products. On the other hand, the use of triisopropoxylvinylsilane (**1e**) completely suppressed the formation of **3** and selectively afforded the alkenylated product **2e**. Although **1e** proved to be the best alkene in terms of the yield and selectivity, we were unable to isolate the pure product **2e** due to the difficulty in separating the byproducts, which were presumably formed by the oligomerization of **1e**. Thus, we decided to employ **1a** as an alkene component for further investigation.[11]

Table 2 shows the scope of the rhodium-catalyzed alkenylation of nitriles using **1a**. Functional groups, such as esters (entries 1), ethers (entries 3, 5, 7, and 8), and amines (entries 4 and 6), and a heteroaromatic ring (entry 12) were tolerated. The selectivity between alkenylation and silylation agreed with the trends of electronic and steric effects observed for our previously reported silylation reaction.[6c] Better selectivity for the alkenylation products was observed with electron-rich substrates due to the relatively slow silylation reaction (entries 3 and 4). It is important to note that, although a small amount of silylated products were formed with several substrates, all the alkenylated products could successfully be isolated in pure form by standard silica gel chromatography. In the case of sterically congested nitriles, the desired alkenylated products were obtained exclusively, presumably due to the sensitivity of the rate of silylation to the steric effect[6a,b] (entries 7−10). Alkenyl cyanides were also applicable to this catalysis to furnish dienylsilanes **14** (entry 13).

A plausible mechanism is illustrated in Scheme 2. A catalyst precursor **A** initially reacts with disilane to generate catalytically active silylrhodium species **B**. Silicon-assisted

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(5) (a) Gooβen, L. J.; Paetzold, J.; Winkel, L. *Synlett* **2002**, 1721. (b) Myers, A. G.; Tanaka, D.; Mannion, M. R. *J. Am. Chem. Soc.* **2002**, *124*, 11250. (c) Tanaka, D.; Myers, A. G. *Org. Lett.* **2004**, *6*, 433. (d) Tanaka, D.; Romeril, S. P.; Myers, A. G. *J. Am. Chem. Soc.* **2005**, *127*, 10323. (e) Hu, P.; Kan, J.; Su, W.; Hong, M. *Org. Lett.* **2009**, *11*, 2341.

(6) (a) Tobisu, M.; Kita, Y.; Chatani, N. *J. Am. Chem. Soc.* **2006**, *128*, 8152. (b) Tobisu, M.; Kita, Y.; Ano, Y.; Chatani, N. *J. Am. Chem. Soc.* **2008**, *130*, 15982. (c) Tobisu, M.; Nakamura, R.; Kita, Y.; Chatani, N. *J. Am. Chem. Soc.* **2009**, *131*, 3174.

(7) For reviews on this topic, see: (a) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (b) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (c) Miura, T.; Murakami, M. *Chem. Commun.* **2007**, 217.

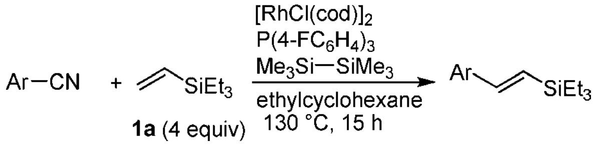
(8) Nakao, Y.; Yada, A.; Satoh, J.; Ebata, S.; Oda, S.; Hiyama, T. *Chem. Lett.* **2006**, *35*, 790.

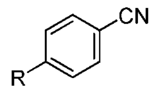
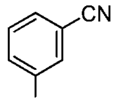
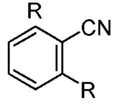
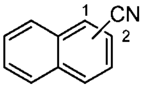
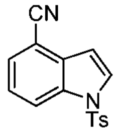
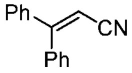
(9) Tobisu, M.; Hyodo, I.; Onoe, M.; Chatani, N. *Chem. Commun.* **2008**, 6013.

(10) Other ligands examined (ligand (yield of **1a**, yield of **2a**)): PPh_3 (53%, 27%), $P(4\text{-}MeOC_6H_4)_3$ (37%, 31%), $P(C_6F_5)_3$ (55%, 14%), $P(2\text{-}MeC_6H_4)_3$ (24%, 74%), PCy_3 (22%, 0%), PBu_3 (25%, 64%), $P(OPh)_3$ (42%, 42%), bipyridine (25%, 10%), IPr (55%, 28%).

(11) For the results using other vinylsilanes, see the Supporting Information.

Table 2. Rh-Catalyzed Alkenylation of Aromatic Nitriles with **1a**[a]

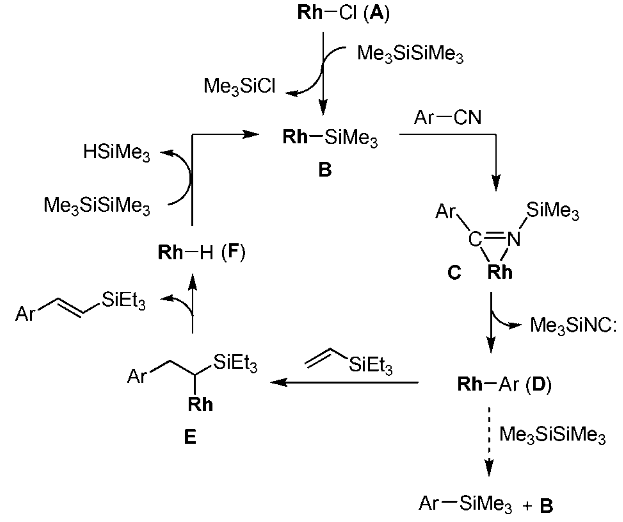


entry	nitrile		yield (%)[b]
1		R = CO_2Me	**2a** 65 (18)
2		R = CF_3	**4** 40 (33)
3[c]		R = OMe	**5** 80 (17)
4[c]		R = NMe_2	**6** 81 (12)
5		R = OMe	**7** 67 (7)
6[d]		R = NMe_2	**8** 75 (16)
7[e]		R = Me	**9** 71 (0)
8		R = OMe	**10** 78 (0)
9[f]		R = Ph	**11** 52 (0)
10		1-CN	**12** 88 (0)
11		2-CN	**13** 62 (16)
12			**14** 82 (11)
13[c]			**15** 41 (0)

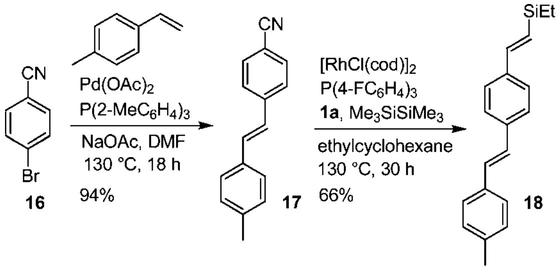
[a] Reaction conditions: nitrile (0.5 mmol), **1a** (2 mmol), hexamethyldisilane (1 mmol), $[RhCl(cod)]_2$ (0.025 mmol), $P(4-FC_6H_4)_3$ (0.05 mmol), ethylcyclohexane (0.5 mL), 130 °C, 15 h. [b] Isolated yield of alkenylated product based on nitrile. Values in the parentheses refer to the yield of the silylated product. [c] Run for 30 h. [d] Run for 40 h. [e] $[RhCl(cod)]_2$ (0.05 mmol) and $P(4-FC_6H_4)_3$ (0.10 mmol) were used. [f] Mesitylene was used as a solvent. Starting nitrile was recovered in 45%.

cleavage of a C−CN bond via η^2-iminoacyl complex **C** then affords arylrhodium **D**.[12] Arylrhodium intermediate **D** adds to vinylsilane to form an alkylrhodium complex **E**, which affords an alkenylated product, along with rhodium hydride **F** via β-hydrogen elimination. Rhodium hydride **F** reacts with disilane to regenerate silylrhodium species **B**.[13] As a minor pathway, arylrhodium **D** can react with disilane to afford a silylated product as we previously reported.[6a,b]

Scheme 2. Plausible Mechanism



The present new variant of the Mizoroki-Heck reaction can provide a unique strategy for the synthesis of π-conjugated molecules. For example, introduction of two different alkenes to an aromatic ring can be attained by the sequential alkenylation of **16** via Pd and Rh catalysis (eq 1).



(1)

Currently, our decyanative Mizoroki−Heck type reaction is limited to the synthesis of alkenylsilanes. Nevertheless, this method should find valuable application in organic synthesis in view of the versatility of alkenylsilanes as intermediates.[14] Particularly useful is the conversion into alkenyl bromides, which can be accomplished by the treatment with NBS at ambient temperature (**20**→**21** in Scheme 3). The potential utility of the decyanative alkenylation/bromination protocol is demonstrated in the iterative synthesis[15] of oligo(phenylenevinylene)s.[16,17] Thus, the conjugated chain could be extended in a streamlined manner by repeating the decyanative-Mizoroki−Heck/bromination/

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[12] (a) Taw, F. L.; White, P. S.; Bergman, R. G.; Brookhart, M. *J. Am. Chem. Soc.* **2002**, *124*, 4192. (b) Taw, F. L.; Mueller, A. H.; Bergman, R. G.; Brookhart, M. *J. Am. Chem. Soc.* **2003**, *125*, 9808. (c) Nakazawa, H.; Kawasaki, T.; Miyoshi, K.; Suresh, C. H.; Koga, N. *Organometallics* **2003**, *23*, 117. (d) Itazaki, M.; Nakazawa, H. *Chem. Lett.* **2005**, *34*, 1054. (e) Nakazawa, H.; Kamata, K.; Itazaki, M. *Chem. Commun.* **2005**, 4004. (f) Nakazawa, H.; Itazaki, M.; Kamata, K.; Ueda, K. *Chem. Asian J.* **2007**, *2*, 882. (g) Ochiai, M.; Hashimoto, H.; Tobita, H. *Angew. Chem., Int. Ed.* **2007**, *46*, 8192.

[13] An alternative mechanism for the catalyst regeneration from **F** is (i) hydrorhodation of **1a** to form $RhCH_2CH_2SiEt_3$, and (ii) the subsequent β-silyl elimination to form $Rh\text{-}SiEt_3$, which also serves as a catalytically active species. If this mechanism is operative, the catalytic reaction should work even with a catalytic amount of disilane. However, the yield of the alkenylated product significantly decreased as the amount of disilane was reduced.

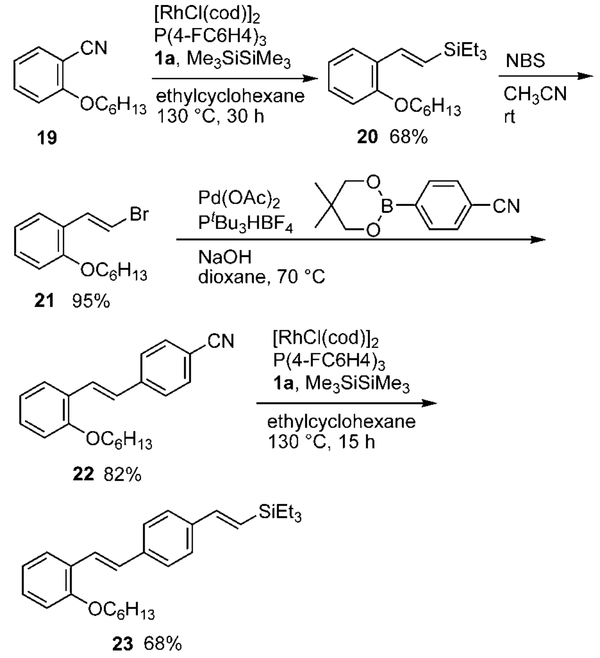
[14] Electrophilic substitution: (a) Fleming, I.; Dunogues, J.; Smithers, R. *Org. React.* **1989**, *37*, 57. Addition to aldehydes: (b) Aikawa, K.; Hioki, Y.-t.; Mikami, K. *J. Am. Chem. Soc.* **2009**, *131*, 13922, and references therein. Coupling with alcohol: (c) Nishimoto, Y.; Kajioka, M.; Saito, T.; Yasuda, M.; Baba, A. *Chem. Commun.* **2008**, 6396.

[15] (a) Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 3565. (b) Wang, C.; Glorius, F. *Angew. Chem., Int. Ed.* **2009**, *48*, 5240.

[16] For iterative synthesis of oligo(phenylenevinylene)s, see: (a) Iwadate, N.; Suginome, M. *Org. Lett.* **2009**, *11*, 1899. (b) Jørgensen, M.; Krebs, F. C. *J. Org. Chem.* **2005**, *70*, 6004.

[17] For the utility of oligo(phenylenevinylene)s in materials, see: Ajayaghosh, A.; Praveen, V. K. *Acc. Chem. Res.* **2007**, *40*, 644.

Scheme 3. Iterative Synthesis of Oligo(phenylenevinylene)s



Suzuki−Miyaura coupling sequence, resulting in a tailored synthesis of asymmetric oligo(phenylenevinylene)s (Scheme 3).

In summary, we have developed a catalytic system that allows the Mizoroki−Heck type alkenylation of nitriles via the cleavage of C−CN bonds. Due to the tolerance of a cyano group under the standard catalytic cross-coupling conditions, the present new variant of the Mizoroki−Heck reaction significantly broadens the range of synthetic strategies for densely elaborated arenes via orthogonal and iterative functionalizations. Further development of the catalytic transformation of C−CN bonds is currently underway in our laboratory.

Acknowledgment. This work was conducted in affiliation with the Program for the Promotion of Environmental Improvement to Enhance Young Researchers' Independence, the Special Coordination Funds for Promoting Science and Technology, MEXT, Japan. Y.K. expresses his special thanks for JSPS Research Fellowship for Young Scientist for financial support and The Global COE (center of excellence) Program "Global Education and Research Center for Bio-Environmental Chemistry" of Osaka University. We also thank the Instrumental Analysis Center, Faculty of Engineering, Osaka University, for their assistance with the HRMS and elemental analyses.

Supporting Information Available: Experimental details and spectroscopic data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL100481H