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Remote Arylative Substitution of Alkenes Possessing an Acetoxy Group via β-Acetoxy Elimination

Kazuma Muto, Takaaki Kumagai, Fumitoshi Kakiuchi, and Takuya Kochi*

Abstract: Palladium-catalyzed "remote arylative substitution" was achieved for the reaction of arylboronic acids with alkenes possessing a distant acetoxy group to provide arylation products having an alkene moiety at the remote position. The use of β-acetoxy elimination as a key step in the catalytic cycle allowed for regioselective formation of unstabilized alkenes after chain walking. This reaction was applicable to various arylboronic acids as well as alkene substrates.

Remote functionalization of organic compounds via alkene isomerization (or chain walking) has been attracting growing attention, because it would provide unique methods to efficiently transform multiple positions of organic molecules in a designed manner.[1] Various reactions in this category have been developed using catalysts containing metals such as Pd,[2,3,4,5] Ni,[6] and Zr,[7] but the types of reactions are still limited, considering the number of classical transition-metal catalyzed reactions. For example, catalytic allylic substitutions have been well studied and used considerably in organic synthesis (Figure 1a), but the corresponding "remote" substitutions have been scarcely explored (Figure 1b).

One of the reasons for the difficulty in expansion of the reaction diversity is that only a limited number of strategies are available for selective product formation by effectively controlling the selectivity of the final step (termination) in the catalytic cycle. Redox-relay Mizoroki-Heck-type reaction[3,4,5] is one of the most extensively studied in this field, and three strategies have been used to terminate the reaction: (i) conversion of alcohols to carbonyl groups (Figure 1c),[3] (ii) formation of π-allyl (or benzylic) intermediates, followed by nucleophilic attack (Figure 1d), [4] and (iii) formation of α,β-unsaturated systems (Figure 1e). [5] Selectivity of all of these reactions essentially relies on the formation of thermodynamically stable products or intermediates. Other types of remote functionalizations involving alkene isomerization mostly use similar termination strategies or formation of bonds at positions where metal-carbon bonds are relatively stabilized such as terminal or benzylic positions.[1b,c]

By taking consideration of the available termination strategies, regioselective formation of a simple alkene, which is not resonance stabilized, is challenging, because this type of alkene can be easily isomerized to give a more thermodynamically stable one or a complex mixture of isomers. In fact, we have reported the chain-walking cycloisomerization of 1,n-dienes to form five

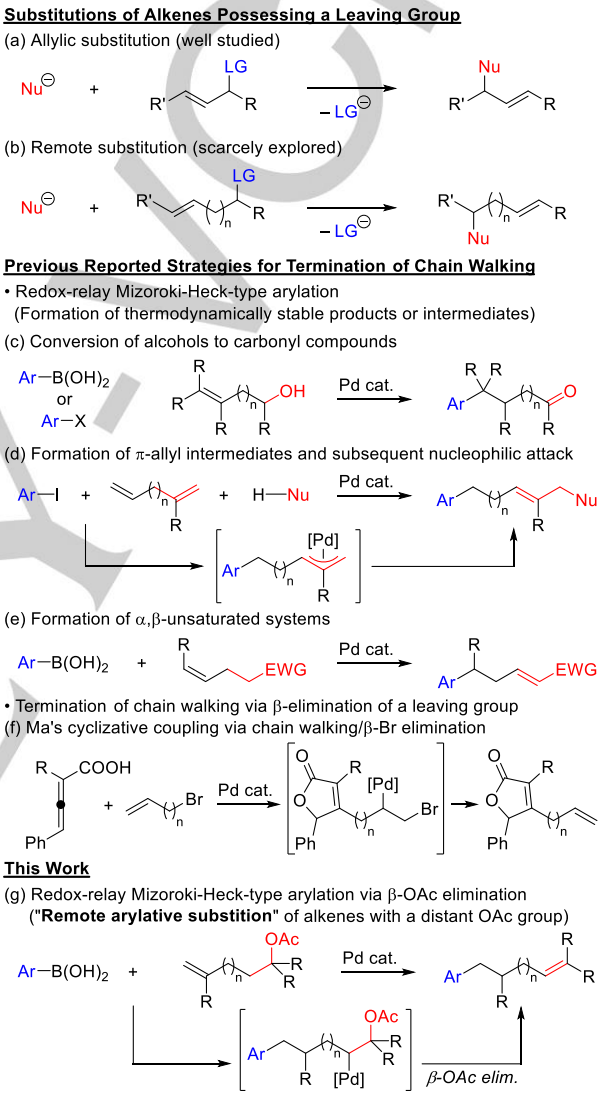

Figure 1. Functionalization of Alkenes via Chain Walking Using Various Termination Strategies.

-membered ring products but could not control the position of the alkene left in the product after chain walking in most cases.[8] In order to form an alkene moiety regioselectively after chain walking, we envisioned that β-acetoxy elimination can be used, because it would irreversibly generate an alkene at the position of the acetoxy group. The use of β-acetoxy elimination for selective formation of alkene has been reported previously.[9,10] Particularly, Sawamura and co-workers developed a palladium-catalyzed regioselective allylic arylation via a carbometalation/β-acetoxy elimination pathway,[9] and we speculated that incorporation of a

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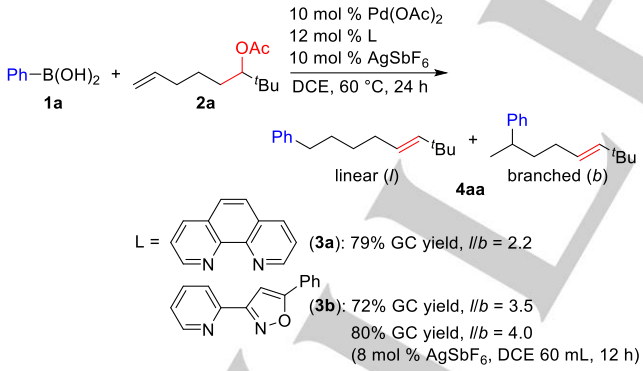
chain-walking mechanism to this reaction may lead to development of an alkene arylation with formation of a new alkene moiety at a remote position. The use of β-elimination of a leaving group in reactions via chain walking has been limited to a few examples such as Ma's palladium-catalyzed reaction of allenoic acids with alkenes with a remote bromo group, which is considered to proceed via allenoic acid cyclization, chain walking, and β-bromo elimination (Figure 1f),[11] and the chain walking/β-X elimination strategy has not been used for simple alkene arylation reactions.

Here we report that palladium-catalyzed "remote arylative substitution" was achieved for the reaction of arylboronic acids with alkenes possessing a distant acetoxy group to provide arylation products having an alkene moiety at the remote position. The use of β-acetoxy elimination as a key step in the catalytic cycle allowed for regioselective formation of unstabilized alkenes in redox-relay Mizoroki-Heck-type arylation. This reaction was applicable to various arylboronic acids and alkene substrates.

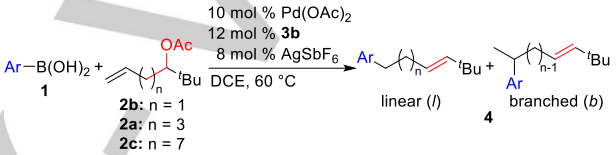
When a reaction of phenylboronic acid (**1a**) with a terminal alkene bearing a remote acetoxy group (**2a**) was performed in the presence of 10 mol % of $Pd(OAc)_2$, 12 mol % of 1,10-phenanthroline (**3a**), and 10 mol % of $AgSbF_6$ in 1,2-dichloroethane (DCE) at 60 ºC for 24 h, using similar reaction conditions to Sawamura's allylic arylation,[9] the remote arylative substitution proceeded to form the alkene moiety regioselectively and gave the desired arylation product **4aa** in 79% GC yield (Scheme 1). However, the product was obtained as a 2.2:1 mixture of linear and branched products. Ligand screening was then conducted to improve the linear/branched ratio and pyridine-isoxazole ligand **3b**[12] was found to provide **4aa** with 3.5:1 selectivity in a slightly lower yield. Optimization of the reaction conditions further improved the selectivity to 4.0:1 and product **4aa** was obtained in 80% GC yield (Tables S2 and S3).



Scheme 1. Remote arylative substitution of terminal alkene **2a** with **1a**

With the optimized reaction conditions in hand, the scope of arylboronic acids was examined using terminal alkenes with various lengths of the methylene chain (Table 1). The reactions of homoallyl acetate **2b** mostly give the corresponding products in good yields with high regioselectivity (entries 1-10). The reaction of **2b** with phenylboronic acid (**1a**) provided the product in 82% isolated yield with a 8.9 linear/branched ratio (entry 1), which was improved to 12:1 and 11:1 for the reaction using 2-methyl- and 3-methylphenylboronic acids (entries 2 and 3). The electronic effect of the substituents were investigated using 4-substituted arylboronic acids (entries 4-10), and it was shown that introduction of electron-withdrawing groups generally provides improved linear/branched ratios. Various reactive functional groups including chloro (entry 7), bromo (entry 8), and cyano (entry 9) groups tolerated the reaction conditions to offer the corresponding products in high yields. A variety of arylboronic acids can also be used for the alkenes possessing a longer chain of methylene spacers. The reactions of **2a** with phenylboronic acid **1a** as well as 2- and 4-substituted arylboronic acids gave the corresponding products in 32-91% yields (entries 11-15). Terminal alkene **2c**, possessing 7 methylene units, can also react with **1a** via chain walking over 7 carbons to give the corresponding product in 64% yield (entry 16).

Table 1. Scope of Arylboronic Acids for the Remote Arylative Substitution of Terminal Alkenes.[a]



entry	Ar	n	time (h)	isolated yield (%)	*l*/*b*
1	Ph (**1a**)	1	48	82 (**4ab**)	8.9
2	2-MeC_6H_4 (**1b**)	1	48	80 (**4bb**)	12
3	3-MeC_6H_4 (**1c**)	1	72	63 (**4cb**)	11
4	4-$MeOC_6H_4$ (**1d**)	1	72	36 (**4db**)	6.3
5	4-FC_6H_4 (**1e**)	1	48	75 (**4eb**)	7.5
6	4-MeC_6H_4 (**1f**)	1	72	59 (**4fb**)	8.3
7	4-ClC_6H_4 (**1g**)	1	48	85 (**4gb**)	8.0
8	4-BrC_6H_4 (**1h**)	1	48	84 (**4hb**)	9.7
9	4-NCC_6H_4 (**1i**)	1	48	93 (**4ib**)	9.8
10	4-$F_3CC_6H_4$ (**1j**)	1	48	75 (**4jb**)	12
11	Ph (**1a**)	3	12	80 (**4aa**)	4.1
12	2-MeC_6H_4 (**1b**)	3	48	32 (**4ba**)	5.7
13	4-MeC_6H_4 (**1f**)	3	12	67 (**4fa**)	3.4
14	4-NCC_6H_4 (**1i**)	3	24	84 (**4ia**)	4.3
15	4-$F_3CC_6H_4$ (**1j**)	3	24	91 (**4ja**)	5.2
16	Ph (**1a**)	7	12	64 (**4ac**)	3.0

[a] Reaction conditions: **1** (0.15 mmol), **2** (0.10 mmol), $Pd(OAc)_2$ (0.010 mmol), **3b** (0.012 mmol), $AgSbF_6$ (0.008 mmol), DCE (60 mL), 60 ºC.

The reactions of terminal alkenes possessing substituents other than a *tert*-butyl group at the α-position of an acetoxy group are shown in Scheme 2. The substrate having an isopropyl group (**2d**) gave the corresponding phenylation product **4ad** in 62% yield with a 9.7 linear/branched ratio, which was improved to 12 for the reaction with 4-trifluoromethylphenylboronic acid (**1j**). Higher linear/branched ratios were observed for the reaction of an alkene possessing a phenyl group (**2e**) with **1a** and **1j**. Substrates derived from tertiary alcohols were also applicable to this reaction. While the reaction of cyclohexane derivative **2f** with **1b** gave product **4af** in 76% yield with a linear/branched ratio of 21, installation of a homoprenyl group on an aromatic ring was achieved in the reaction of **1j** with α,α-dimethylhomoallyl acetate **2g** to give product **4jg** in 63% yield with a 26 linear/branched ratio.

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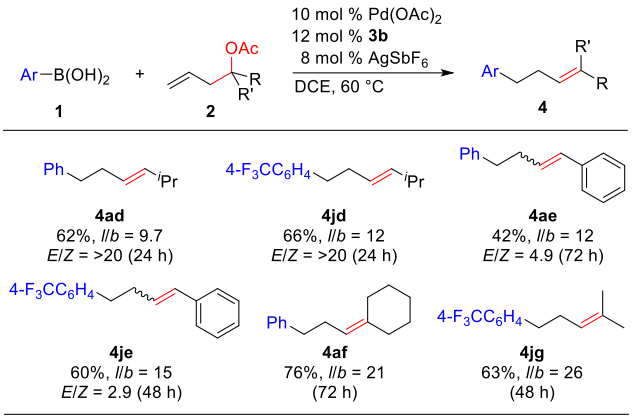


Scheme 2. Scope of terminal alkenes for the remote arylative substitution. Reaction conditions: **1** (0.15 mmol), **2** (0.10 mmol), $Pd(OAc)_2$ (0.010 mmol), **3b** (0.012 mmol), $AgSbF_6$ (0.008 mmol), DCE (60 mL), 60 ºC.

The proposed catalytic cycle for this arylation is shown in Figure 2. Transmetallation between acetoxypalladium species **A** with arylboronic acid **1** generates arylpalladium species **B**. Coordination of **2** and 2,1-insertion gives alkylpalladium species **D**. After chain walking of the palladium center (**D** to **E**) , β-acetoxy elimination provides **4** with regenerating acetoxypalladium species **A**. A key for the success of this reaction is that chain walking occurs by the nondissociative mechanism where alkene exchange does not take place before β-acetoxy elimination, because alkene exchange during the chain walking process would provide a palladium hydride species with a substrate, which leads to the formation of byproducts without an aryl group.

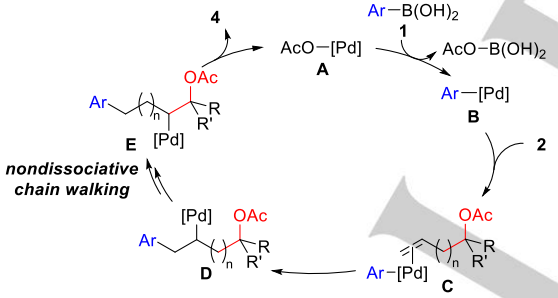
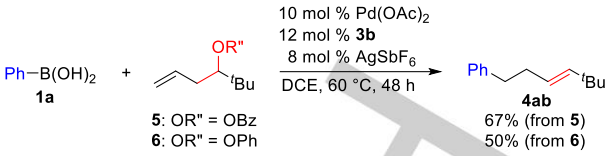


Figure 2. A proposed catalytic cycle.

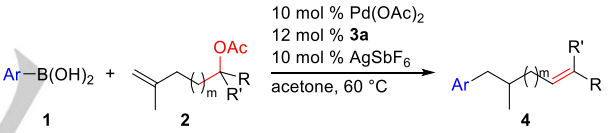
Based on the proposed catalytic cycle, the reaction may be applicable to alkene substrates possessing a leaving group other than acetoxy group. Consequently, the reaction was examined using substrates possessing various leaving groups (Scheme 3). While the reaction of **1a** with benzoate **5** and phenyl ether **6** provided arylation product **4ab** in 67 and 50% yields, respectively, trifluoroacetoxy, butoxy, and phthalimidyl groups were not applicable as leaving groups to this reaction to give less than a trace amount of **4ab**.[13]



Scheme 3. Remote arylative substitution with benzoate **5** and phenyl ether **6**

Next, we explored the reactivity of substrates having 1,1-disubstituted alkenes. After optimization of the reaction conditions (Table S4), it was found that the remote arylative substitution of 1,1-disubstituted alkene **2h** with **1a** provided phenylation product **4ah** with exclusive regioselectivity in 77% isolated yield (82% GC yield), when the reaction was conducted in acetone using **3a** as a ligand (Table 2, entry 1). Regioselective formation of C–C bonds at the terminal position for insertion of 1,1-disubstituted alkenes to Pd–Ar bonds in a redox-relay Mizoroki-Heck-type reaction was reported by Sigman and coworkers.[3d] A variety of arylboronic acids **1** bearing electron-donating and –withdrawing groups were applicable to this reaction and provided the corresponding products in high yields (entries 2-11). The reactions of 1,1-disubstituted alkenes possessing an isopropyl group (**2i**) and two methyl groups (**2j**) instead of a *tert*-butyl group gave products **4ai** and **4aj** in 57 and 53% yields, respectively (entries 12 and 13). Homoallyl acetate **2k** and an alkene substrate possessing 8 methylenes (**2l**) also reacted with **1a** to furnish phenylation products **4ak** and **4al** in good yields (entries 14 and 15).

Table 2. Remote Arylative Substitution of 1,1-Disubstituted Alkenes.[a]



entry	Ar	2	m	R	R'	time (h)	isolated yield (%)
1	Ph (**1a**)	**2h**	2	^{t}Bu	H	4	77 (**4ah**, 82)[b]
2	2-MeC$_6$H$_4$ (**1b**)	**2h**	2	^{t}Bu	H	8	78 (**4bh**)
3	3-MeC$_6$H$_4$ (**1c**)	**2h**	2	^{t}Bu	H	20	78 (**4ch**)
4	4-MeOC$_6$H$_4$ (**1d**)	**2h**	2	^{t}Bu	H	8	75 (**4dh**)
5	4-FC$_6$H$_4$ (**1e**)	**2h**	2	^{t}Bu	H	20	75 (**4eh**)
6	4-MeC$_6$H$_4$ (**1f**)	**2h**	2	^{t}Bu	H	4	79 (**4fh**)
7	4-ClC$_6$H$_4$ (**1g**)	**2h**	2	^{t}Bu	H	8	77 (**4gh**)
8	4-BrC$_6$H$_4$ (**1h**)	**2h**	2	^{t}Bu	H	2	75 (**4hh**)
9	4-NCC$_6$H$_4$ (**1i**)	**2h**	2	^{t}Bu	H	4	74 (**4ih**)
10	4-F$_3$CC$_6$H$_4$ (**1j**)	**2h**	2	^{t}Bu	H	8	73 (**4jh**)
11	4-O$_2$NC$_6$H$_4$ (**1k**)	**2h**	2	^{t}Bu	H	4	73 (**4kh**)
12	Ph (**1a**)	**2i**	2	^{i}Pr	H	3	57 (**4ai**)
13	Ph (**1a**)	**2j**	2	Me	Me	4	53 (**4aj**)
14	Ph (**1a**)	**2k**	0	^{t}Bu	H	4	67 (**4ak**)
15[c]	Ph (**1a**)	**2l**	7	^{t}Bu	H	4	65 (**4al**)

[a] Reaction conditions: **1** (0.75 mmol), **2** (0.5 mmol), $Pd(OAc)_2$ (0.05 mmol), 1,10-phenanthroline (0.06 mmol), $AgSbF_6$ (0.05 mmol), acetone (10 mL), 60 ºC. [b] GC yield is shown in parentheses. [c] **1** (0.15 mmol), **2** (0.1 mmol), $Pd(OAc)_2$ (0.01 mmol), 1,10-phenanthroline (0.012 mmol), $AgSbF_6$ (0.01 mmol), acetone (10 mL), 60 ºC.

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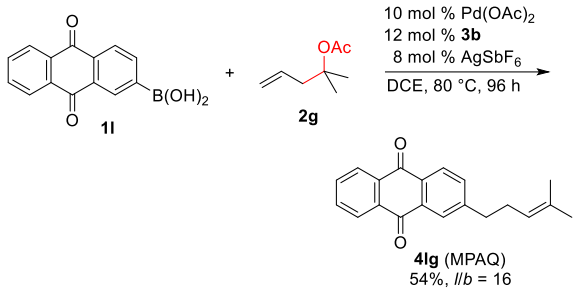
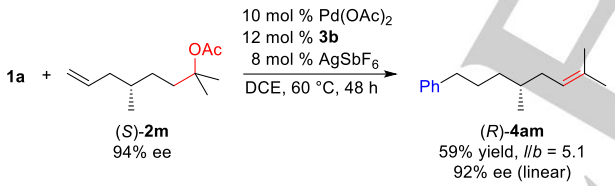
The remote arylative substitution was applied to the synthesis of MPAQ, an antifungal agent isolated from hairy roots of *Sesamum indicum* (Scheme 4).[14] The reaction of boronic acid **1l** with **2g** at 80 ºC for 4 days provided MPAQ (**4lg**) in 54% yield with an excellent linear/branched ratio. This result demonstrates the utility of the reaction for facile installation of an alkyl group containing an alkenyl moiety, such as homoprenyl group, onto aromatic rings.



Scheme 4. Synthesis of MPAQ by the remote arylative substitution

One of the features of the reactions proceeding via nondissociative chain walking is that the configurations of the stereocenters present on the alkyl chain where migration of metal catalysts are maintained.[2d,3d,15] The reaction of **1a** with chiral alkene substrate (*S*)-**2m** (94% ee) provided the corresponding product (*R*)-**4am** with 92% ee (Scheme 5). The high level of retention of the stereochemitry supports the involvement of the nondissociative chain walking process for the remote arylative substitution.



Scheme 5. Remote arylative substitution of chiral alkene substrate (*S*)-**2m**. The enantiomeric excess of (*R*)-**4am** was determined by chiral HPLC analysis after ozonolysis, reduction, and esterification with 3,5-dinitrobenzoyl chloride.

In summary, we developed the palladium-catalyzed remote arylative substitution of alkenes bearing an acetoxy group. The reaction with various alkenes possessing a distant acetoxy group provided arylation products having an alkene moiety at the remote position. A variety of arylboronic acids were also applicable to this reaction. Future studies utilizing this "addition/chain walking/elimination" strategy to other reactions are in progress.

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Conflict of interest

The authors declare no competing financial interest.

Keywords: palladium • chain walking • arylation • alkenes • β-acetoxy elimination

[1] a) I. Franzoni, C. Mazet, *Org. Biomol. Chem.* **2014**, *12*, 233-241. b) A. Vasseur, J. Bruffaerts, I. Marek, *Nat. Chem.* **2016**, *8*, 209-219. c) H. Sommer, F. Julia-Hernandez, R. Martin, I. Marek, *ACS Cent. Sci.* **2018**, *4*, 153-165. d) T. Kochi, S. Kanno, F. Kakiuchi, *Tetrahedron Lett*. **2019**, *60*, 150938.

[2] a) P. Roesle, C. J. Dürr, H. M. Möller, L. Cavallo, L. Caporaso, S. Mecking, *J. Am. Chem. Soc.* **2012**, *134*, 17696-17703. b) S. Aspin, A.-S. Goutierre, P. Larini, R. Jazzar, O. Baudoin, *Angew. Chem.* **2012**, *124*, 10966-10969; *Angew. Chem. Int. Ed.* **2012**, *51*, 10808-10811. c) E. Larionov, L. Lin, L. Guénée, C. Mazet, *J. Am. Chem. Soc.* **2014**, *136*, 16882-16894. d) L. Lin, C. Romano, C. Mazet., *J. Am. Chem. Soc.* **2016**, *138*, 10344-10350. e) D. G. Kohler, S. N. Gockel, J. L. Kennemur, P. J. Waller, K. L. Hull, *Nat. Chem.* **2018**, *10*, 333-340.

[3] a) R. C. Larock, W.-Y. Leung, S. Stolz-Dunn, *Tetrahedron Lett.* **1989**, *30*, 6629-6632. b) E. W. Werner, T.-S. Mei, A. J. Burckle, M. S. Sigman, *Science* **2012**, *338*, 1455-1458. c) T.-S. Mei, E. W. Werner, A. J. Burckle, M. S. Sigman, *J. Am. Chem. Soc.* **2013**, *135*, 6830-6833. d) T.-S. Mei, H. H. Patel, M. S. Sigman, *Nature* **2014**, *508*, 340-344. e) L. Xu, M. J. Hilton, X. Zhang, P.-O. Norrby, Y.-D. Wu, M. S. Sigman, O. Wiest, *J. Am. Chem. Soc*. **2014**, *136*, 1960-1967. f) Z.-M. Chen, M. J. Hilton, M. S. Sigman, *J. Am. Chem. Soc.* **2016**, *138*, 11461-11464. g) S. Singh, J. Bruffaerts, A. Vasseur, I. Marek, *Nat. Commun.* **2017**, *8*, 14200. h) J. Liu, Q. Yuan, F. D. Toste, M. S. Sigman, *Nat. Chem*. **2019**, *11*, 710-715.

[4] a) R. C. Larock, Y. D. Lu, A. C. Bain, C. E. Russell, *J. Org. Chem.* **1991**, *56*, 4589-4590. b) R. C. Larock, Y. Wang, Y. Lu, C. E. Russell, *J. Org. Chem.* **1994**, *59*, 8107-8114. c) Y. Wang, X. Dong, R. C. Larock, *J. Org. Chem.* **2003**, *68*, 3090-3098. d) C. Han, Z. Fu, S. Guo, X. Fang, A. Lin, H. Yao, *ACS Catal.* **2019**, *9*, 4196-4202.

[5] a) C. Zhang, C. B. Santiago, L. Kou, M. S. Sigman, *J. Am. Chem. Soc.* **2015**, *137*, 7290-7293. b) Q. Yuan, M. S. Sigman, *J. Am. Chem. Soc.* **2018**, *140*, 6527-6530. c) Q. Yuan, M. B. Prater, M. S. Sigman, *Adv. Synth. Catal.* **2020**, *362*, 326-330.

[6] a) D. Janssen-Müller, B. Sahoo, S. Z. Sun, R. Martin, *Isr. J. Chem.* **2020**, *60*, 195-206. b) W.-C. Lee, C.-H. Wang, Y.-H. Lin, W.-H. Shih, T.-G. Ong, *Org. Lett.* **2013**, *15*, 5358-5361. c) J. S. Bair, Y. Schramm, A. G. Sergeev, E. Clot, O. Eisenstein, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 13098-13101. d) I. Buslov, J. Becouse, S. Mazza, M. Montandon-Clerc, X. Hu, *Angew. Chem.* **2015**, *127*, 14731-14734; *Angew. Chem., Int. Ed.* **2015**, *54*, 14523-14526. e) Y. He, Y. Cai, S. Zhu, *J. Am. Chem. Soc.* **2017**, *139*, 1061-1064. f) F. Julia-Hernandez, T. Moragas, J. Cornella, R. Martin, *Nature* **2017**, *545*, 84-89. g) M. Gaydou, T. Moragas, F. Juliá-Hernández, R. Martin, *J. Am. Chem. Soc.* **2017**, *139*, 12161-12164. h) F. Chen, K. Chen, Y. Zhang, Y. He, Y.-M. Wang, S. Zhu, *J. Am. Chem. Soc.* **2017**, *139*, 13929-13935. i) L. Peng, Y. Li, Y. Li, W. Wang, H. Pang, G. Yin, *ACS Catal.* **2018**, *8*, 310-313. j) W. Wang, C. Ding, Y. Li, Z. Li, Z. Li, L. Peng, G. Yin, *Angew. Chem.* **2019**, *131*, 4660-4664; *Angew. Chem. Int. Ed.* **2019**, *58*, 4612-4616. k) S.-Z. Sun, C. Romano, R. Martin, *J. Am. Chem. Soc.* **2019**, *141*, 16197-16201. l) S. Guven, G. Kundu, A. Weßels, J. S. Ward, K. Rissanen, F. Schoenebeck, *J. Am. Chem. Soc.* **2021**, *143*, 8375-8380.

[7] a) N. Chinkov, S. Majumbar, I. Marek, *J. Am. Chem. Soc.* **2003**, *125*, 13258-13264. b) N. Chinkov, A. Levin, I. Marek, *Angew. Chem.* **2006**,

118, 479-482; *Angew. Chem. Int. Ed.* **2006**, *45*, 465-468. c) A. Masarwa, D. Didier, T. Zabrodski, M. Schinkel, L. Ackermann, I. Marek, *Nature*, **2014**, *505*, 199-203. d) L. Mola, M. Sidera, S. P. Fletcher, *Aust. J. Chem.* **2015**, *68*, 401-403. e) A. Vasseur, L. Perrin, O. Eisenstein, I. Marek, *Chem. Sci.* **2015**, *6*, 2770-2776. f) X. Wang, X. Cui, S. Li, Y. Wang, C. Xia, H. Jiao, L. Wu, *Angew. Chem.* **2020**, 132, 13710-13714; *Angew. Chem. Int. Ed.* **2020**, *59*, 13608-13612.

[8] a) T. Kochi, T. Hamasaki, Y. Aoyama, J. Kawasaki, F. Kakiuchi, *J. Am. Chem. Soc.* **2012**, *134*, 16544-16547. b) T. Hamasaki, Y. Aoyama, J. Kawasaki, F. Kakiuchi, T. Kochi, *J. Am. Chem. Soc.* **2015**, *137*, 16163-16171. c) T. Hamasaki, F. Kakiuchi, T. Kochi, T. *Chem. Lett.* **2016**, *45*, 297-299.

[9] a) H. Ohmiya, Y. Makida, T. Tanaka, M. Sawamura, *J. Am. Chem. Soc.* **2008**, *130*, 17276-17277. b) H. Ohmiya, Y. Makida, D. Li, M. Tanabe, M. Sawamura, *J. Am. Chem. Soc.* **2010**, *132*, 879-889.

[10] a) X. Lu, *Top. Catal.* **2005**, *35*, 73-86. b) D. Pan, N. Jiao, *Synlett* **2010**, *11*, 1577-1588. c) J. L. Bras, J. Muzart, *Tetrahedron* **2012**, *68*, 10065-10113. d) A. G. Steinig, A. de Meijere, *Eur. J. Org. Chem*. **1999**, *1999*, 1333-1344. e) Q. Zhang, X. Lu, *J. Am. Chem. Soc.* **2000**, *122*, 7604-7605. f) J. Rammauth, O. Poulin, S.; Rakhit, S. P. Maddaford, *Org. Lett.* **2001**, *3*, 2013-2015. g) B. Mariampillai, C. Herse, M. Lautens, *Org. Lett.* **2005**, *7*, 4745-4747. h) M. Lautens, E. Tayama, C. Herse, *J. Am. Chem. Soc*. **2005**, *127*, 72-73. i) K. Shen, X. Han, X. Lu, Z. Hu, *Tetrahedron Lett*. **2017**, *58*, 3768-3771.

[11] a) S. Ma, Z. Yu, *Angew. Chem.* **2003**, *115*, 1999-2001; *Angew. Chem. Int. Ed.* **2003**, *42*, 1955-1957. b) J. Li, S. Yang, H. Jiang, W. Wu, J. Zhao, *J. Org. Chem*. **2013**, *78*, 12477-12486. c) M. Hu, Z. Lin, J. Li, W. Wu, H. Jiang, *Green. Chem*. **2020**, *22*, 5584-5588.

[12] M. Gutiérrez, M. F. Matus, T. Poblete, J. Amigo, G. Vallejos, L. Astudillo, *J. Pharm. Pharmacol.* **2013**, *65*, 1796-1804.

[13] The reaction of **1a** with an alkene without a leaving group, 8,8-dimethylnon-1-ene, was also examined but resulted in formation of a complex mixture of isomers of both the alkene substrate and the phenylation product.

[14] a) T. Ogasawara, K. Chiba, M. Tada, *Phytochemistry* **1993**, *33*, 1095-1098. b) R. N. Syed, H. Laurentin, R. Splivallo, P. Karlovsky, *Int. J. Agric. Biol.* **2015**, *15*, 575-581. c) F. Lavaee, M. Moshaverinia, S. A. MalekHosseini, A. Jamshidzade, M. Zarei, H. Jafarian, P. Haddadi, P. Badiee, *Braz. J. Parm. Sci.* **2019**, *55*, e17479.

[15] Y. Yamasaki, T. Kumagai, S. Kanno, F. Kakiuchi, T. Kochi, *J. Org. Chem.* **2018**, *83*, 9322-9333.

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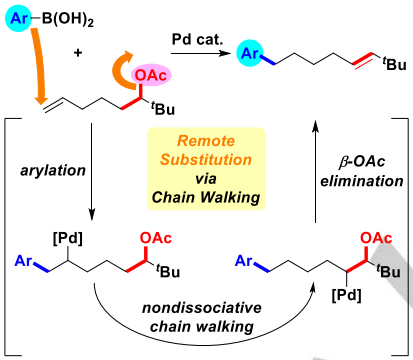
COMMUNICATION

Palladium-catalyzed “remote arylative substitution” was achieved for the reaction of arylboronic acids with alkenes possessing a distant acetoxy group via nondissociative chain walking and β-acetoxy elimination.



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Remote Arylative Substitution of Alkenes Possessing an Acetoxy Group via β-Acetoxy Elimination