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Monocarboxylation and Intramolecular Coupling of Butenylated Arenes via Palladium-Catalyzed C−H Activation Process

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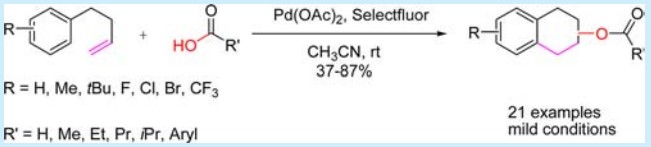
Supporting Information

ABSTRACT: A novel and practical reaction for the direct intramolecular oxidative coupling of butenylated arenes is reported. With the catalysis of $Pd(OAc)_2$, reactions of various butenylated arenes and carboxylic acids with Selectfluor reagent in CH_3CN solution afforded the corresponding monocarboxylation/cyclization products in good yields under mild conditions. This research demonstrated an economic method with the synthesis of 2-tetralyl carboxylic esters, a valuable class of bioactive compounds.



Carboxylic ester is a ubiquitous functional group of organic molecules. The classical strategy for the formation of an ester relies on the condensation of an alcohol with a carboxylic acid. Often, the catalytic addition of carboxylic acids to alkenes, as an alternative method for the generation of esters, provides a more direct and simple route, although photolytic,[1] and Bronsted acid[2] and transition metals such as Pd,[3] Au,[4] Ag,[5] Ru,[6] etc., are usually required as a catalyst.

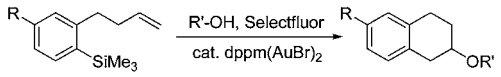
Transition-metal-catalyzed direct cross-coupling via C−H bond activation is another important research topic and has been extensively studied.[7] In comparison with traditional indirect cross-couplings,[8] this direct cross-coupling method is more challenging but advantageous for its atom economy and eco-friendliness. In particular, some Pd-catalyzed direct coupling reactions between arenes and olefins have been reported.[9]

On the basis of the above facts, we note that the Pd-catalyzed tandem reactions including hydrocarboxylation and intramolecular direct cross-coupling of butenylated arenes to construct a useful tetralyl carboxylic ester should be reasonable (Scheme 1). Recently, Toste and co-workers described a gold-catalyzed oxidative coupling[10] of 2-butenylated aryltrimethylsilane[11] using Selectfluor[12] as an oxidant (Scheme 1). 2-Butenylated arylsilanes are necessary for the conversion.

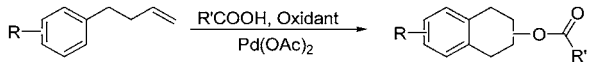
From an academic point of view, it would be highly desirable to directly use an unactivated, instead of activated, coupling partner. Meanwhile, 2-tetralyl carboxylic esters are revealed to be present in numerous biologically active natural products and synthetic molecules, such as isofregenedadiol,[13] ficuselastic acid,[14] taepeenin D,[15] epigallocatechingallate analogues,[16] 25-Nor-D:C-friedooleana-5,7,9-triene-3α-29-diol diacetates,[17] and rotigotine (Figure 1).[18] Therefore, we were interested in developing a more convenient protocol for the synthesis of the compounds.

Scheme 1. Strategies for Monocarboxylation and Direct Intramolecular Coupling

Gold-Catalyzed oxidative coupling reaction with arytrimethylsilanes



This work



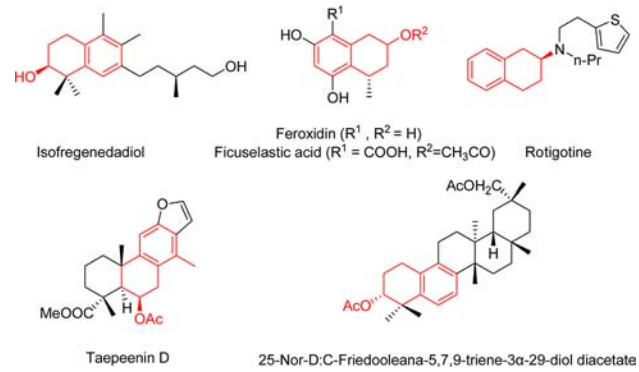


Figure 1. Synthetically and naturally occurring 2-tetralyl carboxylic esters or their derivatives.

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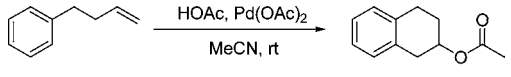
We started our investigations using 4-phenyl-1-butene **1a** as the model substrate. Initially, while $Pd(OAc)_2$ (150 mol %) was used to catalyze the reaction of 4-phenyl-1-butene (1 equiv) and acetic acid (70 equiv) in MeCN under ambient temperature, no target product was detected. The reaction afforded an addition mixture of acetic acid and the C−C double bond of **1a** (Table 1, entry 1).[19] Then, we used $Cu(OAc)_2$ (10 mol %) with $Pd(OAc)_2$ (10 mol %) as catalyst to catalyze the reaction of **1a** (1 equiv) with **2a** (70 equiv) in CH_3CN (Table 1, entry 2). This reaction also failed to give the product, affording a mixture of adducts.[19c] Subsequently, excess $Cu(OAc)_2$ (2.5 equiv) did not give a positive result (Table 1, entry 3). It was also unsuccessful when H_2O_2 or $NaIO_4$ was used as oxidant (Table 1, entries 4 and 5). By referring to Toste's report,[11] we attempted to use Selectfluor as the oxidant to accomplish this reaction. To our delight, use of Selectfluor eventually gave the target product **3a** in 68% yield (Table 1, entry 6).

Table 1. Oxidant Screening for Monocarboxylation and Direct Intramolecular Coupling[a]



1a **3a**

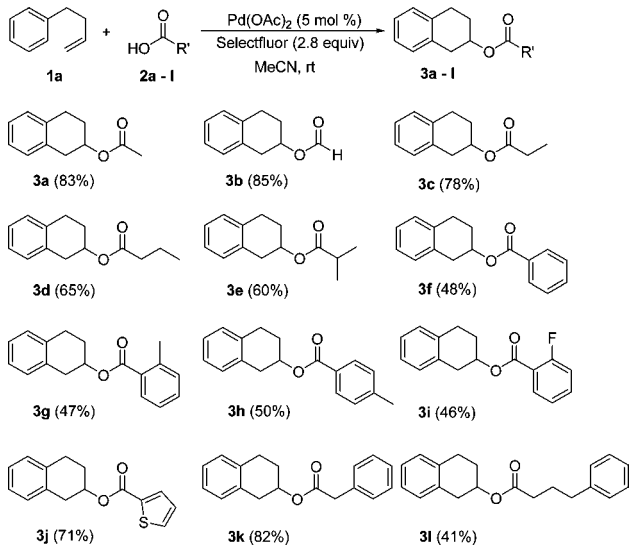
entry	$Pd(OAc)_2$ (mol %)	oxidant (equiv)	result
1	150		nd[b]
2	10	$Cu(OAc)_2$ (0.1)	nd[b]
3	10	$Cu(OAc)_2$ (2.5)	nd[b]
4	10	H_2O_2 (2.5)	nd[b]
5	10	$NaIO_4$ (2.5)	nd[b]
6	10	Selectfluor (2.5)	**3a** (68%)[c]

[a]Conditions: a mixture of **1a** (0.5 mmol), HOAc (2 mL), and $Pd(OAc)_2$ in MeCN was stirred, and then oxidant was added; the mixture was stirred at room temperature overnight. [b]No target product was detected as determined by ^1H NMR analysis. [c]Isolated yield after column chromatography.

On the basis of the above results, we chose Selectfluor as the oxidant to optimize the reaction conditions. After a series of experiments, we found that, among the tested solvents, MeCN was the best, and the amount of acetic acid significantly affected the yield. When HOAc was added in 2 equiv, **3a** was obtained with low yield. With the increase of acetic acid **2a**, the yield was gradually increased until **2a** reached 60 equiv. Then, we identified the following as the optimal reaction condition: $Pd(OAc)_2$ (5 mol %)/Selectfluor (2.8 equiv)/CH_3CN/ambient temperature.[20]

With the optimized conditions in hand, we first examined the substrate scope by treatment of various carboxylic acids with 4-phenyl-1-butene. As shown in Scheme 2, a variety of carboxylic acids **2a−l** were tolerant, affording the products in moderate to good yields. While formic acid **2b**, a small ligand of palladium, gave the product **3b** in 85% yield, the bulky butyric acid **2d** and isobutyric acid **2e** showed low reactivity and gave products **3d** and **3e** in 65 and 60% yield, respectively. Nevertheless, for aromatic acids **2f−l**, yields were moderate, except for phenyl acetic acid **2k** with a yield of 82%. We were surprised to find that **3f** and **3h** were in the solid state, whereas others were oil. From the X-ray structure of **3h** (Figure 2), a special intermolecular $\pi-\pi$ stacking between the phenyl ring of carboxylic acid and that of tetralyl was observed.

Scheme 2. Substrate Scope of Carboxylic Acids[a]



[a]Conditions: a mixture of **1a** (1.0 mmol), **2a−l** (60 equiv), Selectfluor (2.8 equiv), and $Pd(OAc)_2$ (5 mol %) in MeCN was stirred at room temperature overnight. Isolated yield after column chromatography.

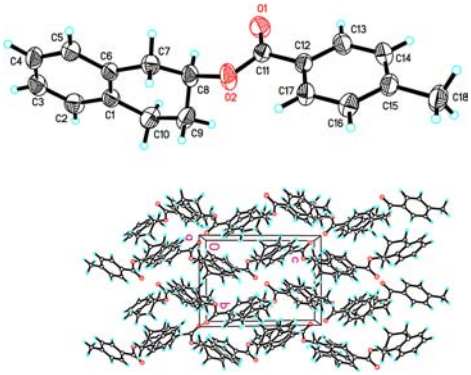


Figure 2. X-ray structure and structure cell of **3h**.

To broaden the range of substrates, various butenylated arenes with formic acid **2b** were tested under the optimized conditions (Table 2). Notably, the presence of substituents on aryls gave a mixture of **4** and **5**. Neutral or electron-rich butenylated arenes **1a−e** gave **4a−e** and **5a−e** in high yields (Table 2, entries 1−4). The substitution position of methyl group in **1b−d** had no significant effect on the yield (Table 2, entries 1−3). Reactions with electron-withdrawing substrates **1f−i** also gave the desired products **4f−i** and **5f−i** in moderate yields (Table 2, entries 5−8). Particularly, **1c** gave a mixture of **4c** and **5c** in an almost 1:1 ratio (Table 2, entry 2). This result shows that the reaction of **1c** is regioselective and gives compounds **4c** (coupling with an ortho-aromatic carbon of methyl and isomerization) and **5c** (coupling with para-aromatic carbon of methyl). Meanwhile, for **1i**, only **4i** was isolated from the reaction mixture (Table 2, entry 8). Reasonably, **1j** gave **4j** as a single isomer in moderate yield (Table 2, entry 9).

On the basis of the obtained results, we therefore propose a plausible mechanism for monocarboxylation and direct intramolecular coupling. A Pd(II)/Pd(IV) process was supposed, and the formation pathway of **4** and **5** is depicted in Scheme 3. In this process, intermediate **B** gave the mixture of **4** and **5** through path a and path b, respectively. Pd(IV) intermediates **E**

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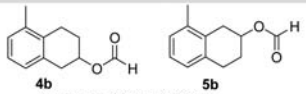
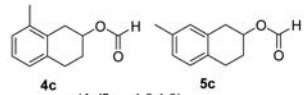
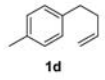
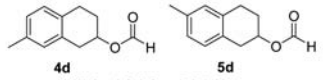
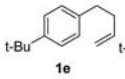
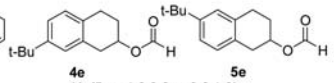
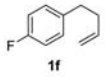
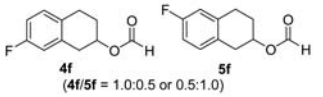
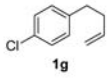
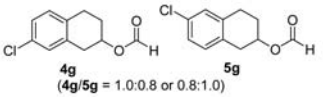
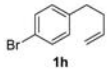
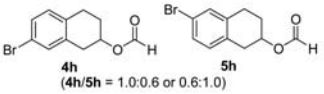
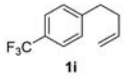
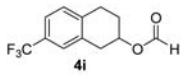
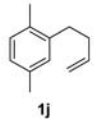
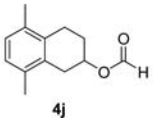
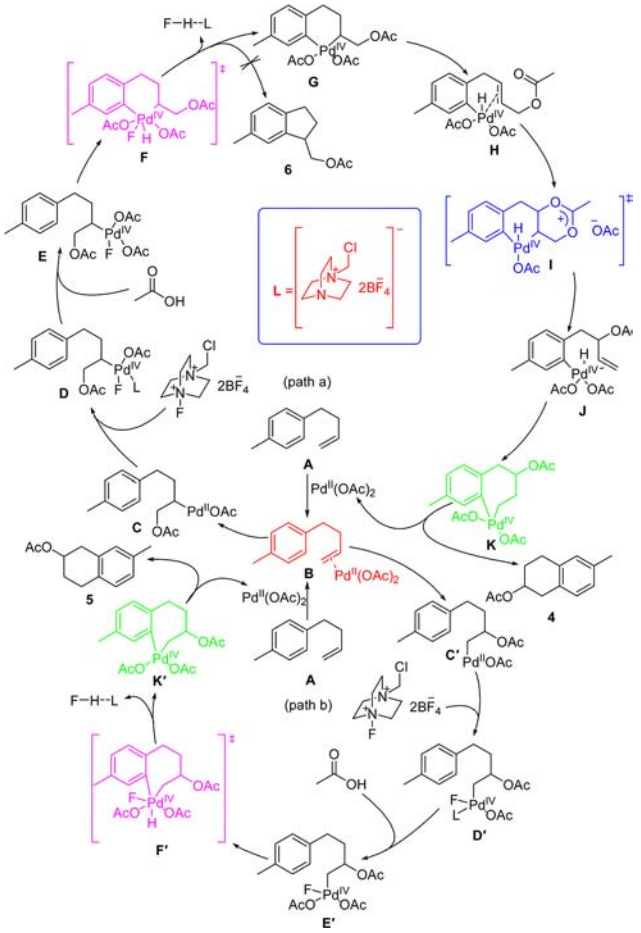
Table 2. Substrate Scope of Butenylated Arene[a]

entry	substrate	product 4/5	yield
1	 1b	 4b / 5b (4b/5b = 1.0:0.6 or 0.6:1.0)	80%
2	 1c	 4c / 5c (4c/5c = 1.0:1.0)	81%
3	 1d	 4d / 5d (4d/5d = 1.0:0.6 or 0.6:1.0)	87%
4	 1e	 4e / 5e (4e/5e = 1.0:0.6 or 0.6:1.0)	84%
5	 1f	 4f / 5f (4f/5f = 1.0:0.5 or 0.5:1.0)	56%
6	 1g	 4g / 5g (4g/5g = 1.0:0.8 or 0.8:1.0)	54%
7	 1h	 4h / 5h (4h/5h = 1.0:0.6 or 0.6:1.0)	50%
8	 1i	 4i	37%
9	 1j	 4j	45%

[a]Conditions: a mixture of **1b–j** (1.0 mmol), **2b** (60 equiv), Selectfluor (2.8 equiv), and $Pd(OAc)_2$ (5 mol %) in MeCN was stirred at room temperature overnight. Isolated yield after column chromatography. The ratio of **4**/**5** was determined by ^{13}C NMR.

and **E**′ promoted C–H activation of arenes to form transition state **F** and **F**′.[21,22] Key intermediate **K** was considered to originate from the Pd(IV)-catalyzed Claisen rearrangement of intermediate **H**. Finally, **K** and **K**′ followed by reductive elimination gave isomers **4** and **5**, respectively. The absence of the generation of pentacyclic compound **6** may be due to the fact that the β-H elimination of **G** to give **H** was more feasible than the reductive elimination of **F** to give **6**.

Scheme 3. Plausible Mechanism for Monocarboxylation and Direct Intramolecular Coupling



In conclusion, we have developed a novel and useful approach for the construction of 2-tetralyl carboxylic ester. This reaction features Pd-catalyzed tandem carboxylation and direct intramolecular coupling with Selectfluor as an oxidant. A series of substrates were tolerated, including various carboxylic acids and differently substituted butenylated arenes. The reaction conditions are mild, and the products were obtained with acceptable yields. Further mechanistic studies are underway and will be demonstrated in due course.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, new compound characterization, and crystal structure data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Anderson, S. W.; Yates, K. *Can. J. Chem.* **1988**, *66*, 2412. (b) Perkowski, A. J.; Nicewicz, D. A. *J. Am. Chem. Soc.* **2013**, *135*, 10334.

(2) (a) Kang, Y.-B.; Gade, L. H. *J. Am. Chem. Soc.* **2011**, *133*, 3658. (b) Kang, Y.-B.; Gade, L. H. *J. Org. Chem.* **2012**, *77*, 1610. (c) Park, J. H.; Park, C. Y.; Song, H. S.; Huh, Y. S.; Kim, G. H.; Park, C. P. *Org. Lett.* **2013**, *15*, 752.

(3) (a) Park, C. P.; Kim, D.-P. *Angew. Chem., Int. Ed.* **2010**, *49*, 6825. (b) Li, Y.; Song, D.; Dong, V. M. *J. Am. Chem. Soc.* **2008**, *130*, 2962. (c) Wang, W.-F.; Wang, F.-J.; Shi, M. *Organometallics* **2010**, *29*, 928. (d) Wang, A.-Z.; Jiang, H.-F.; Chen, H.-J. *J. Am. Chem. Soc.* **2009**, *131*, 3846. (e) Park, C. P.; Lee, J. H.; Yoo, K. S.; Jung, K. W. *Org. Lett.* **2010**, *12*, 2450.

(4) Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2005**, *127*, 6966.

(5) Yang, C.-G.; Reich, N. W.; Shi, Z.-J.; He, C. *Org. Lett.* **2005**, *7*, 4553.

(6) (a) Oe, Y.; Ohta, T.; Ito, Y. *Chem. Commun.* **2004**, 1620. (b) Khusnutdinov, R. I.; Shchadneva, N. A.; Khisamova, L. F.; Dzhemilev, U. M. *Russ. J. Org. Chem.* **2011**, *47*, 155.

(7) (a) Stuart, D. R.; Villemure, E.; Fagnou, K. *J. Am. Chem. Soc.* **2007**, *129*, 12072. (b) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (c) Stuart, D. R.; Fagnou, K. *Science* **2007**, *316*, 1172. (d) Campeau, L. C.; Stuart, D. R.; Leclerc, J. P.; Bertrand-Laperle, M.; Villemure, E.; Sun, H. Y.; Lasserre, S.; Guimond, N.; Lecavallier, M.; Fagnou, K. *J. Am. Chem. Soc.* **2009**, *131*, 3291. (e) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (f) Wasa, M.; Engle, K. M.; Yu, J. Q. *J. Am. Chem. Soc.* **2010**, *132*, 3680. (g) Wang, X.-S.; Leow, D.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 13864.

(8) (a) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461. (b) Xu, L.-M.; Li, B.-J.; Yang, Z.; Shi, Z.-J. *Chem. Soc. Rev.* **2010**, *39*, 712. (c) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417. (d) Sehnal, P.; Taylor, R. J. K.; Fairlamb, I. J. S. *Chem. Rev.* **2010**, *110*, 824. (e) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308.

(9) (a) Jia, C.; Kitamura, T.; Fujiwara, Y. *Org. Lett.* **1999**, *1*, 2097. (b) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (c) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992. (d) Yokota, T.; Tani, M.; Sakaguchi, S.; Ishii, Y. *J. Am. Chem. Soc.* **2003**, *125*, 1476. (e) Yokota, M.; Fujita, D.; Ichikawa, J. *Org. Lett.* **2007**, *9*, 4639.

(10) Jean, M.; Weghe, P. V. D. *Tetrahedron Lett.* **2011**, *52*, 3509.

(11) Brenzovich, W. E.; Brazeau, J.-F.; Toste, F. D. *Org. Lett.* **2010**, *12*, 4728.

(12) (a) Jin, Z.; Xu, B.; Hammond, G. B. *Tetrahedron Lett.* **2011**, *52*, 1956. (b) Ball, L. T.; Lloyd-Jones, G. C.; Russell, C. A. *Chem.—Eur. J.* **2012**, *18*, 2931. (c) Zhang, G.-Z.; Peng, Y.; Cui, L.; Zhang, L.-M. *Angew. Chem., Int. Ed.* **2009**, *48*, 3112. (d) Shan, G.; Yang, X.; Zong, Y.; Rao, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 13606. (e) Zhang, G.-Z; Cui, L.; Wang, Y.-Z.; Zhang, L.-M. *J. Am. Chem. Soc.* **2010**, *132*, 1474. (f) Melhado, A. D.; Brenzovich, W. E., Jr.; Lackner, A. D.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 8885. (g) Tkatchouk, E.; Mankad, N. P.; Benitez, D.; Goddard, W. A., III; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 14293.

(13) Kurhade, S. E.; Sanchawala, A. I.; Ravikumar, V.; Bhuniya, D.; Reddy, D. S. *Org. Lett.* **2011**, *13*, 3690.

(14) Kiem, P. V.; Minh, C. V.; Nhiem, N. X.; Tai, B. H.; Quang, T. H.; Anh, H. L. T.; Cuong, N. X.; Hai, T. N.; Kim, S. H.; Kim, J. K.; Jang, H. D.; Kim, Y. H. *Bull. Korean Chem. Soc.* **2012**, *33*, 3461.

(15) Chatzopoulou, M.; Antoniou, A.; Pitsinos, E. N.; Bantzi, M.; Koulocheri, S. D.; Haroutounian, S. A.; Giannis, A. *Org. Lett.* **2014**, *16*, 3344.

(16) Chen, D.; Pamu, S.; Cui, Q.; Chan, T.-H.; Dou, Q. P. *Bioorg. Med. Chem.* **2012**, *20*, 3031.

(17) Akihisa, T.; Kokke, W. C. M. C.; Kimura, Y.; Tamura, T. *J. Org. Chem.* **1993**, *58*, 1959.

(18) Webster, R.; Boyer, A.; Fleming, M. J.; Lautens, M. *Org. Lett.* **2010**, *12*, 5418.

(19) (a) Kitching, W.; Rappoport, Z.; Winstein, S.; Young, W. G. *J. Am. Chem. Soc.* **1966**, *88*, 2054. (b) Trost, B. M.; Metzner, P. J. *J. Am. Chem. Soc.* **1980**, *102*, 3572. (c) Henderson, W. H.; Check, C. T.; Proust, N.; Stambuli, J. P. *Org. Lett.* **2010**, *12*, 824. (d) Campbell, A. N.; White, P. B.; Guzei, I. A.; Stahl, S. S. *J. Am. Chem. Soc.* **2010**, *132*, 15116. (e) Seayad, J.; Seayad, A. M.; Chai, C. L. L. *Org. Lett.* **2010**, *12*, 1412.

(20) See Supporting Information.

(21) Mei, T.-S.; Wang, X.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 10806.

(22) Engle, K. M.; Mei, T.-S.; Wang, X.-S.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2011**, *50*, 1478.

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