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Synthesis of Catechols from Phenols via Pd-Catalyzed Silanol-Directed C−H Oxygenation

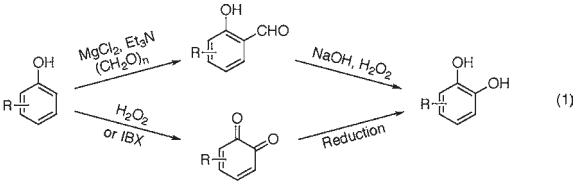
Chunhui Huang, Nugzar Ghavtadze, Buddhadeb Chattopadhyay, and Vladimir Gevorgyan*

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061, United States

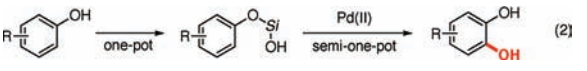
Supporting Information

ABSTRACT: A silanol-directed, Pd-catalyzed C−H oxygenation of phenols into catechols is presented. This method is highly site selective and general, as it allows for oxygenation of not only electron-neutral but also electron-poor phenols. This method operates via a silanol-directed acetoxylation, followed by a subsequent acid-catalyzed cyclization reaction into a cyclic silicon-protected catechol. A routine desilylation of the silacyle with TBAF uncovers the catechol product.

Catechols are widely present in natural products and extensively used in nearly every sector of chemical industries.[1] They are common structural motifs found in many bioactive molecules and drugs (Figure 1).[1a] Due to the regiospecific nature of biotransformations, synthesis of substituted catechols is prevailed by a fermentation of phenols.[2] In addition, a few synthetic procedures exist for transformation of substituted phenols into catechols.[3] One practical procedure involves *ortho*-formylation of phenols followed by a subsequent Dakin oxidation (eq 1, top).[3a] However, this process suffers from low selectivity, particularly for *meta*-substituted phenols.[4] Another method employs oxidation of phenols to *o*-quinones and a subsequent reduction of the latter into catechols (eq 1, bottom). The industrial version of this method employing H_2O_2 oxidation usually provides a mixture of catechol and *para*-hydroquinone,[1a,c] while the method using 2-iodoxybenzoic acid (IBX) as an oxidant is restricted to electron-rich substrates only.[3b] An improved version of the latter method somewhat expands the scope of phenols used; however it provides lower regioselectivity of oxidation.[3c] Thus, the development of efficient, general, and selective methods for conversion of phenols into catechols is warranted. Herein, we wish to report a novel approach toward catechols from phenols via the Pd-catalyzed silanol-directed *ortho* C−H oxygenation (eq 2), a process featuring high site selectivity and a broad functional group tolerance.



(1)



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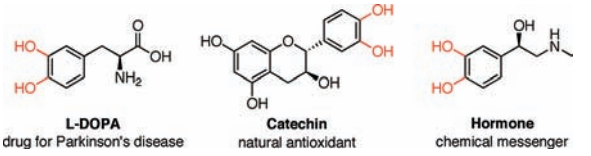
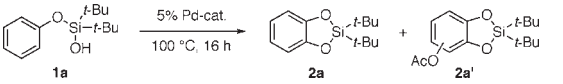


Figure 1. Catechol-containing natural products and pharmaceuticals.

Table 1. Screening of Reaction Conditions for C−O Cyclization



1a 2a 2a'

				yield, %[a]	
entry	Pd cat.	oxidant	solvent	2a	2a′
1[b]	$Pd(OPiv)_2$	$PhI(OAc)_2$ (1.5 equiv)	PhMe	43 (74)	2
2	$Pd(OPiv)_2$	$PhI(OAc)_2$ (1.5 equiv)	PhMe	50 (65)	3
3	$Pd(OAc)_2$	$PhI(OAc)_2$ (1.5 equiv)	PhMe	40 (67)	3
4	$Pd(OTf)_2$	$PhI(OAc)_2$ (1.5 equiv)	PhMe	40 (78)	2
5	$Pd(OPiv)_2$	$PhI(OAc)_2$ (1.5 equiv)	C_6F_6	37 (45)	3
6	$Pd(OPiv)_2$	$PhI(OAc)_2$ (1.5 equiv)	$PhCF_3$	47 (53)	14
7	**$Pd(OPiv)_2$**	**$PhI(OAc)_2$ (2.0 equiv)**	**PhMe**	**58 (79)**	**6**
8	$Pd(OPiv)_2$	$PhI(OAc)_2$ (3.0 equiv)	PhMe	47 (52)	6
9	none	$PhI(OAc)_2$ (1.5 equiv)	PhMe	0	0

[a] GC yields against tetradecane as internal standard, brsm yields in the parentheses (based on recovered starting material). [b] Li_2CO_3 (1 equiv) was added.

Transition-metal-catalyzed directed C−H[5] oxygenation of arenes has emerged as one of the most powerful tools for synthesis of phenol derivatives.[6] Recently, Yu[7] and Liu[8] disclosed an intramolecular hydroxyl group directed Pd-catalyzed oxygenation

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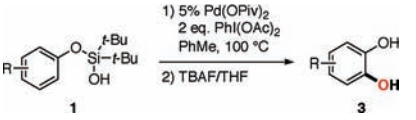
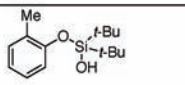
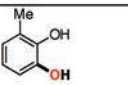
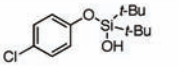
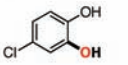
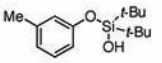
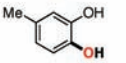
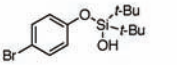
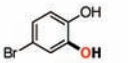
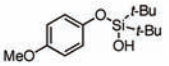
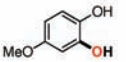
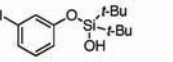
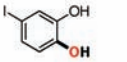
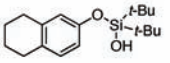
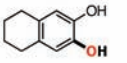
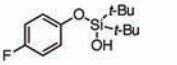
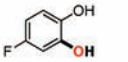
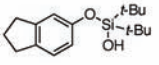
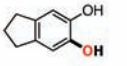
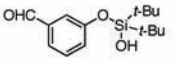
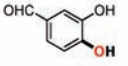
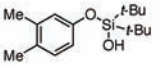
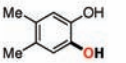
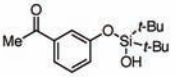
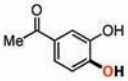
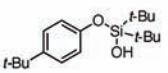
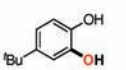
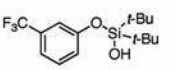
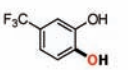
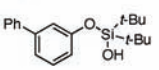
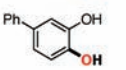
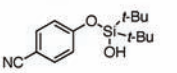
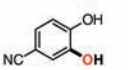
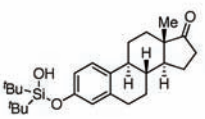
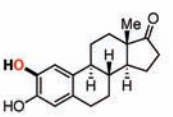
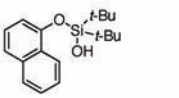
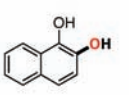
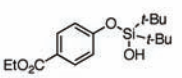
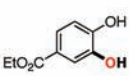
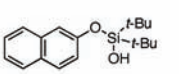
Table 2. Scope of Catechol Synthesis



entry	silanol		catechol		yield, %[a]	entry	silanol		catechol		yield, %[a]
1		**1b**		**3b**	81	12		**1m**		**3m**	84[b,d]
2		**1c**		**3c**	94	13		**1n**		**3n**	83[b,d]
3		**1d**		**3d**	57[b]	14		**1o**		**3o**	70[b,d]
4		**1e**		**3e**	77	15		**1p**		**3p**	60[b,d]
5		**1f**		**3f**	68[c]	16		**1q**		**3q**	47[b,d,e]
6		**1g**		**3g**	93	17		**1r**		**3r**	65[b,d]
7		**1h**		**3h**	78	18		**1s**		**3s**	35[b,d]
8		**1i**		**3i**	87	19		**1t**		**3t**	29[b,d]
9		**1j**		**3j**	88	20		**1u**		**3u**	76[b,d]
10		**1k**		**3k**	76[d]	21		**1v**		**3v**	54[b,d]
11		**1l**		**3l**	62[b,d]						

[a] Isolated yields. [b] Isolated as bis-acetates by further treatment of the catechols with Ac_2O and pyridine in the same pot.[12] [c] Major isomer is shown (34:1). [d] $PhCF_3$ was used instead of PhMe, $PhI(OAc)_2$ (1.5 equiv), 120 °C. [e] 10 mol % $Pd(OPiv)_2$ was used.

of arenes proceeding via a C−H activation/C−O cyclization protocol (eq 3). On the other hand, our group has recently introduced the silanol as a traceless directing group for the Pd-catalyzed *ortho*-alkenylation of phenols.[9,10] Considering the similarity of the OH functionality in alcohols and in silanols, we hypothesized that phenoxy silanol **1** could also undergo the Pd-catalyzed C−H activation/C−O cyclization reaction into silacycle **2**. The latter, upon subsequent desilylation, would furnish catechol **3**.

(3)

Accordingly, phenoxy silanol **1a** was tested in this oxygenation process. The reaction of **1a** under the Pd-catalyzed cyclization conditions developed by Yu[7] provided a 43% GC yield of silacycle **2a** along with 3% of an overoxidized byproduct **2a′** (Table 1, entry 1). Gratifyingly, a better yield of **2a** was obtained in the absence of base[11] (entry 2). $Pd(OPiv)_2$ was found to be superior among different palladium sources tested (entries 2−4). It was found that, during the reaction, toluene was partially oxidized into isomeric tolyl acetates. To avoid that, fluorinated solvents were tested. However, their employment was not beneficial (entries 5−6). Employment of larger amounts of $PhI(OAc)_2$ improved the yield to 58% (79% bsrm, entry 7). A further increase of the oxidant resulted in no improvement (entry 8). Expectedly, there was no reaction without a palladium catalyst (entry 9).

A routine desilylation of **2a** with TBAF quantitatively released catechol **3a** (eq 4). To ease separation, catechol **3a** was efficiently converted into its bis-acetate derivative **4a**.

(4)

Next, the scope of the combined semione-pot cyclization/desilylation procedure from silanols **1** to catechols **3** was

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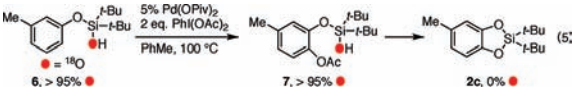
investigated (Table 2). It was found that substrates with electron-donating groups typically reacted faster, providing good to excellent yields of the catechols (**3b**−**h**). Remarkably, in contrast to the previous catechol syntheses,[3] this transformation demonstrated excellent site selectivity, directing the newly installed hydroxyl group to the sterically less hindered C−H site. Of note, estrone highly efficiently and selectively converted into 2-hydroxyestrone (**3j**), an important intermediate of the estrone metabolism in the human body.[13]

Since the existing synthetic methods are marginally efficient and/or selective for oxidation of electron-deficient phenols,[3] it was interesting to probe the generality of this new C−H functionlization method. Thus, oxygenation of *para*-ester-substituted substrate **1k** gave a 24% NMR yield of the cyclization product **2k**. Switching to $PhCF_3$ at elevated temperature (120 °C) dramatically improved the yield of **3k** (entry 10). Moreover, phenols possessing F, Cl, Br, and I reacted well under the modified conditions (entries 11−15). Substrates possessing aldehyde (**1q**) and ketone (**1r**) functionalities were smoothly oxidized into the corresponding catechols in moderate yields (entries 16−17). Phenols possessing CF_3 and CN groups were less efficient providing 35% and 29% yields, respectively (entries 18−19). 1- and 2-Naphthol derivatives were also competent reactants in this oxygenation reaction (entries 20−21). Remarkably, the silanol-directed oxygenation reaction allows access to naphthalene-2,3-diol **3v** from 2-naphthol derivative **1v** (entry 21), demonstrating *orthogonal site selectivity* of this method to the existing techniques, which convert 2-naphthol into regioisomeric naphthalene-1,2-diol **3u**.[3c]

Interestingly, the GC/MS analyses of the oxygenation of **1c** at the early stages of the reaction indicate formation of acetoxylated product **5c**. This was further investigated by a careful monitoring of the reaction under the standard conditions. The reaction profile clearly shows the formation and decay of acetoxylated product **5c** during the reaction course (Figure 2). Meanwhile, increasing amounts of the cyclization product **2c** was also observed from the very beginning of the reaction. In order to understand how the acetoxylated product **5c** is transformed into the silacyle **2c**, several experiments with **5c**, isolated from the reaction mixture, have been performed. Thus, simple heating of **5c** in PhMe at 100 °C for 12 h gave no reaction. However, addition of 2 equiv of HOAc led to a full conversion of **5c** into **2c** within 10 h. Expectedly, **5c** was smoothly transformed into **2c** under the standard reaction conditions. Based on these results, the transformation of the acetoxylated product **5c** into the silacylcle **2c** seems to be mediated by HOAc, which is generated during the reaction course (see Scheme 1).

In order to verify whether silacyle **2c** arises solely through a stepwise route involving acetoxylated product **5c** or it also forms via a direct C−O reductive cyclization,[7] the ^{18}O-labeled silanol **6** was subjected to the standard reaction conditions (eq 5). It was found that ^{18}O-labeled acetoxylated product **7** was formed and then gradually declined during the reaction producing the cyclized product **2c** with no ^{18}O label incorporated (eq 5). It deserves mentioning that throughout the reaction course the abundance of the ^{18}O label in both the starting silanol **6** and the acetoxylated product **7** remained unchanged.



In light of these observations, a plausible reaction pathway for the Pd-catalyzed silanol-directed *ortho* C−H oxygenation is proposed (Scheme 1). First, $Pd(OAc)_2$ (or palladium pivalate) reacts with silanol **1** producing palladacycle **8**,[14] in which silanol acts as a neutral directing group for palladium.[15] Next, Pd^{II} in palladacycle **8** is oxidized by $PhI(OAc)_2$ to a higher oxidation state (Pd^{IV} or Pd^{III})[16] to give intermediate **9**. The direct C−O reductive cyclization from Pd to form **11** was ruled out by the ^{18}O-labeling studies (*vide supra*). Instead, a reductive acetoxylation from **9** regenerates the Pd^{II} catalyst and produces the observed acetoxylated intermediate **10**. The latter, presumably via an acid-catalyzed[17] transesterification into **13** and a subsequent loss of the ^{18}O labeled acetic acid, produces cyclic silyl-protected catechol **2**.

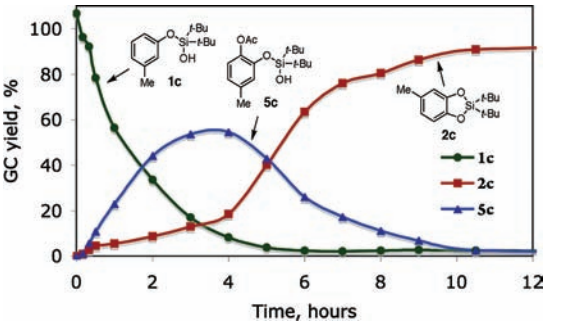
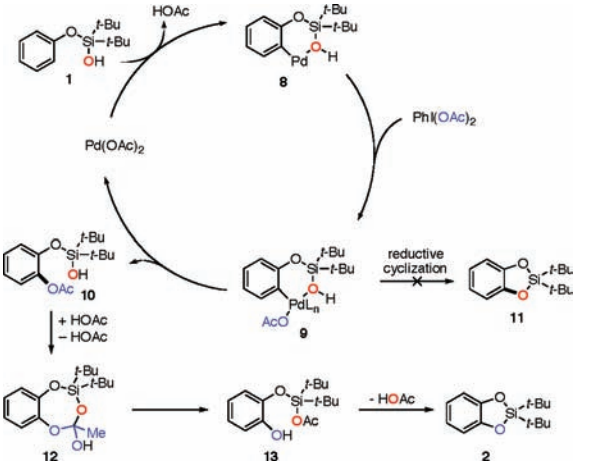


Figure 2. Reaction profile of Pd^{II}-catalyzed silanol-directed C−H acetoxylation and cyclization, picturing the formation and decline of acetoxylated product **5c** as the intermediate in the reaction. Reaction conditions: **1c** (0.2 mmol), $Pd(OPiv)_2$ (0.01 mol), $PhI(OAc)_2$ (0.4 mmol), PhMe (2 mL), 100 °C. The reaction was monitored by GC/MS with tetradecane as the internal standard.

Scheme 1. Plausible Reaction Pathway



In summary, we have developed a semione-pot Pd(II)-catalyzed silanol-directed C−H oxygenation of phenols into catechols. This new method operates via a consecutive C−H acetoxylation/acid-catalyzed transesterification/cyclization sequence. In striking contrast to the known alcohol-[7] and phenol-directed[8] C−O cyclization methods, where the directing group serves as the oxygen source, in our oxygenation method the oxygen atom of the newly installed hydroxyl group is delivered by the oxidant. This new method allows for efficient and site selective construction of substituted catechols, including electron-defficient catechols, which are not easily accessible via existing synthetic approaches.

■ ASSOCIATED CONTENT

Supporting Information. Detailed experimental procedures and charcterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
vlad@uic.edu

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■ REFERENCES

(1) (a) Fiegel, H.; Voges, H.-W.; Hamamoto, T.; Umemura, S.; Iwata, T.; Miki, H.; Fujita, Y.; Buysch, H.-J.; Garbe, D.; Paulus, W. *Phenol Derivatives in Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: New York, 2002. (b) Barner, B. A. *"Catechol" in Encyclopedia of Reagents for Organic Synthesis*; Paquette, L., Eds.; John Wiley and Sons: New York, 2004. (c) Karakhanov, E. A.; Maximov, A. L.; Kardasheva, Y. S.; Skorkin, V. A.; Kardashev, S. V.; Ivanova, E. A.; Lurie-Luke, E.; Seeley, J. A.; Cron, S. L. *Ind. Eng. Chem. Res.* **2010**, *49*, 4607.

(2) (a) Draths, K. M.; Frost, J. W. *J. Am. Chem. Soc.* **1991**, *113*, 9361. (b) Bui, V. P.; Hansen, T. V.; Stenstrøm, Y.; Hudlicky, T. *Green Chem.* **2000**, *2*, 263. (c) Nolan, L. C.; O'Connor, K. E. *Biotechnol. Lett.* **2008**, *30*, 1879. (d) Berberian, V.; Allen, C. C. R.; Sharma, N. D.; Boyd, D. R.; Hardacre, C. *Adv. Synth. Catal.* **2007**, *349*, 727. (e) Prakash, D.; Pandey, J.; Tiwary, B. N.; Jain, R. K. *BMC Biotechnol.* **2010**, *10*, 49. (f) Montersino, S.; Tischler, D.; Gassner, G. T.; van Berkel, W. J. H. *Adv. Synth. Catal.* **2011**, *353*, 2301.

(3) (a) Hansen, T. V.; Skattebøl, L. *Tetrahedron Lett.* **2005**, *46*, 3357. (b) Magdziak, D.; Rodriguez, A. A.; Van De Water, R. W.; Pettus, T. R. R. *Org. Lett.* **2002**, *4*, 285. (c) Pezzella, A.; Lista, L.; Napolitano, A.; d'Ischia, M. *Tetrahedron Lett.* **2005**, *46*, 3541.

(4) Hofsløkken, N. U.; Skattebøl, L. *Acta Chem. Scand.* **1999**, *53*, 258.

(5) For general reviews on transition-metal-catalyzed C−H activation of arenes, see: (a) Kakiuchi, F.; Chatani, N. *Adv. Synth. Catal.* **2003**, *345*, 1077. (b) Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 2439. (c) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (d) Yu, J.-Q.; Giri, R.; Chen, X. *Org. Biomol. Chem.* **2006**, *4*, 4041. (e) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (f) Campeau, L.-C.; Stuart, D. R.; Fagnou, K. *Aldrichimica Acta* **2007**, *40*, 35. (g) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (h) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (i) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (j) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890. (k) Ashenhurst, J. A. *Chem. Soc. Rev.* **2010**, *39*, 540. (l) Satoh, T.; Miura, M. *Synthesis* **2010**, 3395. (m) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293. (n) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740.

(6) For reviews on transition-metal-catalyzed oxygenation of arenes, see: (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (b) Sehnal, P.; Taylor, R. J. K.; Fairlamb, I. J. S. *Chem. Rev.* **2010**, *110*, 824. (c) Muñiz, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9412. (d) Alonso, D. A.; Nájera, C.; Pastor, I. M.; Yus, M. *Chem.—Eur. J.* **2010**, *16*, 5274. (e) Enthaler, S.; Company, A. *Chem. Soc. Rev.* **2011**, *40*, 4912. For recent representative examples, see:(f) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300. (g) Kalyani, D.; Sanford, M. S. *Org. Lett.* **2005**, *7*, 4149. (h) Kim, S. H.; Lee, H. S.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2008**, *49*, 5863. (i) Chernyak, N.; Dudnik, A. S.; Huang, C.; Gevorgyan, V. *J. Am. Chem. Soc.* **2010**, *132*, 8270. (j) Desai, L. V.; Malik, H. A.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 1141. (k) Desai, L. V.; Stowers, K. J.; Sanford, M. S. *J. Am. Chem. Soc.* **2008**, *130*, 13285. (l) Wang, G.-W.; Yuan, T.-T.; Wu, X.-L. *J. Org. Chem.* **2008**, *73*, 4717. (m) Gou, F.-R.; Wang, X.-C.; Huo, P.-F.; Bi, H.-P.; Guan, Z.-H.; Liang, Y.-M. *Org. Lett.* **2009**, *11*, 5726. (n) Zhang, Y.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 14654. (o) Zheng, X.; Song, B.; Xu, B. *Eur. J. Org. Chem.* **2010**, 4376. (p) Racowski, J. M.; Dick, A. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 10974. (q) Wang, G.-W.; Yuan, T.-T. *J. Org. Chem.* **2010**, *75*, 476. (r) Anand, M.; Sunoj, R. B. *Org. Lett.* **2011**, *13*, 4802. (s) Gu, S.; Chen, W. *J. Org. Chem.* **2009**, *74*, 7203. (t) Richter, H.; Beckendorf, S.; Mancheno, O. G. *Adv. Synth. Catal.* **2011**, *353*, 295. (u) Huang, C.; Chernyak, N.; Dudnik, A. S.; Gevorgyan, V. *Adv. Synth. Catal.* **2011**, *353*, 1285.

(7) Wang, X.; Lu, Y.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 12203.

(8) Xiao, B.; Gong, T.-J.; Liu, Z.-J.; Liu, J.-H.; Luo, D.-F.; Xu, J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 9250.

(9) Huang, C.; Chattopadhyay, B.; Gevorgyan, V. *J. Am. Chem. Soc.* **2011**, *133*, 12406.

(10) For *o*-arylation of phenols, see: (a) Bedford, R. B.; Coles, S. J.; Hursthouse, M. B.; Limmert, M. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 112. (b) Bedford, R. B.; Limmert, M. E. *J. Org. Chem.* **2003**, *68*, 8669. (c) Oi, S.; Watanabe, S.-I.; Fukita, S.; Inoue, Y. *Tetrahedron Lett.* **2003**, *44*, 8665. (d) Bajracharya, G. B.; Daugulis, O. *Org. Lett.* **2008**, *10*, 4625. For *o*-alkylation of phenols, see:(e) Lewis, L. N.; Smith, J. F. *J. Am. Chem. Soc.* **1986**, *108*, 2728. (f) Dorta, R.; Tongi, A. *Chem. Commun.* **2003**, 760. (g) Carrión, M. C.; Cole-Hamilton, D. J. *Chem. Commun.* **2006**, 4527. (h) Lewis, J. C.; Wu, J.; Bergman, R. G.; Ellman, J. A. *Organometallics* **2005**, *24*, 5737. For *o*-borylation of phenols, see:(i) Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 7534.

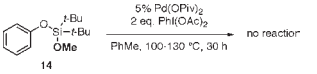
(11) It was shown by Yu's group that the alcohol-directed C−O cyclization may proceed without the base, albeit with lower efficiency (ref 7).

(12) See Supporting Information for details.

(13) (a) Fishman, J.; Cox, R. R.; Gallagher, T. F. *Arch. Biochem.* **1960**, *90*, 318. (b) Kraychy, S.; Gallagher, T. F. *J. Am. Chem. Soc.* **1957**, *79*, 754.

(14) The observed intramolecular kinetic isotope effect (k_H/k_D = 2.6) is in the range for oxygenation reactions proceeding via analogous palladacycles; see: (a) Stowers, K. J.; Sanford, M. S. *Org. Lett.* **2009**, *11*, 4584.(b) See also refs 6a, 6i, 6k.

(15) Notably, the methyl-protected silanol **14** had no reactivity under the standard reaction conditions, suggesting the hydroxyl group of silanol to be crucial for this transformation. Likewise, Liu[8] reported that the OH group of a phenol is required for the formation of hydrogen bonding with the acetate/pivalate group of the Pd(II) catalyst, which is necessary for a successful C−O cyclization.



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(16) For involvement of Pd^{IV} intermediates in C−H functionalization reactions, see: (a) Yoneyama, T.; Crabtree, R. H. *J. Mol. Catal. A: Chem.* **1996**, *108*, 35. (b) Engle, K. M.; Mei, T.-S.; Wang, X.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2011**, *50*, 1478.(c) See also refs 5d, 6a, 6b, 6f, 6h, 7. For involvement of bimetallic Pd^{III} species, see: (d) Powers, D. C.; Geibel, M. A. L.; Klein, J. E. M. N.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050. (e) Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302.

(17) This transesterification process could also take place in the presence of a base. Indeed, the cyclization completed within 10 min upon treatment of **5c** with NaO^{t}Bu in MeOH at room temperature.