ChemInform Abstract: Palladium-Catalyzed Oxidative sp2 C-H Bond Acylation with Alcohols.

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Palladium-Catalyzed Oxidative sp^2 C−H Bond Acylation with Alcohols

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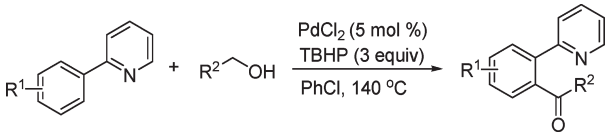
ABSTRACT



An efficient method was developed for the direct acylation of arene sp^2 C−H bonds with alcohols using palladium chloride as a catalyst and peroxide as the oxidant. The alcohols were oxidized to their corresponding aldehydes *in situ* and efficiently coupled with 2-arylpyridines to give aryl ketones in chlorobenzene.

The direct conversion of C−H bonds into C−C bonds can potentially lead to a more efficient synthesis with a reduced number of synthetic operations and thus has attracted great interest.[1] Since the seminal work reported by Murai,[2] great progress has been achieved in the transition-metal-catalyzed activation and subsequent reaction of C−H bonds.[3] The combination of transition metals and directing groups is a useful strategy to facilitate arene C−H bond cleavage[4] and to realize C−C[5] and C−X[6] bond

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(1) (a) Dyker, G. *Handbook of C−H Transformations: Applications in Organic Synthesis*; Wiley-VCH: Weinheim, 2005. (b) Yu, J. Q.; Shi, Z. J. *C−H Activation*; Springer: Berlin, Germany, 2010. (c) *Activation and Functionalization of C−H Bond*; Goldberg, K. I.; Goldman, A. S., Eds.; ACS Symposium Series 885; American Chemical Society: Washington, DC, 2004.

(2) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529.

(3) For representative reviews on C−H functionalization, see: (a) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879. (b) Naota, T.; Takaya, H.; Murahashi, S. I. *Chem. Rev.* **1998**, *98*, 2599. (c) Dyker, G. *Angew. Chem. Int. Ed* **1999**, *38*, 1698. (d) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633. (e) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (f) Crabtree, R. H. *J. Organomet. Chem.* **2004**, *689*, 4083. (g) Goj, L. A.; Gunnoe, T. B. *Curr. Org. Chem.* **2005**, *9*, 671. (h) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (i) Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 2439. (j) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, *107*, 5318. (k) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (l) Campeau, L. C.; Stuart, D. R.; Fagnou, K. *Aldrichimica Acta* **2007**, *40*, 35. (m) Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2008**, *41*, 1013. (n) Li, B. J.; Yang, S.; Shi, Z. *Synlett* **2008**, 949. (o) Diaz-Requejo, M. M.; Pérez, P. J. *Chem. Rev.* **2008**, *108*, 3379. (p) Zhang, M. *Adv. Synth. Catal.* **2009**, *351*, 2243. (q) Chen, X.; Engle, K. M.; Wang, D. H.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (r) Giri, R.; Shi, B.; Engle, K.; Maugel, N.; Yu, J. Q. *Chem. Soc. Rev.* **2009**, *38*, 3242. (s) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (t) Copéret, C. *Chem. Rev.* **2010**, *110*, 656. (u) Mkhalid, I.; Barnard, J.; Marder, T.; Murphy, J.; Hartwig, J. *Chem. Rev.* **2010**, *110*, 890.

(4) (a) Chatani, N. *Directed Metallation*; Springer: Berlin, Germany, 2008. (b) Daugulis, O.; Do, H. Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (c) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624.

(5) For recent selected examples on arene C−H activations and C−C bond formations, see: (a) Tan, K. L.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 2685. (b) Hennessy, E. J.; Buchwald, S. L. *J. Am. Soc. Chem.* **2003**, *125*, 12084. (c) Lane, B. S.; Sames, D. *Org. Lett.* **2004**, *6*, 2897. (d) Campeau, L.; Rousseaux, S.; Fagnou, K. *J. Am. Chem. Soc.* **2005**, *127*, 18020. (d) Rueping, M.; Sugiono, E.; Azap, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 2619. (e) Seregin, I.; Ryabova; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 7742. (f) Shi, Z.; Li, B.; Wan, X.; Cheng, J.; Fang, Z.; Cao, B.; Qin, C.; Wang, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 5554. (g) Yang, S.; Li, B.; Wan, X.; Shi, Z. J. *J. Am. Chem. Soc.* **2007**, *129*, 6066. (h) Ueda, S; Nagasawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6411. (i) Özdemir, I.; Demir, S.; Cetinkaya, B.; Gourlaouen, C.; Maseras, F.; Bruneau, C.; Dixneuf, P. H. *J. Am. Chem. Soc.* **2008**, *130*, 1156. (j) Liégault, B.; Fagnou, K. *Organometallics* **2008**, *27*, 4841. (k) Ackermann, L.; Vicente, R.; Althammer, A. *Org. Lett.* **2008**, *10*, 2299. (l) Wang, D. H.; Mei, T. S.; Yu, J. Q. *J. Am. Chem. Soc.* **2008**, *130*, 17676. (m) Zhao, D.; Wang, W.; Yang, F.; Lan, J.; Yang, L.; Gao, G.; You, J. S. *Angew. Chem., Int. Ed.* **2009**, *48*, 3296. (n) Luo, N.; Yu, Z. K. *Chem.—Eur. J.* **2010**, *16*, 787. (o) Nishikata, T.; Abela, A.; Lipshutz, B. *Angew. Chem., Int. Ed.* **2010**, *49*, 781. (p) Wang, X.; Truesdale, L.; Yu, J. Q. *J. Am. Chem. Soc.* **2010**, *132*, 3648. (q) Wang, D.; Engle, K.; Shi, B.; Yu, J. Q. *Science* **2010**, *327*, 315. (r) Patureau, F.; Glorius, F. J. *Am. Chem. Soc.* **2010**, *132*, 9982. (s) Berman, A.; Bergman, R.; Ellman, J. *J. Org. Chem.* **2010**, *75*, 7863. (t) Xiao, B.; Fu, Y.; Xu, J.; Gong, T.; Dai, J.; Liu, L. *J. Am. Chem. Soc.* **2010**, *132*, 468.

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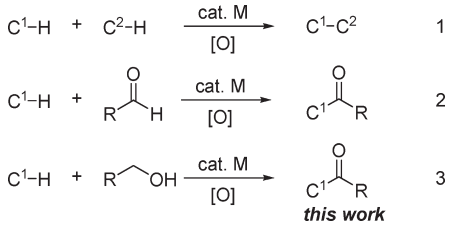
formation. We and others have developed various methods to generate C−C bonds directly from two different simple C−H bonds in the presence of an oxidizing reagent through a cross-dehydrogenative coupling (CDC) catalyzed by copper, palladium, or other transition metals (Scheme 1, eq 1).[7] The C−H bond adjacent to a heteroatom or an unsaturated C−C bond showed unique reactivity toward transition metals with high selectivity.[8] In recent years, the oxidative coupling of two different aryl C−H bonds for the synthesis of an arene−arene linkage has witnessed remarkable progress.[7b] In a challenging fashion, we recently reported the direct cross-coupling of an unactivated arene C−H bond with a cyclic alkane to produce a new C_{sp^3}−C_{sp^2} bond.[9]

Aryl ketones are key functionalities in the pharmaceutical, fragrance, dye, and agrochemical industries.[10] The classical routes to synthesize aryl ketones mainly rely on the Friedel−Crafts acylation of aromatic compounds in the presence of corrosive $AlCl_3$ and oxidation of the corresponding secondary alcohols by chromium reagents.[11] From a synthetic point of view, the direct introduction of carbonyl functional groups onto the aromatic motifs via C−H bond cleavage will both be a more environmentally friendly alternative in aryl ketone synthesis and potentially provide a regioselectivity complementary to classical Friedel−Crafts acylation. However, the CDC reaction of aryl C−H bonds with acyl C−H bonds remains a challenge. Recently, we[12] and others[13] have developed a transition-metal-catalyzed oxidative sp^2 C−H bond acylation with aldehydes. Various ketones can be synthesized efficiently and selectively using aromatic or aliphatic aldehydes as the carbonyl source. Encouraged by these discoveries, it further occurred to us that alcohols could serve as the acylation reagents since alcohols can be readily oxidized into aldehydes.[14] Alcohols are naturally abundant, stable, commercially available, and easy to handle and thus can be potentially used as ideal acylation reagents. *Herein, we report a palladium-catalyzed regioselective acylation of aromatic C−H bonds using alcohols in the presence of peroxide as an oxidant, affording the ketones in good yields.*

Scheme 1. Transition-Metal-Catalyzed CDC Reactions and Direct Acylations from Aldehydes and Alcohols



Our initial investigations were focused on the acylation of 2-phenylpyridine (**1a**) with benzyl alcohol (**2a**), and the results are summarized in Table 1. When 2-phenylpyridine reacted with 3 equiv of benzyl alcohol in the absence of any catalyst using 2 equiv of *tert*-butyl hydroperoxide (TBHP) as the oxidant, no desired product was detected by GC-MS and ^{1}H NMR methods (Table 1, entry 1). A trace amount of the desired product was observed when 5 mol % of PdO was employed (entry 2). Subsequently, various palladium(II) salts were tested for this direct acylation in the presence of TBHP under an atmosphere of air (entries 3−9). Moderate yields were observed when $Pd_2(dba)_3$, $Pd(acac)_2$, and $Pd(COD)Cl_2$ were used as the catalysts. The yields could be further improved by using $Pd(OAc)_2$ and $Pd(CH_3CN)_2Cl_2$. The best result was obtained using $PdCl_2$ as the catalyst, and the desired product was obtained in 86% yield as a single regioisomer (entry 9). Other oxidants were also tested for this transformation: both TBP (*tert*-butyl

(6) (a) Giri, R.; Chen, X.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2005**, *44*, 2112. (b) Hull, K. L.; Anani, W. Q.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 7134. (c) Wan, X.; Ma, Z.; Li, B.; Zhang, K.; Cao, S.; Zhang, S.; Shi, Z. *J. Am. Chem. Soc.* **2006**, *128*, 7416. (d) Chen, X.; Hao, X.; Goodhue, C.; Yu, J. Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790. (e) Li, J. J.; Giri, R.; Yu, J. Q. *Tetrahedron* **2008**, *64*, 6979. (f) Li, J.; Mei, T.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 6452. (g) Zhao, X. D.; Dimitrijević, E.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 3466. (h) Wang, X.; Mei, T.; Yu, J. Q. *J. Am. Chem. Soc.* **2009**, *131*, 7520. (i) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300. (j) Desai, L.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542. (k) Desai, L.; Malik, H.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 1141. (l) Desai, L.; Stowers, K. J.; Sanford, M. S. *J. Am. Chem. Soc.* **2008**, *130*, 13285. (m) Zhang, Y. H.; Shi, B. F.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 6097. (n) Powers, D.; Geibel, M.; Klein, J.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050. (o) Zhang, Y.; Yu, J. Q. *J. Am. Chem. Soc.* **2009**, *131*, 14654. (p) Wang, X.; Lu, Y.; Dai, H.; Yu, J. Q. *J. Am. Chem. Soc.* **2010**, *132*, 12203. (q) Thu, H. Y.; Yu, W. Y.; Che, C. M. *J. Am. Chem. Soc.* **2006**, *128*, 9048. (r) Inamoto, K.; Saito, T.; Katsuno, M.; Sakamoto, T.; Hiroya, K. *Org. Lett.* **2007**, *9*, 2931. (s) Wasa, M.; Yu, J. Q. *J. Am. Chem. Soc.* **2008**, *130*, 14058. (t) Monguchi, D.; Fujiwara, T.; Furukawa, H.; Mori, A. *Org. Lett.* **2009**, *11*, 1607. (u) Wang, Q.; Schreiber, S. L. *Org. Lett.* **2009**, *11*, 5178. (v) Mei, T.; Wang, X.; Yu, J. Q. *J. Am. Chem. Soc.* **2009**, *131*, 10806. (w) Shuai, Q.; Deng, G.; Chua, Z.; Bohle, D.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 632.

(7) For reviews, see: (a) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (b) Ashenhurst, J. A. *Chem. Soc. Rev.* **2010**, *39*, 540. (c) Scheuermann, C. J. *Chem.—Asian J.* **2010**, *5*, 436.

(8) For a review, see: Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. For selected examples, see: (a) Hull, K. L.; Lanni, E. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 14047. (b) Stuart, D. R.; Fagnou, K. *Science* **2007**, *316*, 1172. (c) Whitfiekd, S. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 15142. (d) Stuart, D.; Villemure, E.; Fagnou, K. *J. Am. Chem. Soc.* **2007**, *129*, 12072. (e) Chen, X.; Dobereiner, G.; Hao, X. S.; Giri, R.; Maugel, N.; Yu, J. Q. *Tetrahedron* **2009**, *65*, 3085. (f) Guo, X.; Deng, G.; Li, C.-J. *Adv. Synth. Catal.* **2009**, *351*, 2071. (g) Zhao, X.; Yeung, C.; Dong, V. M. *J. Am. Chem. Soc.* **2010**, *132*, 5837. (h) Wei, Y.; Su, W. P. *J. Am. Chem. Soc.* **2010**, *132*, 16377. (i) Potavathri, S.; Pereira, K.; Gorelsky, S.; Pike, A.; LeBris, A.; DeBoef, B. *J. Am. Chem. Soc.* **2010**, *132*, 14676. (j) He, C.; Fan, S.; Zhang, X. J. *Am. Chem. Soc.* **2010**, *132*, 12850.

(9) (a) Deng, G.; Zhao., L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 6278. (b) Deng, G.; Li, C.-J. *Org. Lett.* **2009**, *11*, 1171. (c) Deng, G.; Ueda, K.; Yanagisawa, S.; Itami, K.; Li, C.-J. *Chem.—Eur. J.* **2009**, *15*, 333.

(10) Surburg, H.; Panten, J. *Common Fragrance and Flavor Materials*, 5th ed.; Wiley-VCH: Weinheim, Germany, 2006.

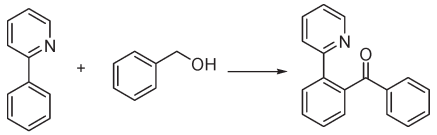
(11) Sartori, G.; Maggi, R. *Advances in Friedel-Crafts Acylation Reactions*; CRC Press: FL, 2010.

(12) (a) Baslé, O.; Bidange, J.; Shuai, Q.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 1145. For decarbonylative arylation using rhodium as a catalyst, see: (b) Shuai, Q.; Yang, L.; Guo, X. Y.; Baslé, O.; Li, C.-J. *J. Am. Chem. Soc.* **2010**, *132*, 12212.

(13) (a) Jia, X.; Zhang, S.; Wang, W.; Luo, F.; Cheng, J. *Org. Lett.* **2009**, *11*, 3120. (b) Tang, B.; Song, R.; Wu, C.; Liu, Y.; Zhou, M.; Wei, W.; Deng, G.; Yin, D.; Li, J. H. *J. Am. Chem. Soc.* **2010**, *132*, 8900.

(14) (a) Tojo, G.; Fernández, M. *Oxidation of Alcohols to Aldehydes and Ketones*; Springer: Berlin, Germany, 2006. (b) Guillena, G.; Ramón, D.; Yus, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2358. (c) Dobereiner, G.; Crabtree, R. *Chem. Rev.* **2010**, *110*, 681.

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

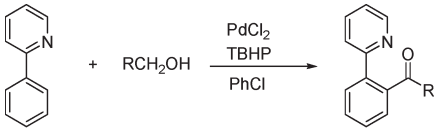
entry	catalyst	oxidant	solvent	yield (%)[b]
1	none	TBHP	PhCl	0
2	PdO	TBHP	PhCl	2
3	$Pd_2(dba)_3$	TBHP	PhCl	42
4	$Pd(acac)_2$	TBHP	PhCl	31
5	$Pd(COD)Cl_2$	TBHP	PhCl	46
6	$Pd(OAc)_2$	TBHP	PhCl	63
7	$Pd(CH_3CN)_2Cl_2$	TBHP	PhCl	73
8	$PdBr_2$	TBHP	PhCl	81
9	$PdCl_2$	TBHP	PhCl	86
10	$PdCl_2$	TBP	PhCl	80
11	$PdCl_2$	dicumyl peroxide	PhCl	76
12	$PdCl_2$	$PhC(CH_3)_2OOH$	PhCl	17
13	$PdCl_2$	$(PhCOO)_2$	PhCl	0
14	$PdCl_2$	O_2 (1 atm)	PhCl	0
15	$PdCl_2$	TBHP	neat	85
16	$PdCl_2$	TBHP	NMP	3
17	$PdCl_2$	TBHP	p-xylene	68
18	$PdCl_2$	TBHP	diglyme	78
19[c]	**$PdCl_2$**	**TBHP**	**PhCl**	**95**

[a] Conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), catalyst (5 mol %), oxidant (2.0 equiv), 140 °C, 24 h in air unless otherwise noted. [b] GC yield. [c] 3 equiv of TBHP were used.

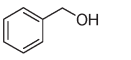
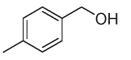
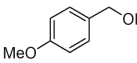
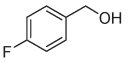
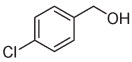
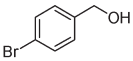
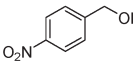
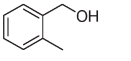
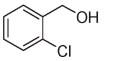
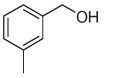
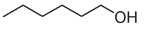
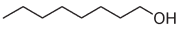
peroxide) and dicumyl peroxide were effective oxidants for the direct acylation, and the desired product was obtained in high yields (entries 10 and 11); other peroxides were less effective, and no desired product was observed when oxygen was used as the sole oxidant (entries 12−14). The effect of solvents on this reaction was also investigated. The reaction was efficient under neat conditions (entry 15). Other solvents, however, significantly decreased the yields (entries 16−18). The yield can be improved to 95% by increasing the oxidant to 3 equiv (entry 19) (after the reaction, only a small amount of leftover benzyl alcohol was observed by GC and a large amount of benzaldehyde was formed).

The direct acylation of 2-phenylpyridine with various primary alcohols was conducted under the optimized reaction conditions, and the results are summarized in Table 2. The reactions with benzylic alcohols bearing electron-donating groups (entries 2 and 3) and electron-withdrawing substituents at the aromatic ring (entries 4 and 5) proceeded to give the desired products in good to excellent yields. A slightly lower yield was obtained when 4-bromobenzyl alcohol was used, and the desired product was achieved in 78% yield (entry 6). The reaction yield decreased dramatically when (4-nitrophenyl)methanol was

Table 2. Scope of the Oxidative Acylation of 2-Phenylpyridine[a]



1a 2 3

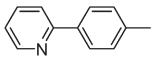
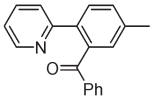
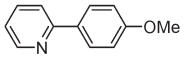
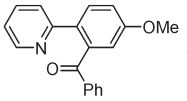
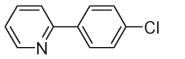
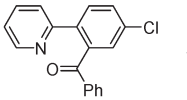
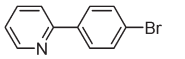
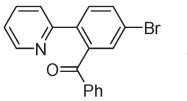
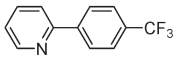
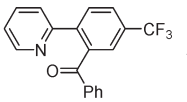
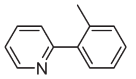
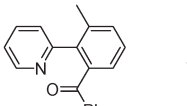
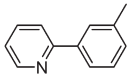
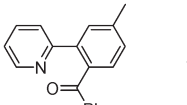
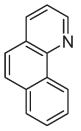
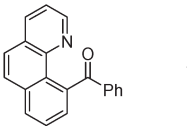
entry	alcohol		product	yield (%)[b]
1		**2a**	**3a**	88
2		**2b**	**3b**	81
3		**2c**	**3c**	65
4		**2d**	**3d**	87
5		**2e**	**3e**	82
6		**2f**	**3f**	78
7[c]		**2g**	**3g**	7
8		**2h**	**3h**	62
9		**2i**	**3i**	76
10		**2j**	**3j**	75
11		**2k**	**3k**	62
12		**2l**	**3l**	67

[a] Conditions: **1a** (0.2 mmol), **2** (0.6 mmol), $PdCl_2$ (5 mol %), oxidant (3 equiv), 140 °C, 24 h in air unless otherwise noted. [b] Isolated yield based on **1a**. [c] GC yield.

used as the substrate (entry 7), and only a 7% yield was observed by the GC method. The position of the substituents on the phenyl ring of benzyl alcohols slightly affected the reaction yield. Moderate to good yields were achieved when (2-methylphenyl)methanol, (2-chlorophenyl)methanol, and (3-methylphenyl)methanol were used (entries 8−10). To our delight, this reaction is not limited to benzyl alcohol and its derivatives. Aliphatic alcohols such as 1-hexanol and 1-octanol were also reactive toward 2-phenylpyridine and gave the desired products in 62% and 67% yields, respectively (entries 11 and 12). It should be noted that the reaction gave the monoacylation products selectively in all cases, and only trace amounts of biacylated products were observed.

The reaction results of 2-phenylpyridine derivatives with benzyl alcohol are presented in Table 3. A series of

Table 3. Reaction of Benzyl Alcohol with 2-Arylpyridines[a]

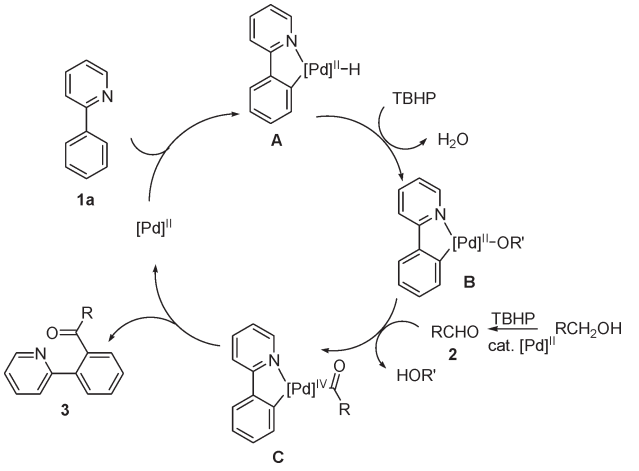
entry	2-arylpyridine		product		yield (%)[b]
1		**1b**		**3m**	83
2		**1c**		**3n**	81
3		**1d**		**3o**	78
4		**1e**		**3p**	63
5		**1f**		**3q**	72
6		**1g**		**3r**	trace
7		**1h**		**3s**	78
8		**1i**		**3t**	89

[a] Conditions: **1** (0.2 mmol), **2a** (0.6 mmol), $PdCl_2$ (5 mol %), TBHP (3 equiv), 140 °C, 24 h in air unless otherwise noted. [b] Isolated yields based on **1**.

functional groups including methyl, methoxy, chloro, and trifluoromethyl were tolerated under the optimal reaction conditions, and the desired products were obtained in good to excellent yields (Table 3, entries 1−5). However, only a trace amount of the acylation product was observed when 2-*o*-tolylpyridine was used as the substrate (entry 6), possibly due to the increased steric effect which prevents the formation of a coplanar conformation of the two aromatic rings. When benzo[*h*]quinoline **1i** was subjected to the procedure, a 89% yield of the acylation product was isolated (entry 8).

(15) Arnold, P. L.; Sanford, M. S.; Pearson, S. M. *J. Am. Chem. Soc.* **2009**, *131*, 13912.

Scheme 2. Tentative Mechanism



A tentative mechanism to rationalize this transformation is illustrated in Scheme 2. The active palladium catalyst reacts with 2-phenylpyridine by chelation-directed C−H activation to generate intermediate **A**.[2] The reaction of **A** with TBHP generates intermediate **B**. The reaction of **B** with aldehyde which is produced from the oxidation of alcohol provides the acyl intermediate **C** based on Sanford's work and our early studies.[12a,15] Finally, the reductive elimination of intermediate **C** affords coupling product **3** and regenerates Pd(II) for further reactions.

In summary, we have demonstrated a novel palladium-catalyzed acylation of arene C−H bonds in the presence of an oxidant. The cheap and readily available benzylic and aliphatic alcohols were oxidized *in situ* to aldehydes and used as acylation reagents. This new methodology enabled cross-coupling with both benzylic alcohols and aliphatic alcohols in good yield with high regioselectivity. Exploration of the substrate scope and reaction mechanism will be further investigated.

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