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Pd-Catalyzed Oxidative Coupling of Arene C−H Bonds with Benzylic Ethers as Acyl Equivalents

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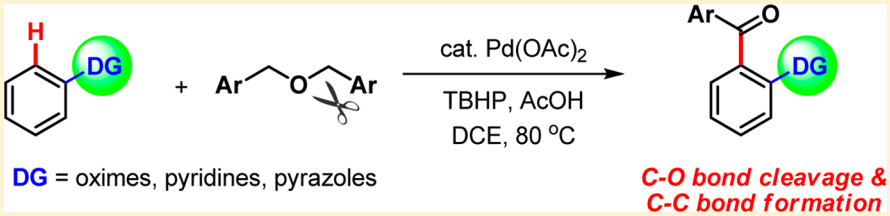
Supporting Information



ABSTRACT: A palladium-catalyzed oxidative coupling of arene C−H bonds with benzylic ethers via C−H bond activation is described. The reaction proceeds efficiently with a broad range of substrates bearing conventional directing groups with excellent functional group compatibility. This protocol potentially provides opportunities to use dibenzyl ethers as new acyl equivalents for catalytic acylation reactions.

INTRODUCTION

Transition-metal-catalyzed selective cross-coupling reactions via C−H bond activation have emerged as an attractive alternative to traditional cross-coupling reactions because of the minimization of stoichiometric metallic waste and the costs associated with the preparation of starting materials.[1] Thus, cross-coupling reactions via C−H bond activation can lead to an improved overall efficiency of the desired transformation. Since the pioneering efforts of Murai,[2] remarkable progress has been made on carbon−carbon cross-coupling reactions via C−H bond activation. In particular, most C−H bond activation processes generally rely on the strategies of directing-group-assisted C−H bond functionalization and dehydrogenative cross-coupling.[3]

Recently, transition-metal-catalyzed oxidative *ortho*-acylation reactions between arene C−H bonds bearing conventional directing groups and aldehydes[4] or alcohols[5] as acyl sources have been described (Figure 1). Catalytic decarboxylative acylations of aromatic C−H bonds using α-oxocarboxylic acids as acyl surrogates have also been reported.[6] Recently, a palladium-catalyzed acylation of inactive C(sp^2)−H bonds via C−H, C−C, and C−O bond cleavage of toluenes,[7] diketones,[8] and carboxylic acids[9], respectively, was reported. In addition, Yang and Wu demonstrated a palladium-catalyzed direct C−H acylation using arylmethyl amines as new acylation reagents.[10]

Benzylic ethers constitute one of the common protecting groups for alcohols. The C−O bond of benzylic ethers is readily cleaved under a variety of either oxidative or reductive conditions.[11] In particular, oxidative reactions of methylene carbons in benzyl ethers are important transformations because they can convert chemically stable moieties into reactive functional groups that are widely used in organic synthesis, including aldehydes, esters, and carboxylic acids. Since the first report on the formation of benzaldehydes from benzyl methyl ethers by Markees in 1958,[12] a number of methods have been developed for the formation of benzaldehydes via the oxidative cleavage of benzylic C−O bonds under various conditions, such as NBS/H_2O,[13] TEMPO,[14] HNO_3,[15] $Cu(NO_3)_2$,[16] and DDQ.[17] However, there has been no report concerning the behavior of benzylic ethers when treated with *tert*-butyl hydroperoxide (TBHP) as a mild oxidant.

As part of an ongoing research program directed toward the development of catalytic acylation reactions of inactive C−H bonds, we became interested in developing oxidative acylation reactions using benzylic ethers. Herein we present the palladium-catalyzed *ortho*-acylation of arene C−H bonds with benzylic ethers in the presence of TBHP to afford aryl ketones.

RESULTS AND DISCUSSION

In previous reports, *O*-methyl oxime has been used as an efficient directing group for C−H bond functionalization. For example, Shi[18] and Cheng[19] applied this directing group to oxidative coupling with arylboronic acids and aryl halides, respectively. In addition, we described a palladium-catalyzed oxidative *ortho*-acylation of *O*-methyl ketoximes from the alcohol oxidation level.[5d] Thus, *O*-methyl ketoxime **1a** was chosen as a model substrate for the oxidative coupling with dibenzyl ether (**1b**), and the selected optimization is summarized in Table 1. As shown in entries 1−5, a range of

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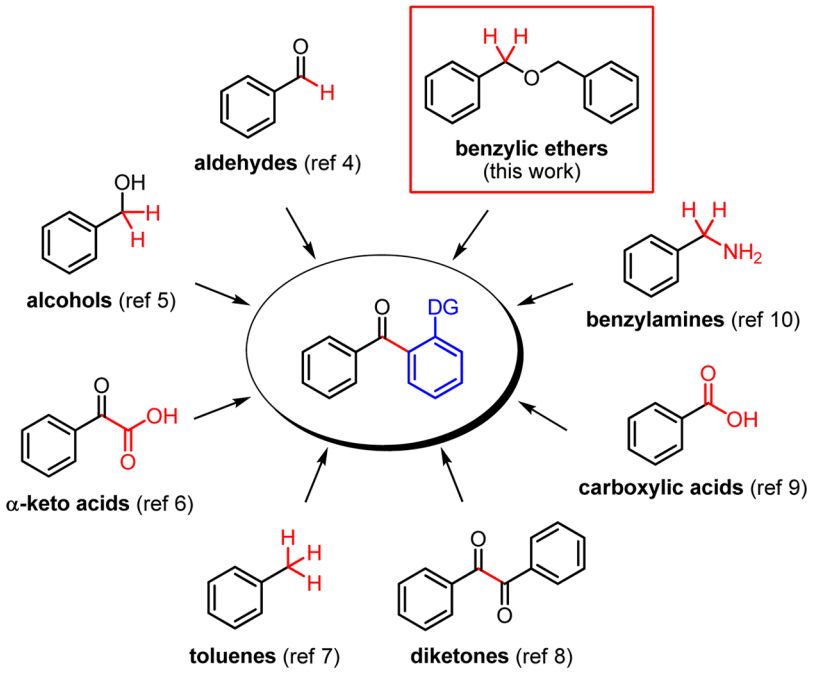
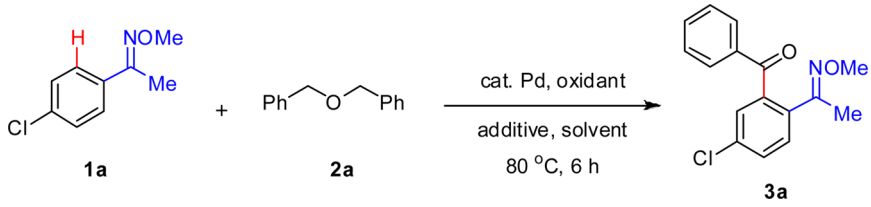


Figure 1. Acyl equivalents for catalytic acylation of arene C−H bonds.

Table 1. Selected Optimization of the Reaction Conditions[a]



entry	catalyst (mol %)	oxidant (equiv)	additive (equiv)	solvent	yield (%)[b]
1	$PdCl_2$ (5)	TBHP (3)		DCE	11
2	$Pd(OAc)_2$ (5)	TBHP (3)		DCE	24
3	$Pd_2(dba)_3$ (5)	TBHP (3)		DCE	N.R.
4	$Pd(TFA)_2$ (5)	TBHP (3)		DCE	22
5	$Pd(OTf)_2$ (5)	TBHP (3)		DCE	8
6		TBHP (3)		DCE	N.R.
7	$Pd(OAc)_2$ (100)			DCE	N.R.
8	$Pd(OAc)_2$ (5)	$(PhCOO)_2$ (3)		DCE	trace
9	$Pd(OAc)_2$ (5)	$Cu(OAc)_2$ (3)		DCE	N.R.
10	$Pd(OAc)_2$ (5)	O_2 gas		DCE	N.R.
11	$Pd(OAc)_2$ (5)	TBHP (3)		MeCN	18
12	$Pd(OAc)_2$ (5)	TBHP (3)		THF	8
13	$Pd(OAc)_2$ (5)	TBHP (3)		DMF	trace
14	$Pd(OAc)_2$ (5)	TBHP (5)		DCE	43
15	$Pd(OAc)_2$ (5)	TBHP (5)	AcOH (3)	DCE	71
16	**$Pd(OAc)_2$ (5)**	**TBHP (6)**	**AcOH (3)**	**DCE**	**85**
17	$Pd(OAc)_2$ (5)	TBHP (7)	AcOH (3)	DCE	84
18	$Pd(OAc)_2$ (5)	TBHP (6)	AcOH (1)	DCE	61
19	$Pd(OAc)_2$ (5)	TBHP (6)	AcOH (3)	DCE	48

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.9 mmol), Pd catalyst (quantity noted), oxidant (quantity noted), additive (quantity noted), and solvent (1 mL) in pressure tubes. [b]Determined by flash column chromatography.

Pd catalysts were screened in the presence of TBHP (300 mol %) as an oxidant, and the use of $Pd(OAc)_2$ afforded our desirable adduct **3a** in 24% yield (entry 2). In the absence of either $Pd(OAc)_2$ or TBHP, no coupling product was observed, even when 100 mol % $Pd(OAc)_2$ was used without TBHP, indicating that both reagents are required in the reaction (entries 6 and 7). Next, our study focused on the use of oxidants such as $(PhCOO)_2$, $Cu(OAc)_2$, and O_2 gas, but the chemical yield was not improved (entries 8−10). Further screening of solvents showed that DCE is superior to other solvents such as MeCN, THF, and DMF (entries 11−13). Logically, it was thought that the formation of **3a** could be

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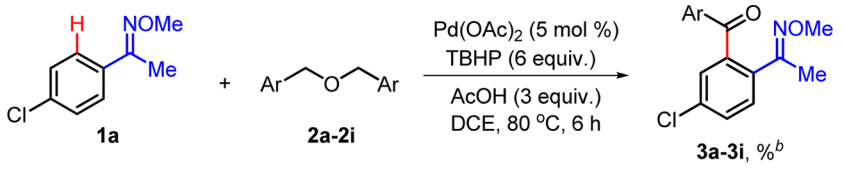
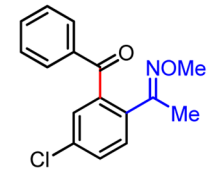
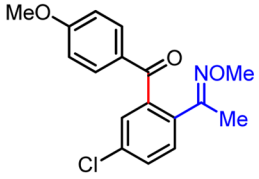
Table 2. Scope of Benzylic Ethers[a]

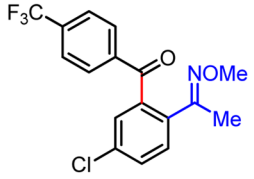




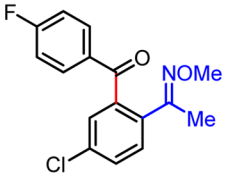
3a, 85%



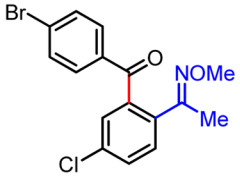
3b, 68%



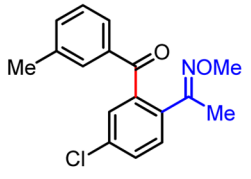
3c, 59%



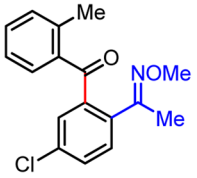
3d, 76%



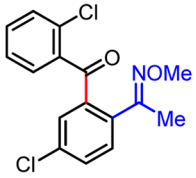
3e, 55%



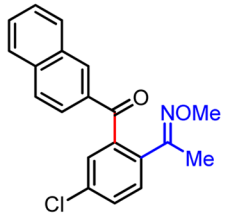
3f, 48%



3g, 84%



3h, 41%[c]



3i, 49%

[a]Reaction conditions: **1a** (0.3 mmol), **2** (0.9 mmol), $Pd(OAc)_2$ (5 mol %), TBHP (6 equiv), AcOH (3 equiv), and DCE (1 mL) at 80 °C for 6 h in pressure tubes. [b]Determined by flash column chromatography. [c]24 h.

increased by increasing the amount of TBHP. Indeed, with 5 equiv of TBHP under otherwise identical conditions, the yield of **3a** was found to be improved to 43% (entry 14). Further investigation revealed that AcOH as an additive is unique in its ability to facilitate high levels of conversion (Table 1, entry 15). After further optimization, the best results were obtained using a treatment of 5 mol % $Pd(OAc)_2$ and 6 equiv of TBHP in the presence of 3 equiv of AcOH additive in DCE solvent at 80 °C for 6 h, which afforded the desired aryl ketone **3a** in high yield (85%; entry 16).

With the optimized reaction conditions in hand, the scope and limitation of benzylic ethers were explored (Table 2). The coupling of *O*-methyl ketoxime **1a** and benzylic ethers **2b**–**h** with electron-donating and electron-withdrawing groups (OMe, Me, CF_3, F, Br, and Cl) was found to be favored in the acylation reaction, regardless of the position of the substituent on the aromatic ring, affording the corresponding products **3b**–**h** in good to high yields. Notably, *p*-bromobenzyl ether (**2e**) was tolerated under these coupling conditions and offers versatile synthetic functionality for further elaboration. In addition, 2,2′-oxybis(methylene)dinaphthalene (**2i**) smoothly underwent this coupling reaction to generate the corresponding product **3i**. Unfortunately, dialkyl ethers and diallylic ethers were found to be unreactive and did not provide the corresponding products.

To further explore the substrate scope and limitation of this process, a broad range of arenes with directing groups were screened to couple with dibenzyl ether (**2a**), as shown in Table 3. The reaction of *para*-substituted *O*-methyl ketoximes **1c** and **1d** found to be favored in the acylation reaction, affording the corresponding products **4c** and **4d** in high yields, whereas **1e** with a strong electron-withdrawing group (CF_3) at the *para* position was found to be relatively less reactive under these reaction conditions. It should be noted that the reaction exclusively afforded the monoacylated products in all cases, and no bisacylation products were observed by ^1H NMR or GC–MS analysis. The acylation of *meta*-substituted *O*-methyl ketoximes preferentially occurred at the less sterically hindered *ortho* position to afford the corresponding products **3f**, **3g**, and **3i** as single regioisomers. However, *m*-fluoroacetophenone *O*-methyl oxime (**1h**) afforded a mixture of regioisomers **4h** (48%) and **4h′** (24%) at the C-6 and C-2 positions, respectively. These results suggest that steric effects of the substrate strongly interfere with the formation of the cyclopalladated intermediate. In addition, this transformation also showed good reactivity toward *ortho*-substituted *O*-methyl ketoxime **1j.** Aldoxime **1k** provided the corresponding product **4k** with significantly decreased reactivity. Notably, in the case of benzophenone **1l** with four *ortho*-C–H bonds, only monoacylation took place, providing the corresponding product **4l** in 72% yield. However, unsymmetrical benzophenone *O*-methyl oxime **1m** provided no significant distribution of products **4m** and **4m′**. After successful exploration of the scope of oximes in the direct acylation, we turned our attention

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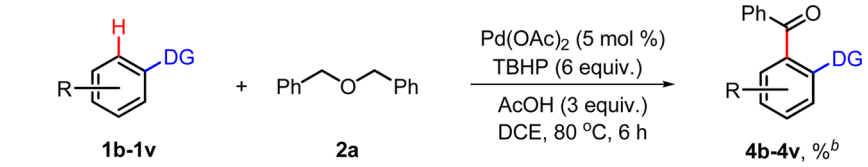
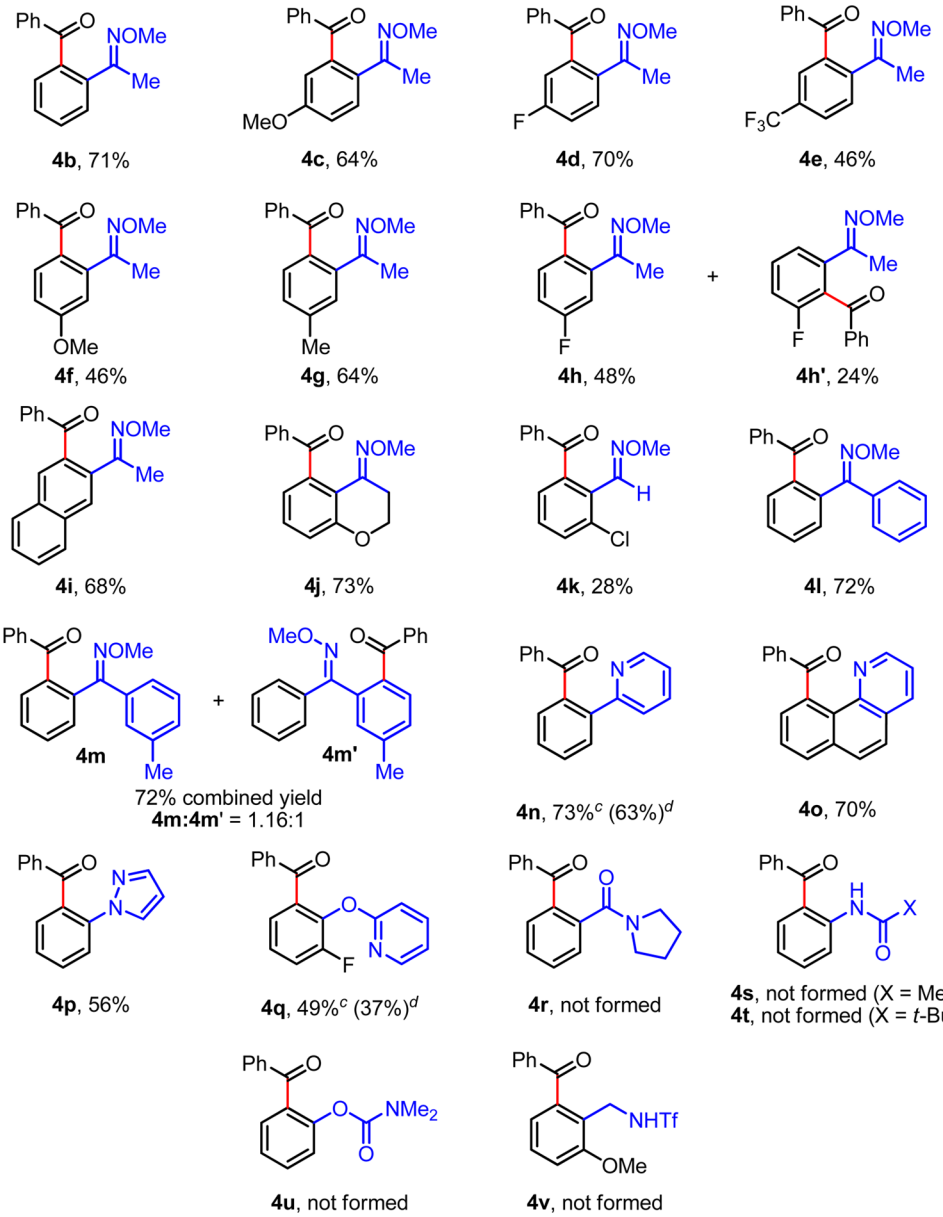
Table 3. Scope of Arenes with Various Directing Groups[a]





[a]Reaction conditions: **1** (0.3 mmol), **2a** (0.9 mmol), $Pd(OAc)_2$ (5 mol %), TBHP (6 equiv), AcOH (3 equiv), and DCE (1 mL) at 80 °C for 6 h in pressure tubes. [b]Determined by flash column chromatography. [c]20 h. [d]Without AcOH.

to substrates bearing various heterocyclic directing groups. We were pleased to see that representative directing groups such as 2-pyridine, quinoline, and 2-pyrazol (**1n−q**) facilitated the *ortho*-C−H acylation under identical reaction conditions. Notably, acylated product **4q** can be readily converted to the corresponding *o*-acylphenol by cleavage of the pyridinyl moiety.[5c] In contrast, a wide range of substrates **1r−v** forming five- or six-membered palladacycle intermediates failed to deliver our desired products under the present reaction conditions.

To gain mechanistic insight, a series of competition experiments were performed, as shown in Schemes 1 and 2. First, an intermolecular competition experiment between dibenzylic ethers **2a** and **2b** was conducted under the standard reaction conditions. Exposure of *O*-methyl ketoxime **1a** to equimolar quantities of **2a** and **2b** provided a separable mixture of **3a** and **3b**, respectively, in 82% combined yield with a ratio of 1:2.4 (Scheme 1, eq 1). An intramolecular competition experiment employing unsymmetrical benzylic ether **2j** under otherwise identical conditions afforded a mixture of **3b** and **3c**

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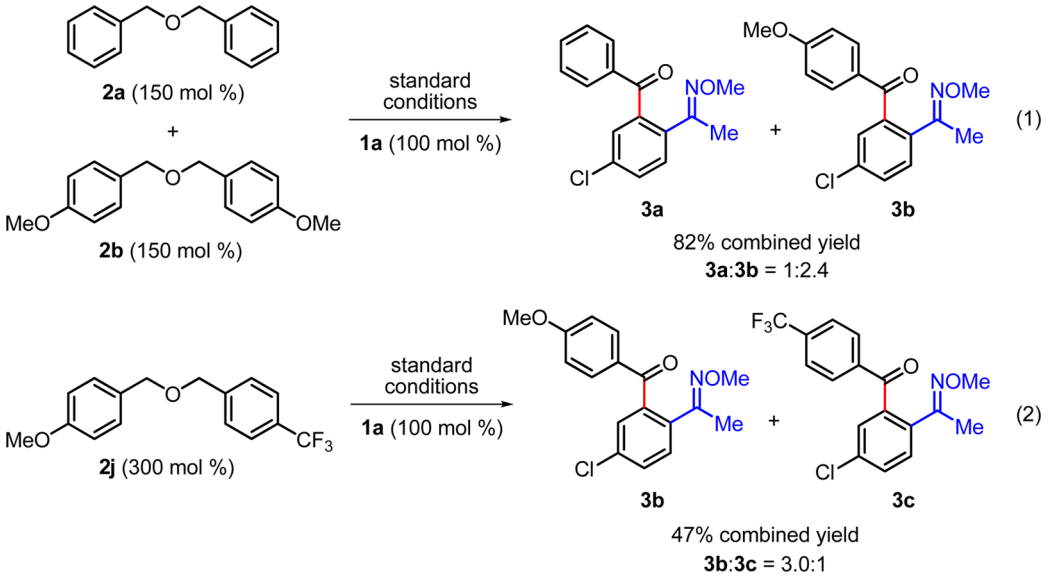
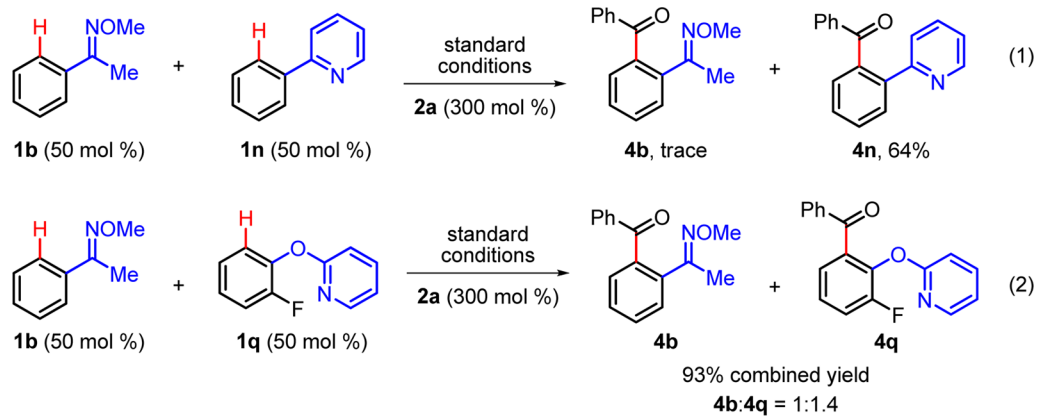
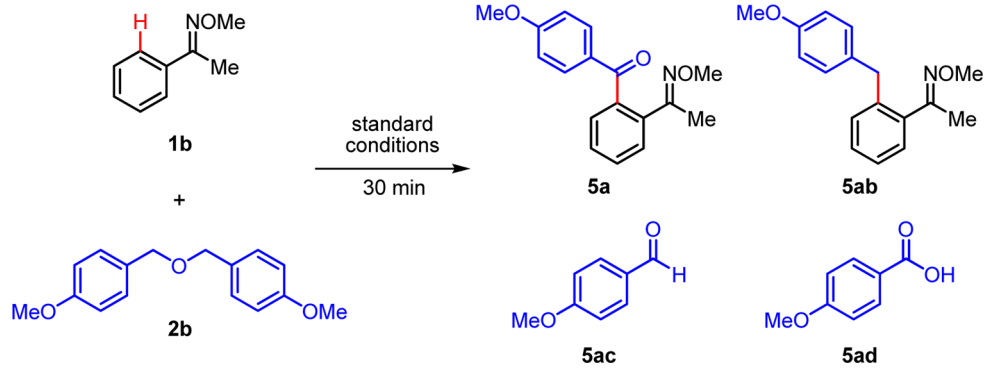
Scheme 1. Competition Experiments with Dibenzylic Ethers



Scheme 2. Intramolecular Competition Experiments between Arenes with Different Directing Groups



Scheme 3. Mechanistic Investigation by LC–MS Analysis



in 47% yield with a 3.0:1 ratio (Scheme 1, eq 2). These results indicate that the benzylic position with an electron-rich moiety may be more rapidly involved in the generation of the acyl radical intermediate.

To further examine the influence of the directing group on this process, intramolecular competition experiments between **1b** and **1n** were performed under the standard reaction conditions (Scheme 2, eq 1). Interestingly, no acylation of **1b** with an oxime directing group was observed, and 2-phenylpyridine (**1n**) exclusively furnished the corresponding product **4n** in 64% yield. In addition, intramolecular competition experiments between *O*-methyl ketoxime **1b** and phenoxypyridine **1q** afforded a mixture of acylated products **4b** and **4q** in 93% combined yield with a 1:1.4 ratio (Scheme 2, eq 2). These observations suggest that the pyridine directing group may coordinate more favorably to the palladium center rather than the oxime directing group irrespective of the kinetic stability of five- or six-membered palladacycles.

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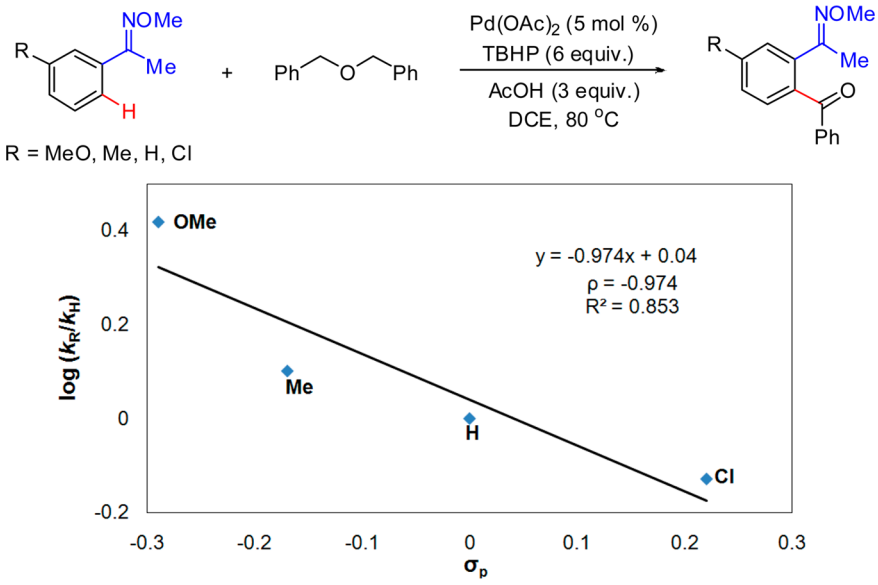
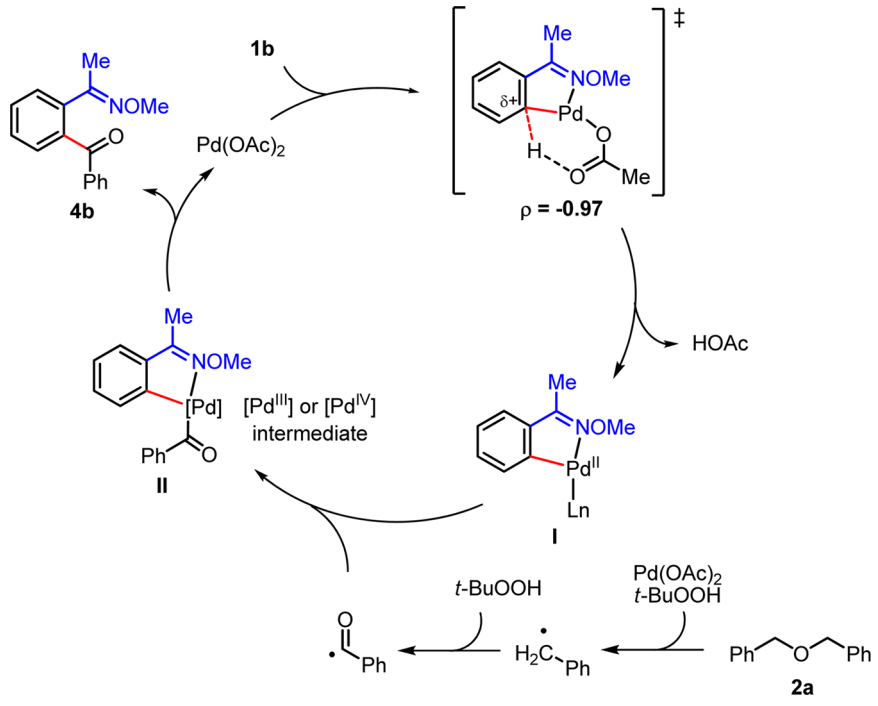


Figure 2. Hammett correlation studies.

Scheme 4. Plausible Reaction Mechanism



To support the mechanistic pathway for this reaction, some related experiments were conducted. The reaction between *O*-methyl ketoxime **1a** and dibenzyl ether (**2a**) in the presence of the radical scavenger ascorbic acid resulted in significantly reduced formation of the acylated product **3a** (<5% yield).[4e,20] This result indicates that the acylation reaction may proceed through a radical pathway. Dibenzylic ether **2b** in the presence of TBHP and $Pd(OAc)_2$ was converted to 4-anisaldehyde and 4-anisic acid as determined by LC−MS analysis. However, significantly decreased amounts of 4-anisaldehyde and 4-anisic acid were detected in the absence of $Pd(OAc)_2$.

A further acylation experiment involving **1b** and **2b** under the standard conditions was carried out to afford acylated compound **5a**, benzylated compound **5ab**, 4-anisaldehyde (**5ac**), and 4-anisic acid (**5ad**) as determined by LC−MS analysis (Scheme 3). These results can be rationalized if the radical initiator TBHP in the presence of the palladium catalyst can undergo C−O bond cleavage to generate benzylic radicals, which may be rapidly oxidized to provide benzoyl radicals in catalytic cycle. Another possible pathway could involve trapping of the benzylic radical intermediate by a palladacycle to afford benzylated product **5ab**, which could further undergo fast oxidation at the benzylic position to generate acylated product **5a**.[7a,21]

The effect of substituents on the reaction kinetics is often derived from the Hammett linear free energy relationship [$\log(k_R/k_H) = \rho\sigma$].[22] A Hammett correlation study on *meta*-substituted *O*-methyl oximes exhibited a linear free energy

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relationship (R^2 = 0.85) between the relative rate constant (k_R/k_H) and the substituent constant (σ) that resulted in a negative Hammett reaction constant (ρ) value of −0.97 (Figure 2). The small negative ρ value reveals that the catalyst−substrate interaction leads to the generation of a partial positive charge (δ+) on the arene ring, thus indicating a strong support for the electrophilic palladation mechanism.[23] Another possible pathway, concerted metalation−deprotonation (CMD), may not be operative in our Pd-catalyzed acylation reaction since this pathway is based on a positive ρ value in the Hammett correlation study, leading to a negative charge on the arene ring.[24]

On the basis of the above mechanistic investigation, a plausible reaction mechanism is depicted in Scheme 4. The oxidative acylation of *O*-methyl ketoxime **1b** is probably initiated by electrophilic palladation of the arene C−H bond to form the five-membered cyclopalladated complex **I**.[25] Dibenzyl ether (**2a**) is oxidized to give benzylic radicals through C−O bond cleavage by TBHP in the presence of the Pd catalyst, and these benzylic radicals can be rapidly converted to reactive benzoyl radicals.[26] The formed palladacycle **I** can react with a benzoyl radical to afford dimeric Pd(III) or Pd(IV) intermediate **II**,[27] which can undergo reductive elimination to give the desired product **4b** and regenerate the Pd(II) catalyst.

CONCLUSION

A directing-group-assisted palladium-catalyzed direct acylation of arenes using dibenzylic ethers as new acyl equivalents has been developed. This transformation has been applied to a wide range of substrates and typically proceeds with excellent levels of regio- and chemoselectivity as well as with high functional group tolerance. Further applications of this method to the synthesis of biologically active compounds are in progress.

EXPERIMENTAL SECTION

Typical Procedure for the Acylation of Arenes (1a−r) with Dibenzyl Ethers (2a−i). To an oven-dried sealed tube containing 1-(4-chlorophenyl)ethanone *O*-methyl oxime (**1a**) (55.1 mg, 0.3 mmol, 100 mol %), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 5 mol %), and dibenzyl ether (**2a**) (178.4 mg, 0.9 mmol, 300 mol %) in DCE (1 mL) were added TBHP (0.35 mL, 1.8 mmol, 600 mol %, 5.0−6.0 M in decane) and AcOH (52 μL, 0.9 mmol, 300 mol %). The reaction mixture was allowed to stir at 80 °C for 6 h, cooled to room temperature, and evaporated onto silica gel. Purification of the product by flash column chromatography (SiO_2, *n*-hexanes/EtOAc = 15:1) provided **3a** (73.5 mg, 0.255 mmol) in 85% yield.

(5-Chloro-2-(1-(methoxyimino)ethyl)phenyl)(phenyl)-methanone (3a). 73.3 mg (85%); colorless oil; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.70 (dd, J = 8.3, 1.3 Hz, 2H), 7.69−7.40 (m, 6H), 3.64 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 196.0, 152.8, 140.3, 137.6, 134.8, 134.6, 132.9, 130.1, 129.3, 128.9, 128.8, 128.4, 61.8, 14.1; IR (KBr) υ 2936, 1671, 1594, 1479, 1449, 1369, 1315, 1283, 1179, 1105, 1048, 827 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{14}ClNO_2$ $[M]^+$ 287.0713, found 287.0713.

(5-Chloro-2-(1-(methoxyimino)ethyl)phenyl)(4-methoxyphenyl)methanone (3b). 64.8 mg (68%); colorless sticky solid; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.69 (dd, J = 6.9, 2.1 Hz, 2H), 7.47−7.39 (m, 3H), 6.89 (dd, J = 6.9, 2.1 Hz, 2H), 3.86 (s, 3H), 3.67 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 194.8, 163.5, 153.1, 140.7, 134.7, 134.6, 131.8, 130.4, 129.8, 129.1, 128.7, 113.7, 61.8, 55.5, 14.4; IR (KBr) υ 2934, 1601, 1510, 1457, 1315, 1254, 1174, 1046, 946, 898, 818, 774 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{16}ClNO_3$ $[M]^+$ 317.0819, found 317.0815.

(5-Chloro-2-(1-(methoxyimino)ethyl)phenyl)(4-(trifluoromethyl)phenyl)methanone (3c). 62.9 mg (59%); yellow solid; mp = 106.5−110.6 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.79 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H), 7.54−7.43 (m, 2H), 7.42 (s, 1H), 3.62 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 194.8, 152.4, 14.6, 139.6, 135.2, 134.3, 130.5, 129.3, 12.8, 127.6, 125.5, 123.5 (q, J_{C-F} = 270.2 Hz), 61.8, 13.7; IR (KBr) υ 2928, 1682, 1589, 1412, 1325, 1271, 1166, 1127, 1067, 902, 856, 826, 776 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{13}ClF_3NO_2$ $[M]^+$ 355.0587, found 355.0579.

(5-Chloro-2-(1-(methoxyimino)ethyl)phenyl)(4-fluorophenyl)methanone (3d). 69.7 mg (76%); light-yellow solid; mp = 95.3−98.2 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.72 (q, J = 3.5 Hz, 2H), 7.49 (q, J = 6.2 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.40 (d, J = 2.2 Hz, 1H), 7.08 (t, J = 8.5 Hz, 2H), 3.63 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 194.5, 165.5 (d, J_{C-F} = 252.9 Hz), 152.6, 140.1, 134.9, 134.4, 134.0 (d, J_{C-F} = 2.4 Hz), 131.8 (d, J_{C-F} = 9.1 Hz), 130.2, 129.0, 128.7, 115.5 (d, J_{C-F} = 22.2 Hz), 61.8, 14.0; IR (KBr) υ 2936, 1723, 1670, 1599, 1508, 1411, 1364, 1263, 1223, 1153, 1047, 956, 824, 773 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{13}ClFNO_2$ $[M]^+$ 305.0619, found 305.0613.

(4-Bromophenyl)(5-chloro-2-(1-(methoxyimino)ethyl)-phenyl)methanone (3e). 60.5 mg (55%); brown solid; mp = 119.8−127.5 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.56−7.50 (m, 5H), 7.45 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 2.1 Hz, 1H), 3.64 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 194.9, 152.5, 139.8, 136.4, 135.0, 134.4, 131.7, 130.6, 130.3, 128.9, 128.8, 127.9, 61.8, 13.9; IR (KBr) υ 2978, 1710, 1591, 1487, 1363, 1266, 1195, 1011, 896, 813, 756 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{13}BrClNO_2$ $[M]^+$ 364.9818, found 364.9811.

(5-Chloro-2-(1-(methoxyimino)ethyl)phenyl)(*m*-tolyl)-methanone (3f). 43.4 mg (48%); colorless oil; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.53−7.43 (m, 5H), 7.35−7.28 (m, 2H), 3.67 (s, 3H), 2.37 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 196.2, 153.0, 140.5, 138.2, 137.5, 134.8, 134.7, 133.7, 130.1, 129.7, 129.0, 128.9, 128.3, 126.6, 61.8, 21.3, 14.3; IR (KBr) υ 2934, 1668, 1587, 1456, 1365, 1266, 1103, 1047, 969, 898, 763 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{16}ClNO_2$ $[M]^+$ 301.0870, found 301.0875.

(5-Chloro-2-(1-(methoxyimino)ethyl)phenyl)(*o*-tolyl)-methanone (3g). 76.0 mg (84%); yellow oil; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.48 (q, J = 5.7 Hz, 2H), 7.38−7.36 (m, 2H), 7.28 (q, J = 0.5 Hz, 1H), 7.20−7.14 (m, 1H), 7.12 (q, J = 7.3 Hz, 1H), 3.77 (s, 3H), 2.57 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.5, 154.5, 141.5, 139.5, 137.2, 135.7, 134.7, 131.8, 131.7, 130.6, 130.5, 129.6, 129.5, 125.2, 61.8, 21.3, 15.1; IR (KBr) υ 2933, 1717, 1668, 1600, 1573, 1457, 1364, 1244, 1101, 1047, 941, 894, 822, 750 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{16}ClNO_2$ $[M]^+$ 301.0870, found 301.0873.

(5-Chloro-2-(1-(methoxyimino)ethyl)phenyl)(2-chlorophenyl)methanone (3h). 39.6 mg (41%); white solid; mp = 94.3−97.2 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.53−7.50 (m, 2H), 7.41 (q, J = 4.3 Hz, 3H), 7.36 (d, J = 8.3 Hz, 1H), 7.30−7.28 (m, 1H), 3.84 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 194.3, 154.6, 140.0, 137.3, 136.0, 134.9, 132.6, 132.4, 131.4, 131.3, 130.9, 130.1, 129.8, 126.5, 62.0, 15.2; IR (KBr) υ 2932, 1682, 1588, 1435, 1317, 1292, 1239, 1102, 1047, 944, 897, 812, 757 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{13}Cl_2NO_2$ $[M]^+$ 321.0323, found 321.0326.

(5-Chloro-2-(1-(methoxyimino)ethyl)phenyl)(naphthalen-2-yl)methanone (3i). 49.6 mg (49%); yellow sticky solid; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.06−7.84 (m, 5H), 7.63−7.48 (m, 5H), 3.60 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 196.0, 152.9, 140.5, 135.5, 135.0, 134.9, 134.7, 132.4, 131.2, 130.2, 129.5, 129.1, 129.0, 128.5, 128.4, 127.9, 126.8, 124.7, 61.8, 14.2; IR (KBr) υ 2932, 1718, 1669, 1573, 1457, 1364, 1244, 1101, 1047, 941, 894, 822, 752 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{20}H_{16}ClNO_2$ $[M]^+$ 337.0870, found 337.0862.

(2-(1-(Methoxyimino)ethyl)phenyl)(phenyl)methanone (4b). 53.9 mg (71%); light-yellow solid; mp = 93.5−99.2 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.71 (dd, J = 8.3, 1.3 Hz, 2H), 7.54−7.44 (m, 5H), 7.39 (t, J = 8.2 Hz, 2H), 3.67 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.6, 154.0, 138.9, 138.2, 136.4, 132.6, 130.2, 129.3, 129.0, 128.6, 128.3, 127.7, 61.7, 14.4; IR (KBr) υ 2935, 1668, 1597,

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1449, 1367, 1313, 1286, 1154, 1048, 928 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{15}NO_2$ $[M]^+$ 253.1103, found 253.1102.

(5-Methoxy-2-(1-(methoxyimino)ethyl)phenyl)(phenyl)-methanone (4c). 54.4 mg (64%); colorless oil; ^1H NMR (700 MHz, $CDCl_3$) δ 7.70 (dd, J = 8.3, 1.2 Hz, 2H), 7.50 (t, J = 7.3 Hz, 1H), 7.41 (d, J = 8.6 Hz, 1H), 7.38 (t, J = 8.2 Hz, 2H), 7.04 (dd, J = 8.6, 2.6 Hz, 1H), 6.98 (d, J = 2.7 Hz, 1H), 3.83 (s, 3H), 3.62 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.3, 159.8, 153.3, 140.3, 138.1, 132.5, 129.2, 128.9, 128.6, 128.2, 115.9, 114.0, 61.5, 55.6, 14.2; IR (KBr) υ 2937, 1669, 1601, 1497, 1414, 1367, 1288, 1177, 1122, 1040, 896 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{17}NO_3$ $[M]^+$ 283.1208, found 283.1212.

(5-Fluoro-2-(1-(methoxyimino)ethyl)phenyl)(phenyl)-methanone (4d). 56.9 mg (70%); yellow solid; mp = 94.6−98.2 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 7.63 (dd, J = 8.3, 1.2 Hz, 2H), 7.46 (t, J = 7.4 Hz, 1H), 7.42−7.40 (m, 1H), 7.34 (t, J = 8.2 Hz, 2H), 7.16−7.13 (m, 1H), 7.11 (dd, J = 8.4, 2.6 Hz, 1H), 3.58 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 196.0, 162.5 (d, J_{C-F} = 247.4 Hz), 152.9, 140.9 (d, J_{C-F} = 6.4 Hz), 137.6, 132.9, 130.3, 129.6 (d, J_{C-F} = 7.5 Hz), 129.3, 128.4, 117.0 (d, J_{C-F} = 21.6 Hz), 116.2 (d, J_{C-F} = 24.0 Hz), 61.7, 14.3; IR (KBr) υ 2937, 1671, 1600, 1578, 1492, 1408, 1369, 1318, 1274, 1178, 1070, 976, 828 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{14}FNO_2$ $[M]^+$ 271.1009, found 271.1009.

(2-(1-(Methoxyimino)ethyl)-5-(trifluoromethyl)phenyl)-(phenyl)methanone (4e). 44.3 mg (46%); yellow oil; ^1H NMR (700 MHz, $CDCl_3$) δ 7.78 (d, J = 8.1 Hz, 1H), 7.71−7.67 (m, 3H), 7.63 (d, J = 8.1 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 8.2 Hz, 2H), 3.66 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 196.1, 152.7, 139.6, 139.5, 137.4, 133.0, 130.7 (q, J_{C-F} = 32.9 Hz), 129.3, 128.5, 128.1, 126.8 (q, J_{C-F} = 3.0 Hz), 125.8 (q, J_{C-F} = 3.0 Hz), 123.6 (q, J_{C-F} = 270.8 Hz), 62.0, 14.1; IR (KBr) υ 2939, 1673, 1450, 1339, 1269, 1175, 1130, 1092, 1048, 840 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{14}F_3NO_2$ $[M]^+$ 321.0977, found 321.0972.

(4-Methoxy-2-(1-(methoxyimino)ethyl)phenyl)(phenyl)-methanone (4f). 39.0 mg (46%); colorless oil; ^1H NMR (700 MHz, $CDCl_3$) δ 7.67 (dd, J = 8.2, 1.2 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.38 (t, J = 8.1 Hz, 2H), 6.95 (d, J = 2.5 Hz, 2H), 6.93 (dd, J = 8.4, 2.5 Hz, 1H), 3.87 (s, 3H), 3.71 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.1, 161.5, 155.0, 139.5, 138.9, 132.5, 131.9, 131.3, 129.6, 128.4, 114.2, 113.6, 61.9, 55.8, 15.4; IR (KBr) υ 2961, 2936, 1767, 1659, 1597, 1420, 1366, 1177, 1140, 1065, 1040, 1001, 928 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{17}NO_3$ $[M]^+$ 283.1208, found 283.1210.

(2-(1-(Methoxyimino)ethyl)-4-methylphenyl)(phenyl)-methanone (4g). 51.3 mg (64%); light-yellow solid; mp = 94.9−99.7 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 7.68 (dd, J = 8.3, 1.3 Hz, 2H), 7.94 (t, J = 7.4 Hz, 1H), 7.38−7.36 (m, 3H), 7.27 (br s, 1H), 7.25−7.23 (m, 1H), 3.68 (s, 3H), 2.42 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.8, 154.7, 140.9, 138.6, 137.0, 136.2, 132.6, 129.6, 129.5, 129.4, 128.7, 61.8, 21.7, 15.0; IR (KBr) υ 2935, 1732, 1663, 1597, 1447, 1365, 1254, 1179, 1071, 918 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{17}NO_2$ $[M]^+$ 267.1259, found 267.1257.

(4-Fluoro-2-(1-(methoxyimino)ethyl)phenyl)(phenyl)-methanone (4h). 39.0 mg (48%); white solid; mp = 142.5−148.8 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 7.67 (dd, J = 8.3, 1.2 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.46 (dd, J = 8.5, 5.7 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H), 7.17 (dd, J = 9.6, 2.5 Hz, 1H), 7.13 (dt, J = 8.3, 2.6 Hz, 1H), 3.67 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 196.7, 163.7 (d, J_{C-F} = 249.6 Hz), 153.3, 139.3 (d, J_{C-F} = 7.5 Hz), 138.3, 135.1 (d, J_{C-F} = 2.9 Hz), 132.9, 131.5 (d, J_{C-F} = 8.9 Hz), 129.5, 128.5, 11.6 (d, J_{C-F} = 21.8 Hz), 115.1 (d, J_{C-F} = 22.6 Hz), 62.0, 14.6; IR (KBr) υ 2934, 1728, 1667, 1580, 1464, 1364, 1265, 1204, 1049, 945 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{14}FNO_2$ $[M]^+$ 271.1009, found 271.1012.

(2-Fluoro-6-(1-(methoxyimino)ethyl)phenyl)(phenyl)-methanone (4h′). 19.5 mg (24%); colorless oil; ^1H NMR (700 MHz, $CDCl_3$) δ 7.78 (dd, J = 7.9, 0.7 Hz, 2H), 7.52 (t, J = 7.3 Hz, 1H), 7.46−7.43 (m, 1H), 7.41 (t, J = 7.8 Hz, 2H), 7.29 (dd, J = 7.8, 0.7 Hz, 1H), 7.14 (t, J = 8.9 Hz, 1H), 3.54 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 193.4, 159.9 (d, J_{C-F} = 246.8 Hz), 152.8 (d, J_{C-F} = 2.1 Hz), 138.2, 137.7 (d, J_{C-F} = 4.3 Hz), 133.2, 130.9 (d, J_{C-F} = 8.9 Hz), 129.8, 128.6, 126.9 (d, J_{C-F} = 19.2 Hz), 123.5 (d, J_{C-F} = 2.8 Hz), 116.4 (d, J_{C-F} = 21.5 Hz), 61.9, 13.8; IR (KBr) υ 2934, 1730, 1667, 1580, 1465, 1364, 1265, 1204, 1051, 945 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{14}FNO_2$ $[M]^+$ 271.1009, found 271.1010.

(3-(1-(Methoxyimino)ethyl)naphthalen-2-yl)(phenyl)-methanone (4i). 61.8 mg (68%); yellow solid; mp = 147.3−154.8 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.94 (s, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.76 (dd, J = 8.2, 1.2 Hz, 2H), 7.60−7.52 (m, 3H), 7.41 (t, J = 7.9 Hz, 2H), 3.71 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.3, 153.8, 138.4, 136.6, 133.6, 132.5, 132.4, 129.5, 129.4, 128.5, 128.3, 128.2, 127.9, 127.6, 127.4, 61.7, 14.2; IR (KBr) υ 2935, 1742, 1681, 1597, 1451, 1365, 1282, 1193, 1053, 872 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{20}H_{17}NO_2$ $[M]^+$ 303.1259, found 303.1261.

(4-(Methoxyimino)chroman-5-yl)(phenyl)methanone (4j). 61.6 mg (73%); white solid; mp = 103.9−105.9 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 7.75 (dd, J = 8.2, 1.2 Hz, 1H), 7.49 (t, J = 7.3 Hz, 1H), 7.38 (t, J = 8.9 Hz, 2H), 7.33 (t, J = 7.7 Hz, 1H), 7.01 (dd, J = 8.3, 1.2 Hz, 1H), 6.89 (dd, J = 7.3, 1.1 Hz, 1H), 4.22 (t, J = 6.2 Hz, 2H), 3.51 (s, 3H), 2.79 (t, J = 6.2 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.3, 156.9, 146.0, 138.9, 137.9, 132.4, 130.4, 129.0, 128.2, 120.9, 118.8, 116.2, 64.9, 61.7, 24.0; IR (KBr) υ 2937, 1673, 1595, 1469, 1318, 1279, 1145, 1079, 945, 850 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{17}H_{15}NO_3$ $[M]^+$ 281.1052, found 281.1049.

(*E*)-2-Benzoyl-6-chlorobenzaldehyde *O*-Methyl Oxime (4k). 23.0 mg (28%); colorless oil; ^1H NMR (700 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.70 (q, J = 7.1 Hz, 2H), 7.54−7.53 (m, 2H), 7.43−7.40 (m, 3H), 7.31−7.30 (m, 1H), 3.60 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 196.3, 143.8, 141.0, 137.4, 134.4, 132.9, 131.1, 130.2, 129.3, 128.4, 128.1, 127.0, 62.1; IR (KBr) υ 2936, 1674, 1597, 1448, 1314, 1280, 1136, 1048, 964, 804, 710 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{15}H_{12}ClNO_2$ $[M]^+$ 273.0557, found 273.0555.

(2-((Methoxyimino)(phenyl)methyl)phenyl)(phenyl)-methanone (4l). 68.1 mg (72%); white solid; mp = 91.5−98.0 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 7.72 (dd, J = 8.2, 1.2 Hz, 2H), 7.50−7.44 (m, 4H), 7.38 (t, J = 8.2 Hz, 2H), 7.31−7.27 (m, 6H), 3.69 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.5, 154.8, 140.0, 138.0, 135.9, 132.7, 132.6, 130.2, 129.8, 129.6, 129.4, 129.2, 129.0, 128.9, 128.2, 128.0, 62.2; IR (KBr) υ 2935, 2897, 2816, 1590, 1484, 1444, 1326, 1165, 1054, 1031, 982, 919, 878 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{21}H_{17}NO_2$ $[M]^+$ 315.1259, found 315.1257.

(2-((Methoxyimino)(*m*-tolyl)methyl)phenyl)(phenyl)-methanone (4m) and (2-((Methoxyimino)(phenyl)methyl)-4-methylphenyl)(phenyl)methanone (4m′). 71.1 mg (72%); colorless oil; ^1H NMR (700 MHz, $CDCl_3$) δ 7.72 (dd, J = 8.3, 1.2 Hz, 2H), 7.69 (dd, J = 8.3, 1.2 Hz, 2H), 7.48−7.43 (m, 5H), 7.39−7.32 (m, 5H), 7.29−7.26 (m, 7H), 7.19 (t, J = 7.6 Hz, 1H), 7.12 (br s, 1H), 7.10 (d, J = 8.2 Hz, 1H), 7.06 (d, J = 7.6 Hz, 2H), 7.03 (br s, 1H), 3.17 (s, 3H), 3.68 (s, 3H), 2.37 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.6, 197.5, 155.3, 155.1, 140.5, 140.1, 138.3, 137.7, 137.4, 136.4, 136.1, 132.9, 132.8, 132.7, 132.6, 130.9, 130.2, 130.1, 129.9, 129.8, 129.7, 129.6, 129.5, 129.4, 129.3, 129.0, 128.3, 128.2, 128.0, 126.8, 62.3, 21.6, 21.5; IR (KBr) υ 2859, 1665, 1630, 1597, 1491, 1447, 1314, 1285, 1150, 1049, 988, 926 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{22}H_{19}NO_2$ $[M]^+$ 329.1416, found 329.1419.

(Phenyl)(2-(pyridin-2-yl)phenyl)methanone (4n). 56.7 mg (73%); light-yellow solid; mp = 104.9−108.4 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.27 (d, J = 4.8 Hz, 1H), 7.69 (d, J = 7.7 Hz, 1H), 7.60 (dd, J = 8.3, 2.8 Hz, 2H), 7.53−7.50 (m, 1H), 7.48−7.40 (m, 4H), 7.29 (t, J = 7.3 Hz, 1H), 7.18 (t, J = 7.4 Hz, 2H), 6.91 (ddd, J = 7.4, 4.8, 1.1 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 198.3, 156.8, 149.1, 139.7, 139.5, 137.9, 136.3, 132.4, 130.2, 129.4, 129.1, 128.8, 128.5, 128.1, 122.7, 122.0; IR (KBr) υ 2923, 1665, 1586, 1448, 1426, 1313, 1280, 1151, 1023, 928, 755 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{18}H_{13}NO$ $[M]^+$ 259.0997, found 259.0999.

(Benzo[*h*]quinolin-10-yl)(phenyl)methanone (4o). 59.4 mg (70%); light-brown solid; mp = 145.5−148.3 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.52 (d, J = 4.3 Hz, 1H), 8.10 (dd, J = 7.9, 1.7 Hz,

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1H), 8.06 (dd, J = 7.9, 1.0 Hz, 1H), 7.91 (d, J = 8.7 Hz, 1H), 7.81−7.79 (m, 3H), 7.75 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 7.1 Hz, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.34−7.31 (m, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 198.7, 147.1, 144.7, 139.3, 139.0, 135.3, 133.8, 131.8, 129.2, 129.0, 128.7, 128.1, 127.9, 127.8, 127.0, 126.4, 126.2, 121.7; IR (KBr) υ 2924, 1668, 1511, 1422, 1314, 1273, 1175, 1005, 914, 892, 837, 730 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{20}H_{13}NO$ $[M]^+$ 283.0997, found 283.0995.

(2-(1*H*-Pyrazol-1-yl)phenyl)(phenyl)methanone (4p). 41.7 mg (56%); white solid; mp = 84.1−87.3 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.64−7.56 (m, 6H), 7.48−7.46 (m, 1H), 7.49−7.38 (m, 2H), 7.28 (t, J = 7.4 Hz, 2H), 6.16 (t, J = 2.1 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 195.9, 141.2, 138.6, 136.8, 133.8, 132.9, 131.3, 129.8, 129.6, 129.1, 128.2, 127.5, 123.3, 107.7; IR (KBr) υ 2923, 1668, 1602, 1519, 1450, 1393, 1274, 1151, 1046, 936, 800, 752 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{16}H_{12}N_2O$ $[M]^+$ 248.0950, found 248.0948.

(3-Fluoro-2-(pyridin-2-yloxy)phenyl)(phenyl)methanone (4q). 43.1 mg (49%); yellow sticky solid; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.01 (d, J = 4.9 Hz, 1H), 7.76 (dd, J = 8.4, 1.2 Hz, 2H), 7.54−7.51 (m, 1H), 7.47 (t, J = 7.4 Hz, 1H), 7.37−7.29 (m, 5H), 6.89 (ddd, J = 7.1, 4.9, 0.9 Hz, 1H), 6.68 (d, J = 8.2 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 194.1, 162.3, 154.7 (d, J_{C-F} = 249.7 Hz), 146.9, 139.2 (d, J_{C-F} = 27.0 Hz), 139.1, 137.1, 135.0, 133.1, 129.9, 128.1, 125.7 (d, J_{C-F} = 7.4 Hz), 125.0 (d, J_{C-F} = 4.1 Hz), 119.0 (d, J_{C-F} = 19.3 Hz), 118.7, 110.7; IR (KBr) υ 2939, 2830, 1669, 1597, 1463, 1429, 1271, 1190, 1143, 1068, 887, 777 cm^{-1}; HRMS (quadrupole, EI) m/z calcd for $C_{18}H_{12}FNO_2$ $[M]^+$ 293.0852, found 293.0851.

■ ASSOCIATED CONTENT

Supporting Information

Spectroscopic data for all compounds. 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) For recent reviews of C−H bond activation, see: (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (b) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (c) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (d) Wencel-Delord, J.; Dröge, T.; Kiu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (e) Baudoin, O. *Chem. Soc. Rev.* **2011**, *40*, 4902. (f) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (g) Bras, J. L.; Muzart, J. *Chem. Rev.* **2011**, *111*, 1170. (h) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236. (i) Mousseau, J. J.; Charette, A. B. *Acc. Chem. Res.* **2013**, *46*, 412. (j) Guobing, Y.; Xiangmei, W.; Minghua, Y. *Org. Biomol. Chem.* **2013**, *11*, 5588.

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

(3) For selected reviews of catalytic dehydrogenative cross-coupling, see: (a) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (b) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (c) Scheuermann, C. J. *Chem.—Asian J.* **2010**, *5*, 436.

(4) For selected examples of C−H acylation using aldehydes, see: (a) Jia, X.; Zhang, S.; Wang, W.; Luo, F.; Cheng, J. *Org. Lett.* **2009**, *11*, 3120. (b) Park, J.; Park, E.; Kim, A.; Lee, Y.; Chi, K.-W.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Org. Lett.* **2011**, *13*, 4390. (c) Sharma, S.; Park, E.; Park, J.; Kim, I. S. *Org. Lett.* **2012**, *14*, 906. (d) Sharma, S.; Park, J.; Park, E.; Kim, A.; Kim, M.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Adv. Synth. Catal.* **2013**, *355*, 332. (e) Chan, C.-W.; Zhou, Z.; Chan, A. S. C.; Yu, W.-Y. *Org. Lett.* **2010**, *12*, 3926. (f) Yang, Y.; Zhou, B.; Li, Y. *Adv. Synth. Catal.* **2012**, *354*, 2916. (g) Sharma, S.; Kim, A.; Park, J.; Kim, M.; Kwak, J. H.; Jung, Y. H.; Park, J. S.; Kim, I. S. *Org. Biomol. Chem.* **2013**, *11*, 7869.

(5) For selected examples of C−H acylation using alcohols, see: (a) Xiao, F.; Shuai, Q.; Zhao, F.; Baslé, O.; Deng, G.; Li, C.-J. *Org. Lett.* **2011**, *13*, 1614. (b) Park, J.; Kim, A.; Sharma, S.; Kim, M.; Park, E.; Jeon, Y.; Lee, Y.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Org. Biomol. Chem.* **2013**, *11*, 2766. (c) Kim, M.; Sharma, S.; Park, J.; Kim, M.; Choi, Y.; Jeon, Y.; Kwak, J. H.; Kim, I. S. *Tetrahedron* **2013**, *69*, 6552. (d) Sharma, S.; Kim, M.; Park, J.; Kim, M.; Kwak, J. H.; Jung, Y. H.; Oh, J. S.; Lee, Y.; Kim, I. S. *Eur. J. Org. Chem.* **2013**, 6656.

(6) For selected examples of C−H acylation using α-oxocarboxylic acids, see: (a) Fang, P.; Li, M.; Ge, H. *J. Am. Chem. Soc.* **2010**, *132*, 11898. (b) Li, M.; Ge, H. *Org. Lett.* **2010**, *12*, 3464. (c) Wang, H.; Guo, L.-N.; Duan, X.-H. *Org. Lett.* **2012**, *14*, 4358. (d) Kim, M.; Park, J.; Sharma, S.; Kim, A.; Park, E.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Chem. Commun.* **2013**, *49*, 925. (e) Park, J.; Kim, M.; Sharma, S.; Park, E.; Kim, A.; Lee, S. H.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Chem. Commun.* **2013**, *49*, 1654. (f) Sharma, S.; Kim, A.; Park, E.; Park, J.; Kim, M.; Kwak, J. H.; Lee, S. H.; Jung, Y. H.; Kim, I. S. *Adv. Synth. Catal.* **2013**, *355*, 667. (g) Yu, L.; Li, P.; Wang, L. *Chem. Commun.* **2013**, *49*, 2368. (h) Li, H.; Li, P.; Zhao, Q.; Wang, L. *Chem. Commun.* **2013**, *49*, 9170. (i) Miao, J.; Ge, H. *Org. Lett.* **2013**, *15*, 2930.

(7) (a) Guin, S.; Rout, S. K.; Banerjee, A.; Nandi, S.; Patel, B. K. *Org. Lett.* **2012**, *14*, 5294. (b) Wu, Y.; Choy, P. Y.; Mao, F.; Kwong, F. Y. *Chem. Commun.* **2013**, *49*, 689.

(8) Zhou, W.; Li, H.; Wang, L. *Org. Lett.* **2012**, *14*, 4594.

(9) Lu, J.; Zhang, H.; Chen, X.; Liu, H.; Jiang, Y.; Fu, H. *Adv. Synth. Catal.* **2013**, *355*, 529.

(10) Zhang, Q.; Yang, F.; Wu, Y. *Chem. Commun.* **2013**, *49*, 6837.

(11) Wuts, P. G. M.; Green, T. W. *Protective Groups in Organic Synthesis*, 4th ed.; Wiley & Sons: New York, 2007; pp 102−120.

(12) Markees, D. G. *J. Org. Chem.* **1958**, *23*, 1490.

(13) Mayhoub, A. S.; Talukdar, A.; Cushman, M. *J. Org. Chem.* **2010**, *75*, 3507.

(14) Pradhan, P. P.; Bobbitt, J. M.; Bailey, W. F. *J. Org. Chem.* **2009**, *74*, 9524.

(15) Strazzolini, P.; Runcio, A. *Eur. J. Org. Chem.* **2003**, 526.

(16) Nishiguchi, T.; Bougauchi, M. *J. Org. Chem.* **1989**, *54*, 3001.

(17) (a) Lee-Ruff, E.; Ablenas, F. J. *Can. J. Chem.* **1989**, *67*, 699. (b) Shen, Z.; Dai, J.; Xiong, J.; He, X.; Mo, W.; Hu, B.; Sun, N.; Hu, X. *Adv. Synth. Catal.* **2011**, *353*, 3031.

(18) Sun, C.-L.; Liu, N.; Li, B.-J.; Yu, D.-G.; Wang, Y.; Shi, Z.-J. *Org. Lett.* **2010**, *12*, 184.

(19) Thirunavukkarasu, V. S.; Parthasarathy, K.; Cheng, C.-H. *Angew. Chem., Int. Ed.* **2008**, *47*, 9462.

(20) Warren, J. M.; Mayer, J. M. *J. Am. Chem. Soc.* **2010**, *132*, 7784.

(21) For oxidation of benzylic C−H bonds by TBHP, see: (a) Brutchey, R. L.; Drake, I. J.; Bell, A. T.; Tilley, T. D. *Chem. Commun.* **2005**, 3736. (b) Yi, C. S.; Kwon, K.-H.; Lee, D. W. *Org. Lett.* **2009**, *11*, 1567.

(22) (a) Hammett, L. P. *J. Am. Chem. Soc.* **1937**, *59*, 96. (b) Bordwell, F. G.; Cornforth, F. J. *J. Org. Chem.* **1978**, *43*, 1763.

(23) (a) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050. (b) Joo, J. M.; Touré, B. B.; Sames, D. *J. Org. Chem.* **2010**, *75*, 4911.

(24) Sun, H.-Y.; Gorelsky, S. I.; Stuart, D. R.; Campeau, L.-C.; Fagnou, K. *J. Org. Chem.* **2010**, *75*, 8180.

(25) For a review of palladacycles, see: Dupont, J.; Consorti, C. S.; Spencer, J. *Chem. Rev.* **2005**, *105*, 2527.

(26) For a review of acyl radicals, see: (a) Chatgilialoglu, C.; Crich, D.; Komatsu, M.; Ryu, I. *Chem. Rev.* **1999**, *99*, 1991. For recent selected examples of acyl radicals, see: (b) Shi, Z.; Glorius, F. *Chem. Sci.* **2013**, *4*, 829. (c) Liu, Z.; Zhang, J.; Chen, S.; Shi, E.; Xu, Y.; Wan, X. *Angew. Chem., Int. Ed.* **2012**, *51*, 3231.
(27) For a selected example of a Pd(III) intermediate, see: (a) Neufeldt, S. R.; Sanford, M. S. *Adv. Synth. Catal.* **2012**, *354*, 3517. For selected examples of Pd(IV) intermediates, see: (b) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177. (c) Muñiz, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9412. (d) Arnold, P. L.; Sanford, M. S.; Pearson, S. M. *J. Am. Chem. Soc.* **2009**, *131*, 13912.