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Palladium-Catalyzed Oxidative Olefination of Phenols Bearing Removable Directing Groups under Molecular Oxygen

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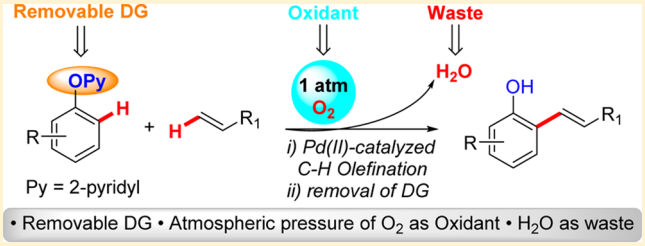
Supporting Information

ABSTRACT: An efficient Pd(II)-catalyzed oxidative olefination of phenols bearing removable directing groups with molecular oxygen as the sole oxidant has been developed. This reaction protocol provides an efficient and robust synthetic tool for the synthesis of *o*-alkenyl phenols under mild conditions.



Transition-metal-catalyzed oxidative cross-coupling reactions have emerged as powerful tools for the construction of new C−C and C−heteroatom bonds in terms of atom and step economy.[1] A number of oxidants such as inorganic salts, BQ, DDQ, IBX, and $PhI(OAc)_2$ have been widely employed in these transformations. However, in order to fulfill the requirements of green chemistry,[2] there is an increasing demand to use oxidants that are environmentally friendly and do not give rise to any waste products. Therefore, molecular oxygen is recognized as the ideal oxidant because it is environmentally friendly, inexpensive, and abundant and has a high efficiency per unit mass of oxidant.[3] However, oxidative functionalization of C−H bonds under mild conditions using atmospheric pressure of molecular oxygen as the sole oxidant still remains a very challenging field.[4]

Fujiwara and Moritani reported the pioneering work on alkenylation of electron-rich arenes with alkenes catalyzed by palladium complexes.[5] Recently, a large variety of oxidative olefinations of aromatic C−H bonds have been reported.[6] Alkenylation through the cleavage of two C−H bonds has become an important transformation in organic synthesis. However, in order to control the regioselectivity, directing groups are usually introduced; nevertheless, the practicality might be restricted when the directing groups cannot be easily removed from the products. Therefore, significant efforts have been directed toward the discovery of efficient and removable directing groups.[7]

Phenol derivatives are common and important structural motifs in bioactive natural products and pharmaceuticals.[8] Many phenol derivatives, such as phenol esters,[9a,b] phenol carbamates,[9c,d] and 2-phenoxypyridines,[9e,h] have been widely employed in C−H activation. Liu and Loh independently reported Rh(III)-catalyzed olefination of phenol carbamates,[9c,d] and more recently, Ackermann reported a ruthenium-catalyzed oxidative alkenylation of phenoxypyridines.[9e] However, stoichiometric amounts of metal oxidant [2.0 equiv of $Cu(OAc)_2 \cdot H_2O$] and additive (0.25 equiv of $AgSbF_6$) have to be used in these reactions, which is not synthetically efficient and beneficial from an environmental point of view. You reported an efficient method for the olefination of arenes with 2-pyridylmethyl as a removable directing group using oxygen as the oxidant,[10] but external additives such as 2 equiv of $KHCO_3$ and an amino acid ligand were still needed. Herein we report a palladium-catalyzed oxidative olefination of phenol derivatives with *molecular oxygen as the sole oxidant that does not require any other additives*. The directing group can be easily removed, providing *o*-alkenylated phenols (Figure 1).

We initiated our studies with the coupling of 2-phenoxypyridine (**1a**) and ethyl acrylate using $Pd(OAc)_2$ (10 mol %) as a catalyst in the presence of an oxidant under atmospheric pressure of O_2 at 100 °C. The desired product **2a** was isolated in 36% yield with a high level of selectivity when $Cu(OAc)_2$ was used as the oxidant (mono:di = 11:1; Table 1, entry 1). Switching to a silver oxidant, such as AgTFA, gave a slightly higher yield with more diolefinated product **2a′** (45%, mono:di = 3.1:1; entry 2). Encouraged by the result that the yield dropped when the atmosphere of O_2 was replaced by N_2 (entry 3), we began to use molecular oxygen as the sole oxidant. We were delighted to find that the yield improved to 60% with the monoolefinated product **2a** produced dominantly (entry 4). A variety of solvents such as DMAc, DMF, and $MeNO_2$ were screened, and the yield improved to 72% when $MeNO_2$ was used as the solvent. However, only moderate selectivity was obtained (entry 7). We recently found that the use of a coordinating solvent such as DMA or DMPU can improve the selectivity.[11] After further optimization, we were pleased to find that the monoolefination of **1a** occurred in 73% yield with high

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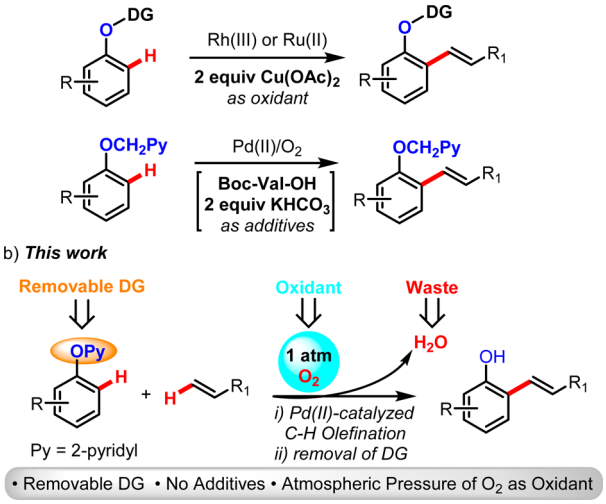


Figure 1. Trasition-metal-catalyzed oxidative olefination of phenol derivatives.

selectivity (mono:di = 13.6:1) when $MeNO_2$ and DMPU were used together (20:1 v/v) as cosolvents (entry 8). An attempt to conduct the reaction under ambient air led to a reduced yield (48%; entry 9).

With the optimized conditions in hand, we further explored the scope of this oxidative olefination reaction. As shown in Table 2, a wide range of phenol derivatives were compatible with the optimized conditions and reacted efficiently with ethyl acrylate to give the corresponding olefinated products in moderate to high yields. Various methyl- and methoxy-substituted phenols could be olefinated to give the desired products in good yields (entries 1−3 and 5−6). However, the *o*-methoxyphenol derivative gave a reduced yield (**2e**, 8%; entry 4), which might be due to weak coordination of the *o*-methoxy group with palladium. Chloro- and trifluoromethoxy-substituted phenols were also compatible with the optimized conditions, albeit affording the products in reduced yields (entries 7−9). Reasonably, 3,5-dimethylphenol derivative **1j** reacted slowly to give the desired product in only 38% yield because of the steric congestion at the *ortho* position (entry 10). The present reaction protocol was successfully extended to other acrylates. Ethyl acrylate, methyl acrylate, and *tert*-butyl acrylate reacted efficiently with **1m** under the optimized reaction conditions to give the corresponding products **2m**−**o** in good to excellent yields (entries 12−14). Unfortunately, styrene was unreactive under the present reaction conditions (entry 15). The presence of the pyridine directing group and the C−H bond at the *ortho* position were found to be essential for the reaction, since **1n**−**p** did not give the desired product, as shown at the bottom of Table 2.

The 2-pyridyl group could be easily removed using a previously reported protocol.[9f] As shown in Scheme 1, the olefinated product **2c** was deprotected by treating it with methyl trifluoromethanesulfonate (MeOTf) to form the corresponding pyridinium in toluene. Subsequently, the crude pyridinium was added into a refluxing Na/MeOH solution to generate **3c** in 68% yield for two steps. Furthermore, the alkenylated phenol **3c** could be converted into the corresponding *o*-alkylated phenol **4c** in 93% yield by hydrogenation.

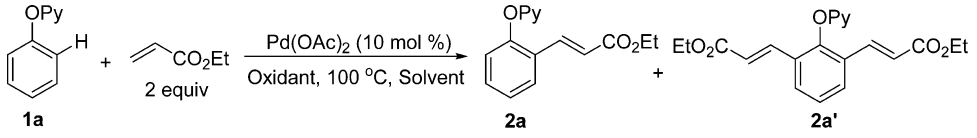
Finally, a plausible mechanism for the present palladium(II)-catalyzed oxidative olefination of 2-phenoxypyridine (**1a**) is proposed on the basis of previous studies (Scheme 2). Coordination of **1a** to palladium acetate is followed by C−H activation to form the dimeric palladacycle **A**.[9g,10] Subsequently, the olefin coordinates with palladacycle **A** via ligand exchange. Either the cyclized intermediate **C** or the uncyclized intermediate **D** is formed via olefin insertion, followed by *β*-hydride elimination to give the desired product **2a** and liberate Pd(0). The Pd(II) is regenerated from the oxidation of Pd(0) by molecular oxygen. DMPU can possibly act as a ligand to improve the monoselectivity and prevent the aggregation of Pd(0).[11]

In conclusion, we have developed a simple and efficient palladium-catalyzed direct C−H olefination of phenol derivatives with a readily removable directing group. This protocol can proceed well with oxygen at atmospheric pressure as the sole oxidant without the need of any other additives, providing an expeditious strategy for the synthesis of *o*-alkenyl or *o*-alkyl phenols.

EXPERIMENTAL SECTION

General Information. Dioxane was dried by sodium and freshly distilled. The other materials and solvents were purchased from commercial suppliers and used without additional purification. NMR spectra were recorded at 400 MHz (^{1}H) and 100 MHz (^{13}C) using

Table 1. Optimization of the Reaction Conditions[a]



Entry	Oxidant	*T* (°C)	Solvent	Yield (%)[d]
1[b]	$Cu(OAc)_2$	100	1,4-dioxane	36 (11:1)
2[b]	AgTFA	100	1,4-dioxane	45 (3.1:1)
3[c]	AgTFA	100	1,4-dioxane	36 (3.5:1)
4	O_2 (1 atm)	100	1,4-dioxane	60 (9:1)
5	O_2 (1 atm)	100	DMAc	65 (3.3:1)
6	O_2 (1 atm)	100	DMF	61 (7.7:1)
7	O_2 (1 atm)	100	$MeNO_2$	72 (5.5:1)
8	O_2 (1 atm)	100	$MeNO_2$:DMPU = 20:1	73 (13.6:1)
9	air (1 atm)	100	$MeNO_2$:DMPU = 20:1	48 (16:1)

[a]Reaction conditions: **1a** (0.2 mmol), $Pd(OAc)_2$ (10 mol %), ethyl acrylate (0.4 mmol), and oxidant in 2 mL of solvent at 100 °C for 24 h. [b]Under O_2. [c]Under N_2. [d]Yields of isolated products after chromatography. Values in parentheses are mono:di ratios.

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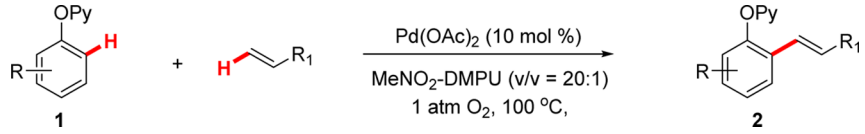
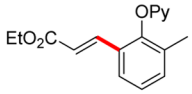
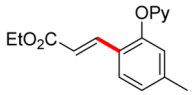
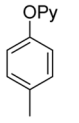
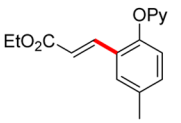
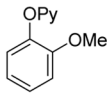
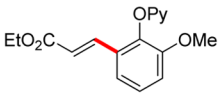
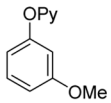
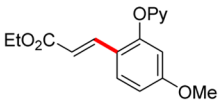
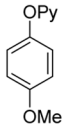
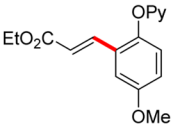
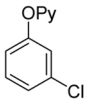
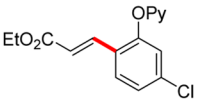
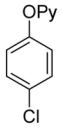
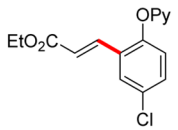
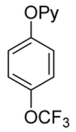
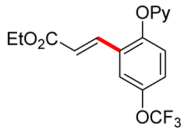
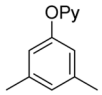
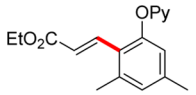
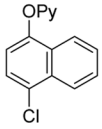
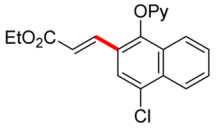
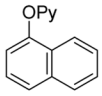
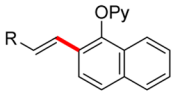
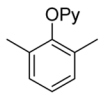
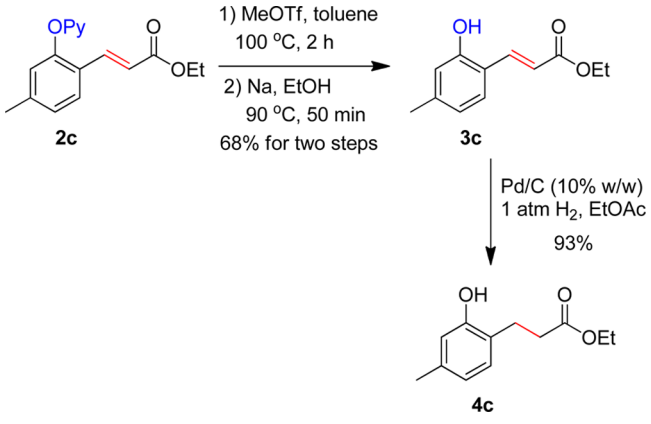
Table 2. Pd-Catalyzed Olefination of Phenol Derivatives[a]



Entry	Substrate	Product	Yield (%)[b]
1	 **1b**	 **2b**	62%
2	 **1c**	 **2c**	88%
3	 **1d**	 **2d**	60% (11:1)
4	 **1e**	 **2e**	8%
5	 **1f**	 **2f**	71%
6	 **1g**	 **2g**	62% (9.3:1)
7	 **1h**	 **2h**	41%
8	 **1i**	 **1i**	56% (7:1)
9	 **1j**	 **2j**	25%
10	 **1k**	 **2k**	38%
11	 **1l**	 **2l**	84%
12 13 14 15	 **1m**		**2m** R = CO_2Et 93% **2n** R = CO_2Me 69% **2o** R = CO_2t-Bu 79% **2p** R = Ph 0%
	 **1n**	 **1o**	 **1p**

[a]Reaction conditions: **1** (0.2 mmol), $Pd(OAc)_2$ (10 mol %), ethyl acrylate (0.4 mmol), and O_2 (1 atm) in $MeNO_2$/DMPU (20:1 v/v) at 100 °C. [b]Yields of isolated products after chromatography. Values in parentheses are mono:di ratios. When no ratio is given, a less than 5% yield of diolefinated product was observed.

Scheme 1. Removal of the Directing Group



TMS as an internal standard. Chemical shifts are given relative to $CDCl_3$ (7.26 ppm for ^1H NMR, 77.16 ppm for ^{13}C NMR). Data are represented as follows: chemical shift (multiplicity, coupling constant(s) in Hz, integration). Multiplicities are denoted as follows: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectroscopy data of the products were collected on an HRMS-TOF instrument using EI ionization.

General Procedure for the Olefination of 2-Phenoxypyridine Derivatives 1 with Acrylates. A mixture of substrate (0.2 mmol), $Pd(OAc)_2$ (10 mol %), ethyl acrylate (0.4 mmol), CH_3NO_2 (2.0 mL), and DMPU (0.1 mL) in a 50 mL Schlenk tube (purged with O_2) was heated at 100 °C for 24 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. Purification of the residue by chromatography with petroleum ether and EtOAc as the eluent provided the desired products.

***(E)*-Ethyl 3-(2-(Pyridin-2-yloxy)phenyl)acrylate (2a).** **2a** was obtained as a yellow oil (74 mg, 68% yield) according to the general procedure. ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (dd, J_1 = 4.8 Hz, J_2 = 2.0 Hz, 1H), 7.89 (d, J = 16.0 Hz, 1H), 7.74–7.66 (m, 2H), 7.4 (dt, J_1

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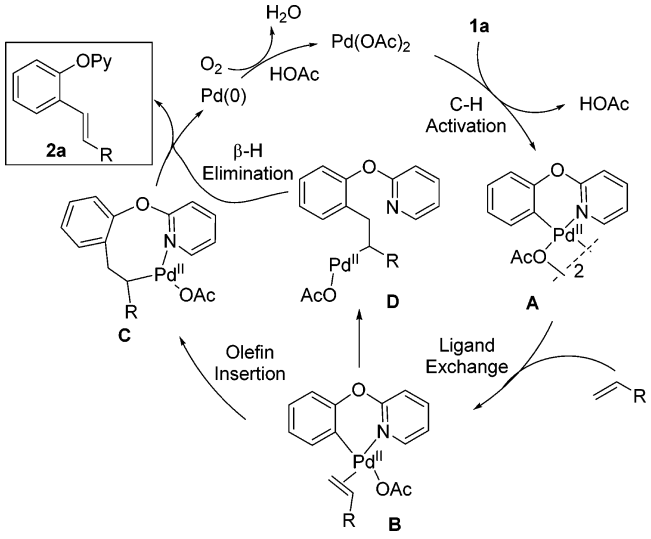
Scheme 2. Proposed Mechanism of Pd(II)-Catalyzed Oxidative Olefination Reaction



= 8.4 Hz, J_2 = 1.6 Hz, 1H), 7.23 (t, J = 7.4 Hz, 1H), 7.10 (d, J = 8.0 Hz, 1H), 7.02−6.97 (m, 2H), 6.47 (d, J = 16.4 Hz, 1H), 4.21 (q, J = 6.6 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 163.6, 153.1, 147.9, 139.8, 139.0, 131.3, 128.2, 127.6, 125.3, 122.5, 120.0, 119.0, 111.9, 60.6, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{16}H_{15}NO_3$ (M^+) 269.1052, found 269.1050.

(2*E*,2′*E*)-Diethyl 3,3′-(2-(Pyridin-2-yloxy)-1,3-phenylene)-diacrylate (2a′). **2a′** was obtained as a white solid (6 mg, 5% yield) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (ddd, J_1 = 5.0 Hz, J_2 = 2.0 Hz, J_3 = 0.8 Hz, 1H), 7.75−7.69, (m, 3H), 7.72 (d, 16.0 Hz, 2H), 7.31 (t, J = 7.8 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.98−6.94 (m, 1H), 6.42 (d, J = 16.4 Hz, 1H), 4.17 (q, J = 7.0 Hz, 4H), 1.26 (t, J = 7.0 Hz, 6H).

(*E*)-Ethyl 3-(3-Methyl-2-(pyridin-2-yloxy)phenyl)acrylate (2b). **2b** was obtained as a white solid (70 mg, 62% yield) according to the general procedure. Mp: 106−107 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (dd, J_1 = 5.0 Hz, J_2 =1.8 Hz, 1H), 7.79 (d, J = 16.0 Hz, 1H), 7.69 (dt, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 7.2 Hz, 1H), 7.19 (t, J = 7.2 Hz, 1H), 6.95−6.93 (m, 2H), 6.42 (d, J = 16.0 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 2.10 (s, 3H), 1.26 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 163.3, 150.9, 147.9, 139.7, 139.3, 133.2, 132.5, 128.4, 125.8, 125.5, 119.9, 118.3, 110.4, 60.5, 16.8, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{17}H_{17}NO_3$ (M^+) 283.1208, found 283.1205.

(*E*)-Ethyl 3-(4-Methyl-2-(pyridin-2-yloxy)phenyl)acrylate (2c). **2c** was obtained as a white solid (100 mg, 88% yield) according to the general procedure. Mp: 101−103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 4.0 Hz, 1H), 7.84 (d, J = 16.0 Hz, 1H), 7.70 (dt, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.04−6.95 (m, 3H), 6.90 (s, 1H), 6.43 (d, J = 16.0 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 2.35 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.7, 163.6, 152.9, 147.9, 142.2, 139.7, 139.0, 128.0, 126.3, 124.6, 122.9, 118.8, 60.4, 21.6, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{17}H_{17}NO_3$ (M^+) 283.1208, found 283.1200.

(*E*)-Ethyl 3-(5-Methyl-2-(pyridin-2-yloxy)phenyl)acrylate (2d). **2d** was obtained as a yellow oil (62 mg, 55% yield) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, J = 3.6 Hz, 1H), 7.84 (d, J = 16.4 Hz, 1H), 7.69 (dt, J_1 = 7.8 Hz, J_2 = 1.6 Hz, 1H), 7.47 (s, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.01−6.96 (m, 3H), 6.46 (d, J = 16.0 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 2.37 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 163.8, 150.7, 147.9, 139.7, 139.1, 134.9, 132.2, 127.2, 122.6, 119.6, 118.7, 111.6, 60.5, 21.0, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{17}H_{17}NO_3$ (M^+) 283.1208, found 283.1211.

(2*E*,2′*E*)-Diethyl 3,3′-(5-Methyl-2-(pyridin-2-yloxy)-1,3-phenylene)diacrylate (2d′). **2d′** was obtained as a white solid (8 mg, 5% yield) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 4.0 Hz, 1H), 7.74 (d, J = 8.8 Hz, 1H), 7.68 (d, J = 16.0 Hz, 2H), 7.51 (s, 2H), 7.06 (d, J = 8.4 Hz, 1H), 6.95 (t, J = 6.0 Hz, 1H), 6.40 (d, J = 16.0 Hz, 2H), 4.17 (q, J = 7.2 Hz, 4H), 2.40 (s, 3H), 1.26 (t, J = 7.0 Hz, 6H).

(*E*)-Ethyl 3-(3-Methoxy-2-(pyridin-2-yloxy)phenyl)acrylate (2e). **2e** was obtained as a yellow solid (10 mg, 8% yield) according to the general procedure. Mp: 113−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 4.0 Hz, 1H), 7.84 (d, J = 16.4 Hz, 1H), 7.67 (m, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.01 (t, J = 8.2 Hz, 1H), 6.95 (t, J = 6.0 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 4.19 (q, J = 7.0 Hz, 2H), 3.72 (s, 3H), 1.28 (t, J = 7.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.0, 163.5, 152.6, 147.6, 141.7, 139.5, 138.9, 129.3, 126.0, 120.4, 119.3, 118.4, 114.2, 110.6, 60.6, 56.2, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{17}H_{17}NO_4$ (M^+) 299.1158, found 299.1161.

(*E*)-Ethyl 3-(4-Methoxy-2-(pyridin-2-yloxy)phenyl)acrylate (2f). **2f** was obtained as a yellow oil (85 mg, 71%) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 3.6 Hz, 1H), 7.81 (d, J = 16.0 Hz, 1H), 7.72 (dt, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.03−6.97 (m, 2H), 6.79 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H), 6.61 (d, J = 2.0 Hz, 1H), 6.35 (d, J = 16.0 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 163.4, 162.2, 154.3, 148.0, 139.8, 138.8, 129.2, 120.2, 119.0, 117.3, 111.9, 111.8, 107.7, 60.4, 55.7, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{17}H_{17}NO_4$ (M^+) 299.1158, found 299.1155.

(*E*)-Ethyl 3-(5-Methoxy-2-(pyridin-2-yloxy)phenyl)acrylate (2g). **2g** was obtained as a yellow oil (57 mg, 56% yield) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 4.0 Hz, 1H), 7.81 (d, J = 16.4 Hz, 1H), 7.68 (dt, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.14 (d, J = 2.4 Hz, 1H), 7.05 (d, J = 9.2 Hz, 1H), 6.98−6.94 (m, 3H), 6.44 (d, J = 16.0 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 164.0, 156.7, 147.8, 146.5, 139.7, 138.9, 128.3, 124.0, 120.0, 118.6, 117.7, 111.7, 111.4, 60.6, 55.7, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{17}H_{17}NO_4$ (M^+) 299.1158, found 299.1157.

(2*E*,2′*E*)-Diethyl 3,3′-(5-Methoxy-2-(pyridin-2-yloxy)-1,3-phenylene)diacrylate (2g′). **2g′** was obtained as a yellow solid (10 mg, 6%) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 4.0 Hz, 1H), 7.72 (d, J = 7.2 Hz, 1H), 7.68 (d, J = 16.0 Hz, 2H), 7.21 (s, 2H), 7.05 (d, J = 8.4 Hz, 1H), 6.95 (t, J = 6.0 Hz, 1H), 6.41 (d, J = 16.0 Hz, 2H), 4.17 (q, J = 7.2 Hz, 4H), 3.87 (s, 3H), 1.26 (t, J = 7.2 Hz, 6H).

(*E*)-Ethyl 3-(4-Chloro-2-(pyridin-2-yloxy)phenyl)acrylate (2h). **2h** was obtained as a yellow solid (50 mg, 41% yield) according to the general procedure. Mp: 75−77 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 3.6 Hz, 1H), 7.82 (d, J = 16.0 Hz, 1H), 7.75 (dt, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.19 (dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H), 7.11 (d, J = 2.0 Hz, 1H), 7.07−7.01 (m, 2H), 6.45 (d, J = 16.0 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 162.9, 153.4, 147.9, 140.0, 137.9, 136.5, 128.9, 126.0, 122.7, 120.2, 119.5, 112.1, 60.7, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{16}H_{14}ClNO_3$ (M^+) 303.0662, found 303.0661.

(*E*)-Ethyl 3-(5-Chloro-2-(pyridin-2-yloxy)phenyl)acrylate (2i). **2i** was obtained as a yellow oil (60 mg, 49% yield) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 4.4 Hz, 1H), 7.79 (d, J = 16.0 Hz, 1H), 7.71 (dt, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H), 7.63 (d, J = 2.0 Hz, 1H), 7.35 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 7.06 (d, J = 8.8 Hz, 1H), 7.02 (t, J = 6.8 Hz, 2H), 6.46 (d, J = 16.0 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 163.2, 151.3, 147.8, 139.9, 137.6, 131.3, 130.6, 129.1, 127.7, 124.1, 121.0, 119.2, 111.9, 60.7, 14.3. HRMS (EI-TOF) m/z: calcd for $C_{16}H_{14}ClNO_3$ (M^+) 303.0662, found 303.0661.

(2*E*,2′*E*)-Diethyl 3,3′-(5-Chloro-2-(pyridin-2-yloxy)-1,3-phenylene)diacrylate (2i′). **2i′** was obtained as a white solid (11 mg, 7% yield) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, J = 4.0 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.65 (s, 2H), 7.63 (d, J = 16.8 Hz, 2H), 7.10 (d, J = 8.4 Hz, 1H), 6.99

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(t, J = 5.8 Hz, 1H), 6.40 (d, J = 16.0 Hz, 2H), 4.18 (q, J = 7.2 Hz, 4H), 1.26 (t, J = 7.0 Hz, 6H).

(*E*)-Ethyl 3-(2-(Pyridin-2-yloxy)-5-(trifluoromethoxy)phenyl)-acrylate (2j). **2j** was obtained as a white solid (37 mg, 25% yield) according to the general procedure. Mp: 42−44 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, J = 3.6 Hz, 1H), 7.82 (d, J = 16.0 Hz, 1H), 7.75 (dt, J_1 = 7.6 Hz, J_2 = 1.8 Hz, 1H), 7.50 (d, J = 1.6 Hz, 1H), 7.26−7.23 (m, 1H), 7.14 (d, J = 9.2 Hz, 1H), 7.06−7.02 (m, 2H), 6.46 (d, J = 16.0 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 163.1, 151.1, 147.8, 145.9, 140.0, 137.6, 128.9, 123.9, 123.8, 121.3, 120.6 (q, J_{C-F} = 256.0 Hz), 120.3, 119.4, 112.0, 60.8, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{17}H_{14}F_3NO_4$ (M^+) 353.0875, found 353.0868.

(*E*)-Ethyl 3-(2,4-Dimethyl-6-(pyridin-2-yloxy)phenyl)acrylate (2k). **2k** was obtained as a yellow oil (45 mg, 38% yield) according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 4.8 Hz, 1H), 7.76 (d, J = 16.4 Hz, 1H), 7.68 (t, J = 5.0 Hz, 1H), 6.98 (t, J = 6.0 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 6.90 (s, 1H), 6.74 (s, 1H), 6.42 (d, J = 16.4 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 2.43 (s, 3H), 2,29 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 163.4, 153.2, 148.0, 140.5, 139.6, 139.5, 138.4, 128.6, 124.0, 122.6, 120.8, 118.6, 111.8, 60.4, 21.4, 21.1, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{18}H_{19}NO_3$ (M^+) 297.1365, found 297.1359.

(*E*)-Ethyl 3-(4-Chloro-1-(pyridin-2-yloxy)naphthalen-2-yl)-acrylate (2l). **2l** was obtained as a white solid (115 mg, 84% yield) according to the general procedure. Mp: 161−163 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 5.2 Hz, 1H), 7.90 (d, J = 16.4 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.85 (s, 1H), 7.74 (dt, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.10 (d, J = 8.0 Hz, 1H), 6.98 (t, J = 6.0 Hz, 1H), 6.51 (d, J = 16.0 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 166.7, 164.2, 148.0, 147.9, 140.1, 137.6, 132.7, 129.8, 129.3, 128.5, 127.8, 125.2, 124.8, 123.8, 123.4, 120.7, 118.8, 110.5, 60.7, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{20}H_{16}ClNO_3$ (M^+) 353.0819, found 353.0817.

(*E*)-Ethyl 3-(1-(Pyridin-2-yloxy)naphthalen-2-yl)acrylate (2m). **2m** was obtained as a white solid (119 mg, 93% yield) according to the general procedure. Mp: 143−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 4.0 Hz, 1H), 8.00 (d, J = 16.0 Hz, 1H), 7.85 (t, J = 7.6 Hz, 2H), 7.75 (s, 2H), 7.72 (dt, J_1 = 7.8 Hz, J_2 = 1.6 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 6.96 (t, J = 5.4 Hz, 1H), 6.54 (d, J = 16.0 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 164.4, 148.9, 148.0, 139.9, 138.7, 135.8, 128.2, 128.1, 127.6, 127.0, 126.1, 124.3, 123.3, 119.9, 118.6, 110.3, 60.6, 14.4. HRMS (EI-TOF) m/z: calcd for $C_{20}H_{17}NO_3$ (M^+) 319.1208, found 319.1201.

(*E*)-Methyl 3-(1-(Pyridin-2-yloxy)naphthalen-2-yl)acrylate (2n). **2n** was obtained as a white solid (85 mg, 69% yield) according to the general procedure. Mp: 154−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 4.8 Hz, 1H), 8.01 (d, J = 16.4 Hz, 1H), 7.84 (t, J = 7.8 Hz, 2H), 7.75−7.69 (m, 3H), 7.50 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.96 (t, J = 6.0 Hz, 1H), 6.55 (d, J = 16.4 Hz, 1H), 3.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 164.4, 149.0, 148.0, 139.9, 138.9, 135.8, 128.2, 128.1, 127.6, 127.0, 126.2, 124.2, 123.3, 119.4, 118.6, 110.3, 51.8. HRMS (EI-TOF) m/z: calcd for $C_{19}H_{15}NO_3$ (M^+) 305.1052, found 305.1055.

(*E*)-*tert*-Butyl 3-(1-(Pyridin-2-yloxy)naphthalen-2-yl)acrylate (2o). **2o** was obtained as a white solid (110 mg, 79% yield) according to the general procedure. Mp: 119−121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 3.6 Hz, 1H), 7.91 (d, J = 16.0 Hz, 1H), 7.84 (d, J = 7.2 Hz, 2H), 7.77−7.69 (m, 3H), 7.49 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.96 (t, J = 6.8 Hz, 1H), 6.47 (d, J = 16.0 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 164.4, 148.8, 148.1, 139.9, 137.6, 135.7, 128.2, 127.4, 126.9, 126.1, 124.4, 123.3, 121.7, 118.5, 110.4, 80.6, 28.3. HRMS (EI-TOF) m/z: calcd for $C_{22}H_{21}NO_3$ (M^+) 347.1521, found 347.1521.

(*E*)-Ethyl 3-(2-Hydroxy-4-methylphenyl)acrylate (3c). **2c** (141 mg, 0.5 mmol) was dissolved in toluene (15 mL), and MeOTf was added under N_2. The reaction mixture was stirred under N_2 at 100 °C for 2 h. The reaction mixture was allowed to cool to ambient temperature. A white solid was obtained when the solvent was evaporated. The solid was dissolved in dry ethanol (5.0 mL) and was added under N_2 to a solution of Na (294 mg, 12 mmol) in dry ethanol (15 mL). The reaction mixture was heated at 80 °C for 15 min. The reaction mixture was allowed to cool to ambient temperature, and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 8:1) to yield **3c** (70 mg, 68%) as a white solid. Mp: 88−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 16.4 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 6.73 (d, J = 6.8 Hz, 1H), 6.65 (s, 1H), 6.56 (d, J = 16.4 Hz, 1H), 6.07 (s, 1H), 4.27 (q, J = 7.2 Hz, 2H), 2.31 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 155.2, 142.4, 140.3, 129.3, 122.1, 119.2, 117.8, 117.1, 60.6, 21.5, 14.5. HRMS (EI-TOF) m/z: calcd for $C_{12}H_{14}O_3$ (M^+) 206.0943, found 206.0943.

Ethyl 3-(2-Hydroxy-4-methylphenyl)propanoate (4c). To a solution of **3c** (41.3 mg, 0.2 mmol) in EtOAc was added 10% Pd/C (4.1 mg), and the reaction mixture was stirred under a hydrogen atmosphere for 6 h. The palladium catalyst was removed by filtration, and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 10:1) to yield **4c** (39 mg, 95%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (s, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.71 (s, 1H), 6.98 (d, J = 7.6 Hz, 1H), 4.14 (q, J = 7.2 Hz, 2H), 2.86 (t, J = 6.4 Hz, 2H), 2.68 (d, J = 6.4 Hz, 2H), 2.27 (s, 1H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 153.3, 137.1, 129.5, 123.4, 120.7, 117.0, 60.4, 34.6, 23.4, 20.1, 13.2. HRMS (EI-TOF) m/z: calcd for $C_{12}H_{16}O_3$ (M^+) 208.1099, found 208.1097.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details and spectral data for all new 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 selected reviews of catalytic C−H bond functionalization, see: (a) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (b) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (c) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (d) Sun, C. L.; Li, B. J.; Shi, Z. J. *Chem. Rev.* **2011**, *111*, 1293. (e) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (f) Kulkarni, A. A.; Daugulis, O. *Synthesis* **2009**, 4087.

(2) Anastas, P. T.; Eghbali, N. *Chem. Soc. Rev.* **2010**, *39*, 301.

(3) For recent reviews of reactions using molecular oxygen as an oxidant, see: (a) Shi, Z.; Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3381. (b) Wu, W.; Jiang, H. *Acc. Chem. Res.* **2012**, *45*, 1736. (c) Piera, J.; Bäckvall, J.-E. *Angew. Chem., Int. Ed.* **2008**, *47*, 3506. (d) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, *107*, 5318. (e) Sigman, M. S.; Jensen, D. R. *Acc. Chem. Res.* **2006**, *39*, 221.

(4) For selected recent examples of reactions using molecular oxygen as an oxidant, see: (a) Steinhoff, B. A.; Guzei, I. A.; Stahl, S. S. *J. Am. Chem. Soc.* **2004**, *126*, 11268. (b) Ueda, S.; Nagasawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6411. (c) Zhang, Y. H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 14654. (d) Izawa, Y.; Pun, D.; Stahl, S. S. *Science* **2011**, *333*, 209. (e) Liu, Q.; Wu, P.; Yang, Y.; Zeng, Z.; Liu, J.; Yi, H.; Lei, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 4666. (f) Zhang, C.; Feng, P.; Jiao, N. *J. Am. Chem. Soc.* **2013**, *135*, 15257. (g) Zhang, G.; Yang, L.; Wang, Y.; Xie, Y.; Huang, H. *J. Am. Chem. Soc.* **2013**, *135*, 8850. (h) Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 4457.

(5) (a) Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, *8*, 1119. (b) Fujiwara, Y.; Moritani, I.; Danno, S.; Asano, R.; Teranishi, S. *J. Am. Chem. Soc.* **1969**, *91*, 7166.

(6) For selected reviews, see: (a) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (b) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (c) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236. (d) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (e) Kozhushkov, S. I.; Ackermann, L. *Chem. Sci.* **2013**, *4*, 886.

(7) For recent examples of the use of removable directing groups, see: (a) Zhang, L.-Q.; Yang, S.; Huang, X.; You, J.; Song, F. *Chem. Commun.* **2013**, *49*, 8830. (b) Sarkar, D.; Melkonyan, F. S.; Gulevich, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2013**, *52*, 10800. (c) Chen, F.-J.; Zhao, S.; Hu, F.; Chen, K.; Zhang, Q.; Zhang, S.-Q.; Shi, B.-F. *Chem. Sci.* **2013**, *4*, 4187. (d) Chen, K.; Hu, F.; Zhang, S.-Q.; Shi, B.-F. *Chem. Sci.* **2013**, *4*, 3906. (e) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965. (f) García-Rubia, A.; Arrayás, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 6511. (g) Huang, C.; Gevorgyan, V. *J. Am. Chem. Soc.* **2009**, *131*, 10844. For selected reviews of the use of removable directing groups, see: (h) Wang, C.; Huang, Y. *Synlett* **2013**, *24*, 145. (i) Rousseau, G.; Breit, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 2450.

(8) Tyman, J. H. P. *Synthetic and Natural Phenols*; Elsevier: New York, 1996.

(9) (a) Dai, H.-X.; Li, G.; Zhang, X.-G.; Stepan, A. F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 7567. (b) Xiao, B.; Fu, Y.; Xu, J.; Gong, T.-J.; Dai, J.-J.; Yi, J.; Liu, L. *J. Am. Chem. Soc.* **2010**, *132*, 468. (c) Gong, T.-J.; Xiao, B.; Liu, Z.-J.; Wan, J.; Luo, D.-F.; Fu, Y.; Liu, L. *Org. Lett.* **2011**, *13*, 3235. (d) Feng, C.; Loh, T.-P. *Chem. Commun.* **2011**, *47*, 10458. (e) Ma, W.; Ackermann, L. *Chem.—Eur. J.* **2013**, *19*, 13925. (f) Ackermann, L.; Diers, E.; Manvar, A. *Org. Lett.* **2012**, *14*, 1154. (g) Chu, J.-H.; Lin, P.-S.; Wu, M.-J. *Organometallic* **2010**, *29*, 4058. (h) Gu, S.; Chen, C.; Chen, W. *J. Org. Chem.* **2009**, *74*, 7203.

(10) Cong, X.; You, J.; Gao, G.; Lan, J. *Chem. Commun.* **2013**, *49*, 662.

(11) Zhang, Q.; Chen, K.; Rao, W.-H.; Zhang, Y.; Chen, F.-J.; Shi, B.-F. *Angew. Chem., Int. Ed.* **2013**, *52*, 13588.

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