JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

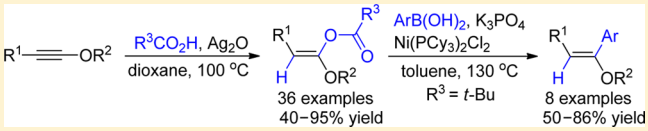
Silver-Catalyzed Regio- and Stereoselective Addition of Carboxylic Acids to Ynol Ethers

Jing Yin, Yihui Bai, Mengyi Mao, and Gangguo Zhu*

Department of Chemistry, Zhejiang Normal University, 688 Yingbin Road, Jinhua 321004, China

Supporting Information

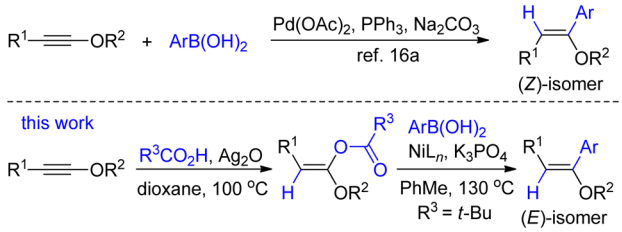
ABSTRACT: A silver-catalyzed *trans* addition of carboxylic acids to ynol ethers is described. The reaction has a broad scope with respect to carboxylic acids and ynol ethers, delivering (*Z*)-α-alkoxy enol esters in good yields with excellent regio- and stereoselectivity. Meaningfully, the Ni-catalyzed selective coupling of alkenyl C−OPiv bonds of (*Z*)-α-alkoxy enol esters with boronic acids enables a convenient route to the access of (*E*)-enol ethers. As such, the two-step procedure, consisted of a hydrocarboxylation and a subsequent Suzuki−Miyaura coupling, offers a formal *trans* hydroarylation of ynol ethers, thus providing a good complementary method to our previous report.



INTRODUCTION

Enol esters are versatile building blocks in organic synthesis and material science. Hence, the development of efficient and general methods for the preparation of these moieties is still of high interest. Specifically, the transition-metal-catalyzed addition of carboxylic acids to acetylenes appears to be an ideal protocol due to its high atom economy.[1,2] Various catalysts, including mercury,[3] ruthenium,[4] rhodium,[5] iridium,[6] palladium,[7] silver,[8] gold,[9] and rhenium,[10,11] have been described for promoting the transformation during the past decades. However, most of the previous reports are restricted to terminal alkynes. The examples on hydrocarboxylation of unsymmetric internal acetylenes are particularly rare,[7,12−14] mainly because of the difficulty in controlling the regio- and stereoselectivity. By means of a $Ru_3(CO)_{12}$/3PPh_3 catalyst system, a highly selective *cis* addition of carboxylic acids to aryl and trifluoromethyl group substituted unsymmetric internal alkynes has been accomplished by the groups of Kawatsura and Itoh.[12] Recently, Lam and co-workers demonstrated that carboxylic acids could add to ynamides, providing α-acyloxyenamides in a highly regio- and stereocontrolled manner.[13] We have initiated a project aiming at the exploration of new applications of ynol ethers,[15−18] including chloroallylation,[15] hydroarylation,[16] and hydroboration[17] processes. For example, a *cis* hydroarylation of ynol ethers with boronic acids as arylating reagents has been developed in our group, giving (*Z*)-enol ethers in high yields (Scheme 1).[16a] In contrast, the *trans* hydroarylation of ynol ethers has not been realized. Herein, we describe a silver-catalyzed stereospecific *trans* addition of carboxylic acids to ynol ethers, furnishing (*Z*)-α-alkoxy enol esters in high yields with excellent regio- and stereoselectivity. Further, the subsequent Ni-catalyzed Suzuki−Miyaura coupling[19] of alkenyl C−OPiv bonds[20] of (*Z*)-α-alkoxy enol esters enables the generation of (*E*)-enol ethers with excellent geometric purity. Notably, the two-step procedure displayed here offers a formal *trans* hydroarylation of ynol ethers, thus providing a good complementary method to our previous report.[16]

Scheme 1. Summary of This Work



RESULTS AND DISCCUSION

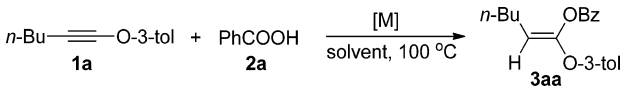
As a model system, the reaction between ynol ether **1a** and benzoic acid **2a** was first investigated. In the presence of 5 mol % of $Ru_3(CO)_{12}$, **3aa** was obtained in 31% yield after stirring in toluene at 100 °C for 10 h, and no other regio- and stereoisomers were observed by GC and NMR analysis (Table 1, entry 1). Further optimization of the catalyst indicated that Ag_2O served as the preferred catalyst for this reaction, affording **3aa** in 65% isolated yield (Table 1, entries 1−12). Pleasingly, the utilization of dioxane instead of toluene as the solvent increased the yield to 88%, whereas the reaction performed under an atmosphere of air resulted in a relatively lower yield (Table 1, entries 17 and 18). Therefore, the optimized conditions for regio- and stereoselective addition of carboxylic acids to ynol ethers comprised 5 mol % of Ag_2O as the catalyst, dioxane as the solvent, and at 100 °C under N_2 atmosphere for 10 h.

Under the optimized reaction conditions, we observed a broad scope with respect to benzoic acids (Table 2). In particular, 4-fluoro, 4-chloro, and 4-bromobenzoic acids

Received: July 17, 2014
Published: September 4, 2014

   dx.doi.org/10.1021/jo501615a | J. Org. Chem. 2014, 79, 9179−9185

Table 1. Optimization of the Reaction Conditions[a]



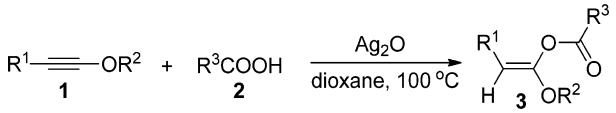
entry	[M]	solvent	yield (%)[b]
1	$Ru_3(CO)_{12}$	toluene	31
2	$ZnCl_2$	toluene	trace
3	CuCl	toluene	12
4	$Cu(OAc)_2$	toluene	17
5	Na_2CO_3	toluene	trace
6	Ag_2O	toluene	65
7	Ag_2CO_3	toluene	53
8	$AgNO_3$	toluene	20
9	AgOAc	toluene	18
10	AgOTf	toluene	trace
11	$PPh_3AuCl/AgOTf$	toluene	trace
12	$PPh_3AuCl/AgSbF_6$	toluene	trace
13	Ag_2O	THF	69
14	Ag_2O	$ClCH_2CH_2Cl$	82
15	Ag_2O	DMF	51
16	Ag_2O	NMP	63
17	Ag_2O	dioxane	88
18[c]	Ag_2O	dioxane	77

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.28 mmol), [M] (5 mol %), solvent (1 mL), under N_2, 100 °C, 10 h. [b]Isolated yield. [c]Under air atmosphere. Bz = benzoyl.

participated well in the present reaction, leaving the halide atoms untouched (Table 2, entries 1−3). However, reaction with 4-iodobenzoic acid as the substrate was sluggish under the same conditions; fortunately, the utilization of 1.2 equiv of Et_3N as the additive significantly improved the yield (Table 2, entry 4). A wide range of functional groups, including NO_2, CN, CO_2Me, Me, OMe, NH_2, OH, pyridyl, and thienyl functionalities, survived well under the reaction conditions, producing (*Z*)-α-alkoxy enol esters **3** in moderate to excellent yields with perfect regio- and stereocontrol, although the addition of Et_3N was also necessary for the transformation of **2j** and **2n** (Table 2, entries 5−14).

Besides benzoic acids, other carboxylic acids were also evaluated. For example, cinnamic acid gave rise to (*Z*)-α-alkoxy enol ester **3ap** in 85% yield under the reaction conditions (Table 2, entry 15). Phenylpropiolic acid (**2q**) was found to be almost unreactive under the standard conditions, probably due to the competitive interaction of the C−C triple bond of **2q** with the silver catalyst. We envisioned that increasing the amounts of Ag_2O might be able to facilitate the reaction. As expected, the use of 2.5 equiv of Ag_2O together with the addition of Et_3N (1.2 equiv) led to the desired product in 73% yield (Table 2, entry 16). As for HOAc, an excess use (5 equiv) of starting material was required for the full conversion (Table 2, entry 17). We were pleased to find that the reaction of pivalic acid with **1a** proceeded smoothly as well, providing the corresponding product in satisfactory yield (Table 2, entry 18). It implied that the steric hindrance of carboxylic acid has little impact on the reaction yield. Furthermore, the silver-catalyzed *trans* addition of 4-fluorophenylacetic acid to **1a** occurred uneventfully, delivering **3at** in 76% yield (Table 2, entry 19). In contrast, no desired products were obtained when CF_3SO_3H or CF_3CO_2H was used, owing to the hydrolysis of ynol ethers in these cases.

Table 2. Scope of Silver-Catalyzed *Trans* Addition of Carboxylic Acids to Ynol Ethers[a]



entry	R^1/R^2 (**1**)	R^3 (**2**)	yield (%)[b]
1	*n*-Bu/3-tol (**1a**)	4-FC_6H_4 (**2b**)	75 (**3ab**)
2	*n*-Bu/3-tol (**1a**)	4-ClC_6H_4 (**2c**)	81 (**3ac**)
3	*n*-Bu/3-tol (**1a**)	4-BrC_6H_4 (**2d**)	77 (**3ad**)
4	*n*-Bu/3-tol (**1a**)	4-IC_6H_4 (**2e**)	73 (**3ae**)[c]
5	*n*-Bu/3-tol (**1a**)	4-$NO_2C_6H_4$ (**2f**)	60 (**3af**)
6	*n*-Bu/3-tol (**1a**)	4-CNC_6H_4 (**2g**)	87 (**3ag**)
7	*n*-Bu/3-tol (**1a**)	4-$CO_2MeC_6H_4$ (**2h**)	84 (**3ah**)
8	*n*-Bu/3-tol (**1a**)	4-MeC_6H_4 (**2i**)	81 (**3ai**)
9	*n*-Bu/3-tol (**1a**)	4-$OMeC_6H_4$ (**2j**)	80 (**3aj**)[c]
10	*n*-Bu/3-tol (**1a**)	4-$NH_2C_6H_4$ (**2k**)	40 (**3ak**)
11	*n*-Bu/3-tol (**1a**)	4-OHC_6H_4 (**2l**)	80 (**3al**)
12	*n*-Bu/3-tol (**1a**)	2-OHC_6H_4 (**2m**)	76 (**3am**)
13	*n*-Bu/3-tol (**1a**)	4-pyridyl (**2n**)	56 (**3an**)[d]
14	*n*-Bu/3-tol (**1a**)	2-thienyl (**2o**)	88 (**3ao**)
15	*n*-Bu/3-tol (**1a**)	(*E*)-styryl (**2p**)	85 (**3ap**)
16	*n*-Bu/3-tol (**1a**)	C≡CPh (**2q**)	73 (**3aq**)[e]
17	*n*-Bu/3-tol (**1a**)	Me (**2r**)	83 (**3ar**)
18	*n*-Bu/3-tol (**1a**)	*t*-Bu (**2s**)	80 (**3as**)
19	*n*-Bu/3-tol (**1a**)	4-$FC_6H_4CH_2$ (**2t**)	76 (**3at**)
20	H/Ph (**1b**)	Ph (**2a**)	90 (**3ba**)
21	$BnCH_2$/3-tol (**1c**)	Ph (**2a**)	85 (**3ca**)
22	allyl/3-tol (**1d**)	Ph (**2a**)	87 (**3da**)
23	allyl/3-tol (**1d**)	*t*-Bu (**2s**)	86 (**3ds**)
24	H/3-tol (**1e**)	Ph (**2a**)	80 (**3ea**)
25	H/3-tol (**1e**)	*t*-Bu (**2s**)	70 (**3es**)
26	*n*-Bu(Et)CH/3-tol (**1f**)	Ph (**2a**)	82 (**3fa**)
27	allyl/Ph (**1g**)	Ph (**2a**)	86 (**3ga**)
28	*n*-Bu/Ph (**1h**)	Ph (**2a**)	82 (**3ha**)
29	*n*-Bu/4-ClC_6H_4 (**1i**)	Ph (**2a**)	85 (**3ia**)
30	Cy/4-ClC_6H_4 (**1j**)	Ph (**2a**)	77 (**3ja**)
31	Ph/Et (**1k**)	Ph (**2a**)	95 (**3ka**)
32	Ph/Et (**1k**)	*t*-Bu (**2s**)	87 (**3ks**)
33	4-FC_6H_4/Et (**1l**)	Ph (**2a**)	93 (**3la**)
34	4-$OMeC_6H_4$/Et (**1m**)	Ph (**2a**)	90 (**3ma**)
35	H/Et (**1n**)	Ph (**2a**)	71 (**3na**)[c,f]

[a]Reaction conditions: **1** (0.25 mmol), **2** (0.28 mmol), Ag_2O (5 mol %), dioxane (1 mL), N_2, 100 °C, 10 h. [b]Isolated yield. [c]Et_3N (0.3 mmol) was added to the standard conditions. [d]**1a** (0.25 mmol), **2n** (0.5 mmol), Ag_2O (5 mol %), Et_3N (0.6 mmol), dioxane (1 mL), N_2, 100 °C, 24 h. [e]Ag_2O (0.7 mmol) and Et_3N (0.3 mmol) were used. [f]Run at room temperature for 4 h.

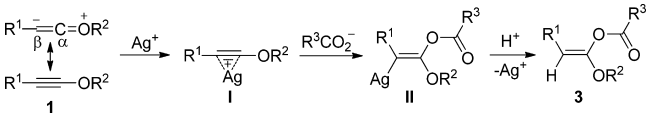
On the other hand, various ynol ethers were successfully applied to the current reaction. For instance, terminal ynol ether **1b** furnished **3ba** in 90% yield (Table 2, entry 20). The addition of **2a** to **1d**, a substrate bearing both C−C triple and C−C double bonds, underwent smoothly to form **3da** in 87% yield with excellent chem-, regio-, and stereoselectivity (Table 2, entry 22). Moreover, increased steric bulk of the R^1 group was well-tolerated, giving **3fa** in 82% yield with excellent regio- and stereocontrol (Table 2, entry 26). Other than alkyl ynol ethers, aromatic substrate **1k** produced hydrocarboxylation products **3ka** and **3ks** in respective yields of 95% and 87% (Table 2, entries 31 and 32). Notably, the electronic effect of the R^1 group has no significant impact on the reaction

dx.doi.org/10.1021/jo501615a | J. Org. Chem. 2014, 79, 9179−9185

efficiency, as demonstrated by the production of **3la** and **3ma** (Table 2, entries 33 and 34). Remarkably, the commercially available ethyl ethynyl ether was also an effective substrate, giving **3na** in 71% yield after reaction at room temperature in the presence of 1.2 equiv of Et_3N for 4 h (Table 2, entry 35). The regio- and stereochemistry of this silver-catalyzed *trans* hydrocarboxylation reaction was determined by the NOE measurements (see the Supporting Information).

A plausible mechanism for this reaction is proposed as shown in Scheme 2. First, the electrophilic addition of a silver cation to

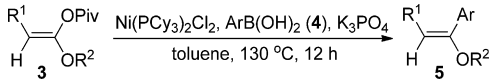
Scheme 2. A Possible Mechanism



C−C triple bonds of ynol ethers forms an intermediate **I**, which can be attacked by the carboxylate anion from the backside to give a silver species **II**. The polarization of C−C triple bonds of ynol ethers stemmed from the electron donation of the oxygen atom may account for the regioselective α-addition of the carboxylate anion.[15−18] Finally, protodemetalation of the C−Ag bond of **II** delivers the *trans* addition products **3** along with the regeneration of the silver catalyst (Scheme 2).

As such, we have developed a direct, efficient, and ligand-free method for the production of (*Z*)-α-alkoxy enol esters in good yields with perfect regio- and stereoselectivity. We noticed that products **3** have two different alkenyl C−O bonds. We envisioned that the selective cross-coupling of C−OCOR^3 bonds over C−OR^2 bonds might result in a stereocontrolled approach to enol ethers. To this end, pivalate **3ks** was treated with 4 mol % of $Ni(PCy_3)_2Cl_2$, 1.2 equiv of $PhB(OH)_2$ (**4a**), and 3.0 equiv of K_2CO_3 in toluene at 130 °C for 12 h; as expected, (*E*)-enol ether **5a**[21] was obtained in 35% yield. Other bases such as KO*t*-Bu, NaOMe, and KF generated **5a** in 10, 66, and 5% yield, respectively. In contrast, the utilization of K_3PO_4 as the base led to the highest yield (86%), and the coupling of the C−OEt bond was not detected (Table 3, entry 1). Then, a brief survey on the scope of boronic acids was conducted. Both 4- and 2-tolylboronic acids worked well for this Suzuki−Miyaura coupling reaction (Table 3, entries 3 and 4). Moreover, **4e**, an electron-poor boronic acid, underwent the facile coupling with **3ks** to form (*E*)-enol ether **5e** in 83% yield (Table 3, entry 5). In addition to **3ks**, other pivalates, including **3as**, **3ds**, and **3es**, were found to be the suitable coupling partners and led to the desired products in reasonable yields (Table 3, entries 6−8). Overall, the procedure involving hydrocarboxylation and subsequent Suzuki−Miyaura coupling offers a formal *trans* hydroarylation of ynol ethers, which provides a good complementary method to our previous efforts to enol ethers.[16]

Table 3. Synthesis of (*E*)-Enol Ethers via the Ni-Catalyzed C−O Bond Coupling[a]



entry	R^1/R^2 (**3**)	Ar (**4**)	yield (%)[b]
1	Ph/Et (**3ks**)	Ph (**4a**)	86 (**5a**)
2	Ph/Et (**3ks**)	4-FC_6H_4 (**4b**)	71 (**5b**)
3	Ph/Et (**3ks**)	4-MeC_6H_4 (**4c**)	74 (**5c**)
4	Ph/Et (**3ks**)	2-MeC_6H_4 (**4d**)	70 (**5d**)
5	Ph/Et (**3ks**)	4-$CF_3C_6H_4$ (**4e**)	83 (**5e**)
6	*n*-Bu/3-tol (**3as**)	Ph (**4a**)	60 (**5f**)
7	allyl/3-tol (**3ds**)	Ph (**4a**)	63 (**5g**)
8	H/3-tol (**3es**)	Ph (**4a**)	50 (**5h**)

[a]Reaction conditions: **3** (0.25 mmol), **4** (0.3 mmol), $Ni(PCy_3)_2Cl_2$ (4 mol %), K_3PO_4 (0.75 mmol), toluene (1 mL), under N_2, 130 °C, 12 h. [b]Isolated yield.

CONCLUSION

In summary, a silver-catalyzed *trans* addition of carboxylic acids to ynol ethers has been realized, which produces (*Z*)-α-alkoxy enol esters in good yields with excellent regio- and stereoselectivity. A wide range of functional substituents, such as NO_2, CN, CO_2Me, Me, OMe, NH_2, OH, pyridyl, thienyl, alkenyl, and alkynyl groups, are well-tolerated in this reaction. Furthermore, the subsequent Ni-catalyzed Suzuki−Miyaura coupling of alkenyl C−OPiv bonds of (*Z*)-α-alkoxy enol esters enables a convenient approach to (*E*)-enol ethers. As such, the two-step procedure[22] developed here offers a formal *trans* hydroarylation of ynol ethers, thereby providing a good complementary method to our previous report. We believe that it will be valuable for the diversity-oriented synthesis.[23]

EXPERIMENTAL SECTION

General. Unless otherwise mentioned, materials obtained from commercial suppliers were used directly without further purification. Toluene, dioxane, and THF were distilled from sodium prior to use. Column chromatography was performed using silica gel (300−400 mesh) with petroleum ether/EtOAc as the eluent. ^1H NMR and ^{13}C NMR spectra were measured on a 600 MHz NMR spectrometer using $CDCl_3$ or DMSO-*d6* as the solvent. Chemical shifts were given in δ relative to TMS, and the coupling constants were given in Hz. High-resolution mass spectra (HRMS) analyses were conducted using a TOF MS instrument with an ESI or APCI source.

General Procedure for the Ag-Catalyzed Regio- and Stereoselective Addition of Carboxylic Acids to Ynol Ethers. To a mixture of **2a** (34 mg, 0.28 mmol) and Ag_2O (3 mg, 0.0125 mmol) was added a solution of **1a** (47 mg, 0.25 mmol) in 1 mL of dioxane under a nitrogen atmosphere. After stirring at 100 °C for 10 h, the reaction mixture was quenched with water, extracted with EtOAc, washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Column chromatography on silica gel (petroleum ether/EtOAc = 30:1) gave 68 mg (yield: 88%) of **3aa** as a colorless oil. ^1H NMR (600 MHz, $CDCl_3$): δ 8.10−8.05 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46−7.43 (m, 2H), 7.22−7.18 (m, 1H), 7.03−6.98 (m, 2H), 6.89 (d, *J* = 7.4 Hz, 1H), 4.81 (t, *J* = 7.6 Hz, 1H), 2.33 (s, 3H), 2.05−2.01 (m, 2H), 1.40−1.30 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.6, 155.6, 148.5, 139.7, 133.7, 130.2, 129.2, 128.5, 128.5, 124.3, 118.5, 114.6, 100.4, 31.4, 24.5, 22.1, 21.3, 13.8; HRMS (ESI) calcd for $C_{20}H_{22}NaO_3$ $(M + Na)^+$ 333.1467, found 333.1461.

Compound ***3ab***. 62 mg, 75% yield, colorless oil; ^1H NMR (600 MHz, $CDCl_3$): δ 8.15−8.04 (m, 2H), 7.22−7.18 (m, 1H), 7.15−7.10 (m, 2H), 7.00−6.98 (m, 2H), 6.90 (d, *J* = 7.5 Hz, 1H), 4.80 (t, *J* = 7.6 Hz, 1H), 2.34 (s, 3H), 2.04−1.99 (m, 2H), 1.41−1.30 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.2 (d, *J* = 255.6 Hz), 162.6, 155.5, 148.4, 139.8, 132.9 (d, *J* = 9.5 Hz), 129.2, 124.8 (d, *J* = 2.8 Hz), 124.4, 118.6, 115.8 (d, *J* = 22.1 Hz), 114.7, 100.4, 31.4, 24.5, 22.1, 21.4, 13.8; HRMS (ESI) calcd for $C_{20}H_{21}FNaO_3$ $(M + Na)^+$ 351.1372, found 351.1371.

Compound ***3ac***. 70 mg, 81% yield, colorless oil; ^1H NMR (600 MHz, $CDCl_3$): δ 7.97−7.90 (m, 2H), 7.38−7.31 (m, 2H), 7.13−7.10 (m, 1H), 6.94−6.80 (m, 2H), 6.82 (d, *J* = 7.5 Hz, 1H), 4.72 (t, *J* = 7.6 Hz, 1H), 2.25 (s, 3H), 1.97−1.91 (m, 2H), 1.33−1.22 (m, 4H), 0.79 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.8, 155.5, 148.4, 140.4, 139.7, 131.6, 129.2, 128.9, 127.0, 124.5, 118.6, 114.7,

dx.doi.org/10.1021/jo501615a | J. Org. Chem. 2014, 79, 9179−9185

100.4, 31.4, 24.5, 22.1, 21.4, 13.8; HRMS (ESI) calcd for $C_{20}H_{21}ClNaO_3$ $(M + Na)^+$ 367.1077, found 367.1077.

Compound **3ad**. 75 mg, 77% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 (d, J = 8.5 Hz, 2H), 7.58 (d, J = 8.5 Hz, 2H), 7.21−7.17 (m, 1H), 7.00−6.97 (m, 2H), 6.89 (d, J = 7.5 Hz, 1H), 4.81 (t, J = 7.6 Hz, 1H), 2.33 (s, 3H), 2.04−1,98 (m, 2H), 1.39−1.30 (m, 4H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.9, 155.4, 148.4, 139.7, 131.9, 131.6, 129.2, 129.0, 127.4, 124.4, 118.5, 114.7, 100.4, 31.4, 24.5, 22.1, 21.3, 13.8; HRMS (ESI) calcd for $C_{20}H_{21}BrNaO_3$ $(M + Na)^+$ 411.0572, found 411.0567.

Compound **3ae**. 80 mg, 73% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.87−7.84 (m, 2H), 7.83−7.80 (m, 2H), 7.26−7.22 (m, 1H), 7.06−7.02 (m, 2H), 6.94 (d, J = 7.5 Hz, 1H), 4.85 (t, J = 7.6 Hz, 1H), 2.38 (s, 3H), 2.08−2.02 (m, 2H), 1.44−1.36 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.1, 155.4, 148.4, 139.7, 137.9, 131.5, 129.2, 128.0, 124.4, 118.5, 114.7, 101.9, 100.4, 31.4, 24.5, 22.1, 21.3, 13.8; HRMS (ESI) calcd for $C_{20}H_{21}INaO_3$ $(M + Na)^+$ 459.0433, found 459.0426.

Compound **3af**. 53 mg, 60% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.30 (d, J = 8.8 Hz, 2H), 8.26−8.23 (m, 2H), 7.23−7.19 (m, 1H), 7.01−6.97 (m, 2H), 6.92 (d, J = 7.5 Hz, 1H), 4.84 (t, J = 7.6 Hz, 1H), 2.34 (s, 3H), 2.07−1.98 (m, 2H), 1.41−1.31 (m, 4H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.8, 155.3, 150.9, 148.2, 139.9, 133.9, 131.3, 129.3, 124.7, 123.7, 118.5, 114.6, 100.6, 31.4, 24.5, 22.1, 21.3, 13.8; HRMS (ESI) calcd for $C_{20}H_{21}NNaO_5$ $(M + Na)^+$ 378.1317, found 378.1309.

Compound **3ag**. 73 mg, 87% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.26−7.22 (m, 1H), 7.04−7.00 (m, 2H), 6.94 (d, J = 7.5 Hz, 1H), 4.86 (t, J = 7.6 Hz, 1H), 2.37 (s, 3H), 2.10−2.00 (m, 2H), 1.44−1.32 (m, 4H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.0, 155.3, 148.2, 139.8, 132.3, 132.3, 130.6, 129.2, 124.6, 118.4, 117.6, 117.1, 114.6, 100.5, 31.3, 24.4, 22.0, 21.3, 13.7; HRMS (ESI) calcd for $C_{21}H_{21}NNaO_3$ $(M + Na)^+$ 358.1419, found 358.1414.

Compound **3ah**. 77 mg, 84% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20−8.10 (m, 4H), 7.26−7.21 (m, 1H), 7.05−7.01 (m, 2H), 6.94 (d, J = 7.5 Hz, 1H), 4.85 (t, J = 7.6 Hz, 1H), 3.98 (s, 3H), 2.37 (s, 3H), 2.10−2.00 (m, 2H), 1.45−1.30 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.0, 162.8, 155.4, 148.4, 139.7, 134.6, 132.3, 130.1, 129.6, 129.2, 124.5, 118.5, 114.7, 100.4, 52.4, 31.4, 24.5, 22.1, 21.3, 13.8; HRMS (ESI) calcd for $C_{22}H_{24}NaO_5$ $(M + Na)^+$ 391.1521, found 391.1521.

Compound **3ai**. 66 mg, 81% yield, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 8.2 Hz, 2H), 7.30−7.21 (m, 3H), 7.06−7.00 (m, 2H), 6.92 (d, J = 7.5 Hz, 1H), 4.83 (t, J = 7.6 Hz, 1H), 2.44 (s, 3H), 2.37 (s, 3H), 2.09−2.01 (m, 2H), 1.42−1.32 (m, 4H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.6, 155.6, 148.6, 144.7, 139.7, 130.3, 129.2, 129.2, 125.8, 124.3, 118.6, 114.7, 100.3, 31.5, 24.5, 22.1, 21.7, 21.4, 13.8; HRMS (ESI) calcd for $C_{21}H_{24}NaO_3$ $(M + Na)^+$ 347.1623, found 347.1622.

Compound **3aj**. 68 mg, 80% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09−8.04 (m, 2H), 7.25−7.20 (m, 1H), 7.05−7.00 (m, 2H), 6.98−6.90 (m, 3H), 4.82 (t, J = 7.6 Hz, 1H), 3.89 (s, 3H), 2.37 (s, 3H), 2.08−2.03 (m, 2H), 1.43−1.35 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.0, 163.3, 155.7, 148.6, 139.6, 132.4, 129.2, 124.3, 120.8, 118.6, 114.7, 113.8, 100.3, 55.5, 31.5, 24.5, 22.1, 21.4, 13.8; HRMS (ESI) calcd for $C_{21}H_{24}NaO_4$ $(M + Na)^+$ 363.1572, found 363.1565.

Compound **3ak**. 33 mg, 40% yield, white solid, mp: 86−89 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.91 (d, J = 8.5 Hz, 2H), 7.25−7.20 (m, 1H), 7.05−7.00 (m, 2H), 6.91 (d, J = 7.4 Hz, 1H), 6.65 (d, J = 8.5 Hz, 2H), 4.80 (t, J = 7.6 Hz, 1H), 4.19 (s, 2H), 2.36 (s, 3H), 2.07−2.01 (m, 2H), 1.42−1.33 (m, 4H), 0.90 (t, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.6, 155.7, 151.6, 148.7, 139.6, 132.4, 129.1, 124.1, 118.6, 117.6, 114.7, 113.7, 100.2, 31.5, 24.5, 22.1, 21.4, 13.8; HRMS (ESI) calcd for $C_{20}H_{24}NO_3$ $(M + H)^+$ 326.1756, found 326.1749.

Compound **3al**. 65 mg, 80% yield, white solid, mp: 63−65 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.02 (d, J = 8.8 Hz, 2H), 7.26−7.20 (m, 1H), 7.04−7.00 (m, 2H), 6.98−6.92 (m, 3H), 4.86 (t, J = 7.6 Hz, 1H), 2.36 (s, 3H), 2.10−2.00 (m, 2H), 1.50−1.30 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.2, 161.4, 155.5, 148.4, 139.7, 132.7, 129.2, 124.4, 120.1, 118.5, 115.6, 114.6, 100.6, 31.4, 24.4, 22.1, 21.3, 13.8; HRMS (ESI) calcd for $C_{20}H_{22}NaO_4$ $(M + Na)^+$ 349.1416, found 349.1414.

Compound **3am**. 62 mg, 76% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.42 (s, 1H), 7.93 (dd, J = 8.0, 1.5 Hz, 1H), 7.56−7.51 (m, 1H), 7.28−7.23 (m, 1H), 7.07−7.02 (m, 3H), 6.96−6.93 (m, 2H), 4.89 (t, J = 7.6 Hz, 1H), 2.39 (s, 3H), 2.10−2.06 (m, 2H), 1.45−1.37 (m, 4H), 0.93 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.5, 162.2, 155.4, 147.8, 139.8, 136.6, 130.3, 129.3, 124.6, 119.4, 118.4, 117.8, 114.6, 111.0, 100.9, 31.4, 24.4, 22.1, 21.4, 13.8; HRMS (ESI) calcd for $C_{20}H_{22}NaO_4$ $(M + Na)^+$ 349.1416, found 349.1396.

Compound **3an**. 44 mg, 56% yield, yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.84 (d, J = 3.2 Hz, 2H), 7.91 (d, J = 5.1 Hz, 2H), 7.26−7.22 (m, 1H), 7.02−6.99 (m, 2H), 6.94 (d, J = 7.5 Hz, 1H), 4.86 (t, J = 7.6 Hz, 1H), 2.37 (s, 3H), 2.06−2.01 (m, 2H), 1.43−1.33 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.2, 155.3, 150.7, 148.2, 139.9, 135.9, 129.3, 124.7, 123.2, 118.5, 114.6, 100.7, 31.4, 24.5, 22.1, 21.4, 13.8; HRMS (ESI) calcd for $C_{19}H_{21}NNaO_3$ $(M + Na)^+$ 334.1419, found 334.1417.

Compound **3ao**. 70 mg, 88% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.92 (d, J = 3.7 Hz, 1H), 7.65 (d, J = 4.9 Hz, 1H), 7.26−7.22 (m, 1H), 7.18−7.13 (m, 1H), 7.04−7.00 (m, 2H), 6.94 (d, J = 7.4 Hz, 1H), 4.83 (t, J = 7.6 Hz, 1H), 2.38 (s, 3H), 2.11−2.05 (m, 2H), 1.44−1.36 (m, 4H), 0.93 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.0, 155.6, 148.4, 139.8, 135.1, 133.9, 131.8, 129.3, 128.1, 124.4, 118.6, 114.8, 100.6, 31.5, 24.5, 22.2, 21.4, 13.9; HRMS (ESI) calcd for $C_{18}H_{20}NaO_3S$ $(M + Na)^+$ 339.1031, found 339.1029.

Compound **3ap**. 71 mg, 85% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.84 (d, J = 16.0 Hz, 1H), 7.59−7.54 (m, 2H), 7.45−7.40 (m, 3H), 7.26−7.23 (m, 1H), 7.04−7.01 (m, 2H), 6.95 (d, J = 7.6 Hz, 1H), 6.52 (d, J = 16.0 Hz, 1H), 4.83 (t, J = 7.6 Hz, 1H), 2.39 (s, 3H), 2.10−2.04 (m, 2H), 1.44−1.38 (m, 4H), 0.95 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.8, 155.7, 148.4, 147.4, 139.7, 134.0, 130.9, 129.3, 129.0, 128.4, 124.4, 118.5, 116.2, 114.8, 100.6, 31.6, 24.6, 22.3, 21.4, 13.9; HRMS (ESI) calcd for $C_{22}H_{24}NaO_3$ $(M + Na)^+$ 359.1623, found 359.1626.

Compound **3aq**. 61 mg, 73% yield, yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.12−8.10 (m, 2H), 7.66−7.60 (m, 1H), 7.52−7.46 (m, 2H), 7.25−7.21 (m, 1H), 7.09−7.00 (m, 3H), 4.84 (t, J = 7.6 Hz, 1H), 2.37 (s, 3H), 2.08−2.04 (m, 2H), 1.43−1.36 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.6, 155.6, 148.6, 139.7, 133.8, 130.2, 129.2, 128.6, 128.5, 126.5, 124.4, 122.2, 118.6, 114.7, 100.4, 31.5, 24.5, 22.2, 21.4, 13.8; HRMS (ESI) calcd for $C_{22}H_{22}NaO_3$ $(M + Na)^+$ 357.1467, found 357.1463.

Compound **3ar**. 52 mg, 83% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.22 (t, J = 7.7 Hz, 1H), 6.96−6.91 (m, 3H), 4.74 (t, J = 7.6 Hz, 1H), 2.37 (s, 3H), 2.18 (s, 3H), 2.02−1.96 (m, 2H), 1.42−1.35 (m, 4H), 0.93 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.8, 155.5, 148.2, 139.7, 129.2, 124.3, 118.4, 114.6, 100.3, 31.4, 24.5, 22.2, 21.4, 20.4, 13.8; HRMS (ESI) calcd for $C_{15}H_{20}NaO_3$ $(M + Na)^+$ 271.1310, found 271.1304.

Compound **3as**. 58 mg, 80% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.21 (t, J = 7.8 Hz, 1H), 6.97−6.91 (m, 3H), 4.72 (t, J = 7.6 Hz, 1H), 2.36 (s, 3H), 2.01−1.95 (m, 2H), 1.43−1.33 (m, 4H), 1.24 (s, 9H), 0.93 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.3, 155.3, 148.7, 139.5, 129.1, 124.3, 118.8, 115.0, 99.3, 38.9, 31.4, 26.1, 24.3, 22.1, 21.3, 13.8; HRMS (ESI) calcd for $C_{18}H_{26}NaO_3$ $(M + Na)^+$ 313.1780, found 313.1774.

Compound **3at**. 65 mg, 76% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25−7.19 (m, 3H), 7.02−6.98 (m, 2H), 6.95−6.85 (m, 3H), 4.74 (t, J = 7.7 Hz, 1H), 3.70 (s, 2H), 2.35 (s, 3H), 1.90−1.86 (m, 2H), 1.35−1.28 (m, 4H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 168.3, 162.1 (d, J = 246.0 Hz), 155.2, 148.1, 139.6, 130.8 (d, J = 8.1 Hz), 129.2, 128.7 (d, J = 3.3 Hz), 124.4, 118.5, 115.4 (d, J = 21.5 Hz), 114.7, 100.1, 39.9, 31.3, 24.3, 22.1, 21.3, 13.7; HRMS (ESI) calcd for $C_{21}H_{23}FNaO_3$ $(M + Na)^+$ 365.1529, found 365.1531.

Compound **3ba**. 54 mg, 90% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.16−8.11 (m, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51−

dx.doi.org/10.1021/jo501615a | J. Org. Chem. 2014, 79, 9179−9185

7.48 (m, 2H), 7.42−7.39 (m, 2H), 7.32−7.29 (m, 2H), 7.20 (t, J = 7.4 Hz, 1H), 4.42 (d, J = 3.3 Hz, 1H), 4.23 (d, J = 3.3 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.7, 156.0, 154.5, 133.8, 130.2, 129.7, 128.5, 128.5, 124.6, 119.4, 80.7; HRMS (ESI) calcd for $C_{15}H_{12}NaO_3$ (M + Na)$^+$ 263.0684, found 263.0681.

Compound ***3ca***. 76 mg, 85% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.11 (d, J = 7.7 Hz, 2H), 7.66 (t, J = 7.3 Hz, 1H), 7.53−7.50 (m, 2H), 7.36−7.33 (m, 2H), 7.28−7.22 (m, 4H), 7.02−6.93 (m, 3H), 4.90 (t, J = 7.6 Hz, 1H), 2.80 (t, J = 7.5 Hz, 2H), 2.44−2.38 (m, 5H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.5, 155.3, 148.9, 141.3, 139.6, 133.8, 130.2, 129.2, 128.5, 128.5, 128.4, 128.3, 125.9, 124.4, 118.5, 114.7, 99.2, 35.5, 26.7, 21.3; HRMS (ESI) calcd for $C_{24}H_{22}NaO_3$ (M + Na)$^+$ 381.1467, found 381.1465.

Compound ***3da***. 64 mg, 87% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.14 (dd, J = 8.3, 1.1 Hz, 2H), 7.67−7.61 (m, 1H), 7.51−7.48 (m, 2H), 7.28−7.24 (m, 1H), 7.09−7.07 (m, 2H), 6.97 (d, J = 7.5 Hz, 1H), 5.90−5.80 (m, 1H), 5.14−5.10 (m, 1H), 5.05−5.03 (m, 1H), 4.85 (t, J = 7.6 Hz, 1H), 2.87−2.78 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.5, 155.2, 149.7, 139.7, 135.9, 133.8, 130.2, 129.2, 128.5, 128.4, 124.7, 119.0, 115.2, 115.2, 96.8, 29.0, 21.3; HRMS (ESI) calcd for $C_{19}H_{18}NaO_3$ (M + Na)$^+$ 317.1154, found 317.1148.

Compound ***3ds***. 59 mg, 86% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.23−7.20 (m, 1H), 6.97−6.92 (m, 3H), 5.85−5.78 (m, 1H), 5.09 (dd, J = 17.1, 1.6 Hz, 1H), 5.02 (dd, J = 10.1, 1.4 Hz, 1H), 4.70 (t, J = 7.6 Hz, 1H), 2.73−2.70 (m, 2H), 2.36 (s, 3H), 1.23 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.3, 155.0, 149.8, 139.6, 136.0, 129.2, 124.7, 119.2, 115.5, 115.1, 95.9, 39.0, 28.9, 26.8, 21.3; HRMS (APCI) calcd for $C_{17}H_{23}O_3$ (M + H)$^+$ 275.1647, found 275.1652.

Compound ***3ea***. 51 mg, 80% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.16−8.10 (m, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.52−7.49 (m, 2H), 7.28 (t, J = 7.8 Hz, 1H), 7.13−7.08 (m, 2H), 7.02 (d, J = 7.5 Hz, 1H), 4.39 (d, J = 3.3 Hz, 1H), 4.20 (d, J = 3.3 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.8, 156.2, 154.4, 139.9, 133.8, 130.2, 129.4, 128.6, 128.5, 125.5, 120.1, 116.4, 80.3, 21.3; HRMS (ESI) calcd for $C_{16}H_{14}NaO_3$ (M + Na)$^+$ 277.0841, found 277.0839.

Compound ***3es***. 41 mg, 70% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26−7.22 (m, 1H), 7.05−6.97 (m, 3H), 4.17 (d, J = 3.1 Hz, 1H), 4.08 (d, J = 3.1 Hz, 1H), 2.37 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.6, 156.2, 154.3, 139.8, 129.3, 125.4, 120.2, 116.5, 79.8, 39.0, 26.8, 21.3; HRMS (ESI) calcd for $C_{14}H_{18}NaO_3$ (M + Na)$^+$ 257.1154, found 257.1139.

Compound ***3fa***. 72 mg, 82% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.13 (d, J = 7.3 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.52−7.49 (m, 2H), 7.27−7.24 (m, 1H), 7.10−7.07 (m, 2H), 6.94 (d, J = 7.5 Hz, 1H), 4.60 (d, J = 10.4 Hz, 1H), 2.39 (s, 3H), 2.22−2.12 (m, 1H), 1.52−1.45 (m, 2H), 1.39−1.28 (m, 6H), 1.00−0.95 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.6, 155.8, 149.1, 139.6, 133.7, 130.1, 129.2, 128.7, 128.5, 124.2, 118.5, 114.6, 105.0, 37.6, 35.0, 29.5, 28.5, 22.7, 21.4, 14.1, 11.9; HRMS (ESI) calcd for $C_{23}H_{28}NaO_3$ (M + Na)$^+$ 375.1936, found 375.1933.

Compound ***3ga***. 60 mg, 86% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.13 (dd, J = 8.2, 1.1 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51−7.48 (m, 2H), 7.42−7.37 (m, 2H), 7.28−7.26 (m, 2H), 7.15 (t, J = 7.4 Hz, 1H), 5.92−5.80 (m, 1H), 5.14−5.10 (m, 1H), 5.07−5.03 (m, 1H), 4.88 (t, J = 7.6 Hz, 1H), 2.85−2.81 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.4, 155.3, 149.6, 135.8, 133.8, 130.2, 129.6, 128.5, 128.4, 123.8, 118.2, 115.3, 97.2, 29.0; HRMS (ESI) calcd for $C_{18}H_{16}NaO_3$ (M + Na)$^+$ 303.0997, found 303.0993.

Compound ***3ha***. 61 mg, 82% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.12 (dd, J = 8.3, 1.2 Hz, 2H), 7.65−7.61 (m, 1H), 7.51−7.48 (m, 2H), 7.38−7.35 (m, 2H), 7.23 (dd, J = 8.7, 1.0 Hz, 2H), 7.12 (t, J = 7.4 Hz, 1H), 4.89 (t, J = 7.6 Hz, 1H), 2.09−2.05 (m, 2H), 1.44−1.35 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.6, 155.6, 148.3, 133.8, 130.2, 129.5, 128.5, 128.5, 123.5, 117.7, 100.8, 31.4, 24.5, 22.1, 13.8; HRMS (ESI) calcd for $C_{19}H_{20}NaO_3$ (M + Na)$^+$ 319.1310, found 319.1309.

Compound ***3ia***. 70 mg, 85% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.10 (d, J = 7.7 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51−7.48 (m, 2H), 7.31 (d, J = 8.9 Hz, 2H), 7.17 (d, J = 8.9 Hz, 2H), 4.87 (t, J = 7.6 Hz, 1H), 2.08−2.04 (m, 2H), 1.42−1.34 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.6, 154.3, 148.3, 134.0, 130.3, 129.6, 129.5, 128.7, 123.0, 119.2, 101.3, 31.4, 24.5, 22.2, 13.9; HRMS (ESI) calcd for $C_{19}H_{19}ClNaO_3$ (M + Na)$^+$ 353.0920, found 353.0904.

Compound ***3ja***. 69 mg, 77% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.15−8.08 (m, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.52−7.49 (m, 2H), 7.33−7.30 (m, 2H), 7.20−7.15 (m, 2H), 4.78 (d, J = 9.6 Hz, 1H), 2.22−2.16 (m, 1H), 1.81−1.61 (m, 5H), 1.30−1.15 (m, 5H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.7, 154.3, 147.2, 133.9, 130.2, 129.5, 128.6, 128.5, 128.4, 119.1, 106.9, 34.6, 33.1, 25.8, 25.6; HRMS (ESI) calcd for $C_{21}H_{21}ClNaO_3$ (M + Na)$^+$ 379.1077, found 379.1073.

Compound ***3ka***. 64 mg, 95% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.26−8.20 (m, 2H), 7.68 (t, J = 7.5 Hz, 1H), 7.56−7.53 (m, 2H), 7.37 (d, J = 7.5 Hz, 2H), 7.27−7.24 (m, 2H), 7.14 (t, J = 7.4 Hz, 1H), 5.46 (s, 1H), 4.14 (q, J = 7.0 Hz, 2H), 1.46 (t, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.4, 152.8, 134.3, 134.0, 130.4, 128.8, 128.7, 128.5, 127.4, 125.8, 91.5, 65.5, 14.4; HRMS (ESI) calcd for $C_{17}H_{16}NaO_3$ (M + Na)$^+$ 291.0997, found 291.0987.

Compound ***3ks***. 54 mg, 87% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30−7.27 (m, 4H), 7.17−7.14 (m, 1H), 5.33 (s, 1H), 4.03 (q, J = 7.0 Hz, 2H), 1.41 (t, J = 7.0 Hz, 3H), 1.31 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 175.1, 152.9, 134.3, 128.1, 127.7, 125.6, 91.0, 65.1, 38.9, 26.9, 14.3; HRMS (APCI) calcd for $C_{15}H_{21}O_3$ (M + H)$^+$ 249.1491, found 249.1488.

Compound ***3la***. 66 mg, 93% yield, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (d, J = 7.8 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.55−7.52 (m, 2H), 7.32−7.29 (m, 2H), 6.95−6.91 (m, 2H), 5.41 (s, 1H), 4.11 (q, J = 7.0 Hz, 2H), 1.44 (t, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.2, 160.8 (d, J = 245.3 Hz), 152.4 (d, J = 1.8 Hz), 134.0, 130.2, 130.1 (d, J = 3.3 Hz), 128.7 (d, J = 7.7 Hz), 128.6, 128.5, 115.2 (d, J = 21.4 Hz), 90.4, 65.4, 14.3; HRMS (ESI) calcd for $C_{17}H_{15}FNaO_3$ (M + Na)$^+$ 309.0903, found 309.0898.

Compound ***3ma***. 67 mg, 90% yield, yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.21 (d, J = 7.3 Hz, 2H), 7.67 (t, J = 7.5 Hz, 1H), 7.55−7.52 (m, 2H), 7.29 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 5.42 (s, 1H), 4.11 (q, J = 7.0 Hz, 2H), 3.76 (s, 3H), 1.44 (t, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.4, 157.6, 151.6, 133.8, 130.2, 128.7, 128.6, 128.4, 126.5, 113.8, 91.2, 65.3, 55.0, 14.3; HRMS (ESI) calcd for $C_{18}H_{18}NaO_4$ (M + Na)$^+$ 298.1205, found 298.1201.

Compound ***3na***. 34 mg, 71% yield, colorless oil; ^{1}H NMR (600 MHz, DMSO): δ 8.04−8.00 (m, 2H), 7.75 (t, J = 7.5 Hz, 1H), 7.60−7.57 (m, 2H), 4.00 (d, J = 3.6 Hz, 1H), 3.97 (d, J = 3.6 Hz, 1H), 3.93 (q, J = 7.0 Hz, 2H), 1.27 (t, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 163.7, 157.1, 134.8, 130.2, 129.6, 128.6, 73.1, 65.3, 14.4; HRMS (ESI) calcd for $C_{11}H_{12}NaO_3$ (M + Na)$^+$ 215.0684, found 215.0673.

General Procedure for the Ni-Catalyzed Coupling of 3 with Boronic Acids. To a mixture of **4a** (37 mg, 0.3 mmol), $Ni(PCy_3)_2Cl_2$ (6.8 mg, 0.01 mmol), and K_3PO_4 (160 mg, 0.75 mmol) was added a solution of **3ks** (62 mg, 0.25 mmol) in 1 mL of toluene under a nitrogen atmosphere. After stirring at 130 °C for 12 h, the reaction mixture was quenched with water, extracted with EtOAc, washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Column chromatography on silica gel (petroleum ether/EtOAc = 50:1) gave 48 mg (yield: 86%) of **5a**[21] as a colorless oil. ^{1}H NMR (600 MHz, DMSO): δ 7.35−7.27 (m, 5H), 7.10 (t, J = 7.6 Hz, 2H), 7.02 (t, J = 7.3 Hz, 1H), 6.91 (d, J = 7.5 Hz, 2H), 5.92 (s, 1H), 3.99 (q, J = 6.9 Hz, 2H), 1.34 (t, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 156.4, 137.2, 136.7, 129.5, 129.1, 128.9, 128.7, 128.4, 125.6, 102.5, 63.8, 15.0.

Compound ***5b***. 43 mg, 71% yield, colorless oil; ^{1}H NMR (600 MHz, DMSO): δ 7.32−7.28 (m, 2H), 7.16−7.11 (m, 4H), 7.05−7.02 (m, 1H), 6.91 (d, J = 7.4 Hz, 2H), 5.93 (s, 1H), 3.99 (q, J = 6.9 Hz, 2H), 1.34 (t, J = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 162.4 (d, J = 245.9 Hz), 155.4, 137.1, 133.0 (d, J = 3.3 Hz), 131.7 (d, J = 8.4 Hz), 129.0, 128.5, 125.7, 115.7 (d, J = 21.6 Hz), 102.6, 63.9, 15.0;

dx.doi.org/10.1021/jo501615a | J. Org. Chem. 2014, 79, 9179−9185

HRMS (APCI) calcd for $C_{16}H_{16}FO$ $(M + H)^+$ 243.1185, found 243.1180.

Compound **5c**. 44 mg, 74% yield, colorless oil; ^{1}H NMR (600 MHz, DMSO): δ 7.16 (d, J = 8.1 Hz, 2H), 7.13−7.08 (m, 4H), 7.01 (t, J = 7.3 Hz, 1H), 6.92 (d, J = 7.3 Hz, 2H), 5.87 (s, 1H), 3.96 (q, J = 6.9 Hz, 2H), 2.30 (s, 3H), 1.33 (t, J = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 156.4, 138.4, 137.4, 133.7, 129.4, 129.3, 128.9, 128.4, 125.5, 102.2, 63.7, 21.4, 15.0; HRMS (APCI) calcd for $C_{17}H_{19}O$ $(M + H)^+$ 239.1436, found 239.1421.

Compound **5d**. 42 mg, 70% yield, colorless oil; ^{1}H NMR (600 MHz, DMSO): δ 7.32−7.26 (m, 2H), 7.18−7.16 (m, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.05−7.02 (m, 2H), 6.99−6.94 (m, 1H), 6.77−6.72 (m, 2H), 5.97 (s, 1H), 3.99 (q, J = 7.0 Hz, 2H), 2.16 (s, 3H), 1.31 (t, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 156.6, 136.9, 136.7, 136.6, 130.7, 129.9, 129.2, 128.4, 127.9, 126.5, 125.4, 103.2, 63.5, 19.3, 15.0; HRMS (APCI) calcd for $C_{17}H_{19}O$ $(M + H)^+$ 239.1436, found 239.1425.

Compound **5e**. 61 mg, 83% yield, colorless oil; ^{1}H NMR (600 MHz, DMSO): δ 7.64 (d, J = 8.3 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.14−7.11 (m, 2H), 7.06 (t, J = 7.3 Hz, 1H), 6.94 (d, J = 7.6 Hz, 2H), 6.04 (s, 1H), 4.01 (q, J = 6.9 Hz, 2H), 1.34 (t, J = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 154.7, 140.7 (q, J = 1.2 Hz), 136.7, 130.3, 129.3 (q, J = 31.5 Hz), 129.2, 128.6, 126.0, 125.5 (q, J = 3.8 Hz), 124.5 (q, J = 272.4 Hz), 103.8, 64.1, 14.9; HRMS (APCI) calcd for $C_{17}H_{16}F_3O$ $(M + H)^+$ 293.1153, found 293.1151.

Compound **5f**. 40 mg, 60% yield, colorless oil; ^{1}H NMR (600 MHz, DMSO): δ 7.45 (d, J = 7.3 Hz, 2H), 7.39−7.36 (m, 2H), 7.32−7.29 (m, 1H), 7.11 (t, J = 7.8 Hz, 1H), 6.80 (s, 1H), 6.76−6.73 (m, 2H), 5.36 (t, J = 7.7 Hz, 1H), 2.24−2.19 (m, 5H), 1.40−1.26 (m, 4H), 0.83 (t, J = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 157.4, 150.1, 139.6, 134.6, 129.7, 128.8, 128.8, 128.7, 123.2, 118.2, 117.0, 114.6, 32.2, 26.8, 22.2, 21.4, 14.2; HRMS (APCI) calcd for $C_{19}H_{23}O$ $(M + H)^+$ 267.1749, found 267.1745.

Compound **5g**. 40 mg, 63% yield, colorless oil; ^{1}H NMR (600 MHz, DMSO): δ 7.53−7.49 (m, 2H), 7.34−7.31 (m, 2H), 7.29−7.26 (m, 1H), 7.13 (t, J = 7.8 Hz, 1H), 6.81−6.76 (m, 2H), 6.71 (dd, J = 8.2, 2.3 Hz, 1H), 6.07 (t, J = 7.4 Hz, 1H), 5.88−5.81 (m, 1H), 5.11−5.06 (m, 1H), 5.03−5.00 (m, 1H), 2.91−2.89 (m, 2H), 2.23 (s, 3H); ^{13}C NMR (151 MHz, DMSO): δ 157.3, 148.9, 139.8, 136.4, 135.2, 129.9, 129.1, 128.6, 125.6, 122.9, 116.3, 116.0, 115.4, 112.6, 30.2, 21.5; HRMS (APCI) calcd for $C_{18}H_{19}O$ $(M + H)^+$ 251.1436, found 251.1434.

Compound **5h**. 26 mg, 50% yield, colorless oil; ^{1}H NMR (600 MHz, DMSO): δ 7.70−7.66 (m, 2H), 7.44−7.37 (m, 3H), 7.26 (t, J = 7.8 Hz, 1H), 6.96−6.86 (m, 3H), 5.28 (d, J = 2.4 Hz, 1H), 4.48 (d, J = 2.3 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (151 MHz, DMSO): δ 158.6, 156.3, 140.0, 135.0, 130.0, 129.5, 129.0, 125.8, 124.7, 120.0, 116.5, 94.3, 21.4; HRMS (APCI) calcd for $C_{15}H_{15}O$ $(M + H)^+$ 211.1123, found 211.1105.

■ ASSOCIATED CONTENT

Supporting Information

Spectroscopic data of products **3** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: gangguo@zjnu.cn (G.Z.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for the financial support from the Natural Science Foundation of Zhejiang Province (LR12B02001 and LY14B020002), the National Science Foundation of China (21172199), and Zhejiang Normal University.

■ REFERENCES

(1) For selected reviews, see: (a) Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1997**, 507. (b) Dixneuf, P. H.; Bruneau, C.; Dérien, S. *Pure Appl. Chem.* **1998**, *70*, 1065. (c) Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* **1999**, *32*, 311. (d) Bruneau, C.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 2176. (e) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (f) Gooßen, L. J.; Rodríguez, N.; Gooßen, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 3100.

(2) For intramolecular versions, see: (a) Chan, D. M. T.; Marder, T. B.; Milstein, D.; Taylor, N. J. *J. Am. Chem. Soc.* **1987**, *109*, 6385. (b) Elgafi, S.; Field, L. D.; Messerle, B. A. *J. Organomet. Chem.* **2000**, *607*, 97. (c) Mas-Marzá, E.; Sanaú, M.; Peris, E. *Inorg. Chem.* **2005**, *44*, 9961. (d) Li, X.; Chianese, A. R.; Vogel, T.; Crabtree, R. H. *Org. Lett.* **2005**, *7*, 5437. (e) Harkat, H.; Weibel, J.-M.; Pale, P. *Tetrahedron Lett.* **2006**, *47*, 6273. (f) Genin, E.; Toullec, P. Y.; Antoniotti, S.; Brancour, C.; Genêt, J.-P.; Michelet, V. *J. Am. Chem. Soc.* **2006**, *128*, 3112. For a review, see: (g) Drozdzak, R.; Allaert, B.; Ledoux, N.; Dragutan, V.; Verpoort, F. *Adv. Synth. Catal.* **2005**, *347*, 1721.

(3) (a) Lemaire, H.; Lucas, H. J. *J. Am. Chem. Soc.* **1955**, *77*, 939. (b) Hudrlik, P. F.; Hudrlik, A. M. *J. Org. Chem.* **1973**, *38*, 4254. (c) Larock, R. C.; Oertle, K.; Beatty, K. M. *J. Am. Chem. Soc.* **1980**, *102*, 1966. (d) Kita, Y.; Akai, S.; Ajimura, N.; Yoshigi, M.; Tsugoshi, T.; Yasuda, H.; Tamura, Y. *J. Org. Chem.* **1986**, *51*, 4150.

(4) (a) Shvo, Y.; Rotem, M. *Organometallics* **1983**, *2*, 1689. (b) Mitsudo, T.-a.; Hori, Y.; Yamakawa, Y.; Watanabe, Y. *J. Org. Chem.* **1987**, *52*, 2230. (c) Doucet, H.; Martin-Vaca, B.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1995**, *60*, 7247. (d) Goossen, L. J.; Paetzold, J.; Koley, D. *Chem. Commun.* **2003**, 706. (e) Kim, H.; Goble, S. D.; Lee, C. *J. Am. Chem. Soc.* **2007**, *129*, 1030. (f) Yi, C. S.; Gao, R. *Organometallics* **2009**, *28*, 6585. (g) Tanaka, K.; Saitoh, S.; Hara, H.; Shibata, Y. *Org. Biomol. Chem.* **2009**, *7*, 4817. (h) Tripathy, J.; Bhattacharjee, M. *Tetrahedron Lett.* **2009**, *50*, 4863. (i) Willem, Q.; Nicks, F.; Sauvage, X.; Delaude, L.; Demonceau, A. *J. Organomet. Chem.* **2009**, *694*, 4049. (j) Nicks, F.; Aznar, R.; Sainz, D.; Muller, G.; Demonceau, A. *Eur. J. Org. Chem.* **2009**, 5020. (k) Berger, S.; Haak, E. *Tetrahedron Lett.* **2010**, *51*, 6630. (l) Nishiumi, M.; Miura, H.; Wada, K.; Hosokawa, S.; Inoue, M. *Adv. Synth. Catal.* **2010**, *352*, 3045. (m) Tan, S. T.; Fan, W. Y. *Eur. J. Inorg. Chem.* **2010**, 4631. (n) Cadierno, V.; Francos, J.; Gimeno, J. *Organometallics* **2011**, *30*, 852.

(5) Lumbroso, A.; Vautravers, N. R.; Breit, B. *Org. Lett.* **2010**, *12*, 5498.

(6) Nakagawa, H.; Okimoto, Y.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2003**, *44*, 103.

(7) (a) Lambert, C.; Utimoto, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 5323. (b) Wakabayashi, T.; Ishii, Y.; Murata, T.; Mizobe, Y.; Hidai, M. *Tetrahedron Lett.* **1995**, *36*, 5585. (c) Wolf, L. B.; Tjen, K. C. M. F.; ten Brink, H. T.; Blaauw, R. H.; Hiemstra, H.; Schoemaker, H. E.; Rutjes, F. P. J. T. *Adv. Synth. Catal.* **2002**, *344*, 70. (d) Wang, Y.; Burton, D. J. *J. Org. Chem.* **2006**, *71*, 3859. (e) Lu, X.; Zhu, G.; Ma, S. *Tetrahedron Lett.* **1992**, *33*, 7205. (f) Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505. (g) Zhao, L.; Lu, X.; Xu, W. *J. Org. Chem.* **2005**, *70*, 4059. (h) Song, J.; Shen, Q.; Xu, F.; Lu, X. *Tetrahedron* **2007**, *63*, 5148. (i) Tang, D.-J.; Tang, B.-X.; Li, J.-H. *J. Org. Chem.* **2009**, *74*, 6749.

(8) Ishino, Y.; Nishiguchi, I.; Nakao, S.; Hirashima, T. *Chem. Lett.* **1981**, 641.

(9) (a) Chary, B. C.; Kim, S. *J. Org. Chem.* **2010**, *75*, 7928. (b) Wang, Y.; Wang, Z.; Li, Y.; Wu, G.; Cao, Z.; Zhang, L. *Nat. Commun.* **2014**, DOI: 10.1038/ncomms4470.

(10) Hua, R.; Tian, X. *J. Org. Chem.* **2004**, *69*, 5782.

(11) For a DABCO-promoted addition of carboxylates to electron-deficient alkynes, see: Fan, M.-J.; Li, G.-Q.; Liang, Y.-M. *Tetrahedron* **2006**, *62*, 6782.

(12) Kawatsura, M.; Namioka, J.; Kajita, K.; Yamamoto, M.; Tsuji, H.; Itoh, T. *Org. Lett.* **2011**, *13*, 3285.

(13) Smith, D. L.; Goundry, W. R. F.; Lam, H. W. *Chem. Commun.* **2012**, *48*, 1505.

(14) Tsukada, N.; Takahashi, A.; Inoue, Y. *Tetrahedron Lett.* **2011**, *52*, 248.
(15) Cai, H.; Yuan, Z.; Zhu, W.; Zhu, G. *Chem. Commun.* **2011**, *47*, 8682.
(16) (a) Bai, Y.; Yin, J.; Kong, W.; Mao, M.; Zhu, G. *Chem. Commun.* **2013**, *49*, 7650. (b) Cui, W.; Ying, J.; Zheng, R.; Cheng, C.; Bai, Y.; Zhu, G. *J. Org. Chem.* **2014**, *79*, 3487.
(17) Cui, W.; Mao, M.; He, Z.; Zhu, G. *J. Org. Chem.* **2013**, *78*, 9815.
(18) For the synthesis of ynol ethers employed in this paper, see: (a) Jouvin, K.; Bayle, A.; Legrand, F.; Evano, G. *Org. Lett.* **2012**, *14*, 1652. (b) Tanaka, R.; Miller, S. I. *Tetrahedron Lett.* **1971**, *12*, 1753. (c) Moyano, A.; Charbonnier, F.; Greene, A. E. *J. Org. Chem.* **1987**, *52*, 2919. For recent reports on ynol ethers, see: (d) Miyauchi, Y.; Noguchi, K.; Tanaka, K. *Org. Lett.* **2012**, *14*, 5856. (e) Tran, V.; Minehan, T. G. *Org. Lett.* **2012**, *14*, 6100. (f) Verrier, C.; Carret, S.; Poisson, J.-F. *Org. Lett.* **2012**, *14*, 5122. (g) Minami, Y.; Shiraishi, Y.; Yamada, K.; Hiyama, T. *J. Am. Chem. Soc.* **2012**, *134*, 6124. (h) Minami, Y.; Yamada, K.; Hiyama, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 10611. (i) Graf, K.; Rühl, C. L.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 12727. (j) Alford, J. S.; Davies, H. M. L. *J. Am. Chem. Soc.* **2014**, *136*, 10266. For a recent review, see: (k) Evano, G.; Gaumont, A.-C.; Alayrac, C.; Wrona, I. E.; Giguere, J. R.; Delacroix, O.; Bayle, A.; Jouvin, K.; Theunissen, C.; Gatignol, J.; Silvanus, A. C. *Tetrahedron* **2014**, *70*, 1529 and references therein.
(19) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
(20) For the Ni-catalyzed Suzuki−Miyaura coupling of C−OPiv bonds, see: (a) Guan, B.-T.; Wang, Y.; Li, B.-J.; Yu, D.-G.; Shi, Z.-J. *J. Am. Chem. Soc.* **2008**, *130*, 14468. (b) Sun, C.-L.; Wang, Y.; Zhou, X.; Wu, Z.-H.; Li, B.-J.; Guan, B.-T.; Shi, Z.-J. *Chem.—Eur. J.* **2010**, *16*, 5844. (c) Quasdorf, K. W.; Tian, X.; Garg, N. K. *J. Am. Chem. Soc.* **2008**, *130*, 14422. (d) Ramgren, S. D.; Hie, L.; Ye, Y.; Garg, N. K. *Org. Lett.* **2013**, *15*, 3950. (e) Zhou, Q.; Srinivas, H. D.; Dasgupta, S.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 3307. For recent reviews on the cross-coupling of C−O bonds, see: (f) Li, B.-J.; Yu, D.-G.; Sun, C.-L.; Shi, Z.-J. *Chem.—Eur. J.* **2011**, *17*, 1728. (g) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. *Chem. Rev.* **2011**, *111*, 1346. (h) Yamaguchi, J.; Muto, K.; Itami, K. *Eur. J. Org. Chem.* **2013**, 19.
(21) Caputo, R.; Longobardo, L.; Palumbo, G.; Pedatella, S. *Synlett* **1995**, 1274. Of note, the hydrolysis of **5** was observed in $CDCl_3$; as such, DMSO-*d*6 was used for the NMR measurements.
(22) So far, the one-pot hydrocarboxylation/Suzuki−Miyaura coupling process was unsuccessful.
(23) Burke, M. D.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 46.

dx.doi.org/10.1021/jo501615a | *J. Org. Chem.* 2014, 79, 9179−9185