JOC The Journal of Organic Chemistry

Article

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Iron-Catalyzed Cross-Dehydrogenative Coupling Esterification of Unactive C(sp^3)–H Bonds with Carboxylic Acids for the Synthesis of α-Acyloxy Ethers

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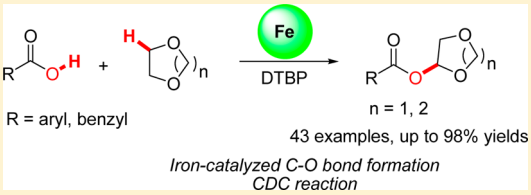
Supporting Information

ABSTRACT: An iron-catalyzed oxidative esterification reaction between unactivated C(sp^3)–H bonds from symmetric and asymmetric ethers and carboxylic acids using di-*tert*-butyl peroxide (DTBP) as the oxidant via a cross dehydrogenative coupling (CDC) reaction was established, which tolerates a wide range of cyclic ether substrates to react with aromatic acids and phenylacetic acid, providing an efficient method for the preparation of α-acyloxy ethers with good to excellent yields. Intermolecular competing kinetic isotope effect (KIE) experiments were also carried out, which indicate that C(sp^3)–H bond cleavage may be the rate-determining step of this CDC reaction.



INTRODUCTION

Direct C–H functionalization for the formation of C–C and C–X (X = O, S, N, P, etc.) bonds catalyzed by transition metals has become one of the most useful tools in organic chemistry owing to its remarkable potential for step economy, atom economy, and environmental sustainability.[1] In the past years, oxidative C(sp)–H and C(sp^2)–H cross couplings for various C–C bond-forming reactions have received special research attention and made great progress.[2] However, oxidative couplings involving C(sp^3)–H bonds remain challenging due to their low reactivity and the lack of a coordination site for the transition-metal catalyst.[3]

Functionalization of C(sp^3)–H bonds adjacent to the oxygen of ethers represents one of the hot topics in the research of C(sp^3)–H bond activation, and some developments have taken place recently.[4] The Li group developed Fe-catalyzed N-alkylation of azoles via oxidation of unactivated C(sp^3)–H bonds of ethers in 2010.[5] Later, the Wang group demonstrated a Cu-catalyzed cross-dehydrogenative coupling reactions of (benzo)thiazoles with cyclic ethers using $K_2S_2O_8$ as an oxidant.[6] Very recently, the Lei group reported oxidative arylation of cyclic ethers catalyzed by nickel.[7] Our group also developed an iron-catalyzed decarboxylative alkenylation of cyclic ethers with cinnamic acids via a radical process.[8] Encouraged by these results, we then tried to realize the oxidative arylation of cyclic ethers with more easily available aromatic carboxylic acids with iron as catalyst (Scheme 1). Surprisingly, the expected product 2-(4-methoxyphenyl)-1,4-dioxane was not observed. Instead, we found that 4-methoxybenzoic acid reacted with 1,4-dioxane directly through a cross dehydrogenative coupling (CDC) process,[9] giving an unexpected α-acyloxy ether product of 1,4-dioxan-2-yl 4-methoxybenzoate with 89% isolated chemical yield.

C–H activating esterification has also attracted attentions in the past few years, which proceeds through oxidative coupling reactions from common starting materials with high atom economy. Several transition-metal catalysts, including palladium,[10] copper,[11] rhodium,[12] and platinum,[13] have been developed for this new C–H activating esterification reaction. In addition, a metal-free methodology using Bu_4NI as a catalyst has also been employed for C–H activating esterification.[14] However, to the best of our knowledge, no reports of iron-catalyzed oxidative C(sp^3)–H activating esterification of ethers are known. The readily available and nontoxic iron catalysts are highly attractive for chemical synthesis from environmental and economic points of view.[15] Therefore, the development of iron-catalyzed C–O cross-coupling methods would be of a great value. Herein, we report an iron-catalyzed dehydrogenative cross-coupling reaction for C–O bond formation to construct α-acyloxy ethers using DTBP as the oxidant.

RESULTS AND DISCUSSION

The initial choice of reaction conditions was focused on using 4-methoxybenzoic acid (**1a**) and 1,4-dioxane as substrates with $Fe(acac)_3$ as catalyst. Among a wide range of oxidant candidates, such as TBHP (5–6 M in decane), $K_2S_2O_8$, H_2O_2 (30% aqueous solution), and TBPB (Table 1, entries 2–5), DTBP was found to be the most effective oxidant, giving 89% chemical yield (entry 1). The iron(III) acetylacetonate was found to be the best choice of catalyst, and the other tested iron compounds, such as Fe_2O_3 and $FeCl_3$, did not give any improvement (entries 6 and 7). No significant increase in the yield of **5a** was observed with the use of more than 2 equiv of

Received: January 25, 2014
Published: April 11, 2014

   dx.doi.org/10.1021/jo500192h | J. Org. Chem. 2014, 79, 3847–3855

Scheme 1. Decarboxylative and Dehydrogenative Cross-Coupling Reactions

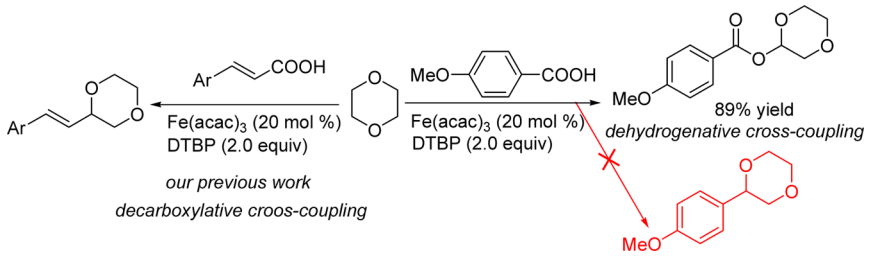
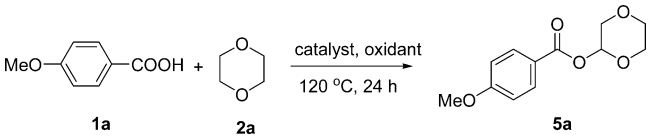


Table 1. Optimization of Typical Reaction Conditions[a]



1a 2a 5a

entry	catalyst (amt, mol %)	oxidant	yield, %[b]
1	$Fe(acac)_3$ (20)	DTBP[g]	89
2[c]	$Fe(acac)_3$ (20)	TBHP[h]	46
3	$Fe(acac)_3$ (20)	$K_2S_2O_8$	N.D.
4	$Fe(acac)_3$ (20)	H_2O_2[d]	trace
5	$Fe(acac)_3$ (20)	TBPB	21
6	Fe_2O_3 (20)	DTBP	34
7	$FeCl_3$ (20)	DTBP	23
8[e]	$Fe(acac)_3$ (20)	DTBP	85
9	$Fe(acac)_3$ (10)	DTBP[f]	67
10	$Fe(acac)_3$ (20)		N.D.
11		DTBP	N.D.

[a]Catalytic conditions: 4-methoxybenzoic acid (2 mmol), 1,4-dioxane (4 mL), iron catalyst (20 mol %), oxidant (2.0 equiv), 120 °C, 24 h. [b]Isolated yield based on carboxylic acid. [c]TBHP (5−6 M in decane). [d]30% aqueous solution. [e]130 °C. [f]3.0 equiv. [g]DTBP = di-*tert*-butyl peroxide. [h]TBHP = *tert*-butyl hydroperoxide.

DTBP (entry 8). Finally, an examination of the loading amount of $Fe(acac)_3$ catalyst demonstrated that 20 mol % was needed for this reaction (67% yield, entry 9). Furthermore, the reaction did not proceed without the use of iron catalyst or DTBP (entries 10 and 11).

With the optimized reaction conditions in hand, we next explored the benzoic acid scope of this iron-catalyzed oxidative esterification reaction (Scheme 2). As shown in Scheme 2, the process has a broad scope, with groups such as methoxy, methyl, ethyl, *tert*-butyl, *n*-propoxy, phenyl, phenoxy, bromo, and ethoxy, giving good to excellent yields of 62−96% (**5a**−**m**,**o**−**x**). Ortho-, meta-, and para-substituted benzoic acids could all work in this system. Slightly lower yields were observed in the cases of ortho-substituted benzoic acids in comparison to their para or meta analogues, possibly due to steric hindrance (**5a**−**c**,**p**−**r**,**u**−**v**). Variation of substituents on the aromatic ring showed obvious effects on the reaction efficiency. The reaction with benzoic acids substituted with an electron-donating group afforded the expected product with excellent yields (**5u**, 96% yield). However, benzoic acids substituted with an electron-withdrawing group, such as 4-bromobenzoic acid, afforded the corresponding product in only 62% yield (**5m**). Even more, the reaction did not work when benzoic acid contained a nitro substituent group (**5n**). Notably, disubstituted and trisubstituted benzoic acids also worked well in the reaction and gave the desired products (**5o**−**x**). In addition, a highly electron-rich substrate, 3,4,5-trimethoxybenzoic acid, afforded the corresponding α-acyloxy ethers in the highest yield (96% **5u**) .

To prove the synthetic utility of the methodology, heteroaryl carboxylic acids and fused aryl carboxylic acids were subjected to the reaction under the optimized conditions (Scheme 3). As shown in Scheme 3, these reactions proceeded smoothly, giving the desired products in good to excellent yields (73−98%). Thiophene-2-carboxylic acid afforded a better yield than 1-methyl-1*H*-pyrrole-2-carboxylic acid (97% for **6a** and 89% for **6d**). Notably, a double-heteroatom aryl carboxylic acid, 2,4-dimethylthiazole-5-carboxylic acid, also gave the desired product in excellent yield (94%, **6e**). In addition, 1-naphthoic acid, 2-naphthoic acid, and 4-methyl-1-naphthoic acid were also good reaction partners, providing the corresponding products in 82%, 85%, and 86% yields, respectively (**6f**−**h**). Furthermore, it is also noteworthy that 1-methyl-1*H*-indole-3-carboxylic acid and benzo[*b*]thiophene-2-carboxylic acid could provide the corresponding products in good yields (**6i**,**j**).

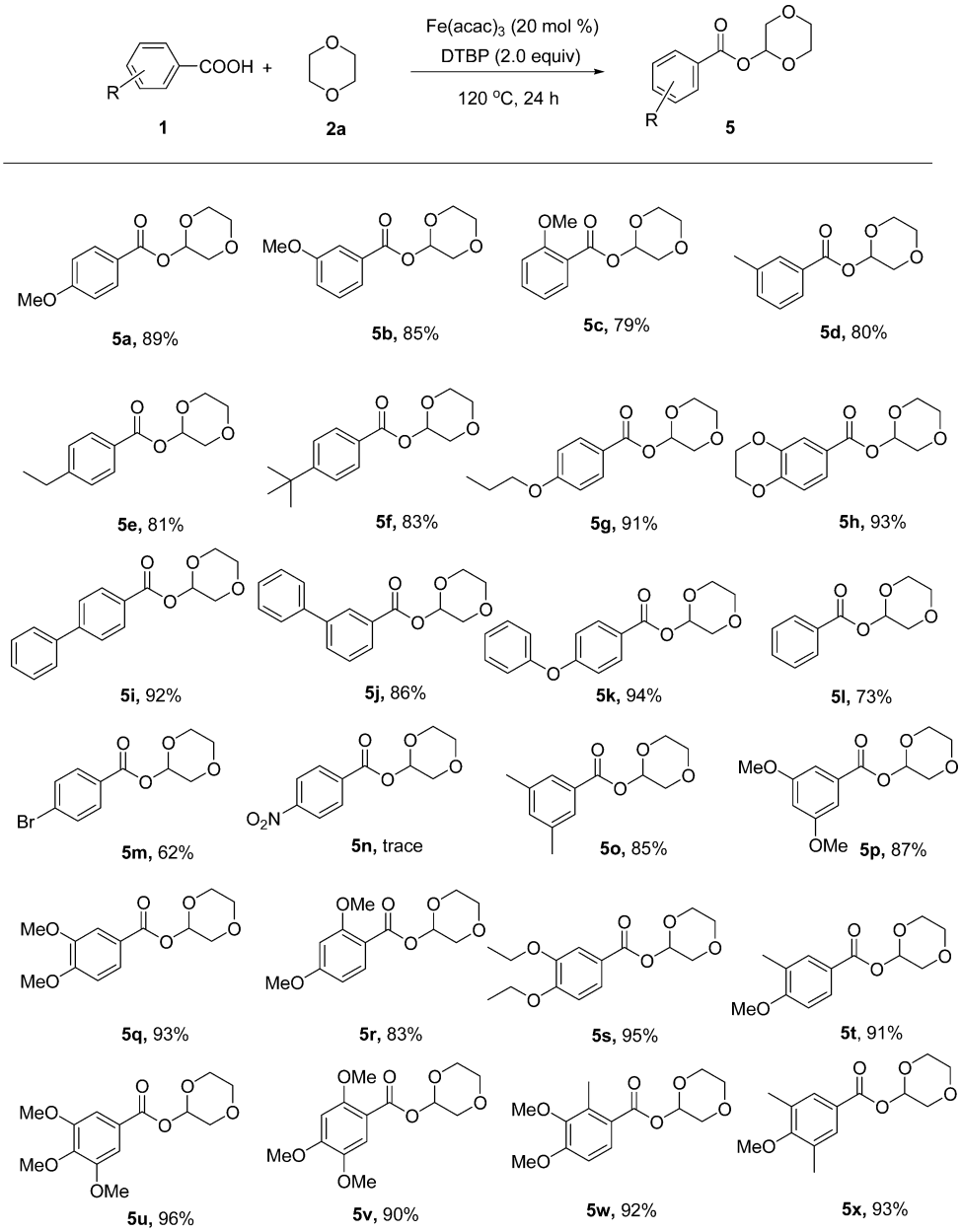
After testing the coupling reaction with a symmetric ether, 1,4-dioxane, we then tried to extend the reaction substrate scope to an asymmetric ether as substrate, to investigate the reactivity and regioselectivity of this system. 1,3-Dioxolane, an asymmetric ether, was then used in this oxidative esterification reaction which has not been thus far achieved under CDC reactions (Scheme 4). We began our investigation by examining the coupling of 4-methoxybenzoic acid and 1,3-dioxolane under the optimized conditions. Surprisingly, the expected product 1,3-dioxolan-2-yl 4-methoxybenzoate was not observed. Instead, we obtained 1,3-dioxolan-4-yl 4-methoxybenzoate (**7a**) in 86% yield, which was identified by its ^{1}H NMR and ^{13}C NMR spectra. As illustrated in Scheme 4, benzoic acids containing methoxy, methyl, ethyl, *tert*-butyl, phenyl, and phenoxy groups could all react well with 1,3-dioxolane to afford the corresponding α-acyloxy ethers in good yields (**7a**−**e**). In addition, thiophene-2-carboxylic and thiophene-3-carboxylic acids were also good reaction partners, providing the corresponding products in 90% and 87% yields, respectively (**7f**,**g**). Furthermore, the reactions have excellent regioselectivities, and only one regioisomer is detected for all cases.

Thereafter, the scope of this protocol was evaluated using other C(sp^3)−H bonds as the cross-coupling partners with thiophene-2-carboxylic acid (Scheme 5). The substrate methoxybenzene coupled well with thiophene-2-carboxylic acid under our optimized conditions to give the corresponding product in 82% yield (**8a**). Remarkably, the protocol was also successfully utilized for the esterification of cyclohexene in 42% yield (**8b**). Disappointingly, tetrahydrofuran, 2,5-dihydrofuran, toluene, and benzyl ether could not react with thiophene-2-carboxylic acid under the current conditions (**8c**−**f**).

Finally, we examined whether other types of acids were suitable substrates for this oxidative esterification reaction.

dx.doi.org/10.1021/jo500192h | J. Org. Chem. 2014, 79, 3847−3855

Scheme 2. Coupling of 1,4-Dioxane with Substituted Benzoic Acids[a]



[a]Catalytic conditions: **1** (2.0 mmol), 1,4-dioxane **2a** (4.0 mL), DTBP (2.0 equiv), 120 °C, 24 h. Isolated yield based on **1**.

Phenylacetic acid (**4**) was used in this system to react with 1,4-dioxane under the typical reaction conditions. We were pleased to find that the reaction proceeded well and gave the corresponding product **9** in 62% yield (Scheme 6).

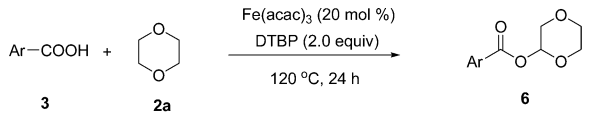
To investigate the details of the mechanism for this iron-catalyzed oxidative esterification of ethers with carboxylic acids, a series of controlled experiments were carried out. No desired product was observed by addition of TEMPO as a radical inhibitor. In addition, an intermolecular competing kinetic isotope effect (KIE) experiment was carried out (Scheme 7). As a result, a significant KIE was observed with $k_H/k_D = 3$ (the KIE was determined by ^{1}H NMR spectroscopy by analyzing the ratio of **6a** and [**D**]**6a**). This indicates that C(sp^3)−H bond cleavage may be one of the rate-determining steps of this procedure.

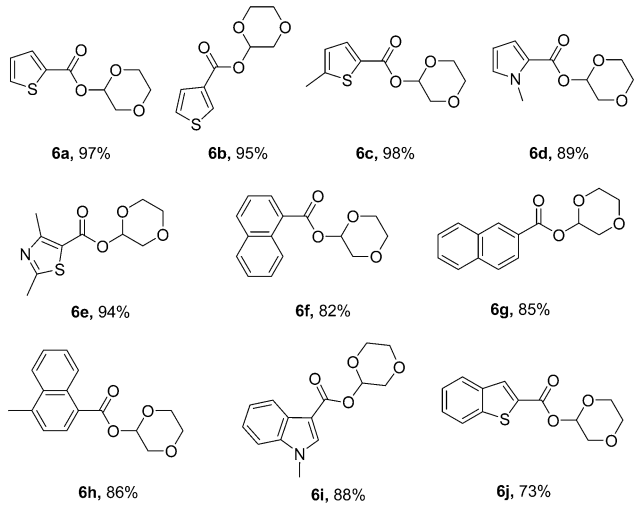
On the basis of the above results and the literature reports,[8,16] a plausible radical oxidative coupling mechanism containing a μ-oxo, μ-carboxylate diiron(III) intermediate is illustrated in Scheme 8. At the beginning, the iron catalyst reacts with carboxylic acid and the oxidant DTBP, forming the μ-oxo, μ-carboxylate diiron(III) intermediate **A** (methane monooxygenase model system).[17] The intermediate **A** is further oxidized to give the Fe(IV) intermediate **B**. Then, intermediate **B** reacts with a cyclic ether to generate intermediate **C**.[17b,18] Subsequently, the intermediate **C** undergoes a cross-coupling process, giving the final product **5a** and catalyst Fe(III) intermediate **A**.

According to a previous report on the stereoelectronic effects in hydrogen atom abstraction from ethers[19] and the mechanism proposed above (Scheme 8), the abnormal regioselectivity of the reaction on the substrate 1,3-dioxolane could be explained.

dx.doi.org/10.1021/jo500192h | J. Org. Chem. 2014, 79, 3847−3855

Scheme 3. Coupling of 1,4-Dioxane to Heteroaryl Carboxylic Acids and Fused Aryl Carboxylic Acids[a]

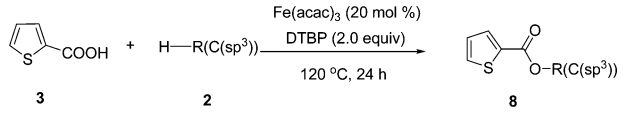


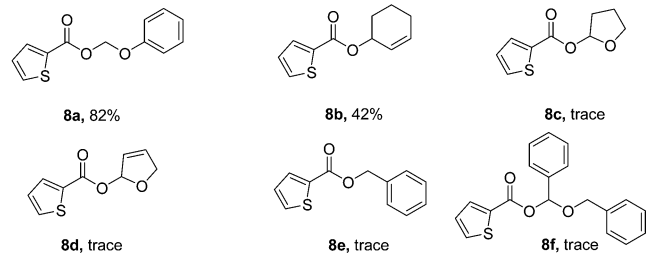


[a]Catalytic conditions: **3** (2.0 mmol), 1,4-dioxane (4.0 mL), DTBP (2.0 equiv), 120 °C, 24 h. Isolated yield based on **3**.

If the radical forms at the Ha position (path b, Scheme 9), it will be a bridgehead radical, which is notoriously very difficult to form.[19] Thus, for the Fe-catalyzed radical reaction of this substrate containing two oxygen atoms, the regioselectivity is abnormal, and the reaction happens selectively at the Hb position and proceeds through path a to give the final products **7**.

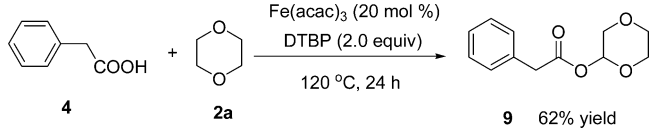
Scheme 5. Substrate Scope for the Iron-Catalyzed Oxidative Esterification of Other C(sp^3)−H Bonds with Thiophene-2-carboxylic Acid[a]





[a]Catalytic conditions: thiophene-2-carboxylic acid (2.0 mmol), **2** (4.0 mL), DTBP (2.0 equiv), 120 °C, 24 h. Isolated yield based on thiophene-2-carboxylic acid.

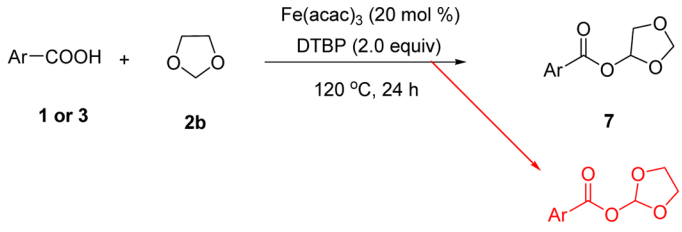
Scheme 6. Coupling of 1,4-Dioxane with Phenylacetic Acid[a]

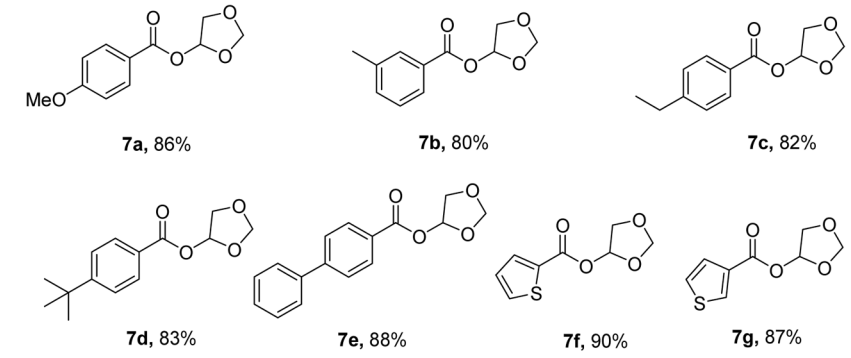


[a]Catalytic conditions: phenylacetic acid (2.0 mmol), **2a** (4.0 mL), DTBP (2.0 equiv), 120 °C, 24 h. Isolated yield based on phenylacetic acid.

Finally, the different pathways for the current cross-dehydrogenative coupling of benzoic acid and our previous cross-decarboxylative coupling of cinnamic acids[8] have been

Scheme 4. Coupling of 1,3-Dioxolane with Aromatic Carboxylic Acids[a]

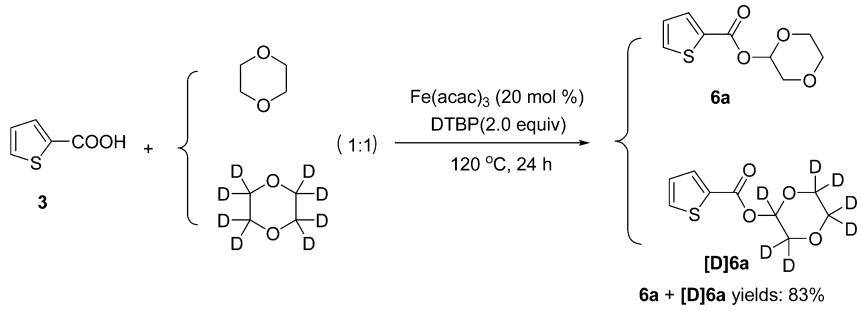




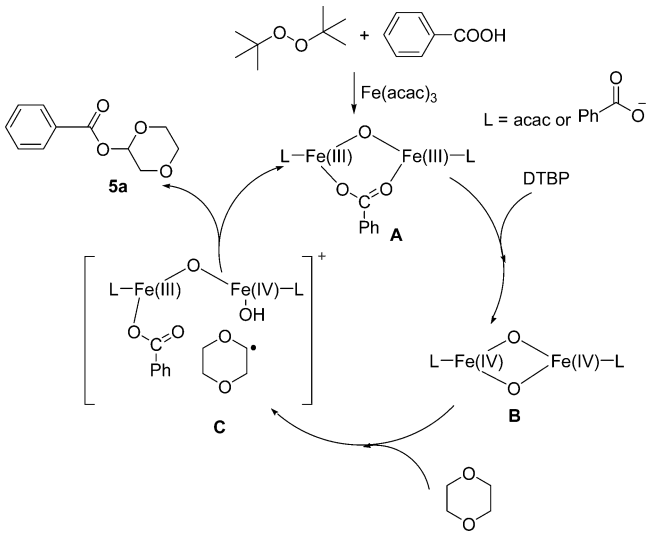
[a]Catalytic conditions: aromatic carboxylic acids (2.0 mmol), 1,3-dioxolane (**2b**; 4.0 mL), DTBP (2.0 equiv), 120 °C, 24 h. Isolated yield based on aromatic carboxylic acids.

dx.doi.org/10.1021/jo500192h | J. Org. Chem. 2014, 79, 3847−3855

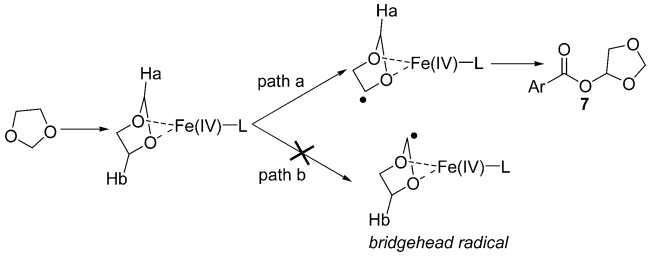
Scheme 7. KIE Studies



Scheme 8. Possible Mechanism



Scheme 9. Regioselectivity of the Reaction on 1,3-Dioxolane

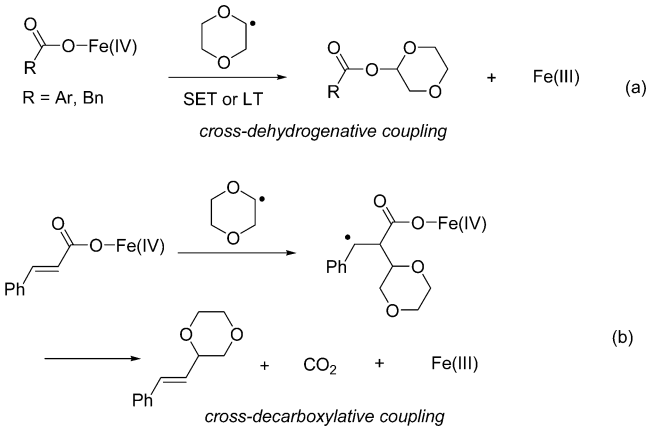


investigated (Scheme 10). For the current reaction with benzoates and phenylacetate as substrates, the cyclic ether radical intermediate reacts with the Fe(IV) carboxylate intermediate through either a single electron transfer process (SET) or a ligand transfer process (LT), giving the final cross dehydrogenative coupling products without decarboxylation (Scheme 10a).[11d,20] However, for our previous system with cinnamic acids as substrates, the reaction goes through a different pathway, which consists of the addition of the cyclic ether radical intermediate to a C−C double bond. Then, releasing CO_2 gives the final cross decarboxylative coupling products (Scheme 10b).[8]

CONCLUSION

In conclusion, an efficient procedure for the $Fe(acac)_3$-catalyzed direct esterification of unactivated $C(sp^3)$−H bonds with DTBP as an oxidant has been reported. This is a novel method for the construction of C−O bonds using iron as

Scheme 10. Different Pathways for Reactions of Benzoates and Cinnamic Acids



catalyst via a CDC reaction. Furthermore, this reaction provides a useful strategy for the synthesis of substituted α-acyloxy ethers. Various carboxylic acids and several symmetric and asymmetric ethers were well tolerated in this catalytic system with moderate to excellent chemical yields and completely controlled regioselectivities. The mechanism of this reaction has also been studied through an intermolecular competing kinetic isotope effect (KIE) experiment. Further studies on iron-catalyzed C−O bond formation reactions are currently being investigated in our laboratory.

EXPERIMENTAL SECTION

General Procedure of the Fe-Catalyzed Oxidative Esterification Reaction. In a Schlenk tube equipped with a magnetic stir bar were added $Fe(acac)_3$ (141 mg, 0.4 mmol) and 4-methoxybenzoic acid (304 mg, 2.0 mmol). 1,4-Dioxane (4.0 mL, 30−50 mmol) and DTBP (di-*tert*-butyl peroxide, 4 mmol, 753 μL) were added. The resulting reaction mixture was stirred at 120 °C for 24 h. After the required reaction time, the mixture was cooled to room temperature. The reaction mixture was extracted with dichloromethane. The organic phases were evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/dichloromethane 2/1) to afford the corresponding product.

*1,4-Dioxan-2-yl 4-Methoxybenzoate (**5a**).*[21] Colorless oil. Yield: 424 mg (89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10−8.04 (m, 2H), 6.94−6.88 (m, 2H), 6.05 (s, 1H), 4.21−4.15 (m, 1H), 3.87−3.81 (m, 5H), 3.79 (dd, J = 4.1, 1.9 Hz, 2H), 3.68−3.61 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.7, 163.6, 131.8, 121.8, 113.5, 89.3, 67.7, 66.0, 61.6, 55.3.

*1,4-Dioxan-2-yl 3-Methoxybenzoate (**5b**).* Colorless oil. Yield: 405 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74−7.66 (m, 1H), 7.61 (dd, J = 2.6, 1.5 Hz, 1H), 7.34 (dd, J = 9.1, 6.9 Hz, 1H), 7.10 (ddd, J = 8.3, 2.7, 0.9 Hz, 1H), 6.08 (t, J = 1.8 Hz, 1H), 4.20 (ddd, J = 11.9, 7.5,

dx.doi.org/10.1021/jo500192h | J. Org. Chem. 2014, 79, 3847−3855

5.6 Hz, 1H), 3.86 (d, J = 1.9 Hz, 2H), 3.83 (d, J = 5.2 Hz, 3H), 3.81−3.76 (m, 2H), 3.65 (dt, J = 11.7, 2.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 159.2, 130.7, 129.1, 121.8, 119.2, 114.0, 89.5, 67.38, 65.6, 61.4, 54.9. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{12}H_{14}O_5]$ 238.0841, found 238.0845.

*1,4-Dioxan-2-yl 2-Methoxybenzoate (**5c**).* White solid, mp 63−64 °C. Yield: 376 mg (79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85−7.79 (m, 1H), 7.45−7.39 (m, 1H), 6.95−6.89 (m, 2H), 6.02 (d, J = 1.6 Hz, 1H), 4.20−4.10 (m, 1H), 3.87−3.82 (m, 3H), 3.80 (d, J = 2.0 Hz, 2H), 3.76−3.70 (m, 2H), 3.65−3.55 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 159.3, 133.7, 131.5, 119.8, 119.1, 111.8, 89.3, 67.5, 65.8, 61.4, 55.7. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{12}H_{14}O_5]$ 238.0841, found 238.0843.

*1,4-Dioxan-2-yl 3-Methylbenzoate (**5d**).* Colorless oil. Yield: 355 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (dd, J = 4.1, 1.4 Hz, 2H), 7.24−7.13 (m, 2H), 5.94 (t, J = 1.8 Hz, 1H), 4.10−4.02 (m, 1H), 3.72 (d, J = 1.7 Hz, 2H), 3.70−3.61 (m, 2H), 3.50 (dt, J = 11.8, 2.6 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.7, 137.7, 133.6, 129.8, 129.3, 127.9, 126.6, 89.3, 67.3, 65.6, 61.3, 20.7. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{12}H_{14}O_4]$ 222.0892, found 222.0895.

*1,4-Dioxan-2-yl 4-Ethylbenzoate (**5e**).* Colorless oil. Yield: 382 mg (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.2 Hz, 2H), 6.08 (s, 1H), 4.24−4.18 (m, 1H), 3.88 (d, J = 1.9 Hz, 2H), 3.81 (dd, J = 6.6, 2.5 Hz, 2H), 3.71−3.60 (m, 1H), 2.70 (q, J = 7.6 Hz, 2H), 1.28−1.25 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 150.1, 129.8, 127.7, 127.0, 89.4, 67.6, 65.9, 61.5, 28.7, 15.0. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{13}H_{16}O_4]$ 236.1049, found 236.1052.

*1,4-Dioxan-2-yl 4-(tert-Butyl)benzoate (**5f**).*[14a] Colorless oil. Yield: 438 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10−8.04 (m, 2H), 7.49−7.45(m, 2H), 6.09 (t, J = 1.8 Hz, 1H), 4.21 (dt, J = 12.1, 6.5 Hz, 1H), 3.87 (d, J = 2.0 Hz, 2H), 3.80 (dd, J = 6.9, 2.5 Hz, 2H), 3.65 (dt, J = 11.7, 2.6 Hz, 1H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 156.8, 129.5, 126.7, 125.1, 89.3, 67.6, 65.8, 61.4, 34.8, 30.8.

*1,4-Dioxan-2-yl 4-Propoxybenzoate (**5g**).* White solid, mp 37−39 °C. Yield: 484 mg (91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05−7.95 (m, 2H), 6.90−6.84 (m, 2H), 6.02 (t, J = 1.9 Hz, 1H), 4.20−4.10 (m, 1H), 3.91 (t, J = 6.6 Hz, 2H), 3.82 (d, J = 1.9 Hz, 2H), 3.75 (dd, J = 6.6, 2.6 Hz, 2H), 3.61 (dt, J = 11.8, 2.7 Hz, 1H), 1.82−1.72 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 163.1, 131.7, 121.5, 113.9, 89.2, 69.4, 67.6, 65.8, 61.5, 22.1, 10.2. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{14}H_{18}O_5]$ 266.1154, found 266.1159.

*1,4-Dioxan-2-yl 2,3-Dihydrobenzo[b][1,4]dioxine-6-carboxylate (**5h**).* White solid, mp 98−100 °C. Yield: 495 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 6.7 Hz, 2H), 6.89 (d, J = 8.9 Hz, 1H), 6.04 (s, 1H), 4.28 (d, J = 9.0 Hz, 4H), 4.23−4.14 (m, 1H), 3.86 (s, 2H), 3.80 (d, J = 4.7 Hz, 2H), 3.65 (d, J = 11.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 147.9, 142.9, 123.4, 122.5, 118.9, 116.9, 89.3, 67.5, 65.8, 64.3, 63.7, 61.4. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{13}H_{14}O_6]$ 266.0790, found 266.0791.

*1,4-Dioxan-2-yl [1,1′-Biphenyl]-4-carboxylate (**5i**).* White solid, mp 83−84 °C. Yield: 495 mg (92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.60−7.52 (m, 2H), 7.41 (t, J = 7.4 Hz, 2H), 7.38−7.31 (m, 1H), 6.10 (s, 1H), 4.27−4.15 (m, 1H), 3.92−3.81 (m, 2H), 3.80−3.73 (m, 2H), 3.64−3.60 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 145.5, 139.3, 130.0, 128.5, 128.1, 127.8, 126.8, 126.6, 89.4, 67.4, 65.6, 61.3. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{17}H_{16}O_4]$ 284.1049, found 284.1044.

*1,4-Dioxan-2-yl [1,1′-Biphenyl]-3-carboxylate (**5j**).* Colorless oil. Yield: 488 mg (86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (t, J = 1.6 Hz, 1H), 8.15−8.09 (m, 1H), 7.85−7.79 (m, 1H), 7.69−7.60 (m, 2H), 7.55 (t, J = 7.7 Hz, 1H), 7.48 (dd, J = 10.3, 4.7 Hz, 2H), 7.40 (dd, J = 8.3, 6.4 Hz, 1H), 6.14 (t, J = 1.7 Hz, 1H), 4.33−4.20 (m, 1H), 3.93 (d, J = 1.9 Hz, 2H), 3.85 (dd, J = 6.7, 2.5 Hz, 2H), 3.70 (dt, J = 11.7, 2.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.1, 141.6, 139.9, 132.0, 130.2, 128.8, 128.8, 128.6, 128.4, 127.7, 127.1, 89.9, 67.7, 66.0, 61.8. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{17}H_{16}O_4]$ 284.1049, found 284.1043.

*1,4-Dioxan-2-yl 4-Phenoxybenzoate (**5k**).* Light yellow oil. Yield: 564 mg (94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09−7.98 (m, 2H), 7.34−7.27 (m, 2H), 7.10 (t, J = 7.4 Hz, 1H), 6.99 (d, J = 7.7 Hz, 2H), 6.96−6.87 (m, 2H), 6.01 (s, 1H), 4.19−4.06 (m, 1H), 3.79 (d, J = 1.7 Hz, 2H), 3.73−3.68 (m, 2H), 3.59−3.53 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 161.7, 155.0, 131.6, 129.6, 124.1, 123.5, 119.6, 116.8, 89.2, 67.3, 65.6, 61.2. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{17}H_{16}O_5]$ 300.0998, found 300.0995.

*1,4-Dioxan-2-yl Benzoate (**5l**).*[14d] Colorless oil. Yield: 304 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05−7.99 (m, 2H), 7.50−7.43 (m, 1H), 7.38−7.32 (m, 2H), 5.99 (t, J = 2.0 Hz, 1H), 4.12−4.06 (m, 1H), 3.80−3.74 (m, 2H), 3.74−3.66 (m, 2H), 3.61−3.49 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 133.1, 129.6, 129.5, 128.2, 89.6, 67.5, 65.8, 61.5.

*1,4-Dioxan-2-yl 4-Bromobenzoate (**5m**).*[14d] White solid, mp 98−100 °C. Yield: 353 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.5 Hz, 2H), 6.03 (s, 1H), 4.21−4.09 (m, 1H), 3.83 (d, J = 1.6 Hz, 2H), 3.80−3.74 (m, 2H), 3.68−3.57 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 131.5, 131.1, 128.4, 128.3, 89.8, 67.5, 65.8, 61.5.

*1,4-Dioxan-2-yl 3,5-Dimethylbenzoate (**5o**).* Colorless oil. Yield: 401 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 2H), 7.07 (s, 1H), 5.96 (t, J = 1.9 Hz, 1H), 4.10 (ddd, J = 12.0, 7.8, 5.3 Hz, 1H), 3.76 (d, J = 2.0 Hz, 2H), 3.74−3.65 (m, 2H), 3.54 (dt, J = 11.8, 2.6 Hz, 1H), 2.24 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.1, 137.7, 134.7, 129.3, 127.2, 89.3, 67.5, 65.8, 61.4, 20.8. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{13}H_{16}O_4]$ 236.1049, found 236.1051.

*1,4-Dioxan-2-yl 3,5-Dimethoxybenzoate (**5p**).* White solid, mp 51−53 °C. Yield: 466 mg (87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 1.8 Hz, 2H), 6.65 (d, J = 2.0 Hz, 1H), 6.05 (s, 1H), 4.25−4.14 (m, 1H), 3.86 (d, J = 1.3 Hz, 2H), 3.84−3.76 (m, 8H), 3.72−3.61 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 160.5, 131.4, 107.4, 105.7, 89.9, 67.6, 65.9, 61.7, 55.4. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{13}H_{16}O_6]$ 268.0947, found 268.0952.

*1,4-Dioxan-2-yl 3,4-Dimethoxybenzoate (**5q**).* Colorless oil. Yield: 499 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (dd, J = 8.4, 2.0 Hz, 1H), 7.59 (d, J = 2.0 Hz, 1H), 6.90 (d, J = 8.5 Hz, 1H), 6.07 (t, J = 1.9 Hz, 1H), 4.24−4.16 (m, 1H), 3.94 (s, 6H), 3.88 (d, J = 2.1 Hz, 2H), 3.83−3.75 (m, 2H), 3.67 (dt, J = 11.7, 2.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4, 152.9, 148.2, 123.6, 121.6, 111.6, 109.8, 89.2, 67.4, 65.6, 61.4, 55.6, 55.54. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{13}H_{16}O_6]$ 268.0947, found 268.0949.

*1,4-Dioxan-2-yl 2,4-Dimethoxybenzoate (**5r**).* White solid, mp 102−103 °C. Yield: 445 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.5 Hz, 1H), 6.54−6.46 (m, 2H), 6.06 (d, J = 1.7 Hz, 1H), 4.28−4.18 (m, 1H), 3.90 (s, 3H), 3.88−3.84 (m, 5H), 3.81 (dd, J = 7.0, 2.6 Hz, 2H), 3.67 (dt, J = 11.6, 2.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 163.7, 161.8, 134.0, 111.4, 104.5, 98.8, 89.1, 67.8, 66.0, 61.7, 55.8, 55.3. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{13}H_{16}O_6]$ 268.0947, found 268.0951.

*1,4-Dioxan-2-yl 3,4-Diethoxybenzoate (**5s**).* Colorless oil. Yield: 562 mg (95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 8.4 Hz, 1H), 7.57 (s, 1H), 6.86 (d, J = 8.5 Hz, 1H), 6.04 (s, 1H), 4.22−4.08 (m, 5H), 3.85 (s, 2H), 3.79 (d, J = 6.2 Hz, 2H), 3.65 (d, J = 11.8 Hz, 1H), 1.50−1.42 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 153.1, 148.0, 123.9, 121.7, 113.9, 111.4, 89.4, 67.7, 66.0, 64.5, 64.3, 61.7, 14.5, 14.4. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{15}H_{20}O_6]$ 296.1260, found 296.1263.

*1,4-Dioxan-2-yl 4-Methoxy-3-methylbenzoate (**5t**).* White solid, mp 64−66 °C. Yield: 459 mg (91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (dd, J = 8.6, 2.1 Hz, 1H), 7.80 (d, J = 1.4 Hz, 1H), 6.74 (d, J = 8.6 Hz, 1H), 5.97 (t, J = 1.9 Hz, 1H), 4.17−4.06 (m, 1H), 3.78 (d, J = 2.1 Hz, 2H), 3.77 (s, 3H), 3.74−3.69 (m, 2H), 3.57 (dt, J = 11.8, 2.7 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 161.5, 131.7, 129.4, 126.2, 121.0, 108.8, 89.0, 67.5, 65.7, 61.4, 55.0, 15.71. HRMS (TOF MS EI$^+$): m/z calcd for $[C_{13}H_{16}O_5]$ 252.0998, found 252.0993.

*1,4-Dioxan-2-yl 3,4,5-Trimethoxybenzoate (**5u**).* White solid, mp 104−105 °C. Yield: 572 mg (96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (s, 2H), 6.08 (t, J = 2.0 Hz, 1H), 4.25−4.15 (m, 1H), 3.93 (s, 6H), 3.92 (s, 3H), 3.92−3.89 (m, 2H), 3.84 (dd, J = 6.6, 2.7 Hz, 2H), 3.70 (dt, J = 11.8, 2.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8,

dx.doi.org/10.1021/jo500192h | J. Org. Chem. 2014, 79, 3847−3855

152.8, 142.5, 124.5, 107.0, 89.9, 67.7, 65.9, 61.8, 60.8, 56.2. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{14}H_{18}O_7$] 298.1053, found 298.1050.

*1,4-Dioxan-2-yl 2,4,5-Trimethoxybenzoate (**5v**).* White solid, mp 92−94 °C. Yield: 536 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (s, 1H), 6.55 (s, 1H), 6.06 (s, 1H), 4.27−4.15 (m, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.87 (s, 3H), 3.86 (d, J = 1.8 Hz, 2H), 3.81−3.76 (m, 2H), 3.66 (dt, J = 11.6, 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 155.6, 153.4, 141.8, 113.8, 109.3, 97.1, 88.8, 67.2, 65.4, 61.2, 56.3, 55.7, 55.3. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{14}H_{18}O_7$] 298.1053, found 298.1052.

*1,4-Dioxan-2-yl 3,4-Dimethoxy-2-methylbenzoate (**5w**).* White solid, mp 39−41 °C. Yield: 519 mg (92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, J = 8.7 Hz, 1H), 6.69 (d, J = 8.7 Hz, 1H), 5.95 (s, 1H), 4.08 (dd, J = 11.6, 6.0 Hz, 1H), 3.80 (s, 3H), 3.77 (s, 2H), 3.70 (d, J = 5.8 Hz, 2H), 3.67 (s, 3H), 3.57 (d, J = 11.5 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.2, 156.0, 147.2, 135.3, 127.9, 121.7, 108.4, 89.1, 67.7, 65.8, 61.6, 60.0, 55.4, 13.1. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{14}H_{18}O_6$] 282.1103, found 282.1101.

*1,4-Dioxan-2-yl 4-Methoxy-3,5-dimethylbenzoate (**5x**).* White solid, mp 101−102 °C. Yield: 495 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 2H), 5.99 (s, 1H), 4.22−4.10 (m, 1H), 3.80 (d, J = 2.0 Hz, 2H), 3.77−3.70 (m, 2H), 3.68 (s, 3H), 3.59 (dt, J = 11.7, 2.5 Hz, 1H), 2.25 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 161.1, 130.8, 130.4, 124.6, 89.2, 67.5, 65.7, 61.4, 59.2, 15.7. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{14}H_{18}O_5$] 266.1154, found 266.1152.

*1,4-Dioxan-2-yl Thiophene-2-carboxylate (**6a**).*[14d] White solid, mp 48−49 °C. Yield: 415 mg (97%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90−7.80 (m, 1H), 7.62−7.52 (m, 1H), 7.09 (dt, J = 8.7, 4.8 Hz, 1H), 6.02 (s, 1H), 4.19−4.13 (m, 1H), 3.86−3.82(m, 2H), 3.80−3.74 (m, 2H), 3.68−3.58 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 133.9, 133.0, 133.0, 127.7, 89.7, 67.5, 65.8, 61.5.

*1,4-Dioxan-2-yl Thiophene-3-carboxylate (**6b**).* Colorless oil. Yield: 407 mg (95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (dd, J = 3.0, 1.0 Hz, 1H), 7.59 (dd, J = 5.1, 1.0 Hz, 1H), 7.33 (dd, J = 5.1, 3.1 Hz, 1H), 6.04 (s, 1H), 4.24−4.12 (m, 1H), 3.86 (d, J = 1.9 Hz, 2H), 3.79 (dd, J = 6.7, 2.5 Hz, 2H), 3.65 (dt, J = 11.7, 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 133.3, 132.8, 127.7, 125.9, 89.2, 67.4, 65.7, 61.4. HRMS (TOF MS EI$^+$): m/z calcd for [$C_9H_{10}O_4S$] 214.0300, found 214.0296.

*1,4-Dioxan-2-yl 5-Methylthiophene-2-carboxylate (**6c**).* Colorless oil. Yield: 467 mg (98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 3.7 Hz, 1H), 6.69 (dd, J = 3.7, 1.0 Hz, 1H), 5.91 (t, J = 1.8 Hz, 1H), 4.11−4.06 (m, 1H), 3.74 (d, J = 2.0 Hz, 2H), 3.71−3.66 (m, 2H), 3.54 (dt, J = 11.6, 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2, 148.4, 134.2, 130.1, 126.1, 89.2, 67.3, 65.6, 61.30, 15.3. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{10}H_{12}O_4S$] 228.0456, found 228.0461.

*1,4-Dioxan-2-yl 1-Methyl-1H-pyrrole-2-carboxylate (**6d**).*[21] White solid, mp 48−49 °C. Yield: 376 mg (89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03 (dd, J = 4.0, 1.8 Hz, 1H), 6.76 (t, J = 2.0 Hz, 1H), 6.06 (dd, J = 4.0, 2.5 Hz, 1H), 5.93 (t, J = 2.0 Hz, 1H), 4.15−4.03 (m, 1H), 3.86 (s, 3H), 3.81−3.74 (m, 2H), 3.74−3.69 (m, 2H), 3.56 (dt, J = 11.9, 2.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 129.9, 121.3, 118.4, 107.6, 88.2, 67.4, 65.6, 61.3, 36.3.

*1,4-Dioxan-2-yl 2,4-Dimethylthiazole-5-carboxylate (**6e**).* Light yellow oil. Yield: 457 mg (94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.87 (s, 1H), 4.04−3.98 (m, 1H), 3.72−3.70 (m, 2H), 3.68−3.63 (m, 2H), 3.52 (dt, J = 11.8, 2.5 Hz, 1H), 2.58 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 160.6, 160.2, 120.8, 89.5, 67.3, 65.6, 61.3, 19.0, 17.0. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{10}H_{13}NO_4S$] 243.0565, found 243.0568.

*1,4-Dioxan-2-yl 1-Naphthoate (**6f**).*[15] Light yellow oil. Yield: 423 mg (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.03 (d, J = 8.7 Hz, 1H), 8.36 (dd, J = 7.3, 1.2 Hz, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.64 (ddd, J = 8.5, 6.9, 1.4 Hz, 1H), 7.58−7.49 (m, 2H), 6.22 (t, J = 1.8 Hz, 1H), 4.32−4.22 (m, 1H), 4.01−3.90 (m, 2H), 3.90−3.82 (m, 2H), 3.72 (dt, J = 11.8, 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 134.0, 133.8, 131.5, 130.9, 128.5, 127.9, 126.2, 126.0, 125.7, 124.4, 89.8, 67.9, 66.1, 61.8.

*1,4-Dioxan-2-yl 2-Naphthoate (**6g**).*[14d] White solid, mp 88−89 °C. Yield: 439 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (s, 1H), 8.10 (dd, J = 8.6, 1.7 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 8.5 Hz, 2H), 7.49 (tdd, J = 14.8, 7.0, 1.3 Hz, 2H), 6.15 (s, 1H), 4.27−4.21 (m, 1H), 3.94−3.85 (m, 2H), 3.83−3.73 (m, 2H), 3.64 (dt, J = 11.7, 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 135.3, 132.0, 131.1, 129.0, 128.1, 127.9, 127.4, 126.6, 126.3, 124.9, 89.6, 67.5, 65.7, 61.4.

*1,4-Dioxan-2-yl 4-Methyl-1-naphthoate (**6h**).* White solid, mp 59−61 °C. Yield: 468 mg (86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.13 (d, J = 8.6 Hz, 1H), 8.25 (d, J = 7.4 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.67−7.60 (m, 1H), 7.56−7.50 (m, 1H), 7.30 (d, J = 7.5 Hz, 1H), 6.20 (s, 1H), 4.30−4.19 (m, 1H), 3.97−3.88 (m, 2H), 3.83−3.76 (m, 2H), 3.68 (dt, J = 11.7, 2.5 Hz, 1H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 140.7, 132.5, 131.3, 130.5, 127.2, 126.0, 125.7, 125.1, 124.1, 124.1, 89.4, 67.6, 65.8, 61.5, 19.7. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{16}H_{16}O_4$] 272.1049, found 272.1044.

*1,4-Dioxan-2-yl 1-Methyl-1H-indole-3-carboxylate (**6i**).*[21] Yellow solid, mp 94−96 °C. Yield: 459 mg (88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25−8.19 (m, 1H), 7.79 (s, 1H), 7.32−7.22 (m, 3H), 6.10 (t, J = 2.0 Hz, 1H), 4.23−4.17 (m, 1H), 3.87 (d, J = 2.0 Hz, 2H), 3.81−3.76 (m, 2H), 3.70 (s, 3H), 3.63 (dt, J = 11.8, 2.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 136.9, 135.6, 126.3, 122.6, 121.8, 121.3, 109.6, 105.8, 88.2, 67.9, 65.9, 61.5, 33.0.

*1,4-Dioxan-2-yl Benzo[b]thiophene-2-carboxylate (**6j**).* White solid, mp 67−68 °C. Yield: 385 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.87 (t, J = 7.8 Hz, 2H), 7.46−7.39 (m, 2H), 6.10 (s, 1H), 4.30−4.22 (m, 1H), 3.90 (d, J = 1.9 Hz, 2H), 3.86−3.80 (m, 2H), 3.69 (dd, J = 11.8, 1.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 142.4, 138.5, 132.9, 131.2, 127.1, 125.5, 124.9, 122.6, 90.1, 67.6, 66.0, 61.6. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{13}H_{12}O_4S$] 264.0456, found 264.0459.

*1,3-Dioxolan-4-yl 4-Methoxybenzoate (**7a**).* Light yellow oil. Yield: 385 mg (86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 6.55 (dd, J = 4.1, 1.9 Hz, 1H), 5.14 (d, J = 18.1 Hz, 2H), 4.11 (ddd, J = 11.3, 9.5, 3.0 Hz, 2H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.1, 163.5, 131.5, 121.4, 113.4, 95.4, 94.1, 70.3, 55.1. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{11}H_{12}O_5$] 224.0685, found 224.0684.

*1,3-Dioxolan-4-yl 3-Methylbenzoate (**7b**).* Light yellow oil. Yield: 333 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.80 (m, 2H), 7.40−7.30 (m, 2H), 6.57 (dd, J = 4.1, 2.0 Hz, 1H), 5.16 (d, J = 20.6 Hz, 2H), 4.13 (qd, J = 9.5, 3.1 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 138.1, 134.1, 130.1, 129.2, 128.2, 126.8, 95.7, 94.5, 70.5, 21.0. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{11}H_{12}O_4$] 208.0736, found 208.0731.

*1,3-Dioxolan-4-yl 4-Ethylbenzoate (**7c**).* Light yellow oil. Yield: 364 mg (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03−7.89 (m, 2H), 7.25 (d, J = 8.3 Hz, 2H), 6.58 (dd, J = 4.2, 1.9 Hz, 1H), 5.16 (d, J = 16.6 Hz, 2H), 4.13 (ddd, J = 11.4, 9.5, 3.1 Hz, 2H), 2.69 (q, J = 7.6 Hz, 2H), 1.24 (t, J = 7.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 150.2, 129.7, 127.8, 126.7, 95.6, 94.3, 70.5, 28.8, 15.0. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{12}H_{14}O_4$] 222.0892, found 222.0895.

*1,3-Dioxolan-4-yl 4-(tert-Butyl)benzoate (**7d**).* Light yellow oil. Yield: 415 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11−7.85 (m, 2H), 7.44 (d, J = 8.5 Hz, 2H), 6.58 (dd, J = 4.1, 1.9 Hz, 1H), 5.15 (d, J = 17.0 Hz, 2H), 4.18−4.08 (m, 2H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.3, 156.8, 129.4, 126.4, 125.1, 95.4, 94.2, 70.3, 34.7, 30.7. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{14}H_{18}O_4$] 250.1205, found 250.1208.

*1,3-Dioxolan-4-yl [1,1′-Biphenyl]-4-carboxylate (**7e**).* White solid, mp 86−87 °C. Yield: 475 mg (88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J = 8.3 Hz, 2H), 7.64 (dd, J = 18.5, 7.8 Hz, 4H), 7.43 (dt, J = 26.0, 7.2 Hz, 3H), 6.63 (dd, J = 3.8, 2.0 Hz, 1H), 5.20 (d, J = 22.7 Hz, 2H), 4.22−4.12 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 145.9, 139.5, 130.1, 128.7, 128.1, 127.9, 127.0, 126.9, 95.7, 94.5, 70.5. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{16}H_{14}O_4$] 270.0892, found 270.0894.

*1,3-Dioxolan-4-yl Thiophene-2-carboxylate (**7f**).* Light yellow oil. Yield: 360 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, J = 3.7, 1.1 Hz, 1H), 7.59 (dd, J = 5.0, 1.1 Hz, 1H), 7.10 (dd, J = 4.9, 3.9 Hz, 1H), 6.54 (dd, J = 4.1, 1.9 Hz, 1H), 5.15 (d, J = 15.8 Hz, 2H), 4.12

dx.doi.org/10.1021/jo500192h | J. Org. Chem. 2014, 79, 3847−3855

(qd, J = 9.5, 3.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2, 134.1, 133.2, 132.8, 127.8, 95.8, 94.6, 70.5. HRMS (TOF MS EI$^+$): m/z calcd for [$C_8H_8O_4S$] 200.0143, found 200.0144.

*1,3-Dioxolan-4-yl Thiophene-3-carboxylate (**7g**).* Light yellow oil. Yield: 348 mg (87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (dd, J = 3.0, 1.2 Hz, 1H), 7.52 (dd, J = 5.1, 1.2 Hz, 1H), 7.31 (dd, J = 5.1, 3.1 Hz, 1H), 6.54 (dd, J = 4.1, 2.0 Hz, 1H), 5.15 (d, J = 18.9 Hz, 2H), 4.11 (qd, J = 9.5, 3.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 133.4, 132.6, 127.6, 126.0, 95.5, 94.1, 70.3. HRMS (TOF MS EI$^+$): m/z calcd for [$C_8H_8O_4S$] 200.0143, found 200.0141.

*Phenoxymethyl Thiophene-2-carboxylate (**8a**).* Yellow solid, mp 45–47 °C. Yield: 384 mg (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, J = 3.8, 1.2 Hz, 1H), 7.60 (dd, J = 5.0, 1.2 Hz, 1H), 7.40–7.30 (m, 2H), 7.14–7.06 (m, 4H), 5.98 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 156.9, 134.3, 133.3, 132.8, 129.6, 127.9, 122.8, 116.2, 86.2. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{12}H_{10}O_3S$] 234.0351, found 234.0354.

*Cyclohex-2-en-1-yl Thiophene-2-carboxylate (**8b**).*[14e] Colorless oil. Yield: 175 mg (42%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (dd, J = 3.7, 1.2 Hz, 1H), 7.53 (dd, J = 5.0, 1.2 Hz, 1H), 7.10–7.06 (m, 1H), 6.04–5.96 (m, 1H), 5.85–5.78 (m, 1H), 5.49–5.43 (m, 1H), 2.10–1.65 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 134.4, 133.1, 132.9, 132.1, 127.6, 125.4, 68.9, 28.3, 24.8, 18.8.

*1,4-Dioxan-2-yl 2-Phenylacetate (**9**).* White solid, mp 48–49 °C. Yield: 275 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.21 (m, 5H), 5.83 (t, J = 1.7 Hz, 1H), 4.03–3.93 (m, 1H), 3.76–3.65 (m, 6H), 3.52 (dt, J = 11.7, 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 133.3, 129.0, 128.3, 126.9, 89.3, 67.3, 65.7, 61.3, 41.0. HRMS (TOF MS EI$^+$): m/z calcd for [$C_{12}H_{14}O_4$] 222.0892, found 222.0890.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectra of the KIE experiment and ^{1}H and ^{13}C NMR spectra for compounds **5**–**9**. 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.

■ ACKNOWLEDGMENTS

We gratefully acknowledge financial support from the National Natural Science Foundation of China (No. 21102071) and the Fundamental Research Funds for the Central Universities (No. 1107020522 and No. 1082020502). The Jiangsu 333 program (for Y.P.) and Changzhou Jin-Feng-Huang program (for J.H.) are also acknowledged.

■ REFERENCES

(1) For reviews on transition-metal-catalyzed C–H functionalization, see: (a) Chen, X.; Engle, K. M.; Wang, D. H.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094–5115. (b) Daugulis, O.; Do, H. Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074–1086. (c) Li, C. J. *Acc. Chem. Res.* **2009**, *42*, 335–344. (d) Coperet, C. *Chem. Rev.* **2010**, *110*, 656–680. (e) Werner, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 4714–4728. (f) Sun, C. L.; Li, B. J.; Shi, Z. J. *Chem. Rev.* **2011**, *111*, 1293–1314. (g) Campbell, A. N.; Stahl, S. S. *Acc. Chem. Res.* **2012**, *45*, 851–863. (h) Kozhushkov, S. I.; Ackermann, L. *Chem. Sci.* **2013**, *4*, 886–896.

(2) (a) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215–1292. (b) Shi, W.; Liu, C.; Lei, A. *Chem. Soc. Rev.* **2011**, *40*, 2761–2776. (c) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780–1824. (d) Wu, Y. N.; Wang, J.; Mao, F.; Kwong, F. Y. *Chem. Asian J.* **2014**, *9*, 26–47l. (e) Li, D. D.; He, C. L.; Cai, H. T.; Wang, G. W. *Chin. J. Org. Chem.* **2013**, *33*, 203–223.

(3) (a) Chatani, N.; Asaumi, T.; Yorimitsu, S.; Ikeda, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **2001**, *123*, 10935–10941. (b) DeBoef, B.; Pastine, S. J.; Sames, D. *J. Am. Chem. Soc.* **2004**, *126*, 6556–6557. (c) Song, C. X.; Cai, G. X.; Farrell, T. R.; Jiang, Z. P.; Li, H.; Gan, L. B.; Shi, Z. J. *Chem. Commun.* **2009**, *40*, 6002–6004. (d) Liu, W.; Liu, J.; Ogawa, D.; Nishihara, Y.; Guo, X.; Li, Z. *Org. Lett.* **2011**, *13*, 6272–6275. (e) Zhang, B.; Cui, Y.; Jiao, N. *Chem. Commun.* **2012**, *48*, 4498–4500. (f) Cui, Z.; Shang, X.; Shao, X. F.; Liu, Z. Q. *Chem. Sci.* **2012**, *3*, 2853–2858. (g) Liu, X.; Sun, B.; Xie, Z.; Qin, X.; Liu, L.; Lou, H. *J. Org. Chem.* **2013**, *78*, 3104–3112. (h) Ju, L.; Yao, J.; Wu, Z.; Liu, Z.; Zhang, Y. *J. Org. Chem.* **2013**, *78*, 10821–10831. (i) Rouquet, G.; Chatani, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 11726–11743.

(4) For selected examples, see: (a) Conejero, S.; Paneque, M.; Poveda, M. L.; Santos, L. L.; Carmona, E. *Acc. Chem. Res.* **2010**, *43*, 572–580. (b) Cheng, K.; Huang, L. H.; Zhang, Y. H. *Org. Lett.* **2009**, *11*, 2908–2911. (c) Liu, X.; Sun, B.; Xie, Z.; Qin, X.; Liu, L.; Lou, H. X. *J. Org. Chem.* **2013**, *78*, 3104–3112.

(5) Pan, S.; Liu, J.; Li, H.; Wang, Z.; Guo, X.; Li, Z. *Org. Lett.* **2010**, *12*, 1932–1935.

(6) Xie, Z.; Cai, Y.; Hu, H.; Lin, C.; Jiang, J.; Chen, Z.; Wang, L.; Pan, Y. *Org. Lett.* **2013**, *15*, 4600–4603.

(7) Liu, D.; Liu, C.; Li, H.; Lei, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 4453–4456.

(8) Zhao, J.; Zhou, W.; Han, J.; Li, G.; Pan, Y. *Tetrahedron Lett.* **2013**, *54*, 6507–6510.

(9) For selected recent reviews and examples on cross-dehydrogenative coupling, see: (a) Girard, S. A.; Knauber, T.; Li, C. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 74–100. (b) Wu, Y.; Wang, J.; Mao, F.; Kwong, F. Y. *Chem. Asian J.* **2014**, *9*, 26–47. (c) Zhao, J. C.; Fang, H.; Xie, C.; Han, J. L.; Li, G. G.; Pan, Y. *Asian J. Org. Chem.* **2013**, *2*, 1044–1047. (d) Zhou, S. B.; Wang, J.; Lin, D.; Zhao, F.; Liu, H. *J. Org. Chem.* **2013**, *78*, 11204–11212. (e) Jia, Z.; Nagano, T.; Li, X.; Chan, A. S. C. *Eur. J. Org. Chem.* **2013**, 858–861. (f) Nobuta, T.; Tada, N.; Fujiya, A.; Kariya, A.; Miura, T.; Itoh, A. *Org. Lett.* **2013**, *15*, 574–577.

(10) (a) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300–2301. (b) Chen, M. S.; Prabagaran, N.; Labenz, N. A.; White, M. C. *J. Am. Chem. Soc.* **2005**, *127*, 6970–6971. (c) Covell, D. J.; White, M. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 6448–6451.

(11) (a) Eames, J.; Watkinson, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 3567–3571. (b) Tan, Q.; Hayashi, M. *Adv. Synth. Catal.* **2008**, *350*, 2639–2644. (c) Rout, S. K.; Guin, S.; Ghara, K. K.; Banerjee, A.; Patel, B. K. *Org. Lett.* **2012**, *14*, 3982–3985. (d) Priyadarshini, S.; Joseph, P. J. A.; Kantam, M. L. *RSC Adv.* **2013**, *3*, 18283–18287. (e) Rout, S. K.; Guin, S.; Banerjee, A.; Khatun, N.; Gogoi, A.; Patel, B. K. *Org. Lett.* **2013**, *15*, 4106–4109.

(12) Ye, Z.; Wang, W.; Luo, F.; Zhang, S.; Cheng, J. *Org. Lett.* **2009**, *11*, 3974–3977.

(13) Lee, J. M.; Chang, S. *Tetrahedron Lett.* **2006**, *47*, 1375–1379.

(14) (a) Chen, L.; Shi, E.; Liu, Z.; Chen, S.; Wei, W.; Li, H.; Xu, K.; Wan, X. *Chem. Eur. J.* **2011**, *17*, 4085–4089. (b) Niu, L.; Yang, H.; Yang, D.; Fu, H. *Adv. Synth. Catal.* **2012**, *354*, 2211–2217. (c) Huang, J.; Li, L.-T.; Li, H.-Y.; Husan, E.; Wang, P.; Wang, B. *Chem. Commun.* **2012**, *48*, 10204–10206. (d) Zhang, S.; Guo, L.-N.; Wang, H.; Duan, X.-H. *Org. Biomol. Chem.* **2013**, *11*, 4308–4311. (e) Shi, E.; Shao, Y.; Chen, S.; Hu, H.; Liu, Z.; Zhang, J.; Wan, X. *Org. Lett.* **2012**, *14*, 3384–3387.

(15) For representative reviews on iron chemistry, see: (a) Fürstner, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 1364–1367. (b) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500–1511. (c) Correa, A.; Mancheño, O. G.; Bolm, C. *Chem. Soc. Rev.* **2008**, *37*, 1108–1117. (d) Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217–6254.

(16) (a) Yang, H.; Yan, H.; Sun, P.; Zhu, Y.; Lu, L.; Liu, D.; Rong, G.; Mao, J. *Green Chem.* **2013**, *15*, 976–981. (b) Zhao, J.; Fang, H.; Han, J.; Pan, Y. *Beilstein J. Org. Chem.* **2013**, *9*, 1718–1723.

(17) (a) White, M. C.; Doyle, A. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2001**, *123*, 7194–7195. (b) Tshuva, E. Y.; Lippard, S. J. *Chem. Rev.* **2004**, *104*, 987–1012. (c) Legros, J.; Bolm, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 4225–4228.

(18) (a) Costas, M.; Chen, K., Jr.; Que, L. *Coord. Chem. Rev.* **2000**, *200−202*, 517−544. (b) Wallar, B. J.; Lipscomb, J. D. *Chem. Rev.* **1996**, *96*, 2625−2657.
(19) Malatesta, V.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 609−614.
(20) For selected examples on single electron or ligand transfer reactions, see: (a) Kochi, J. K. *Science* **1967**, *155*, 415−424. (b) Marcus, R. A. *Pure Appl. Chem.* **1997**, *69*, 13−29. (c) Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3464−3484.
(21) Liu, Z. Q.; Zhao, L.; Shang, X.; Cui, Z. *Org. Lett.* **2012**, *14*, 3218−3221.