Iron-Catalyzed Oxidative C−H/C−H Cross-Coupling between Electron-Rich Arenes and Alkenes

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S *Supporting Information*
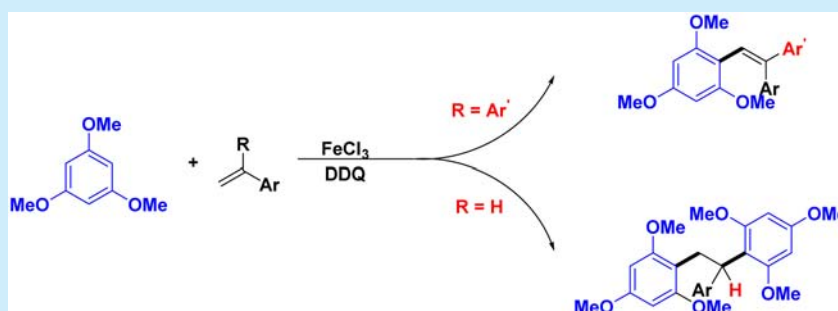
ABSTRACT: A novel oxidative C−H/C−H cross-coupling reaction between electron-rich arenes and alkenes is established utilizing $FeCl_3$ as the catalyst and DDQ as the oxidant. Interestingly, direct arylation products are obtained with diaryl-ethylenes and double arylation products are obtained with styrene derivatives, which show high chemoselectivity and good substrate scope. A radical trapping experiment and EPR (electron paramagnetic resonance) experiments indicate that this reaction proceeds through a radical pathway in which DDQ plays a key role in the aryl radical formation. XAFS (X-ray absorption fine structure) experiments reveal that the oxidation state of the iron catalyst does not change during the reaction, suggesting that $FeCl_3$ might be used as a Lewis acid. Finally, a detailed mechanism is proposed for this transformation.

Transition-metal catalyzed oxidative C−H/C−H cross-coupling reactions have attracted much attention because these transformations provide an ideal synthetic mode for constructing C−C bonds.[1] In recent years, tremendous advances have been presented in this field. For example, activated C−H compounds could be employed as substrates,[2] and some inert C−H compounds could be overcome and tolerated in these transformations as well.[3] However, in most of these cases, late transition metals, such as palladium, ruthenium, rhodium, and platinum, were used as catalysts.[1f,3g,4] However, it is well-known that first-row transition metals are less expensive and have no toxicity.[5] Therefore, more chemists shifted their attention to the inexpensive and nontoxic first-row transition metals, especially copper and iron, which have shown some unique catalytic features recently.[2a,6]
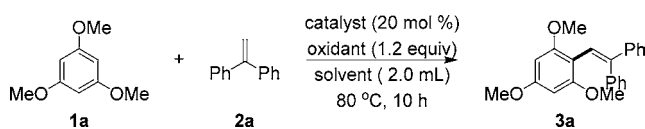
Iron is one of the most abundant, inexpensive, and environmentally friendly metals on the earth. It not only plays an important role in the life reactivity[7] but also is widely used in organic synthesis as a catalyst for oxidation and Friedel−Crafts reactions.[8] Recently, iron salts have been also disclosed as excellent potential catalysts for coupling reactions since cross-coupling reactions between organometallic reagents and halides

were realized in the presence of iron salts.[6d,e,9] Thereafter, iron-catalyzed oxidative cross-coupling reactions of arenes and organometallic reagents,[10] aldehydes and alkenes,[11] and phenols and alkenes[12] and cross-dehydrogenation-coupling (CDC) reactions[13] were demonstrated. Nevertheless, to date, no example has been reported on the iron-catalyzed oxidative cross-coupling between arenes and alkenes. Hence, this work communicates an $FeCl_3$-catalyzed direct oxidative C−H/C−H cross-coupling reaction between arenes and alkenes toward the synthesis of triaryl-ethylene or triaryl-ethane.

We commenced the oxidative cross-coupling between arenes and alkenes by employing 1,3,5-trimethoxybenzene (**1a**) and 1,1-diphenylethylene (**2a**) as substrates. The desired product **3a** was obtained when **1a** and **2a** were mixed in the presence of $FeCl_3$ (20 mol %) and DDQ (1.2 equiv) in DME at 80 °C for 10 h (Table 1, entry 1). This result encouraged us to make a further optimization. First, several iron salts were tested; however, less favorable results were obtained (entries 2 and 3). It turned

Table 1. Condition Optimization for the Oxidative Cross-Coupling of 1a and 2a[a]

entry	catalyst	oxidant	solvent	yield (%)[b]
1	FeCl₃	DDQ	DME	35
2	Fe₂(SO₄)₂	DDQ	DME	trace
3	Fe(acac)₃	DDQ	DME	trace
4	–	DDQ	DME	trace
5	FeCl₃	TCQ	DME	30
6	FeCl₃	BQ	DME	trace
7	FeCl₃	DDQ	CH₃CN	55
8	FeCl₃	DDQ	DCE	34
9	FeCl₃	DDQ	toluene	33
10	FeCl₃	DDQ	DMF	5
11[c]	FeCl₃	DDQ	CH₃CN	24
12[d]	FeCl₃	DDQ	CH₃CN	17
13[e]	**FeCl₃**	**DDQ**	**CH₃CN**	78(76)[f]

[a]All of the reactions were performed with **1a** (0.2 mmol, 33.6 mg), **2a** (0.2 mmol, 36.0 mg), catalyst (20 mol %), and oxidant (0.24 mmol) in 2.0 mL of solvent in Schlenk tubes at 80 °C for 10 h under N₂. [b]Yield determined by GC analysis with naphthalene as the internal standard. [c]FeCl₃ (40 mol %). [d]FeCl₃ (2 mol %). [e]**1a** (1.0 mmol, 168.2 mg), **2a** (0.2 mmol, 36.0 mg), FeCl₃ (20 mol %), DDQ (0.4 mmol, 90.8 mg), and CH₃CN (1.0 mL) in Schlenk tubes at 80 °C for 10 h under N₂. [f]Isolated yield in parentheses.
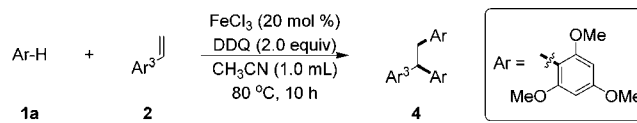
out that an iron salt was necessary for this transformation, since only a trace amount of the desired product could be observed without iron salts (entry 4). Other oxidants, such as tetrachloro-*p*-benzoquinone (TCQ) and *p*-benzoquinone (BQ), were also examined for this transformation, but less favorable yields were obtained (entries 5 and 6). CH₃CN afforded the best yield compared to 1,2-dichloroethane (DCE), toluene, and DMF (entries 7–10). Better results were not obtained when increasing or decreasing the amount of FeCl₃ (entries 11 and 12). Finally, the best yield was obtained when **1a** (1.0 mmol), **2a** (0.2 mmol), FeCl₃ (0.04 mmol), and DDQ (0.4 mmol) were combined in CH₃CN (1.0 mL) at 80 °C for 10 h (entry 13).

With the optimized conditions in hand, the substrate scope of this iron-catalyzed oxidative C−H/C−H cross-coupling reaction between arenes and alkenes was explored. As shown in Scheme 1, various diaryl-ethylenes are suitable for this transformation. For example, 2,2′-(ethene-1,1-diyl)dinaphthalene reacts with **1a** smoothly to give the desired product in 68% yield (**3b**). 1,1-Diphenylethylenes bearing an electron-withdrawing group (CF₃) or electron-donating group (CH₃) is suitable for this reaction (**3c** and **3g**). 1,1-Diphenylethylene with a halogen substituent such as chloride, bromide, and fluoride are all tolerated to produce the corresponding products (**3d**, **3e**, **3f**, **3h**), which enable a potential application in further functionalization. As shown in Table 2, when substituted styrenes are tested for this transformation, corresponding triaryl-ethane instead of triaryl-ethylene are produced (**4a**, **4b**, **4c**, and **4d**).

Subsequently, in order to understand the role of the iron catalyst in this coupling reaction, some experiments were performed. First, a radical-trapping experiment was carried out by employing TEMPO as the radical scavenger. Only a trace amount of **3a** was obtained when 2 equiv of TEMPO were added (eq 1), suggesting that this coupling reaction might proceed

Scheme 1. FeCl₃-Catalyzed Oxidative C−H/C−H Cross-Coupling between Arenes and Diaryl-ethylenes[a]
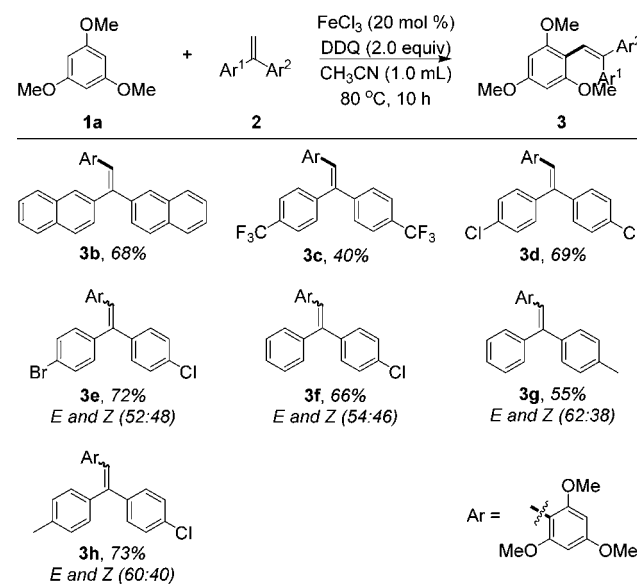
[a]**1a** (1.5 mmol, 252.3 mg), **2** (0.3 mmol), FeCl₃ (20 mol %), DDQ (0.6 mmol, 136.2 mg) and CH₃CN (1.0 mL) in Schlenk tubes at 80 °C for 10 h under N₂. Yields were obtained by isolating the pure products. The ratios of *trans* and *cis* isomers were obtained from ¹H NMR spectra.

Table 2. Oxidative Cross-Coupling of Substituted Styrenes and 1a[a]

entry	Ar³	yield (%)[b]
1	*p*-BrC₆H₄	67
2	*m*-BrC₆H₄	58
3	*p*-ClC₆H₄	66
4	*p*-FC₆H₄	48

[a]All of the reactions were performed with **1a** (1.5 mmol, 252.3 mg), **2** (0.3 mmol), FeCl₃ (20 mol %), DDQ (0.6 mmol, 136.2 mg), and CH₃CN (1.0 mL) in Schlenk tubes at 80 °C for 10 h under N₂. [b]Yields were obtained by isolating the pure products.
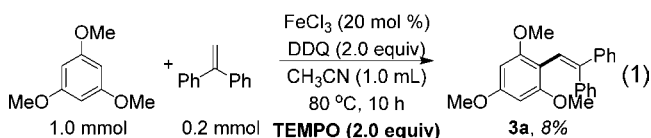
through a radical pathway. Hence, various EPR experiments were done afterward. As shown in Figure 1, strong radical signals are observed in the mixture of **1a** and DDQ in CH₃CN at 80 °C after the addition of 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO). Moreover, when 1-bromo-3,5-dimethoxybenzene (**2a**) in lieu of **1a** is employed to react with DDQ, similar strong radical signals are detected. These phenomena disclose that DDQ could react with arenes to produce radicals. Since distinguishing *g* values were obtained, we guessed that the radical signals originated from arenes. No new signal is found in the reaction mixture of **1a** and FeCl₃ after the addition of DMPO, indicating that DDQ instead of FeCl₃ initiated the formation of the radical.[12a]
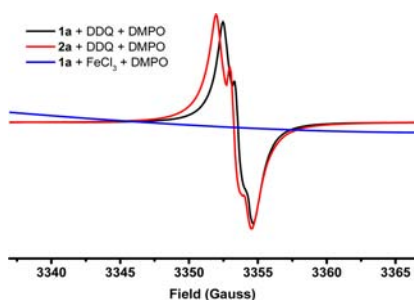
Figure 1. EPR spectra (X band, 9.4 GHz, rt) of (a) reaction mixture of **1a** and DDQ (b) reaction mixture of **2a** and DDQ (c) reaction mixture of **1a** and FeCl₃, with the addition of DMPO under standard conditions.

As described in Table 1, FeCl₃ is essential for this oxidative coupling reaction. To elucidate the role of FeCl₃, XAFS spectroscopy was employed. As shown in Figure 2 and Table 3,
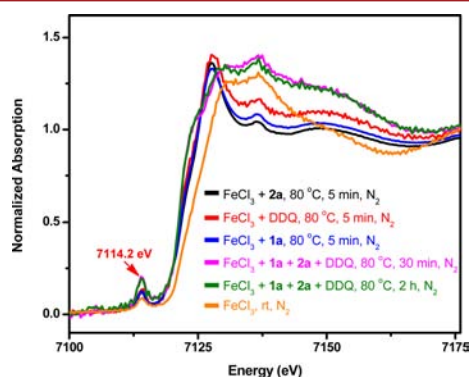

Figure 2. XANES spectra of various Fe species. The mole ratio of FeCl₃ and **1a** or **2a** or DDQ or CH₃CN was determined according to the standard conditions.

Table 3. Summary of the XANES Results

sample	conditions	pre-edge energy^a (eV)	oxidation state
Fe foil	air	N.A.	0
FeCl₂	N₂	7112.7	II
FeCl₃	CH₃CN, rt, N₂	7114.2	III
FeCl₃ + **1a**	CH₃CN, 80 °C, N₂, 5 min	7114.1	III
FeCl₃ + **2a**	CH₃CN, 80 °C, N₂, 5 min	7114.0	III
FeCl₃ + DDQ	CH₃CN, 80 °C, N₂, 5 min	7114.2	III
FeCl₃ + **1a** + **2a** + DDQ	CH₃CN, 80 °C, N₂, 30 min	7114.1	III
	CH₃CN, 80 °C, N₂, 2 h	7114.2	III

^{a}The pre-edge energy was determined from the maximum of the pre-edge peak.

the pre-edge energy of the mixture of FeCl₃ and **1a** or **2a** or DDQ is the same as that of the authentic FeCl₃ sample, indicating that the oxidation state of the iron species in these mixtures is +3, and no redox process occurs between FeCl₃ and **1a** or **2a** or DDQ under the current reaction conditions. In addition, the FeCl₃ catalyzed oxidative cross-coupling reaction of **1a** and **2a** was also monitored by XAFS. Compared with FeCl₃, the iron species in the reaction mixture provide the identical pre-edge energy at 7114.2 eV; i.e., the oxidation state of the iron species might not change during the reaction. Therefore, FeCl₃ is envisioned as an important Lewis acid for the transformation. To support this assumption, other Lewis acids were employed for this coupling reaction. The desired product could be obtained in 65% yield when
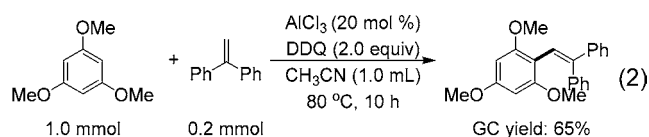
a catalytic amount of AlCl₃ is utilized (eq 2). This result confirms that FeCl₃ might play a role as a Lewis acid in the overall reaction.

Based on the current results, a putative mechanism was proposed and is illustrated in Scheme 2. Initially, an electron-rich

Scheme 2. Proposed Mechanism
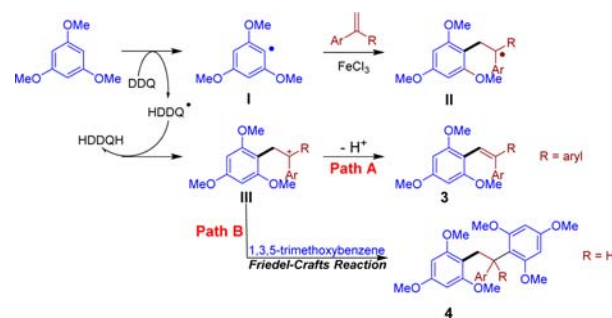
arene is oxidized to produce the aryl radical **I** in the presence of DDQ. Then, an alkene traps the aryl radical to yield the radical intermediate **II**. This radical species is subsequently oxidized by losing one electron and affords the cationic intermediate **III**. There are two optional pathways for the cationic species. When the R group involved in **III** is an aryl, a deprotonation process produces the desired triaryl-enthylene **3**. But if the R group is an H atom, a Friedel−Crafts alkylation process occurrs between **III** and the arene, and the product **4** is obtained. The steric hindrance of the R group might be the key reason for the two selective products. As FeCl₃ was determined to be an important Lewis acid, it might play two roles. By coordinating with the O atom of DDQ, FeCl₃ might help increase the oxidative capacity to facilitate the formation of radical **I**. It also could promote the radical addition process by coordinating and decreasing the electron density on the double bond of the alkene, as radical **I** is electron-rich and would likely react with the electron-deficient alkene.

In conclusion, a novel oxidative C−H/C−H cross-coupling reaction between electron-rich arenes and alkenes was established utilizing FeCl₃ as the catalyst and DDQ as the oxidant. The reaction selectivity changed through the utilization of different alkene substrates. Preliminary mechanistic investigations indicate that radicals were involved in the overall process. DDQ plays a key role in the formation of aryl radicals; meanwhile, FeCl₃ might act as an important Lewis acid to promote this transformation. Finally, a putative mechanism was proposed, while a detailed mechanism is currently under investigation in our laboratory and will be reported in the near future.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experiment details and spectral data for all compounds are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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