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Iron-Catalyzed Acyloxyalkylation of Styrenes Using Hypervalent Iodine Reagents

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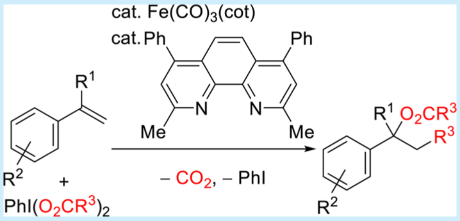
Supporting Information

ABSTRACT: Iron-catalyzed acyloxyalkylation of styrene derivatives using hypervalent iodine reagents was achieved. The acyloxyalkylation reaction proceeded using various types of styrenes and hypervalent iodine reagents. The acyloxyalkylated products were obtained in moderate to good yields without loss of the functional groups. The reaction proceeded via the formation of radical species derived from hypervalent iodine reagents by decarboxylation.



In recent decades, complexes and salts of second- and third-row transition metals, such as palladium, ruthenium, rhodium, and iridium, have emerged as powerful catalysts.[1] The utilization of these metals as catalysts, however, is limited by their relatively high cost and toxicity. On the other hand, iron is the most abundant transition metal in the geosphere, and iron catalysts have recently received much attention in synthetic organic chemistry.[2]

Transition-metal-catalyzed difunctionalization of alkenes is an important topic because the reactions can introduce two new functional groups in only one step to efficiently construct highly functionalized structures of pharmaceuticals and natural products.[3−6] Acyloxyalkylation of alkenes remains challenging; however, examples are quite rare.[7,8] Combined osmium-promoted Sharpless epoxidation and successive alkylation of the formed epoxides are a well-known traditional oxyalkylation of alkenes, but the osmium catalyst is highly toxic and the epoxidation and successive alkylation require two steps, features that do not meet the current requirements of organic reactions. Buchwald and co-workers recently realized a rapid synthesis of enantiomerically enriched lactones by copper-catalyzed enantioselective radical oxyalkylation of alkenes (Figure 1a, upper row).[9] Zhu and co-workers achieved copper(II)-catalyzed oxyalkylation of alkenes with alkylnitriles (Figure 1a, lower row).[10] Wang and co-workers recently reported the first example of a rhenium-catalyzed oxyalkylation of styrenes with hypervalent iodine reagents,[11] which act as both an oxidant and alkylation reagent in the difunctionalization of styrenes (Figure 1b, upper row), but visible light irradiation is required for many hypervalent iodine reagents.

We successfully replaced the rhenium catalyst in this reaction with an iron catalyst (Figure 1b, lower row). Iron-catalyzed acyloxyalkylation is economical and environmentally benign, and the reaction requires no visible light irradiation.

We optimized the reaction conditions using 1-(*tert*-butyl)-4-vinylbenzene (**1a**) and iodobenzene diacetate (**2a**) as model substrates (Table 1). The desired reaction did not proceed in the presence of catalytic amounts of $Fe(CO)_3$(cot) and phenanthroline (**L1**) (entry 1). Acyloxyalkylated product **3aa**, however, was obtained using **L2** or **L3** as a ligand (entries 2 and 3). The desired product **3aa** was not formed by introducing electoron-withdrawing or -donating groups on the phenyl groups of the phenanthroline derivatives (entries 4 and 5).

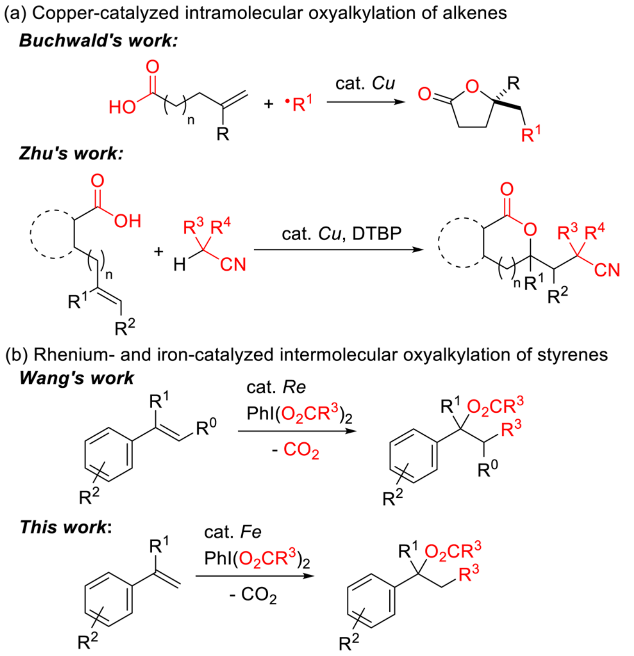


Figure 1. Transition-metal-catalyzed radical acyloxyalkylation of alkenes.

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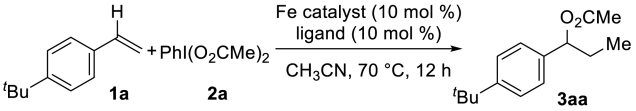
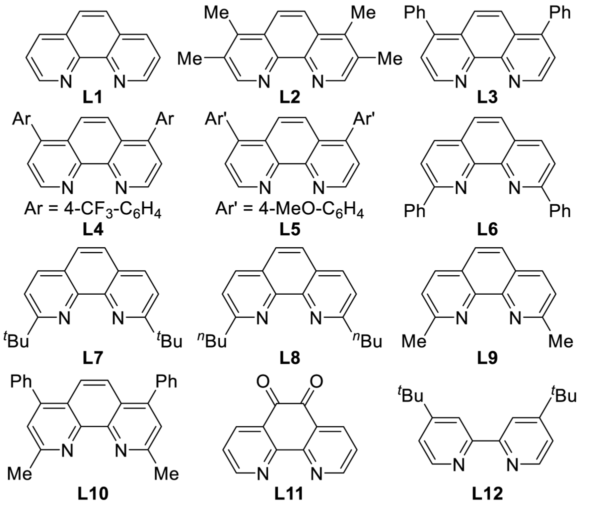
Table 1. Optimization of Reaction Conditions of Alkene Acyloxyalkylation[a]

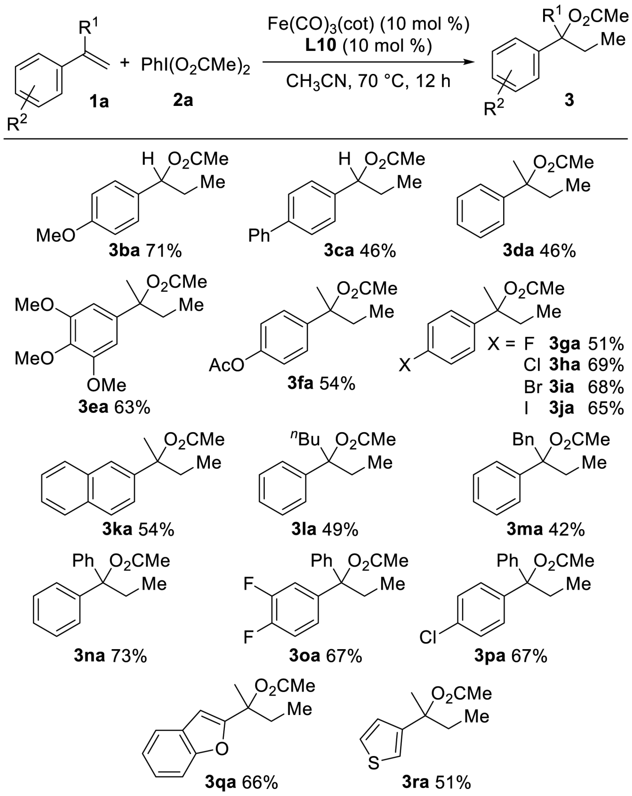


entry	Fe catalyst	ligand	yield [%][b]
1	$[Fe(CO)_3(cot)]$	**L1**	0
2	$[Fe(CO)_3(cot)]$	**L2**	23
3	$[Fe(CO)_3(cot)]$	**L3**	12
4	$[Fe(CO)_3(cot)]$	**L4**	0
5	$[Fe(CO)_3(cot)]$	**L5**	0
6	$[Fe(CO)_3(cot)]$	**L6**	7
7	$[Fe(CO)_3(cot)]$	**L7**	20
8	$[Fe(CO)_3(cot)]$	**L8**	15
9	$[Fe(CO)_3(cot)]$	**L9**	20
10	$[Fe(CO)_3(cot)]$	**L10**	53[c]
11	$[Fe(CO)_3(cot)]$	**L11**	0
12	$[Fe(CO)_3(cot)]$	**L12**	3
13	$[Fe(OAc)_2]$	**L10**	50



[a] Reaction conditions: **1a** (0.250 mmol, 1.0 equiv), **2a** (0.325 mmol, 1.3 equiv), iron catalyst (0.0500 mmol, 10 mol %), ligand (0.0500 mmol, 10 mol %), CH_3CN (1.0 mL), 70 °C, 12 h. cot = cyclooctatetraene. [b] Yield determined by ^1H NMR using 1,1,2,2-tetrachloroethane as an internal standard. [c] Isolated yield.

Scheme 1. Reactions between Several Styrenes 1 and (Diacetoxyiodo)benzene (2a)[a]



[a] Reaction conditions: **1** (0.250 mmol, 1.0 equiv), **2a** (0.3250 mmol, 1.3 equiv), $Fe(CO)_3(cot)$ (0.0500 mmol, 10 mol %), **L10** (0.0500 mmol, 10 mol %), CH_3CN (1.0 mL), 70 °C, 12 h.

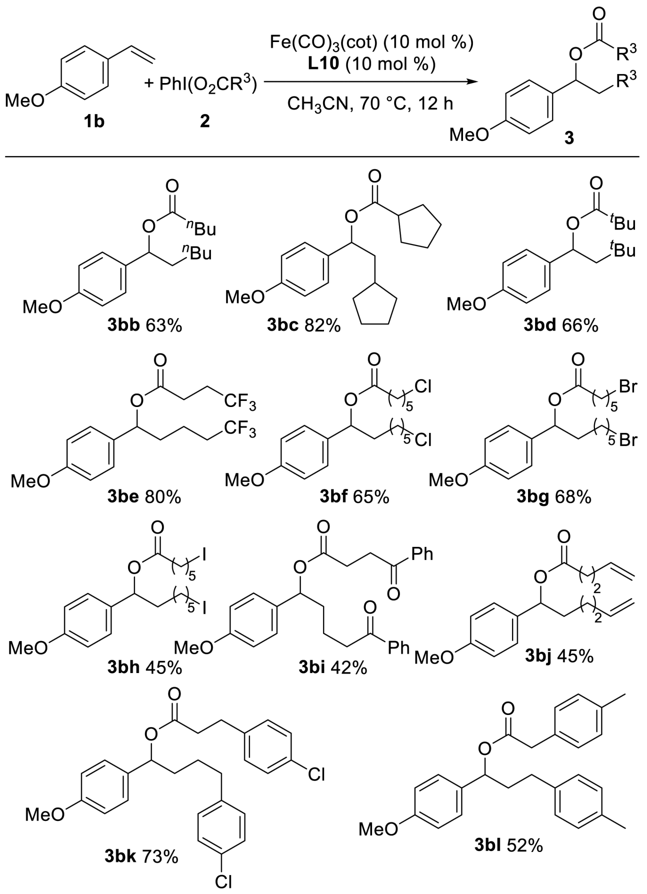
Phenanthrolines **L6**–**L9** with substituents at the 2- and 9-positions promoted the desired reaction (entries 6–9). 2,9-Dimethyl-4,7-diphenyl-1,10-phenanthroline (**L10**) afforded the best result, and **3aa** was obtained in 53% yield (entry 10). The desired product **3aa** was not formed using 9,10-phenanthrenedione (**L11**) or 4,7-di(*tert*-butyl)bipyridine (**L12**) as a ligand (entries 11 and 12). Acyloxyalkylated product **3aa** was also obtained in 50% yield using $Fe(OAc)_2$ as a catalyst (entry 13). Other iron complexes and salts gave **3aa** in lower yields.[12]

The substrate scope of styrenes was investigated next (Scheme 1). Styrene derivatives **1b** and **1c** gave target products **3ba** and **3ca**. α-Methylstyrenes **1d**–**1k** also produced the desired products **1da**–**1ka** in moderate to good yields without loss of the functional groups. The corresponding acyloxyalkylated products **3la**–**3pa** were also afforded using α-butyl-, α-benzyl-, and α-phenylstyrenes **1l**–**1p**. Five-membered heteroaromatic compounds with a vinyl group, **1q** and **1r**, also provided the corresponding oxtalkylated products **3qa** and **3ra** in 66% and 51% yields, respectively.

Next, we investigated several hypervalent iodine reagents (Scheme 2). In all entries, no visible light irradiation was necessary to produce radical species from the hypervalent iodine reagents. Hypervalent iodine reagents **2b**–**2d** bearing primary, secondary, and tertiary alkyl groups produced the corresponding acyloxyalkylated products **3bb**–**3bd** in 63%–82% yields. In a previous study by Wang, no results of the use of any hypervalent iodine reagents containing functional groups were reported (Figure 1b, lower row).[7] We therefore investigated hypervalent iodine reagents **2e**–**2j** bearing functional groups, such as trifluoromethyl and carbonyl groups as well as chlorine, bromine, and iodine atoms. As a result, the corresponding acyloxyalkylated products **3be**–**3bj** were obtained in moderate to good yields without loss of the functional groups. The desired products **3bk** and **3bl** were also obtained using hypervalent iodine reagents **2k** and **2l** bearing 4-chlorophenyl and 4-methylbenzyl groups.

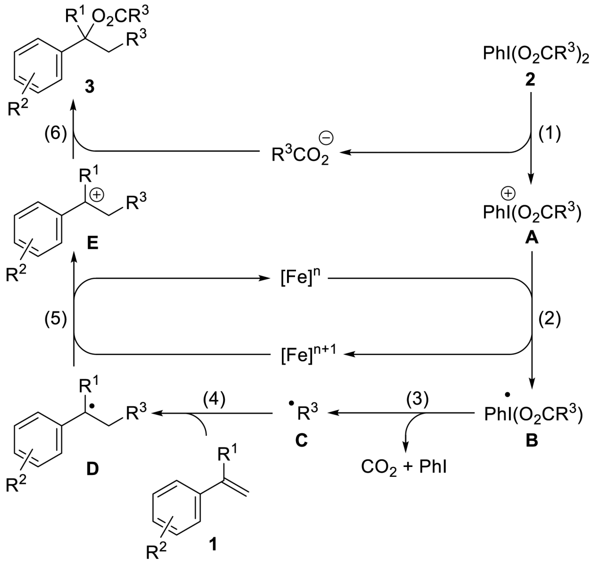
To elucidate the reaction mechanism, we conducted a reaction in the presence of 1.0 equiv of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) as a radical scavenger. As a result, the acyloxyalkylation reaction did not proceed at all. This result indicated that the acyloxyalkylation reaction proceeded via a radical pathway. The proposed mechanism for the iron-catalyzed acyloxyalkylation of styrene derivatives using hypervalent iodine reagents is shown in Scheme 3, based on the

Scheme 2. Reactions between Styrene 1b and (Diacyloxyiodo)benzene 2[a]



[a] Reaction conditions: **1b** (0.250 mmol, 1.0 equiv), **2** (0.325 mmol, 1.3 equiv), Fe(CO)$_3$(cot) (0.0500 mmol, 10 mol %), **L10** (0.0500 mmol, 10 mol %), CH$_3$CN (1.0 mL), 70 °C, 12 h.

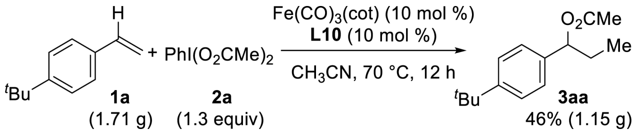
Scheme 3. Proposed Reaction Mechanism



previous report:[11] (1) Generation of cationic specie **A** and carboxylate anion; (2) oxidation of **A** by Fe^n to give radical iodine intermediate **B**; (3) decomposition of **B** to form radical species **C** with the formation of carbon dioxide and iodobenzene; (4) addition of **C** to styrene derivative **1** to give benzyl radical **D**; (5) oxidation of **D** by [Fe]$^{n+1}$ to form benzyl cation **E**; and (6) addition of the carbozylate to **E** to produce the desired product **3**.

The desired product **3aa** was also obtained even in gram scale (Scheme 4). Treatment of 1.71 g of **1a** with **2a** in the presence of catalytic amounts of Fe(CO)$_3$(cot) and **L4** gave 1.15 g of **3aa** in 46% yield.

Scheme 4. Gram-Scale Reaction



In summary, we successfully developed an iron-catalyzed acyloxyalkylation of styrene derivatives using hypervalent iodine reagents. The choice of phenanthroline ligands was important to promote the reaction. In a similar previously reported rhenium-catalyzed reaction, visible light irradiation was necessary for many hypervalent iodine reagents. The present reaction, however, required no irradiation. The reaction proceeded in moderate to good yields, even in gram scale, using a variety of styrenes and hypervalent iodine reagents without loss of the functional groups. Compared with the rhenium-catalyzed reaction, the scope of hypervalent iodine reagents with functional groups was expanded. We hope that the present result will provide useful insight into synthetic organic chemistry using iron catalysts.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b00923.

Experimental procedures and compound characterization data of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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(12) Fe(0) powder, 41%; $[FeCp^*(CO)_2]_2$, 30%; $Fe(acac)_2$, 38%; $Fe(OTf)_2$, 0%; $Fe(ClO_4)_2$, 12%; FeS, 34%; FeF_2, 24%; $FeCl_2$, 19%; $FeBr_2$, 25%; Fe_3O_4, 0%; $Fe(OEt)_3$, 26%; $Fe(OTf)_3$, 0%.