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Cp*Co(III)-catalyzed *ortho* C—H amidation of 2-pyridinyl ferrocenes with 1,4,2-dioxazol-5-ones

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ortho-Amidation of 2-pyridinyl ferrocenes with 1,4,2-dioxazol-5-ones was achieved *via* Cp*Co(III)-catalyzed direct C-H bond functionalization reaction. In the presence of Cp*Co(CO)I$_2$, in combination with AgPF$_6$ and AgOPiv, a wide range of ferrocene-based amidated products were obtained in up to 96% yield under mild reaction conditions. A gram-scale reaction proceeded smoothly with high efficiency. Isoquinoline and pyrimidine are also suitable directing groups in this transformation.

1. Introduction

Over the past decade, transition-metal catalyzed C—H functionalization reaction has proved to be an increasingly powerful method in modern organic synthesis [1–7]. These reactions mostly rely on costly second or third row transition metals, such as Pd, Ru, Rh, Ir, Au etc. In the past several years, significant efforts have been directed towards the use of cheaper first-row transition metals [8–19]. Among these catalysts, high-valent cobalt(III) has attracted much attention, and enormous advances have been accomplished [14–17] since the pioneering work reported by the group of Kanai and Matsunaga in 2013 [20]. Compared with Cp*Rh(III) and Cp*Ir(III) species, the Cp*Co(III) complex displayed higher Lewis acidity and more hard nature [17] leading to unique reactivity and selectivity, which could be complementary to those enabled by the Rh(III)/Ir(III) catalysts [21–30].

Ferrocene derivatives are among the most efficient ligands or catalysts in organic synthesis [31–40]. As shown in Fig. 1, most of these ligands contain heteroatoms, such as P, S and N etc., attached to ferrocene directly, which posed challenges for the synthesis. In terms of atom and step economies, it is highly attractive to diversify ferrocene backbone by direct C—H bond functionalization. However, to date main efforts focused on C—C bond formation *via* C—H bond functionalization to ferrocene [41–63]. Very recently, we reported a Rh-catalyzed direct C—H amidation of ferrocenylpyridines [64] using 1,4,2-dioxazol-5-ones as the nitrogen source [65–84]. In line with our interest in the transition-metal-catalyzed C—H bond functionalization process, we envisaged that the introduction of nitrogen on ferrocene might be possible by using cheaper cobalt catalyst. Herein, we report our results on cobalt-catalyzed amidation of ferrocenes by employing N-containing heteroarenes as directing groups.

2. Experimental

2.1. Materials

Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purified and dried according to standard methods prior to use. 2-Pyridylferrocene derivatives **1** [64] and dioxazolones **2** [67] were synthesized according to the reported procedure.

2.2. Procedure for Cp*Co(III)-catalyzed ortho C-H amidation reaction

To a 25 mL oven-dried sealed tube containing a magnetic stirrer bar, AgPF$_6$ (11.4 mg, 0.045 mmol, 0.15 equiv) and AgOPiv (6.3 mg, 0.03 mmol, 0.1 equiv) were added in the glovebox. After moved out from glovebox, ferrocenyl pyridine **1** (0.3 mmol, 1.0 equiv),

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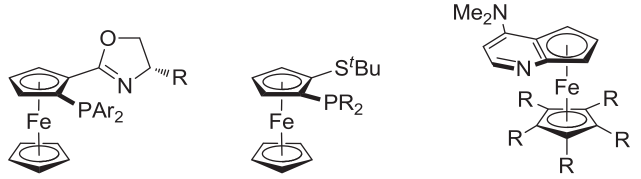


Fc-Phox Fesulphos planar chiral DMAP

Fig. 1. Representative heteroatom-containing chiral ferrocene-based ligands.

dioxazolone **2** (0.36 mmol, 1.2 equiv), Cp*Co(CO)I_2 (7.1 mg, 0.015 mmol, 5 mol%) and DCE (1.5 mL) were added under an argon atmosphere. Then the tube was sealed and the resulting mixture was stirred at 70 °C for indicated time. After the reaction was complete, the reaction mixture was diluted with EtOAc (10 mL) and filtered through a short pad of silica gel. Volatiles were evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (acetone/petroleum ether = 1/40, v/v) affording desired products.

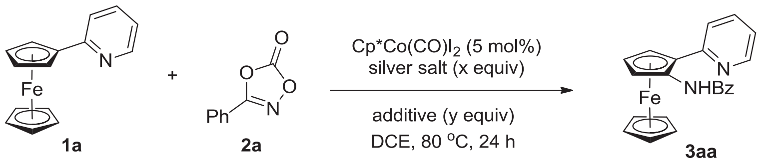
3. Results and discussion

Initially we chose 2-ferrocenylpyridine (**1a**) and 3-phenyl-1,4,2-dioxazol-5-one (**2a**) as the model substrates to optimize the reaction conditions. As shown in Table 1, in the presence of 5 mol% of Cp*Co(CO)I_2, 0.2 equiv of $AgNTf_2$ and 0.2 equiv of NaOAc, the reaction of **1a** (0.1 mmol) with **2a** (1.2 equiv) in DCE at 80 °C afforded the desired product **3aa** in 6% yield detected by NMR (Table 1, entry 1). The addition of acidic, neutral or basic additive provided no positive effect on the yield (Table 1, entries 2–4). To our delight, an increased conversion was found when AgOPiv was used instead of NaOAc (Table 1, entry 6, 24%). After screening several silver salts, the combination of $AgPF_6$ (0.15 equiv) and AgOPiv (0.10 equiv) gave the optimal results (Table 1, entry 9, 95%). These results indicated that the silver salts likely facilitated the formation of cationic Cp*Co(III) and activated amidating reagent [85,86]. Control experiments were performed, and it was found that both silver salts were essential (Table 1, entries 10–12). Moreover, 90% yield was obtained in 0.3 mmol scale at slightly lower temperature (70 °C) (Table 1, entry 14). Thus, the optimal reaction conditions were obtained as the following: Cp*Co(CO)I_2 (5 mol%), $AgPF_6$ (0.15 equiv), AgOPiv (0.1 equiv), **2a** (1.2 equiv), DCE (0.2 M) at 70 °C.

Under the optimal reaction conditions, the substrate scope of amidation reaction of ferrocenes was then explored. As summarized in Table 2, substrates with the methyl group on various site of pyridine (**1b**–**1d**) could react with **2a** smoothly, giving **3ba**–**3da** in good yields (55–87%). When the 6-methyl group was introduced to the pyridine, no product was observed. Likely, the steric hindrance played more important role for cobalt, which has a smaller radius than rhodium [64]. The 3-O^{i}Pr substituted pyridinyl ferrocene **1e** was also suitable for the amidation reaction, giving **3ea** in 85% yield. Furthermore, when isoquinoline and pyrimidine were employed as the directing groups, their desired products **3fa**, **3ga** were obtained in 96% and 44% yield, respectively. With regarding to substrates **1h**–**j** bearing a substituent on the other Cp ring, the corresponding products were obtained with diminished yields (22–43%) under slightly modified conditions. Particularly, there was no diamidation product observed for substrate **1j** even when 2.4 equiv of **2a** were used. Of particular note, a gram scale reaction of **1a** with **2a** could also perform well to give 84% yield.

For the scope of dioxazolone, aryl, heteroaryl and alkyl substituted dioxazolones **2** were tested under the optimal reaction conditions (Table 3). Dioxazolones **2b**–**h** bearing an aryl group with varied electronic property reacted with **1a** smoothly, and their corresponding products (**3ab–3ah**) were obtained in good yields

Table 1
Optimization of reaction conditions.[a]



Entry	Silver (x equiv)	Additive (y equiv)	**3aa** (%)[b]
1	$AgNTf_2$ (0.2)	NaOAc (0.2)	6%
2	$AgNTf_2$ (0.2)	PivOH (0.5)	trace
3	$AgNTf_2$ (0.2)	KH_2PO_4 (0.5)	6%
4	$AgNTf_2$ (0.2)	Et_3N (0.5)	trace
5	$AgNTf_2$ (0.2)	AgOAc (0.2)	4%
6	$AgNTf_2$ (0.2)	AgOPiv (0.2)	24%
7	$AgSbF_6$ (0.2)	AgOPiv (0.2)	21%
8	$AgPF_6$ (0.2)	AgOPiv (0.2)	69%
9	$AgPF_6$ (0.15)	AgOPiv (0.1)	95%
10	–	AgOPiv (0.1)	–
11	$AgPF_6$ (0.15)	CsOPiv (0.1)	trace
12	–	–	–
13[d]	$AgPF_6$ (0.15)	AgOPiv (0.1)	94%
14[e]	**$AgPF_6$ (0.15)**	**AgOPiv (0.1)**	**90%**[c]

[a] Conditions: **1a** (0.1 mmol), **2a** (1.2 equiv), Cp*Co(CO)I_2 (5 mol%), silver salt (x equiv), additive (y equiv), DCE (0.2 M), 80 °C, 24 h.
[b] Detected by ^1H NMR with CH_2Br_2 as an internal standard.
[c] Isolated yield.
[d] 70 °C, 3.5 h.
[e] **1a** (0.3 mmol) was used, 70 °C, 5.5 h.