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Co(II)-Catalyzed Regioselective Cross-Dehydrogenative Coupling of Aryl C−H Bonds with Carboxylic Acids

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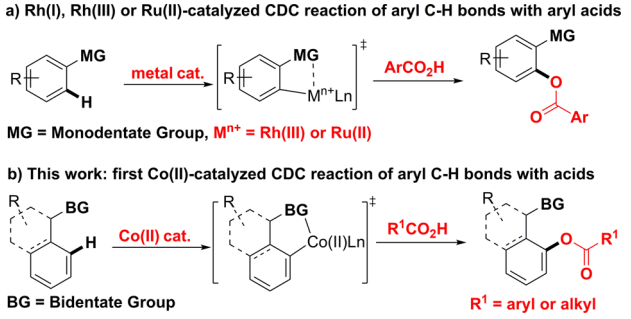
Supporting Information

ABSTRACT: A cobalt(II)-catalyzed regioselective aryl C−H bond oxygenation between arenes and aryl or aliphatic carboxylic acids under bidendate-chelation assistance is developed. This method provides an efficient approach to acyoxy-substituted arenes with a broad range of functional group tolerance. Furthermore, this reaction system could be further applied to the preparation of polyfunctional naphthylenes.

Aryl esters are commonly encountered in pharmaceutical molecules, natural products, and synthetic intermediates.[1] The traditional synthetic methodologies for these compounds relied on cross-coupling reactions of arenols or arylsilicons with carbonyl compounds.[2] In comparison, a transition-metal-catalyzed cross-dehydrogenative coupling (CDC) strategy provides an atom- and step-economic platform to assemble aryl esters.[3] In this regard, heteroatom-containing directing groups have been identified as versatile auxiliaries to enable the CDC reaction of aryl C−H bonds with acids. To date, Ackermann,[4] Cheng,[5] and Zhou[6] reported that sulfoximine and pyridine groups could efficiently enhance the CDC reaction of arenes with acids via a C−H activation process in the presence of Rh and Ru catalysts (Scheme 1a), respectively. Unfortunately, these transformations have been limited to noble transition metals and aryl carboxylic acids. Therefore, developing inexpensive metal-catalyzed C−H oxygenations with a broad substrate scope is desired.

Scheme 1. Transition-Metal-Catalyzed CDC of Aryl C−H Bonds with Acids



Recently, much attention has been turned to developing catalysts of earth-abundant first row transition metals due to its low cost and environmental benignity. Particularly for the cobalt catalysts, the existing examples of C−H functionalization demonstrated that a cobalt-based catalytic system could also be applied to the CDC reaction via a cyclometalation process.[7] In this context, although Glorius,[8] Song,[9] and Niu[10] successively reported cobalt-catalyzed cross-dehydrogenative coupling reactions of aryl C−H bonds with amines, thiols, and alcohols using different chelating auxilaries, the cobalt-catalyzed CDC reaction of aryl C−H bonds with acids has not yet been well-established.[11] More recently, we described a cobalt(III)-catalyzed [4 + 1] cycloaddition of 2-arylpyridines with aldehydes through aryl C−H activation, in which cobalt catalysts play a dual role as a metal catalyst and Lewis acid.[12] To further expand the catalytic versatility of cobalt catalysts in organic transformations, herein we report a novel Co(II)-catalyzed CDC reaction of aryl C−H bonds with acids via bidentate-chelation assistance, in which the substrate scope of acids could be further extended to both aryl and aliphatic acids (Scheme 1b).

Innitially, the cobalt-catalyzed CDC reaction of 1-acylamido-substituted naphthalene (**1a**, 0.10 mmol) with benzoic acid (**2a**, 0.15 mmol) was performed by employing AgOAc (2.0 equiv) as an oxidant in the presence of $NaHCO_3$ (2.0 equiv) in toluene (2.0 mL) at 120 °C under an Ar atmosphere for 12 h. Among a variety of cobalt catalysts, inexpensive $Co(OAc)_2$ proved to be the most effective for installing a benzoxyl group into the 8-position of naphthalen-1-ylamine **1a** and furnished

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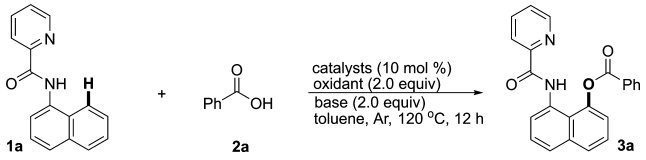
the desired aryl ester **3a** in 52% yield (compare Table 1 entries 1−4 with 5). In contrast, other transition metal catalysts such as

Table 1. Optimization of the Reaction Parameters[a]



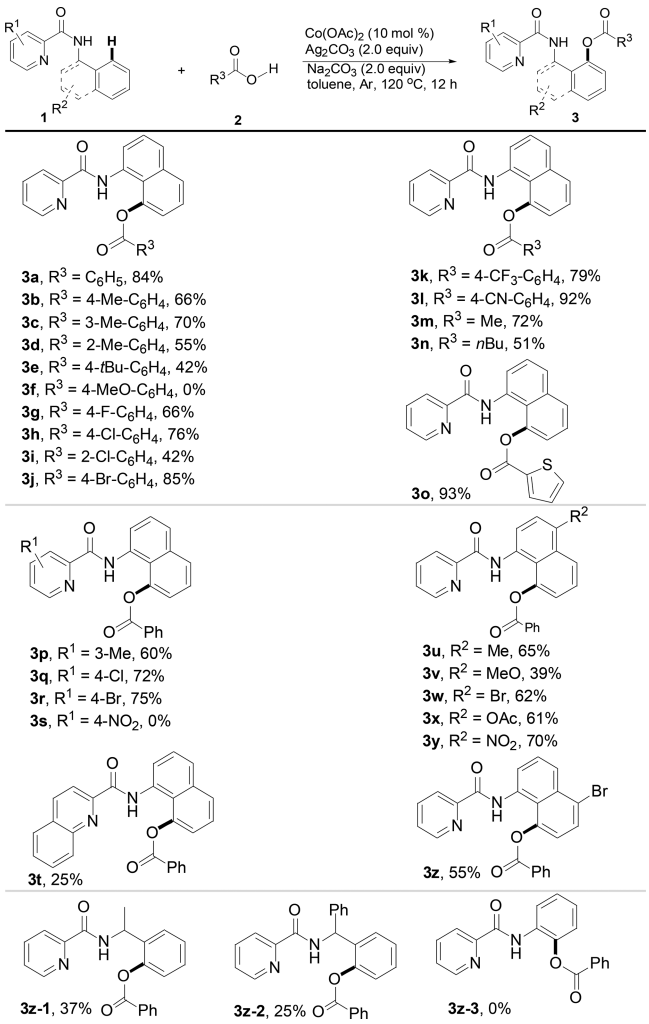
entry	catalysts	oxidant	base	yield[b] (%)
1	$Co(acac)_2$	AgOAc	$NaHCO_3$	44
2	$CoCl_2$	AgOAc	$NaHCO_3$	35
3	$CoSO_4{\cdot}7H_2O$	AgOAc	$NaHCO_3$	24
4	$Co(acac)_3$	AgOAc	$NaHCO_3$	45
5	$Co(OAc)_2$	AgOAc	$NaHCO_3$	52
6	$Pd(OAc)_2$	AgOAc	$NaHCO_3$	0
7	$RuCl_3$	AgOAc	$NaHCO_3$	0
8	$Cu(OAc)_2$	AgOAc	$NaHCO_3$	<5
9	$[Cp^*RhCl_2]_2$	AgOAc	$NaHCO_3$	0
10	$Co(OAc)_2$	$Cu(OAc)_2$	$NaHCO_3$	35
11	$Co(OAc)_2$	MnO_2	$NaHCO_3$	0
12	$Co(OAc)_2$	O_2	$NaHCO_3$	0
13	$Co(OAc)_2$	$K_2S_2O_8$	$NaHCO_3$	0
14	$Co(OAc)_2$	Ag_2CO_3	$NaHCO_3$	73
15	$Co(OAc)_2$	Ag_2CO_3	NaOAc	71
16	$Co(OAc)_2$	Ag_2CO_3	K_2CO_3	76
17	$Co(OAc)_2$	Ag_2CO_3	Na_2CO_3	83
18	$Co(OAc)_2$	Ag_2CO_3	Na_2CO_3	62[c]
19	$Co(OAc)_2$	Ag_2CO_3	Na_2CO_3	48[d]
20	$Co(OAc)_2$	Ag_2CO_3	Na_2CO_3	43[e]

[a]Unless otherwise noted, all the reactions were carried out using pyridine-2-carboxylic acid naphthalen-1-ylamide (**1a**) (0.10 mmol) and benzoic acid (**2a**, 0.15 mmol) with cobalt catalysts (10 mol %) in the presence of oxidant (2.0 equiv) and base (2.0 equiv) in toluene (2.0 mL) at 120 °C for 12 h under Ar in a sealed reaction tube. Followed by flash chromatography on SiO_2. [b]Isolated yield. [c]DCE was used as solvent. [d]1,4-Dioxane was used as solvent. [e]The reaction temperature was 100 °C.

$Pd(OAc)_2$, $RuCl_3$, $Cu(OAc)_2$, and $[Cp^*RhCl_2]_2$ could not enable this transformation (entries 6−9). Subsequently, we employed $Co(OAc)_2$ as catalysts, switched the AgOAc oxidant to other oxidants, and soon found that Ag_2CO_3 could significantly increase the yield of **3a** from 52% to 73% (compare entries 10−13 with 14). Except Ag_2CO_3, AgOAc, and $Cu(OAc)_2$, the other oxidants including MnO_2, O_2, and $K_2S_2O_8$ were not effective at all (entries 11−13). Moreover, we also continued to evaluate the effect of bases on this CDC reaction of 1-acylamido-substituted naphthalene **1a** with benzoic acid **2a**, and Na_2CO_3 was found to be a suitable base which could further improve the yield of **3a** from 73% to 83% (compare entries 14−16 with 17). It should be noted that utilization of other solvents or changing the reaction temperature did not favor this transformation (entries 18−20).

With the optimized catalytic system in hand, we then examined its versatility in the cross-dehydrogenative coupling between pyridine-2-carboxylic acid naphthalen-1-ylamide (**1a**) and various carboxylic acids (**2**). As summarized in Scheme 2, the aryl C−H bond oxygenations are successful for both electron-rich (**3b**−**3f**) and electron-poor (**3g**−**3l**) aryl carboxylic acids. Among them, *ortho*- or *meta*- or *para*-alkyl-substituted benzoic acids could afford 42−66% yields of aryl

Scheme 2. Substrate Scope[a,b]



[a]All the reactions were carried out using *N*-naphthyl-2-pyridylcarboxamides or *N*-benzyl-2-pyridylcarboxamides (**1**) (0.10 mmol) and carboxylic acids (**2**, 0.15 mmol) with $Co(OAc)_2$ catalysts (10 mol %) in the presence of Ag_2CO_3 (2.0 equiv) and Na_2CO_3 (2.0 equiv) in toluene (2.0 mL) at 120 °C for 12 h under Ar in a sealed reaction tube. Followed by flash chromatography on SiO_2. [b]Isolated yield.

esters (**3b**−**3e**), and 2- or 4-halobenzoic acids could also lead to 42−85% yields of the cross-coupling products (**3g**−**3j**). Particularly, 4-trifluoromethylbenzoic acid and 4-cynobenzoic acids could still exhibit excellent reactivity with 79% and 92% yields for **3k** and **3l**, respectively. Most importantly, aliphatic acids and thiophene-2-carboxylic acid are also reactive, thus showing the broad compatibility of the reaction conditions (**3m**−**3o**). The structure of **3o** was already unambiguously assigned by its single crystal X-ray analysis.[13] It should be noted that 4-alkoxybenzoic acid could not be converted into the corresponding arylester **3f** possibly due to the stonger electron-donating methoxyl group improving the pK_a value of aryl acid and decreasing its reactivity.

Subsequently, we further investigated the effect of the substituted pyridine ring from *N*-(1-naphthyl)-2-pyridyl carboxamides on this transformation. It was found that the *ortho*-Csp^2−H bond oxygenation was obviously dependent on the electronic properties of substituents at the 3- or 4-position of the pyridine ring. For examples, 3-methyl-2-pyridyl

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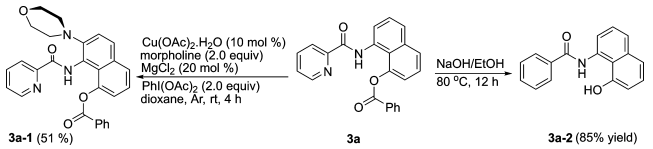
carboxamide and 4-halo-2-pyridyl carboxamides could be effectively converted to the desired aryl esters (**3q**−**3r**) in 60−75% yields, but 4-nitro-2-pyridyl carboxamide could not tolerate this reaction system (**3s**), and quinoline-2-carboxylic acid naphthalen-1-ylamide only afforded a 25% yield of aryl C−H oxygenation product (**3t**). In comparsion, the effect of the substituted naphthalene moiety from carboxamides in this transformation indicated that 1-carboxamido-4-or 5-substituted naphthalenes could all furnish moderate to good yields of aryl esters **3u**−**3z**, regardless of whether electron-deficient or -rich substituents were introduced into the 4- or 5-position of the naphthalene ring. Gratifyingly, the aryl C−H oxygenation could still be extended to *N*-benzyl substituted 2-pyridyl carboxamides, providing the corresponding phenyl esters **3z-1** and **3z-2** in acceptable yields. Unfortunately, *N*-phenyl-pyridine-2-carboxylic acid amide did not give the desired Csp^2−H oxygenation product **3z-3**.

The synthetic utility of the cobalt(II)-catalyzed regioselective aryl C−H bond oxygenation by means of pyridyl assistance was performed for the postsynthetic diversification of naphthyl ester **3a** (Scheme 3). As we know, different types of aryl esters could

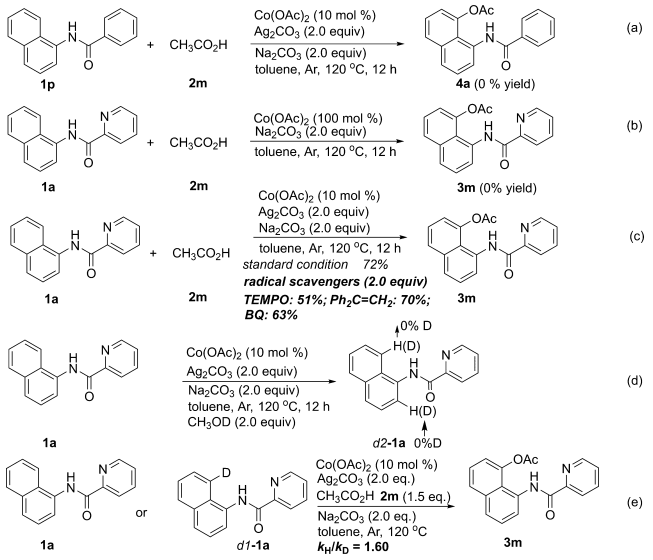
Scheme 3. Synthetic Application for This Transformation



be widely used to assemble complex molecules in synthetic chemistry. We therefore continued to employ a pyridyl ring as a directing group to regioselectively install an amino group at the 7-position of the 1,8-disubstituted naphthalene ring of ester **3a** in 51% yield under a $Cu(OAc)_2$ catalytic system.[14] This method could conveniently produce 1-acyloxy-7,8-diamino-substituted naphthalene **3a-1** in 52% yields. Of course, benzoic acid 8-[(pyridine-2-carbonyl)amino]naphthalen-1-yl ester (**3a**) could be easily converted into *N*-(8-hydroxynaphthalen-1-yl)benzamide (**3a-2**, 81% yield) in the presence of NaOH, in which the pyridine moiety was also replaced by the phenyl group (Scheme 3).

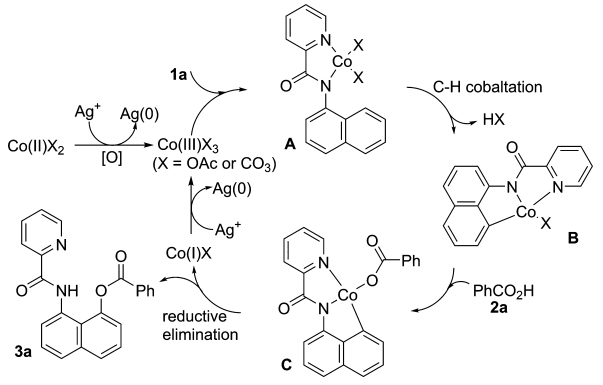
Several control experiments were carried out to gain some insight into the possible mechanism (Scheme 4). Initially, the Co(II)-catalyzed CDC reaction of *N*-naphthalen-1-yl-benzamide (**1p**) and acetic acid (**2m**) was performed under the standard reaction conditions, no desired aryl C−H oxygenation product **4a** was formed (Scheme 4a). This experiment demonstrated that pyridine "N" plays a key role in chelation assistance. Also, a $Co(OAc)_2$-promoted CDC reaction without the presence of Ag_2CO_3 suggested that the active Co(III) species was possibly involved in this aryl C−H oxygenation (Scheme 4b). It was still found that the addition of the typical radical scavengers including TEMPO, 1,1-diphenylethene, and *p*-benzoquinone (BQ) (2.0 equiv) did not significantly reduce the yields of this reaction[15] (Scheme 4c), implying that a radical mechanism should not be ruled out. In addition, the H/D exchange experiment of carboxamide **1a** in the absence of acids showed that no deuterium incorporation occurred, which suggested that the transformation perhaps proceeded through an irreversible cyclometalation pathway (Scheme 4d).[16] Finally, the kinetic isotope effect (KIE) has been determined through parallel experiments, and the corresponding KIE value (k_H/k_D = 1.60) further indicated that Csp2−H bond-breaking was possibly involved in the rate-limiting step of this reaction (Scheme 4e) (see Supporting Information (SI) for more details).

Scheme 4. Preliminary Mechanistic Studies



On the basis of the above-mentioned results and previous reports,[17] a plausible mechanism is proposed in Scheme 5.

Scheme 5. Proposed Mechanism



First, treatment of $Co(OAc)_2$ with Ag_2CO_3 produces an active cobalt(III) catalyst (CoX_3).[17b,18] Then, pyridyl *N*- and amide *N*-coordination of substrate **1a** to Co(III) species followed by naphthyl Csp^2−H bond activation affords a bis-chelated metallacyclic Co(III) complex **B** via a concerted metalation/deprotonation process. Subsequently, the ligand-exchange process between benzoic acid **2a** and Co(III) complex **B** gives the intermediate **C**, which further undergoes reductive elimination to yield the corresponding naphthyl ester **3a** and generates the Co(I) salts. The oxidation of Co(I) to Co(III) by oxidant Ag_2CO_3 continues the catalytic cycles.

In conclusion, we have developed an efficient and convenient approach for aryl Csp^2−H bond oxygenation of naphthylalenes with aryl and aliphatic acids employing inexpensive $Co(OAc)_2$ as the catalyst. This transformation could proceed smoothly under bidendate-chelation assistance to regioselectively assemble acyoxy-substituted naphthylenes. These naphthyl esters could be further converted to more complex naphthylene analogues.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b01942.

Detailed experimental procedures, characterization data, copies of ^{1}H NMR and ^{13}C NMR spectra for all isolated compounds (PDF)

Crystallographic data for **3o** (CIF)

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Notes

The authors declare no competing financial interest.

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(13) See SI for the single crystal structure and data of **3o**.

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