Ester Transfer Reaction of Aromatic Esters with Haloarenes and Arenols by a Nickel Catalyst

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Supporting Information Placeholder

ABSTRACT: A catalytic ester transfer reaction of aromatic esters with aryl halides/arenols was developed. The present reaction can transfer an ester functional group from certain aromatic esters to haloarenes. This ester transfer reaction involves two oxidative additions— one from the C–C bond of the aromatic ester and one from the C–halogen bond of haloarenes— onto a nickel catalyst. The utilization of a Ni/dcypt catalyst capable of cleaving both chemical bonds was a key for the reaction progress. Furthermore, naphthol-based aryl electrophiles were also applicable to the catalytic system via C–O bond activation.

Development of novel substitution reactions of aromatic cores is a continually important topic in organic synthesis. Classically, C–N or C–Br bonds on arenes have been constructed by an electrophilic aromatic substitution. Cross-coupling-based strategies such as Buchwald–Hartwig amination and Ullmann condensation have also been utilized for this purpose.[1] For the synthesis of arenecarboxylic acids and related esters, the carbonylative reactions using CO have found wide use (Figure 1A).[2] However, this gaseous manipulation is preferably avoided, owing to its cumbersome reaction set-up and toxicity. Several alternative methods using safety CO surrogates have been developed to synthesize aromatic esters while avoiding the handling of CO gas.[3]

Meanwhile, functional group metathesis reactions have been emerging as a conceptually distinct synthetic strategy.[4] In 2018, Morandi and Arndtsen independently reported a functional group metathesis of aroyl chlorides and aryl iodides catalyzed by a Pd-Xantphos complex (Figure 1B).[5] These methods used an oxidative addition and a reductive elimination of two distinct chemical bonds (C–I and C–Cl) as a reversible chemical process. Enlightened by these reports, we turned our attention to use aromatic esters instead of moisture-sensitive aroyl chlorides. Our campaign to study the decarbonylative transformation of aromatic esters revealed that the use of Ni- or Pd-dcypt (dcypt: 3,4-bis(dicyclohexylphosphino)thiophene) catalysts was effective to formally cleave the C–C bond of aromatic esters through oxidative additions of the C(acyl)–O bond followed by decarbonylation.[6,7] Moreover, the same catalysts can also enable the oxidative addition of aryl halides or arenols.[8] Thus, there is an opportunity to extend the functional group metathesis strategy to the reaction of aromatic esters with aryl halides as well as arenols. Such a reaction would also give aromatic esters as chemically stable products compared with the corresponding aroyl chlorides. We herein report our efforts toward the development of an ester transfer reaction from aromatic esters to haloarenes as well as arenols.

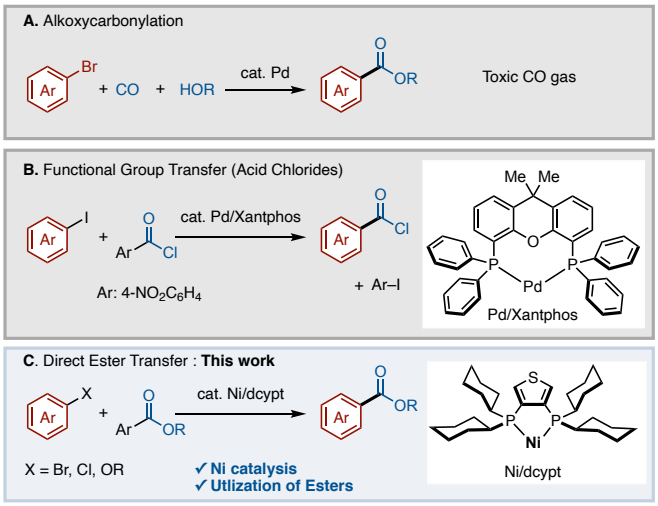
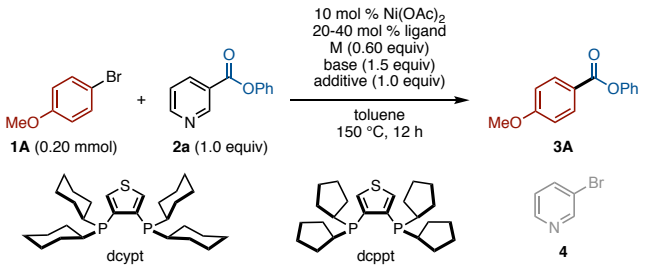


Figure 1. Catalytic synthesis of aromatic carboxylates. (A) Alkoxycarbonylation (B) functional group transfer using acyl chlorides (C) direct ester transfer.

At the outset, we optimized reaction conditions by using 4-bromoanisole (**1A**) and phenyl nicotinate (**2a**) as model substrates (Table 1). In line with our hypothesis, under the influence of $Ni(OAc)_2$/dcypt catalyst with Zn and Na_2CO_3, the reaction of **1A** and **2a** gave the ester transferred product **3A** in 42% yield (Table 1, entry 1). A structurally related thiophene-based ligand dcppt (3,4-bis(dicyclopentylphosphino)thiophene), also produced **3A** in a slightly lower yield (Table 1, entry 2). Interestingly, although dcype (1,2-

bis(dicyclohexylphosphino)ethane) was known to affect decarbonylative couplings,[6] this was totally ineffective in the present reaction (Table 1, entry 3). Xantphos, which is effective for Morandi's as well as Arndtsen's transfer reaction,[5] did not lead to the production of **3A** (Table 1, entry 4). Other typical phosphine ligands such as dppp and PPh_3 did not work at all in the present reaction (Table 1, entries 5 and 6). Although NHC-based ligands can affect the decarbonylative reaction of aromatic esters,[6] IPr did not delivered **3A** (Table 1, entry 7). Through the screening of ligands, unfortunately, Ar–Br **4** as a possible co-product was not observed. In this study, we used Zn powder as a reductant of Ni(II) to generate the active Ni(0) species. A similar effect can be expected for Sn and Mn powder, however, they decreased the reaction yield (Table 1, entries 8 and 9).[9] Although the reaction does not seem to require the base, the addition of Na_2CO_3 improved the reaction yield (Table 1, entries 1, 10–12). Of note, we did not obtain **3A** when palladium catalysis was used instead of nickel (Table 1, entry 13). Further improvement was achieved by the addition of DMAP, in which **3A** was generated in 60% yield (Table 1, entry 14). Using another pyridine base, 2,6-lutidine also resulted in a slight improvement though but not as much as when using DMAP (Table 1, entry 15). Other nucleophilic nitrogen bases, DBU and DABCO, did not increase the reaction yield (Table 1, entries 16 and 17). Although the role of DMAP is totally unclear at this stage, we consider the two possible roles of DMAP: One is that DMAP could support the oxidative addition of aromatic esters to the nickel catalyst through the generation of a transient aroyl-DMAP species.[10] Another role is that DMAP would work as a co-ligand of nickel.[11] Through the above studies, we identified the optimized conditions as $Ni(OAc)_2$/dcypt/Zn/Na_2CO_3/DMAP catalysis.

Table 1. Optimization of Reaction Conditions[a]

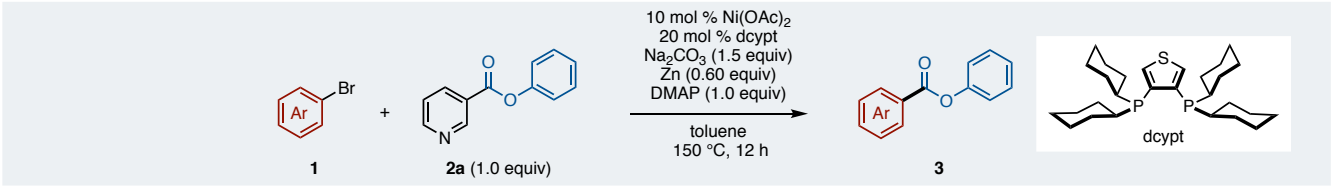


entry	ligand	M	base	additive	3A/%[b]
1	dcypt	Zn	Na_2CO_3	–	42
2	dcppt	Zn	Na_2CO_3	–	36
3	dcype	Zn	Na_2CO_3	–	0
4	Xantphos	Zn	Na_2CO_3	–	0
5	dppp	Zn	Na_2CO_3	–	0
6	PPh_3	Zn	Na_2CO_3	–	0
7[c]	IPr·HCl	Zn	Na_2CO_3	–	0
8	dcypt	Sn	Na_2CO_3	–	17
9	dcypt	Mn	Na_2CO_3	–	34
10	dcypt	Zn	$CaCO_3$	–	26
11	dcypt	Zn	NaOAc	–	28
12	dcypt	Zn	none	–	24
13[d]	dcypt	Zn	Na_2CO_3	–	0
14	dcypt	Zn	Na_2CO_3	DMAP	60
15	dcypt	Zn	Na_2CO_3	lutidine	45
16	dcypt	Zn	Na_2CO_3	DBU	37
17	dcypt	Zn	Na_2CO_3	DABCO	33

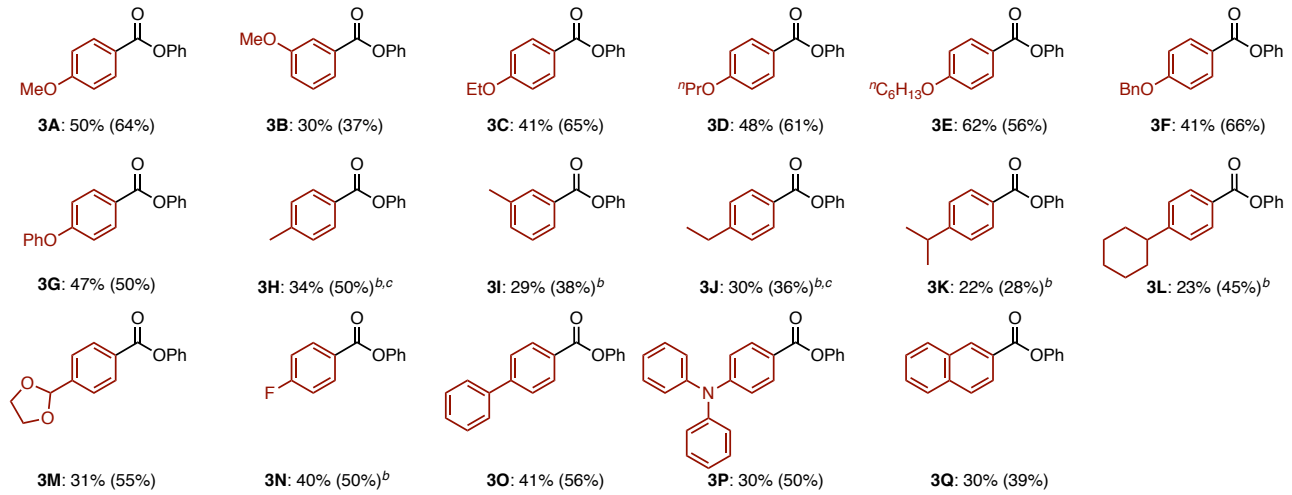
[a] Conditions: **1A** (0.20 mmol), **2a** (0.20 mmol), $Ni(OAc)_2$ (10 mol %), ligand (bidentate, 20 mol %; monodentate, 40 mol %), M (0.60 equiv), base (1.5 equiv), additive (1.0 equiv), toluene (0.80 mL), 150 °C, 12 h. [b] GC yield. [c] NaO*t*-Bu (25 mol %) was added. [d] $Pd(OAc)_2$ (10 mol %) was used instead of $Ni(OAc)_2$.

With the optimized conditions, we next investigated the substrate scope using **2a** as an ester source (Scheme 1). Electron-donating aryl bromides generally reacted to give the corresponding aromatic esters. *m*-Anisyl bromide (**1B**) reacted less efficiently than *p*-anisyl bromide (**1A**). Several aryl bromides with alkoxy groups including phenoxy were reacted to give the corresponding aromatic esters in moderate yields (**3C**–**3G**). Less electron-rich aryl bromides such as *m*- or *p*-alkylphenyl bromides also underwent to the present reaction, albeit affording lower yields of products **3H**–**3L** when compared to the alkoxylated arenes. Unfortunately, at this stage, *o*-substituted aryl bromides showed poor reactivity, affording the corresponding product in less than 20% yield (see the Supporting Information). Acetal (**3M**) and fluoro (**3N**) groups were tolerated under the reaction conditions. Triarylamine-based aromatic ester **3P** was successfully synthesized by the present method in 30% yield. Furthermore, naphthalene ester **3Q** was also produced.

Scheme 1. Substrate Scope [a]



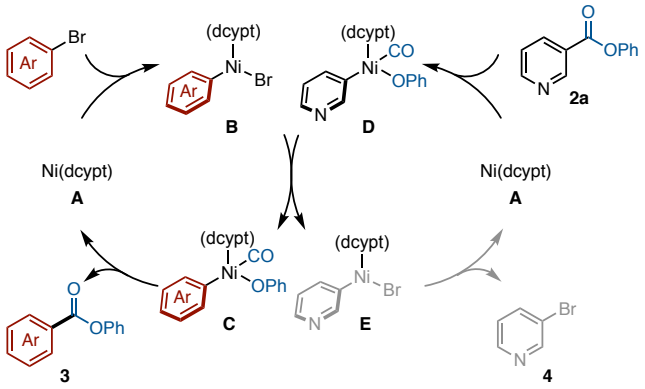
Structure of **3**



[a] Conditions: **1** (0.20 mmol), **2a** (0.20 mmol), $Ni(OAc)_2$ (10 mol %), dcypt (20 mol %), Zn powder (0.60 equiv), Na_2CO_3 (1.5 equiv), DMAP (1.0 equiv), toluene (0.80 mL), 150 °C, 12 h. Numbers in parenthesis show NMR yield. [b] inseparable mixture with phenyl benzoate. Isolated yields were determined by ^1H NMR ratio. [c] 170 °C, 24 h. [d] 2-Chloronaphthalene (**4**) was used without DMAP.

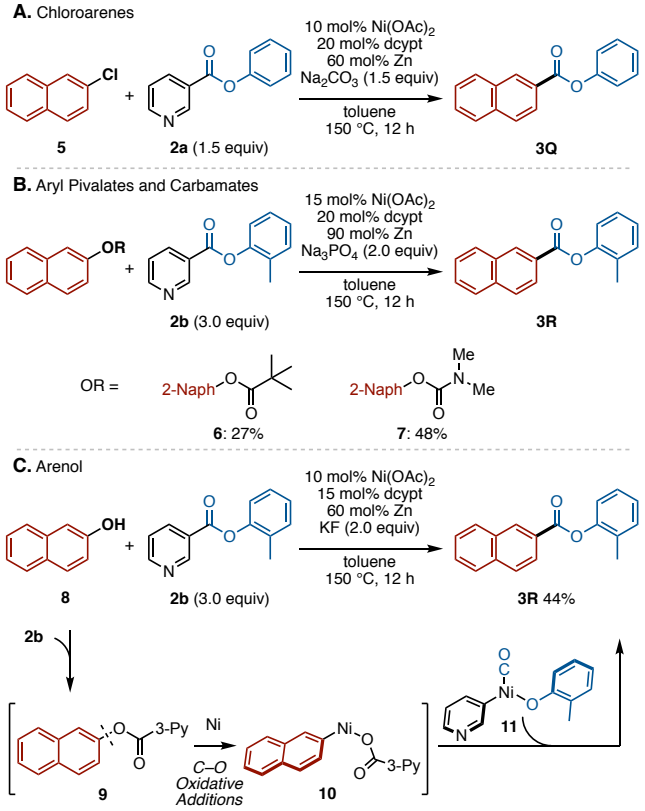
A plausible mechanism of this reaction is illustrated in Scheme 2. Ni/dcypt cleaves the C–Br bond of an aryl bromide and the C–C bond of phenyl nicotinate (**2a**) to generate Ar–Ni–Br (**B**) and Py–Ni(CO)–OPh (**D**) species, respectively. Similarly to the Arndtsen's work,[5] these intermediates could transmetalate to give Ar–Ni(CO)–OPh (**C**) and Py–Ni–Br (**E**). Reductive elimination from **C** would give ester transferred product **3**. On the other hand, reductive elimination from **E** could release bromopyridine **4** as co-product. However, we did not detect this species. The reason is totally unclear at this stage, but we speculate that reduction of **E** by the action of Zn powder, or the dimerization of **F** by nickel-complexes[12] might be involved as undesired pathways.

Scheme 2. Proposed Mechanism.



In addition to bromoarenes, chloroarenes were found reactive in the present reaction (Scheme 3A). 2-Chloronaphthalene (**5**) participated in this reaction, giving **3Q** in acceptable yield (50% yield). Furthermore, the Ni/dcypt catalyst is known to oxidatively add into inert C–O bonds.[13] Hypothesizing that C–O-based aryl electrophiles can participate in the present system, we subjected several C–O aryl electrophiles with *o*-tolyl ester **2b** (Scheme 3B).[14] Although the yields were moderate, we found that pivalates and carbamates underwent the ester transfer reaction under slightly modified conditions. With the success utilizing aryl pivalates in the present system, we wondered that direct esterification of Ar–OH would be possible. As expected, simple arenol **8** could be transformed to aromatic esters **3R** in 44% yield (Scheme 3C). In this case, **2b** occupies dual roles; one is an ester source, and the other is an activator of the Ar–OH group via the in-situ formation of ester **9**. Subsequent oxidative addition of **9** (C(aryl)–O) to Ni/dcypt, followed by transmetalation between **10** and **11** produced **3R**. In this arenol-based reaction, we did not obtain the corresponding 3-hydroxypyridine derivatives at all.

Scheme 3. Ester Transfer using Aryl Chlorides and Arenols.



In summary, we have developed a Ni-catalyzed ester transfer reaction between aryl halides and aromatic esters. As an alternative to aryl halides, we successfully utilized phenol-based aryl electrophiles to give ester-transferred product as well. Although the yield and scope of the method have room for improvement, the present result, particularly the utilization of Ar–OH as a starting material, could find use in synthetic chemistry as a way of creating valuable products from inexpensive feedstocks. Further studies focusing on the development of other ester transfer reactions and elucidation of the mechanism are underway in our laboratory.

ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures and spectroscopic data for compounds including ^{1}H-, ^{13}C NMR spectra (PDF)

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Notes

No competing financial interests have been declared.

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(14) When using simple phenyl ester **2a**, it was found that C(aryl)–O and C(acyl)–O oxidative additions on **2a** were competitive. The *o*-methyl group probably suppressed the undesired C(aryl)–O oxidative addition by steric hinderance.

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