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Metal-free synthesis of aryl esters by coupling aryl carboxylic acids and aryl boronic acids

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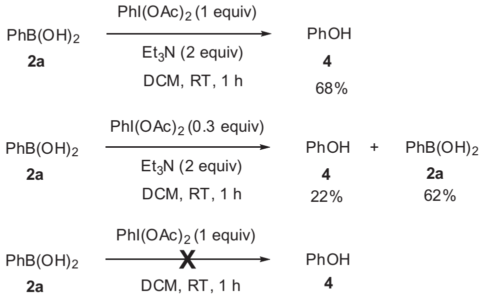
ABSTRACT

A facile synthesis of aryl esters is developed by coupling aryl carboxylic acids and aryl boronic acids in the presence of $PhI(OAc)_2$ and carbonyl diimidazole. A wide range of functional groups were tolerant to the metal-free reaction condition that led to the desired products in good yields.

Esters are an omnipresent functional group in chemistry. In particular, aryl esters are the most abundant subunit found in natural products, agrochemicals, pharmaceuticals, and polymers.[1] Besides, they serve as versatile building blocks in synthesis.[2] Accordingly, the synthetic routes to produce such systems have generated ample interest among synthetic chemists.[3] Conventionally, aryl esters are prepared via the esterification process which involves coupling of aryl carboxylic acid and phenol under acidic or basic conditions and thus restricting the use of substrates bearing sensitive functional groups.[4] Carbodiimide based coupling agents are useful, but separation of the by-product urea derivatives from the final product poses difficulties. Similarly, in the Mitsunobu reaction, multiple purifications are needed to isolate the pure esters.[5] Baeyer–Villiger oxidation of ketone often displayed low regioselectivity.[6] Thus, the development of mild and efficient protocol to access aryl ester is highly desirable.

In recent years, carbon—oxygen bond forming reactions have progressed rapidly with the aid of transition-metal catalyst.[7] Such a bond is present in aryl ester and thus serves as an ideal target substrate for demonstrating new protocols. As a result, methods are being developed to prepare aryl esters by coupling of aryl carboxylic acids with counterparts other than phenol. In this connection, aryl trimethoxysilane was used as a coupling partner in the presence of a copper reagent to acquire aryl ester.[8] The olofsson group illustrated the coupling of diaryliodonium salt with aryl carboxylic acid to prepare sterically congested aryl esters by employing a metal-free strategy.[9] Concurrently, aryl boronic acid has emerged as a valuable reagent due to its commercial availability and easy handling. In recent years, it has been transformed to various groups.[10] Recently, Cheng and co-workers developed a copper based Chan-Lam method to couple aryl boronic acid with aryl carboxylic acid.[11] A similar strategy was later demonstrated by the Liu group.[12] However to the best of our knowledge, a metal-free approach has not been developed so far to couple the aryl boronic acid. From the synthetic perspective, metal-free synthesis is a beneficial approach since it involves the utilization of inexpensive and environmentally benign reagents and also avoids the disposal of residual metallic waste obtained during the reaction.[13,14] Along these lines, we began to investigate the synthesis of aryl ester and herein, we disclose the coupling of aryl carboxylic acid and boronic acid under metal-free condition (Scheme 1).



Scheme 1. Control experiments.

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Table 1
Optimization of the reaction conditions[a]

$$\underset{\textbf{1a}}{\text{PhCOOH}} + \underset{\textbf{2a}}{\text{PhB(OH)}_2} \xrightarrow[\text{CDI (1 equiv), Et}_3\text{N (5 equiv)}]{\text{Reagent}} \underset{\textbf{3aa}}{\text{PhCOOPh}}$$

Entry	Reagent	Solvent	Temp/time (h)	Yield[b] (%)
1	NaOCl	EtOAc	rt, 12	NR
2	$Ca(OCl)_2$	EtOAc	rt, 12	NR
3	$PhI(OAc)_2$	EtOAc	rt, 6	12
4	$PhI(OAc)_2$/oxone	EtOAc	rt, 3	NR
5[c]	$PhI(OAc)_2$	DCM	rt, 3	22
6	$PhI(OAc)_2$	toluene	rt, 3	15
7	$PhI(OAc)_2$	CH_3CN	rt, 3	12
8	$PhI(OAc)_2$	DCM	rt, 3	65

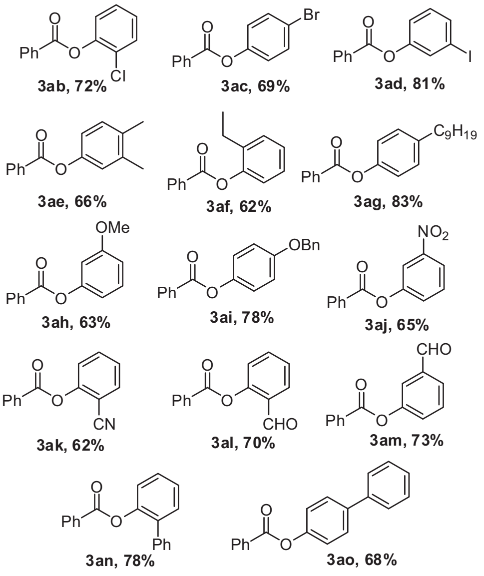
[a] Reactions were performed with benzoic acid **1a** (1 mmol), phenyl boronic acid **2a** (1 mmol), solvent (5 mL), carbonyl diimidazole (1 mmol), reagent (1 mmol), and triethylamine (5 mmol).

[b] Isolated yield.

[c] 30 mol % of $PhI(OAc)_2$ was used.

Table 2
Coupling of benzoic acid with various aryl boronic acids

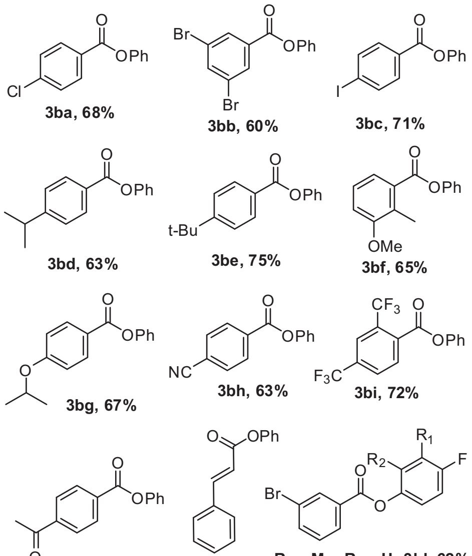
$$\underset{\textbf{1a}}{\text{PhCOOH}} + \underset{\textbf{2}}{\text{ArB(OH)}_2} \xrightarrow[\text{CDI (1 equiv), Et}_3\text{N (5 equiv), DCM, rt, 3 h}]{\text{PhI(OAc)}_2\text{ (1 equiv)}} \underset{\textbf{3a}}{\text{PhCOOAr}}$$



3ab, 72% **3ac, 69%** **3ad, 81%**
3ae, 66% **3af, 62%** **3ag, 83%**
3ah, 63% **3ai, 78%** **3aj, 65%**
3ak, 62% **3al, 70%** **3am, 73%**
3an, 78% **3ao, 68%**

Table 3
Coupling of phenyl boronic acid with various aryl carboxylic acids

$$\underset{\textbf{1}}{\text{ArCOOH}} + \underset{\textbf{2a}}{\text{PhB(OH)}_2} \xrightarrow[\text{CDI (1 equiv), Et}_3\text{N (5 equiv), DCM, rt, 3 h}]{\text{PhI(OAc)}_2\text{ (1 equiv)}} \underset{\textbf{3b}}{\text{ArCOOPh}}$$



3ba, 68% **3bb, 60%** **3bc, 71%**
3bd, 63% **3be, 75%** **3bf, 65%**
3bg, 67% **3bh, 63%** **3bi, 72%**
3bj, 67% **3bk, 64%**
R_1 = Me; R_2 = H; 3bl, 62%
R_1 = H; R_2 = F; 3bm, 67%

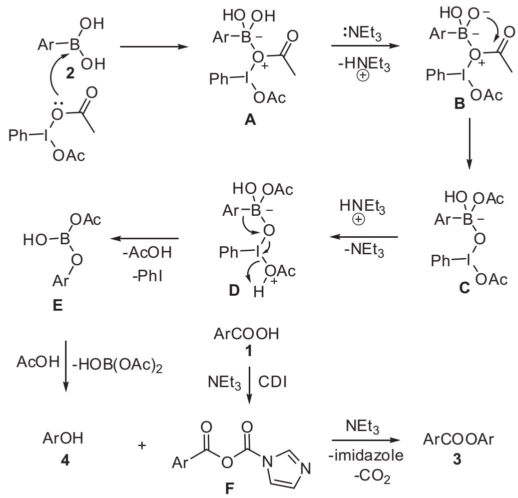
To initiate this study, the model substrates, benzoic acid **1a** and phenyl boronic acid **2a** with carbonyl diimidazole (1 equiv) and triethyl amine (5 equiv) were subjected to various conditions as shown in Table 1. Under sodium hypochlorite and calcium hypochlorite conditions, no product was obtained whereas phenyl iodiacetate (30 mol %) alone gave **3aa** *albeit* in low yield (entry 3). Conversely, the addition of oxone with phenyl iododiacetate was found unsuccessful (entry 4). However, aryl ester **3aa** was obtained in 65% yield with one equivalent of phenyl iododiacetate.[15] A quick screening of various solvents such as toluene, acetonitrile, and DCM revealed that the latter is found to be the best solvent for this transformation (65%).

Having the optimized condition in hand, benzoic acid **1a** was subjected to coupling with various aryl boronic acids **2** as depicted in Table 2. Phenyl boronic acid substituted with halo units such as chloro, bromo, and iodo[16] furnished the corresponding aryl esters in good yields. Methyl, ethyl, nonyl, benzyloxy, and methoxy containing phenyl boronic acid as well as nitro and cyano substituted boronic acid smoothly delivered the desired products (**3ae–ak**). Aryl esters (**3al–3am**) with formyl group were synthesized in good yields. In general, the formyl group is susceptible to oxidation, remained unaffected during the reaction and signifies the mild nature of the condition. Biphenyl boronic acids also transformed smoothly to the aryl esters (**3an–3ao**).

After the synthesis of various aryl benzoates **3a**, it was planned to couple the phenyl boronic acid **2a** with benzoic acids bearing different functional groups (Table 3). As expected, halo substituted benzoic acids underwent a smooth coupling reaction. Benzoic acids embedded with electron donating as well as withdrawing groups led to the aryl esters in good yields. Also, cinnamic acid afforded the unsaturated ester. Monofluoro and difluoro substituted phenyl boronic acids provided the corresponding aryl esters.

To understand the mechanism of the transformation, phenyl boronic acid **2a** was stirred with 1 equiv of phenyl iododiacetate and 2 equiv of triethyl amine in DCM at RT for 1 h, phenol **4** was obtained in 65% yield whereas the same reaction with only 0.3 equiv of phenyl iododiacetate gave only 22% of **4** and 62% unreacted phenyl boronic acid (Scheme 1). Thus it is clear that phenol is the intermediate of this reaction. Further, in the absence of triethylamine, no phenol formation was observed. This shows that triethylamine is essential for the conversion of aryl boronic acid to phenol and also used for the mixed anhydride formation from aryl carboxylic acid.

Based on the result, a possible mechanism is proposed as shown in Scheme 2. Aryl boronic acid **2** and phenyl iodoacetate give a Lewis adduct **A**. Triethylamine is expected to abstract a proton from the boronic acid **A** to form **B** which on intramolecular acetyl transfer followed by protonation led to **D**. This species undergoes an aryl migration to generate **E** which on exchange with in situ generated AcOH afforded phenol **4**. Finally, phenol and mixed anhydride **F** generated from aryl carboxylic acid and carbodiimidazole produced aryl ester **3**.



Scheme 2. Possible mechanism for the metal-free aryl ester synthesis.

In conclusion, a convenient and metal-free synthesis of aryl esters by employing the coupling of aryl boronic acid with aryl carboxylic acid is demonstrated. A wide range of functional groups were found to be tolerant under the reaction condition. The condition is mild and provided the desired products in good yields. A possible mechanism is proposed for this metal-free synthesis.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.02.079.

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15. *Typical procedure for aryl ester synthesis*: To a mixture of benzoic acid **1a** (1 mmol), carbonyl diimidazole (1 mmol), triethylamine (5 mmol), and PhI(OAc)$_2$ (0.32 g, 1 mmol) in DCM (5 mL) was added phenyl boronic acid **2a** (1 mmol) at rt. The reaction mixture was stirred for 3 h. The mixture was evaporated under reduced pressure to obtain a residue which was purified by a silica gel (60–120) column chromatography with petroleum ether–ethyl acetate (8:2) as an eluent to obtain aryl ester **3a** in 65% yield.
16. *3-Iodophenyl benzoate* (***3ad***): white solid; yield 81%; mp 78–79 °C, ^{1}H NMR (400 MHz CDCl$_3$) δ: 7.16–7.20 (m, 1H), 7.24–7.27(m, 1H), 7.56–7.52 (m, 2H), 7.69–7.63 (m, 2H) 8.23 (d, 1H, $J = 5.7$ Hz). ^{13}C NMR (100 MHz CDCl$_3$) δ: 93.7, 121.4, 128.7, 129.1, 130.2, 130.8, 130.9, 133.9, 135.0, 151.2, 164.7. GCMS: 324.