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Ligand free palladium catalyzed decarboxylative cross-coupling of aryl halides with oxalate monoester salts

Yan Li [a], Huan-Huan Chen [a], Chu-Fei Wang [a], Xiao-Lan Xu [b,c,*], Yi-Si Feng [a,c,*]

[a] School of Chemical Engineering, Hefei University of Technology, Hefei 230009, PR China
[b] School of Basic Medicine, Anhui Medical University, Hefei 230032, PR China
[c] Anhui Key Laboratory of Controllable Chemistry Reaction & Material Chemical Engineering, Hefei 230009, PR China

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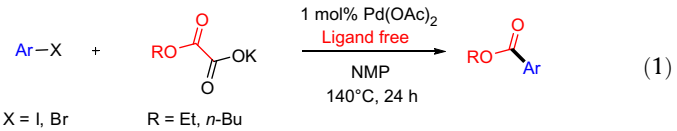
ABSTRACT

Ligand free Pd-catalyzed decarboxylative cross-coupling of potassium oxalate monoester and derivatives with aryl iodides and bromides is described. Functionalized aromatic esters can be efficiently synthesized via this method with only 1.0 mol % $Pd(OAc)_2$ catalyst without any phosphine ligand. This method illustrates an inexpensive and operationally simple method for the preparation of aromatic esters and acids, which is especially beneficial for a large scale synthesis.

Carboxylic acids are cheap and environmentally benign compounds. They can be used as an ideal *d*-synthon equivalent in the cross coupling reactions.[1] After the pioneer work of Goossen et al.,[2] many transition-metal catalyzed redox neutral decarboxylative cross-coupling reactions have been developed, recent examples include the ketone synthesis by Goossen,[3] biaryl synthesis by Forgione,[4] diaryl alkyne synthesis by Lee,[5] Jiao,[6] and other groups,[7] and aromatic ester synthesis by Liu.[8] Other recent studies by Miura,[9] Larros,[10] Su,[11] and other groups[12] also highlight the synthetic utility of related decarboxylative reactions. However, in most reports on Pd-catalyzed redox neutral decarboxylative couplings, especially when aryl halides are used as aryl electrophiles, an expensive, toxic, and often sensitive phosphine ligand was required. For a more desirable transformation, the use of expensive and sensitive ligands always makes an increase in the cost, especially on a relative large scale. Ligand free palladium catalyzed Heck[13] and Suzuki[14] couplings have been widely studied, but there is almost no report on the ligandless redox neutral decarboxylative cross-coupling.



(1)

In 2009, Liu et al. found a redox neutral decarboxylative coupling for the synthesis of aromatic esters via the decarboxylation of potassium oxalate monoester. In Liu's reports, a bidentate phosphine ligand (dppp) is necessary. During our study on the synthesis of aromatic carboxylic esters via this methodology, we find that for aryl iodides and some aryl bromides this transformation can be achieved under a ligand free condition with only 1 mol % palladium acetate catalyst (Eq. 1). This new discovery illustrates that like Heck and Suzuki couplings, in some cases for palladium catalyzed redox neutral decarboxylative couplings, a ligandless condition is feasible.

Our study started with an investigation on Pd-catalyzed decarboxylative cross-coupling of potassium 2-ethoxy-2-oxoacetate[15,16] with iodobenzene in the presence of 1 mol % $Pd(TFA)_2$ in NMP at 150 °C. The desired product was obtained in 83% yield (Table 1, entry 1). As we know, $Pd(TFA)_2$ is prepared from $Pd(OAc)_2$ through complex process. To avoid wasting a lot of reagents, $Pd(OAc)_2$ was used instead of $Pd(TFA)_2$ as catalyst in this reaction while the yield decreased to 79% (entry 2). To our delight, the yield slightly rose to 82% when the temperature was reduced to 140 °C (entry 3). A scan of commercially available palladium precursors such as $PdCl_2$, $Pd_2(allyl)_2Cl_2$, and $Pd_2(dba)_3$ revealed that $Pd(OAc)_2$ was the best choice (entries 5–7). Furthermore, using DMSO, DMAc, DMF, or DMI as solvents gave lower yields than NMP (entries 8–11). To make further improvement on the yield of the reaction, we tested to change the reaction temperature (entries 16–19) and time (entries 12–15) in the system. The results showed that

* Corresponding authors. Tel.: +86 551 2904353; fax: +86 551 2904405.
E-mail addresses: xlxu@ustc.edu (X.-L. Xu), ysfeng@hfut.edu.cn (Y.-S. Feng).

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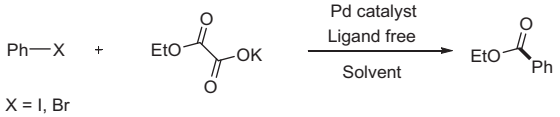
Table 1
Pd-catalyzed decarboxylative cross-coupling of potassium 2-ethoxy-2-oxoacetate with aryl halides[a]



Entry	X	Pd Source	Time (h)	Temp (°C)	Solvent	Yield[b] (%)
1	I	$Pd(TFA)_2$	24	150	NMP	83
2	I	$Pd(OAc)_2$	24	150	NMP	79
3	I	$Pd(OAc)_2$	24	140	NMP	82
4	I	$Pd(TFA)_2$	24	140	NMP	82
5	I	$PdCl_2$	24	140	NMP	80
6	I	$Pd_2(allyl)_2Cl_2$	24	140	NMP	78
7	I	$Pd_2(dba)_3$	24	140	NMP	76
8	I	$Pd(OAc)_2$	24	140	DMSO	24
9	I	$Pd(OAc)_2$	24	140	DMAc	36
10	I	$Pd(OAc)_2$	24	140	DMF	54
11	I	$Pd(OAc)_2$	24	140	DMI	43
12	I	$Pd(OAc)_2$	26	140	NMP	80
13	I	$Pd(OAc)_2$	16	140	NMP	80
14	I	$Pd(OAc)_2$	12	140	NMP	73
15	I	$Pd(OAc)_2$	8	140	NMP	69
16	I	$Pd(OAc)_2$	24	160	NMP	78
17	I	$Pd(OAc)_2$	24	130	NMP	78
18	I	$Pd(OAc)_2$	24	120	NMP	75
19	I	$Pd(OAc)_2$	24	110	NMP	72
20	Br	$Pd(OAc)_2$	24	140	NMP	<5

[a] Reaction conditions: aryl halides (0.5 mmol), oxalate monoester salts (0.75 mmol), NMP (1 mL), and Pd source (1 mol %) at 140 °C under Ar atmosphere for 24 h.
[b] GC yields (average of two runs), using naphthalene as the internal standard.

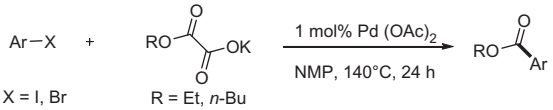
140 °C and 24 h respectively were the best reaction conditions. To our disappointment, when bromobenzene was used as alternative reagent, the yield of the desired product was less than 5%.

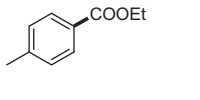
Overall, by using $Pd(OAc)_2$ as catalyst, without any ligand and additive, we obtained the optimal catalytic system for the Pd-catalyzed decarboxylative cross-coupling of oxalate monoester salts with iodobenzene[17] (entry 3).

With the optimized conditions in hand, we next explored the scope of this reaction with various aryl iodides and bromides (Table 2). To our satisfaction, the reaction took place easily to give a good yield and was applicable to a broad range of aryl iodides carrying both electron-donating and electron-withdrawing functional groups (**3a**–**3h**). Ortho-substituted substrates (**3e**, **3f**) and halogenated heterocycles, such as pyridine (**3i**), thiophene (**3j**), diphenyl (**3k**), and naphthalene (**3l**) also gave good yields. However, only the decarboxylative cross-coupling of aryl bromides with electron-withdrawing groups including nitro (**3m**, **3n**) and nitrile (**3o**, **3p**) with potassium 2-ethoxy-2-oxoacetate in this catalytic system was applicable. In addition, the reactions of potassium 2-butoxy-2-oxoacetate with aryl iodides were subsequently investigated. It was clear that the reactions of electron-rich (**3r**–**3t**), electron-poor (**3u**) aryl iodides, or halogenated heterocycles (**3v**–**3x**) with potassium 2-butoxy-2-oxoacetate all gave the desired products in moderate yields.

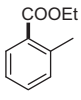
Although nonactivated aryl bromides were not desired substrates, we thought that the combination of the Finkelstein halide exchange and decarboxylative coupling in a one pot manner may make the utilization of nonactivated aryl bromides successful. By using this new protocol we synthesized biphenyl-4-carboxylic acid

Table 2
Decarboxylative cross-coupling scope with respect to aryl halides[a,b]

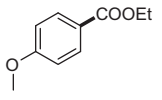




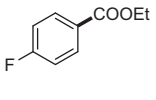
88%
3a



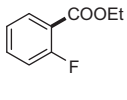
86%
3b



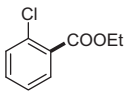
84%
3c



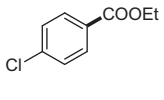
64%
3d



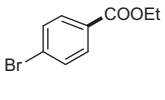
44%
3e



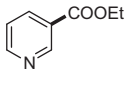
73%
3f



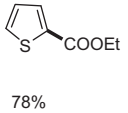
80%
3g



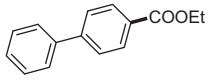
77%
3h



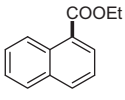
79%
3i



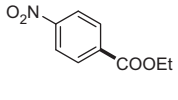
78%
3j



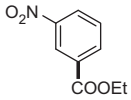
80%
3k



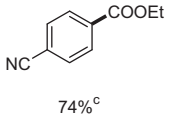
90%
3l



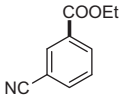
76%[c]
3m



74%[c]
3n



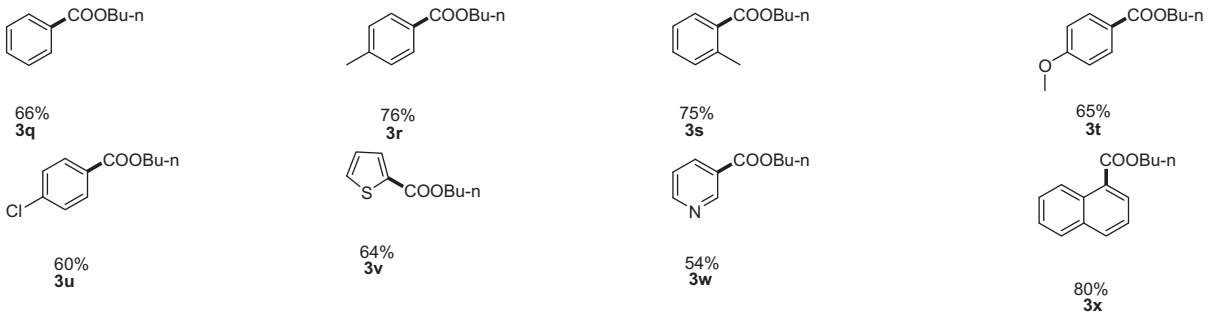
74%[c]
3o



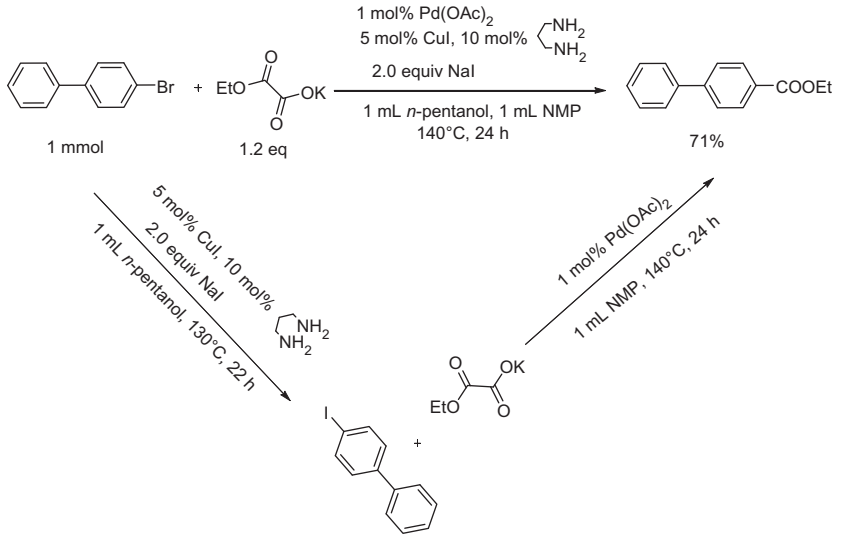
70%[c]
3p

(*continued on next page*)

Table 2 (*continued*)



[a] Reaction conditions: aryl halides (1 mmol), oxalate monoester salts (1.2 mmol), NMP (1 mL), and $Pd(OAc)_2$ (1 mol %) at 140 °C under Ar atmosphere for 24 h.
[b] Isolated yields.
[c] Using bromobenzene derivatives.



Scheme 1. One-pot manner synthesis of biphenyl-4-carboxylic acid ethyl ester from bromobenzene derivatives.

ethyl ester from bromobenzene derivatives in a one-pot manner (Scheme 1). Our work started by an investigation of Cu-catalyzed halogen exchange in aryl halides reported by Buchward.[18] In this work, CuI and 1,3-diamine were used as catalyst and ligand in the conversion of the aryl bromides into aryl iodides. Based on this study, we used 1 mol % $Pd(OAc)_2$ and 5 mol % CuI as catalysts, 10 mol % 1,3-propanediamine as ligand, 2.0 equiv NaI, *n*-pentanol, and NMP as solvent in the decarboxylative cross-coupling of potassium 2-ethoxy-2-oxoacetate with 4-bromobiphenyl. The desired product was obtained in 71% yield.

In conclusion, we have developed an inexpensive and operationally simple protocol for Pd-catalyzed decarboxylative aromatic ester synthesis from aryl halides under ligand free condition. This new catalytic system was suitable for iodobenzene and some activated bromobenzene derivatives, and we achieved the utilization of nonactivated bromobenzene via the combination of copper catalyzed aromatic Finkelstein halide exchange reaction and decarboxylative cross-coupling. Due to the convenient operation, versatility, and environmental friendliness of this procedure, we hope the newly developed ligand free catalytic system could be applied not only in laboratory but also in large-scale production.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.08.076. These data include MOL files and InChiKeys of the most important compounds described in this article.

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16. Synthesis of Potassium Oxalate monoesters. According to the literature procedure, a 100 mL flask was charged with diethyl oxalate (13.5 mL, 0.1 mol), potassium acetate (9.8 g, 0.1 mol), and ethanol (20 mL) as solvents. Subsequently water (1.8 mL, 0.1 mol) was added via syringe. The mixture was stirred under reflux condition (90 °C oil bath) for 3 h, and a lot of white crystal solid was obtained. The mixture was allowed to cool to room temperature and 20 mL diethyl ether was added. The white crystal was filtrated, washed with ethanol and diethyl ether, and dried under vacuum at 30 °C for 2 h.
17. General experimental procedure. An oven-dried Schlenk-tube (10 mL) was charged with Pd source (1 mol %), and ethyl potassium oxalate (0.75 mmol). The tube was evacuated and backfilled with argon (this procedure was repeated three times). After that, iodobenzene (0.5 mmol) and NMP (1.0 mL) were added by syringe under a counter flow of argon at room temperature. The reaction vessel was closed and then placed under stirring in a preheated oil bath. The reaction mixture was stirred for 24 h. Upon completion of the reaction, the mixture was cooled to room temperature and diluted with ethyl acetate, and analyzed by gas chromatography. Selected spectral and analytical data for *4-methylbenzoic acid ethyl ester* (**3a**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (t, 3H, J = 7.2 Hz), 2.39 (s, 3H), 4.36 (q, 2H, J = 7.1 Hz), 7.22 (d, 2H, J = 8.4 Hz), 7.93 (d, 2H, J = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.4, 21.7, 60.8, 127.8, 129.1, 129.6, 143.4, 166.7. HRMS calcd $C_{10}H_{12}O_2$: 164.0837. Found: 164.0826. *4-Chlorobenzoic acid ethyl ester* (**3g**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (t, 3H, J = 7.0 Hz), 4.36 (q, 2H, J = 7.1 Hz), 7.38–7.42 (m, 2H), 7.96–7.99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.4, 61.3, 128.8, 129.0, 131.0, 139.3, 165.8. HRMS calcd $C_9H_9ClO_2$: 184.0291. Found: 184.0282. *4-Nitrobenzoic acid ethyl ester* (**3m**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (t, 3H, J = 7.0 Hz), 4.43 (q, 2H, J = 7.2), 8.20–8.23 (m, 2H), 8.27–8.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.3, 62.0, 123.4, 130.7, 135.9, 150.5, 164.7. HRMS calcd $C_9H_9NO_4$: 195.0532. Found: 195.0545.
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