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Pd(II)-Catalyzed Decarboxylative Cross-Coupling of Potassium Aryltrifluoroborates with α-Oxocarboxylic Acids at Room Temperature

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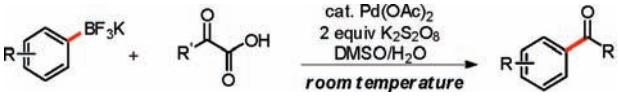
ABSTRACT



A novel Pd-catalyzed decarboxylative cross-coupling of potassium aryltrifluoroborates with α-oxocarboxylic acids is performed at room temperature. This reaction provides an efficient access to aryl ketones under mild conditions.

Transition-metal-catalyzed decarboxylative coupling has emerged as a powerful method for C−C bond formation, and numerous studies have been carried out in this area in recent years.[1] Aside from the well-established decarboxylative allylation of esters,[2] decarboxylative cross-coupling of carboxylic acids with activated or unactivated (hetero) arenes has been of recent interest,[3] and significant progress has been made to improve substrate scope and product diversity.

Ketones are important functional groups in medicine and biologically active natural products. Aryl ketone formation through Pd-catalyzed decarboxylative cross coupling was first reported by Goossen and co-workers using aryl halides with potassium α-oxocarboxylates in the presence of a Cu(I) source (eq 1).[4] Recently, palladium(II)-catalyzed decarboxylative acylation of arenes with α-oxocarboxylic acids was also reported from our laboratory (eq 2).[5] However, these processes suffer either from high reaction temperatures (eq 1) or restricted

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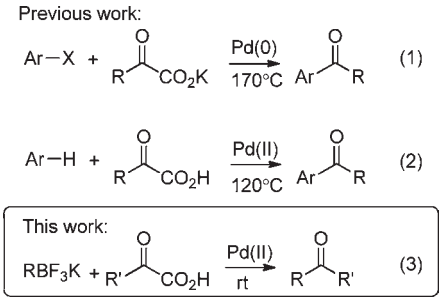
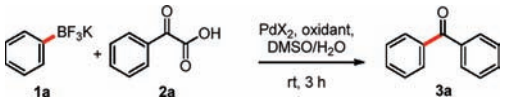
substrate scope (eq 2), which limits their potential application. Palladium-catalyzed cross-coupling of anhydrides, carboxylic acids, or α-carboxylic acids with boronic acids, developed by the groups of Goossen and Yamamoto, provides an alternative approach for aryl ketone formation.[6] However, this method is not compatible with the presence of bromine or iodine atoms, limiting the substrate scope. As such, realization of aryl ketone formation through decarboxylative cross-coupling reactions with improved substrate scope under mild conditions is highly desirable. In our continuing effort to develop mild decarboxylative couplings, herein we report a novel room-temperature approach to aryl ketones via palladium-catalyzed decarboxylative cross coupling of potassium aryltrifluoroborates[7] with α-oxocarboxylic acids (eq 3).



Early reports demonstrated that under mild conditions, decarboxylation of α-oxocarboxylic acids, oxalic acids and oxamic acids could be realized by the combination of a catalytic amount of a silver(I) salt and stoichiometric persulfate.[8] Recently, in a C−H acylation of acetanilides with α-oxocarboxylic acids discovered in our laboratory, it was demonstrated that decarboxylation could also be effectively performed by a catalytic Pd(II) source with stoichiometric persulfate as the oxidant at room temperature[9] On the basis of these studies, we initiated an investigation of decarboxylative coupling using potassium aryltrifluoroborates (**1a**) with phenylglyoxylic acid (**2a**) in the presence of 5 mol % of $Pd(TFA)_2$ and 2 equiv of $(NH_4)_2S_2O_8$ at room temperature. After extensive solvent screening, $DMSO/H_2O$ (2:3, v/v) was found to be optimal, and the desired product **3a** was obtained in 90% yield (Table 1, entry 3). Further optimization of the reaction conditions demonstrated that the most efficient system is the combination of catalytic $Pd(OAc)_2$ with stoichiometric $K_2S_2O_8$ as oxidant, providing **3a** in 98% yield in 3 h (entry 10). It was then noted that high yields could also be obtained with reduced amounts of the catalyst (entries 12 and 13).

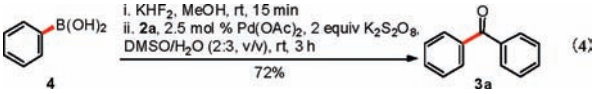
Table 1. Optimization of Reaction Conditions[a]



entry	PdX_2 (mol %)	oxidant (equiv)	$DMSO/H_2O$ (v/v)	yield[b] (%)
1	$Pd(TFA)_2$ (5)	$(NH_4)_2S_2O_8$ (2)	3:1	67
2	$Pd(TFA)_2$ (5)	$(NH_4)_2S_2O_8$ (2)	1:1	79
3	$Pd(TFA)_2$ (5)	$(NH_4)_2S_2O_8$ (2)	2:3	90
4	$Pd(TFA)_2$ (5)	$(NH_4)_2S_2O_8$ (2)	1:2	87
5	$Pd(TFA)_2$ (5)	$(NH_4)_2S_2O_8$ (2)	1:3	85
6	$Pd(OAc)_2$ (5)	$(NH_4)_2S_2O_8$ (2)	2:3	93
7	$PdBr_2$ (5)	$(NH_4)_2S_2O_8$ (2)	2:3	91
8	$[Pd(MeCN)_4](BF_4)_2$ (5)	$(NH_4)_2S_2O_8$ (2)	2:3	83
9	$PdCl_2$ (5)	$(NH_4)_2S_2O_8$ (2)	2:3	72
10	$Pd(OAc)_2$ (5)	$K_2S_2O_8$ (2)	2:3	98
11	$Pd(OAc)_2$ (5)	$K_2S_2O_8$ (1.2)	2:3	60
12	**$Pd(OAc)_2$ (2.5)**	**$K_2S_2O_8$ (2)**	**2:3**	**94 (90[c])**
13	$Pd(OAc)_2$ (1)	$K_2S_2O_8$ (2)	2:3	83
14[d]	$Pd(OAc)_2$ (2.5)	$K_2S_2O_8$ (2)	2:3	21

[a] Conditions: **1a** (0.3 mmol), **2a** (0.6 mmol), PdX_2, oxidant (0.6 mmol), 3 mL solvent, rt, 3 h. [b] Yields measured by GC using an internal standard based on **1a**. [c] Isolated yield based on **1a**. [d] Compound **1a** was replaced by phenylboronic acid (**4**).

It is of note that this transformation could also be carried out in a one-pot process from phenylboronic acid (**4**) through in situ formation of potassium phenyltrifluoroborate followed by decarboxylative coupling with phenylglyoxylic acid (**2a**) in 72% yield under unoptimized conditions (eq 4).



As shown in Table 2, electron-donating substituents and halogens (**3b−j**) on phenylglyoxylic acid are well-tolerated under the optimal catalytic conditions. Substrates with strong electron-withdrawing groups such as ester and nitro gave, at best, only trace amounts of the desired product. Additionally, the sterically hindered substrate **1l** gave rise to the desired product **3l** in good yield, which had failed for Pd(0)/Cu(I)-catalyzed decarboxylative acylation in a previous report.[4a] Furthermore, aliphatic α-oxocarboxylic acids also provided good to excellent yields of products (**3o−q**).

The compatibility of substituted potassium phenyltrifluoroborates (**1b−n**) is surveyed in Table 3. In general,

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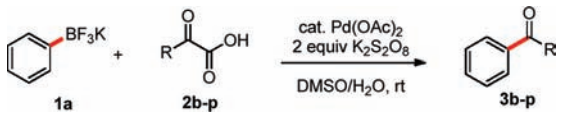
Table 2. Scope of α-Oxocarboxylic Acids[a]



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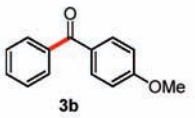
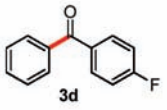
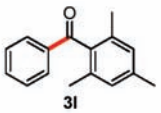
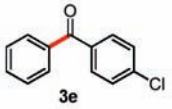
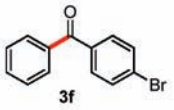
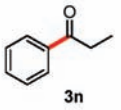
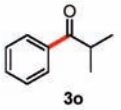
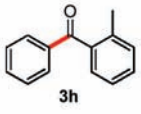
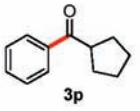
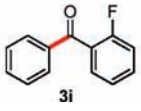
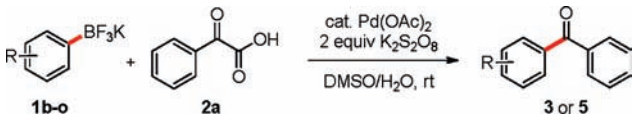
 3b	86	 3j	85
 3c	91	 3k	89[c]
 3d	77	 3l	70[c]
 3e	95	 3m	78[c]
 3f	87	 3n	73[c]
 3g	95	 3o	83[c]
 3h	98	 3p	90[c]
 3i	97		

[a] Conditions: **1a** (0.3 mmol), **2b**−**j** (0.6 mmol), $Pd(OAc)_2$ (0.0075 mmol), $(NH_4)_2S_2O_8$ (0.6 mmol), 3 mL of DMSO/H_2O (2:3, v/v), rt, 3 h. [b] Isolated yields based on **1a**. [c] $Pd(OAc)_2$ (0.015 mmol), **2k**−**p** (0.9 mmol).

Table 3. Scope of Potassium Aryltrifluoroborates[a]



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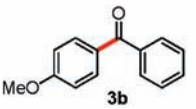
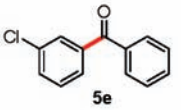
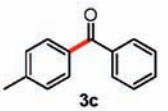
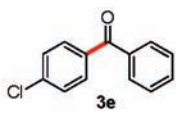
 3b	82	 5e	67
 3c	95	 5f	83
 3e	90	 5g	54
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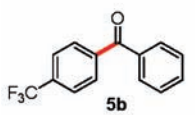
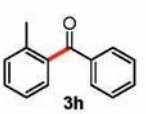
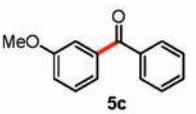
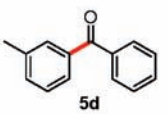
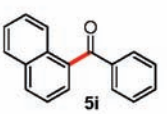
 5b	41	 3h	69
 5c	98	 5h	45
 5d	98	 5i	64[c]

[a] Conditions: **1b**−**o** (0.3 mmol), **2a** (0.6 mmol), $Pd(OAc)_2$ (0.0075 mmol), $(NH_4)_2S_2O_8$ (0.6 mmol), 3 mL of DMSO/H_2O (2:3, v/v), rt, 3 h. [b] Isolated yields based on **1**. [c] $Pd(OAc)_2$ (0.015 mmol) in DMSO/H_2O (8:1, v/v).

electron-donating groups provided higher yields when compared with electron-withdrawing groups. *o*-Substituted substrates (**3g**, **3h**, and **5h**) gave lower yields when compared with *meta*- or *para*-substituted substrates due to steric effects. In addition, potassium 1-naphthylborate also provided a good yield of product **5i**.

In summary, an efficient, room-temperature approach to palladium-catalyzed decarboxylative cross coupling of potassium aryltrifluoroborates with α-oxocarboxylic acids has been developed. In view of the importance of aryl ketones in organic chemistry and medicinal chemistry, and the readily availability and stability of potassium aryltrifluoroborates, this novel method will find broad use in organic synthesis.

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Supporting Information Available. Experimental procedures and spectroscopic data (NMR) for all newly identified compounds. This material is available free of charge via the Internet at http://pubs.acs.org