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One-Pot Synthesis of Arylketones from Aromatic Acids via Palladium-Catalyzed Suzuki Coupling

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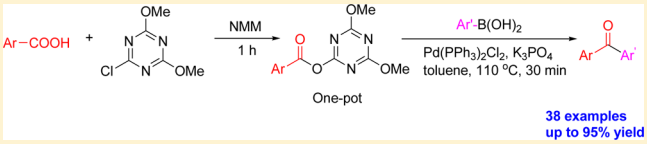
Supporting Information

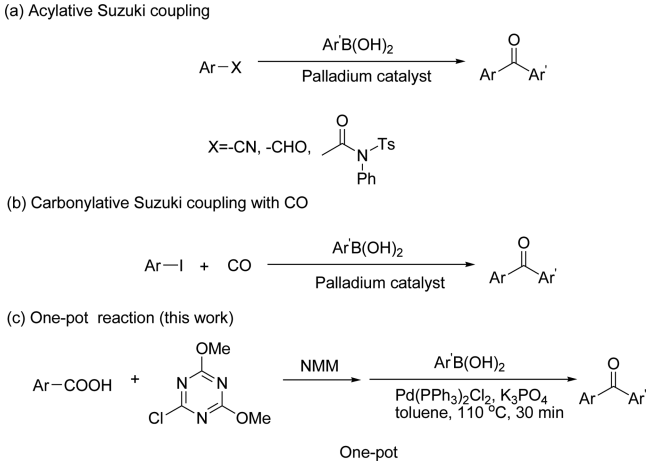
ABSTRACT: A palladium-catalyzed one-pot procedure for the synthesis of aryl ketones has been developed. Triazine esters when coupled with aryl boronic acids provided aryl ketones in moderate to excellent yields (up to 95%) in the presence of 1 mol % $Pd(PPh_3)_2Cl_2$ for 30 min.



Arylketones are commonly used compounds in the preparation of pharmaceuticals[1] and materials[2] and act as useful building blocks in organic chemistry.[3] Compared with the traditional Friedel−Crafts acylation, transition-metal-catalyzed acylative Suzuki coupling is a more effective way of obtaining aryl ketones, due to high functional group tolerance, regioselectivity, and the mild reaction conditions employed. Transition-metal-catalyzed cross-coupling reaction between an aryl boronic acid and an electrophile, including anhydrides,[4] acyl chlorides,[5] esters,[6] nitriles,[7] aldehydes,[8] and amides,[9] to form a series of symmetrical or asymmetric ketones was developed in recent years (Scheme 1, a).

Carbonylative Suzuki coupling utilizing the C1 building block carbon monoxide is yet another approach for the synthesis of aryl ketones which utilizes a transition-metal-catalyzed coupling reaction (Scheme 1, b).[10] However, this approach should be operated under rigorously controlled conditions, due to the high toxicity and flammability of carbon monoxide.

Scheme 1. Pd-Catalyzed Carbonylative Suzuki Cross-Couplings



Cleavage of carbon−oxygen bonds is generally regarded as more difficult than cleavage of carbon−halogen bonds, due to the higher bond dissociation energy of C−O bond.[11] During the past few years, a series of C−O electrophiles such as pivalates,[12] acetates,[13] carbamates,[14] carbonates,[15] sulfonates,[16] sulfamates,[17] and sulfuryl fluoride[18] have been investigated as conveniently available coupling partners in metal-catalyzed cross-coupling reactions.

It is well-known that 2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMT) is an easily obtained reagent used in the preparation of the corresponding heteroaryl ethers[19] or esters[20] which, in turn, can be employed as powerful coupling partners. The strongly polar nature of the 1,3,5-triazine facilitates the cleavage of the C−O bond in the ester, and the oxygenated 1,3,5-triazine possesses good leaving group potential which could accelerate the transmetalation process in the catalytic cycle of cross-coupling reactions.[21] Carboxylic acids or amino acids 1,3,5-triazine esters are reacted with a Grignard/CuI reagent to give the corresponding ketones in nearly quantitative yields.[22] In this type of reactions, functional group tolerance for the Grignard/CuI reagent needed to be improved. However, the reaction times are typically long and involve two-step procedures.

On the basis of the difficulties outlined in the proceeding sections, and considering the general utility of aryl ketones, we set out to develop of a convenient and practical way of synthesizing aryl ketones directly from aromatic acids. Hence, we are reporting a facile, palladium-catalyzed Suzuki coupling which employs a triazine ester as key intermediate to the synthesis of aryl ketones in one pot. First, aromatic carboxylic acids are reacted with 2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMT) under very mild conditions to provide the corresponding triazine ester. Subsequent treatment of the

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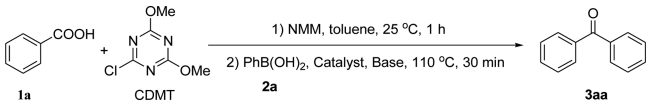
triazine ester with an aryl boronic acid in the presence of a palladium catalyst resulted in a cross-coupling reaction to give aryl ketones in high yields. This is the first example of a facile synthesis of a diverse range of aryl ketones from aromatic acids and aryl boronic acid in a one-pot procedure (Scheme 1, c).

Benzoic acid **1a** and phenylboronic acid **2a** were chosen as general substrates for the one-pot synthesis of benzophenone (Table 1). We first carried out the one-pot reaction in two

Table 1. Effects of Catalyst, Solvent, and Base[a]



1a CDMT 2a 3aa

entry	catalyst (mol %)	base	solvent	yield[c] (%)
1	$Pd(OAc)_2$ (5)	Na_2CO_3	toluene	26
2	$PdCl_2$ (5)	Na_2CO_3	toluene	35
3	$Pd(PPh_3)_2Cl_2$ (5)	Na_2CO_3	toluene	61
4	$Pd(PPh_3)_2Cl_2$ (5)	Na_2CO_3	DMSO	trace
5	$Pd(PPh_3)_2Cl_2$ (5)	Na_2CO_3	DMF	21
6	$Pd(PPh_3)_2Cl_2$ (5)	Na_2CO_3	1,4-dioxane	trace
7	$Pd(PPh_3)_2Cl_2$ (5)	ND	toluene	trace
8	$Pd(PPh_3)_2Cl_2$ (5)	K_2CO_3	toluene	66
9	$Pd(PPh_3)_2Cl_2$ (5)	$CsCO_3$	toluene	70
10	$Pd(PPh_3)_2Cl_2$ (5)	K_3PO_4	toluene	83
11	$Pd(PPh_3)_2Cl_2$ (5)	KF	toluene	77
12	$Pd(PPh_3)_2Cl_2$ (1)	K_3PO_4	toluene	85
13	$Pd(PPh_3)Cl_2$ (0.1)	K_3PO_4	toluene	65
14[b]	$Pd(PPh_3)_2Cl_2$ (1)	K_3PO_4	toluene	39
15	$Pd(OAc)_2$ (1)	K_3PO_4	toluene	63

[a]Reaction conditions (unless otherwise noted): **1a** (0.5 mmol), CDMT (0.5 mmol), NMM (0.5 mmol), solvent (3 mL) were premixed in a 10 mL flask at rt. for 1 h; after charging catalyst, base, and **2a** (0.5 mmol), the mixture was stirred and heated at 110 °C for 30 min. [b]Stirred and heated at 80 °C for 1 h. [c]Isolated yield.

sequential steps, first reacting the aromatic acid and CDMT in toluene, using 4-methylmorpholine (NMM) as base at room temperature for 1 h, thus providing the triazine ester. Second, further reaction of the triazine ester with equal molar phenylboronic acid in the presence of 5 mol % $Pd(OAc)_2$ catalyst with Na_2CO_3 as base resulted in benzophenone at low yield (26%). Through modification of the palladium catalyst, the yield of benzophenone increased significantly, for example, $PdCl_2$, provided 35% yield, $Pd(PPh_3)_2Cl_2$, provided 61% yield (Table 1, entries 1−3).

The solvent also plays a crucial role in determining the yield. In nearly every case, the reactions using toluene as solvent had a higher yield than those of the corresponding reaction which used the polar solvents DMSO, DMF, or 1,4-dioxane (Table 1, entries 4−6). It was found that benzophenone cannot be obtained by reacting triazine ester with phenylboronic acid under the same conditions without base (Table 1, entry 7). The identity of the base also influenced the yield of benzophenone; for example, changing the base from Na_2CO_3 to either K_2CO_3, Cs_2CO_3, KF, or K_3PO_4 gave rise to an increase in yield in this protocol.

Through further optimization of the catalyst loading to 1 mol %, the yield of the desired product increased to 85%.

The high yield obtained with the optimized conditions encouraged us to extend this approach to substituted aromatic acids and aryl boronic acids to synthesize the variety of aryl ketones.

The scope and limitations of this acylative Suzuki cross-coupling reaction were explored using aromatic or heterocyclic acids under the optimized reaction conditions (Table 2). To investigate the influence of electronic factors, a series of aromatic acids (**1b**−**1g**) with electron-withdrawing groups in the *para*-position were coupled to phenylboronic acid, which provided the aryl ketone with yields in the range of 43−90%. The 4-methoxy and 3-methoxy benzoic acids (**1h**, **1i**) were examined as electron-donating substrates with excellent yield. Further, the methoxy and methyl in the *ortho*-position on benzene resulted in decreasing yield, indicating that steric effects are also a factor. Other aromatic acids **1m** and **1n** provided 46% and 85% yield, respectively. These results demonstrated that both electron-donating and electron-withdrawing groups at the aromatic ring are tolerated, except in the case where the aromatic acid bears a functionality in the *ortho*-position, which provides steric hindrance, for the examples **1j** and **1l**. The bulky cyclopentyl and 1-adamantyl acids were coupled to phenyl boronic acid to give the corresponding ketones with 65% and 90% yield, respectively.

In this catalytic system, both electron-deficient and electron-rich aryl boronic acids demonstrated good reactivity and provided the desired products in moderate to excellent yields in short reaction times (**2b**−**2p**). Coupling of 2-methyl (**2d**) or 2,4-dimethyl (**2f**) phenyl boronic acids with triazine esters gave the corresponding sterically hindered ketones in 92% and 91% yield, respectively (Table 3). Furthermore, heteroaryl ketones **3nt** (77%), **3nu** (57%), **3vt** (55%), and **3wt** (61%) could be synthesized via this approach from 2-thiophenecarboxylic acid and heteroaryl boronic acids. To our delight, the scope of the aryl boronic acid was wide in this one-pot reaction, with high functional group compatibility and negligible steric hindrance effects.

On the basis of our observations and the known palladium chemistry, a possible mechanism for the palladium-catalyzed acylative Suzuki coupling reaction is proposed (Scheme 2): Oxidative addition of the triazine ester to the Pd(0)-species to generate an acylpalladium(II) complex **II**; transmetalation between acylpalladium(II) and the arylboronic acid to create the complex **III**; and, finally, reductive elimination to form the new C−C bond and regeneration of Pd(0)-species.

In conclusion, a one-pot reaction was developed for the synthesis of asymmetric aryl ketones using aromatic triazine esters as electrophiles. The procedure employs low catalyst loadings and has demonstrated tolerance to a variety of functional groups. Compared with the previous transition-metal-catalyzed protocols, this facile palladium-catalyzed Suzuki cross-coupling reaction has greater efficiency due to the two reactions sequence being carried out in a one-pot procedure. This is particularly important in large-scale synthesis of asymmetric aryl ketones.

EXPERIMENTAL SECTION

General Procedure: For the synthesis of Benzophenone 3. A mixture of the 2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMT) (1.00 mmol, 175.6 mg), benzoic acid (1.00 mmol, 122.1 mg), and 4-methylmorpholine (1.00 mmol, 101.2 mg) in toluene (5 mL) was stirred at room temperature for 1 h. After reaction completion monitoring by TLC, the flask was charged with $Pd(PPh_3)_2Cl_2$ (0.01 mmol, 7.0 mg), K_3PO_4 (2.00 mmol, 424.5 mg), and phenylboronic acid (1.00 mmol, 121.9 mg) before standard cycles of evacuation and backfilling with dry nitrogen. The mixture was stirred and heated at 110 °C for 30 min. After cooling to room temperature, the mixture was filtrated through a short pad of silica gel; then, the silica gel was

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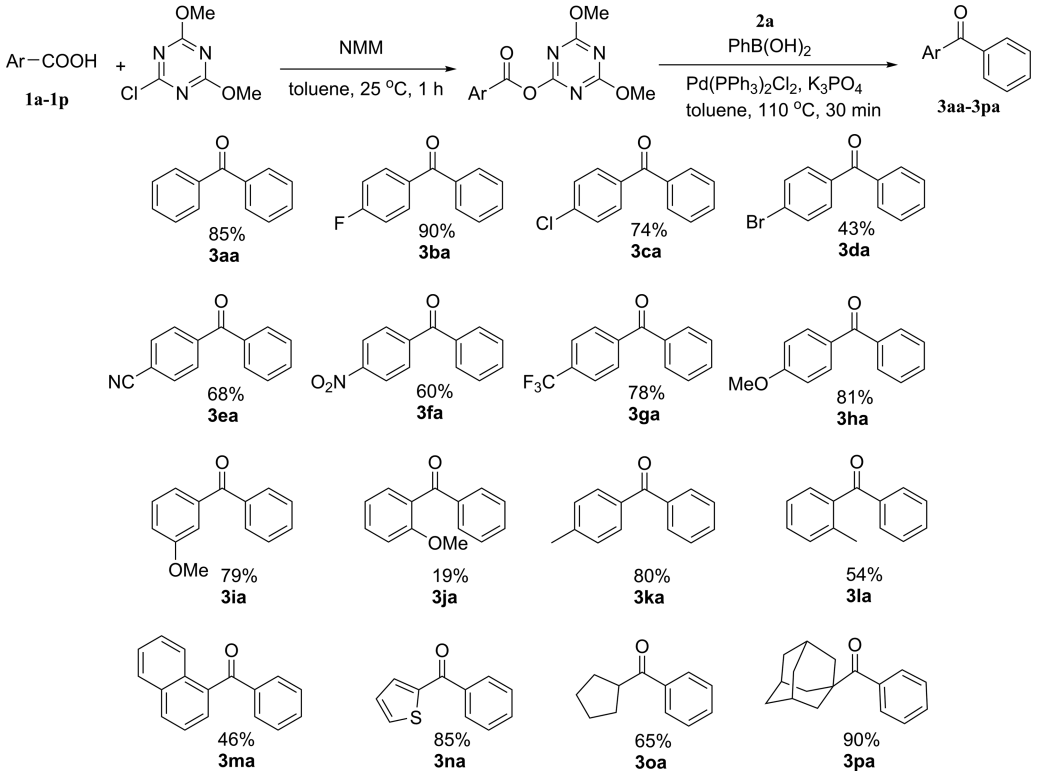
Table 2. Scope of Acylative Suzuki Coupling of Phenylboronic Acid 2a with Various Aromatic Acids 1a−1p



washed with CH_2Cl_2 (3 × 15 mL) and the organic phases were combined. After the solvent was removed, the crude product was purified by silica gel column chromatography (petroleum ether/dichloromethane = 5:1) to give benzophenone, **3aa**. This approach also could be run in 10 mmol scale to give 83% benzophenone.

Benzophenone (***3aa***).[5b] Following the general procedure, **3aa** was isolated as a white solid (155 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85−7.78 (m, 4H), 7.61−7.56 (m, 2H), 7.50−7.45 (m, 4H).

(4-Fluorophenyl)(phenyl)methanone (***3ba***).[10e] Following the general procedure, **3ba** was isolated as a white solid (181 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.6, 5.5 Hz, 2H), 7.78−7.70 (m, 2H), 7.56 (d, J = 7.2 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.14 (t, J = 8.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −106.00.

(4-Chlorophenyl)(phenyl)methanone (***3ca***).[5b] Following the general procedure, **3ca** was isolated as a white solid (160 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (dt, J = 4.2, 3.7 Hz, 4H), 7.62−7.58 (m, 1H), 7.52−7.45 (m, 4H).

(4-Bromophenyl)(phenyl)methanone (***3da***).[23a] Following the general procedure, **3da** was isolated as a white solid (113 mg, 43%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, J = 8.2, 1.2 Hz, 2H), 7.69−7.57 (m, 5H), 7.49 (t, J = 7.7 Hz, 2H).

4-Benzoylbenzonitrile (***3ea***).[5b] Following the general procedure, **3ea** was isolated as a white solid (141 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.2 Hz, 2H), 7.84−7.72 (m, 4H), 7.65 (s, 1H), 7.52 (t, J = 7.7 Hz, 2H).

(4-Nitrophenyl)(phenyl)methanone (***3fa***).[5b] Following the general procedure, **3fa** was isolated as a pale yellow solid (137 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41−8.29 (m, 2H), 7.97−7.90 (m, 2H), 7.81 (dd, J = 8.2, 1.1 Hz, 2H), 7.66 (dd, J = 10.6, 4.3 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H).

Phenyl(4-(trifluoromethyl)phenyl)methanone (***3ga***).[5b] Following the general procedure, **3ga** was isolated as a white solid (195 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.1 Hz, 2H), 7.84−7.78 (m, 2H), 7.76 (d, J = 8.2 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.05 (s, 1H).

(4-Methoxyphenyl)(phenyl)methanone (***3ha***).[5b] Following the general procedure, **3ha** was isolated as a white solid (172 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.7 Hz, 2H), 7.78−7.70 (m, 2H), 7.55 (d, J = 7.1 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 3.88 (s, 3H).

(3-Methoxyphenyl)(phenyl)methanone (***3ia***).[4c] Following the general procedure, **3ia** was isolated as a colorless oil (167 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.8 Hz, 2H), 7.56 (d, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.40−7.30 (m, 3H), 7.13 (s, 1H), 3.84 (s, 3H).

(2-Methoxyphenyl)(phenyl)methanone (***3ja***).[5b] Following the general procedure, **3ja** was isolated as a colorless oil (41 mg, 19%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, J = 5.1, 3.3 Hz, 2H), 7.59−7.51 (m, 1H), 7.47 (ddd, J = 8.4, 7.6, 1.7 Hz, 1H), 7.42 (dd, J = 10.6, 4.8 Hz, 2H), 7.36 (dd, J = 7.5, 1.7 Hz, 1H), 7.04 (td, J = 7.5, 0.8 Hz, 1H), 6.99 (d, J = 8.4 Hz, 1H), 3.72 (s, 3H).

Phenyl(p-tolyl)methanone (***3ka***).[5b] Following the general procedure, **3ka** was isolated as a white solid (157 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 7.9 Hz, 2H), 7.55 (t, J = 7.1 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 2.41 (s, 3H).

Phenyl(o-tolyl)methanone (***3la***).[10e] Following the general procedure, **3la** was isolated as a colorless oil (106 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.9 Hz, 2H), 7.57 (s, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.39 (s, 1H), 7.30 (s, 2H), 7.24 (s, 1H), 2.33 (s, 3H).

Naphthalen-1-yl(phenyl)methanone (***3ma***).[5b] Following the general procedure, **3ma** was isolated as a white solid (107 mg, 46%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.95−7.90 (m, 1H), 7.87 (dd, J = 8.3, 1.2 Hz, 2H), 7.61−7.55 (m, 2H), 7.55−7.48 (m, 3H), 7.45 (dd, J = 10.8, 4.7 Hz, 2H).

Phenyl(thiophen-2-yl)methanone (***3na***).[5b] Following the general procedure, **3na** was isolated as a pale yellow oil (160 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dt, J = 8.4, 1.6 Hz, 2H), 7.72 (dd, J = 5.0, 1.1 Hz, 1H), 7.64 (dd, J = 3.8, 1.1 Hz, 1H), 7.61−7.57 (m, 1H), 7.51−7.47 (m, 2H), 7.16 (dd, J = 4.9, 3.8 Hz, 1H).

Cyclopentyl(phenyl)methanone (***3oa***).[23b] Following the general procedure, **3oa** was isolated as a colorless oil (113 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.0 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 3.76−3.67 (m, 1H), 1.92 (dd, J = 12.7, 6.0 Hz, 4H), 1.80−1.46 (m, 4H).

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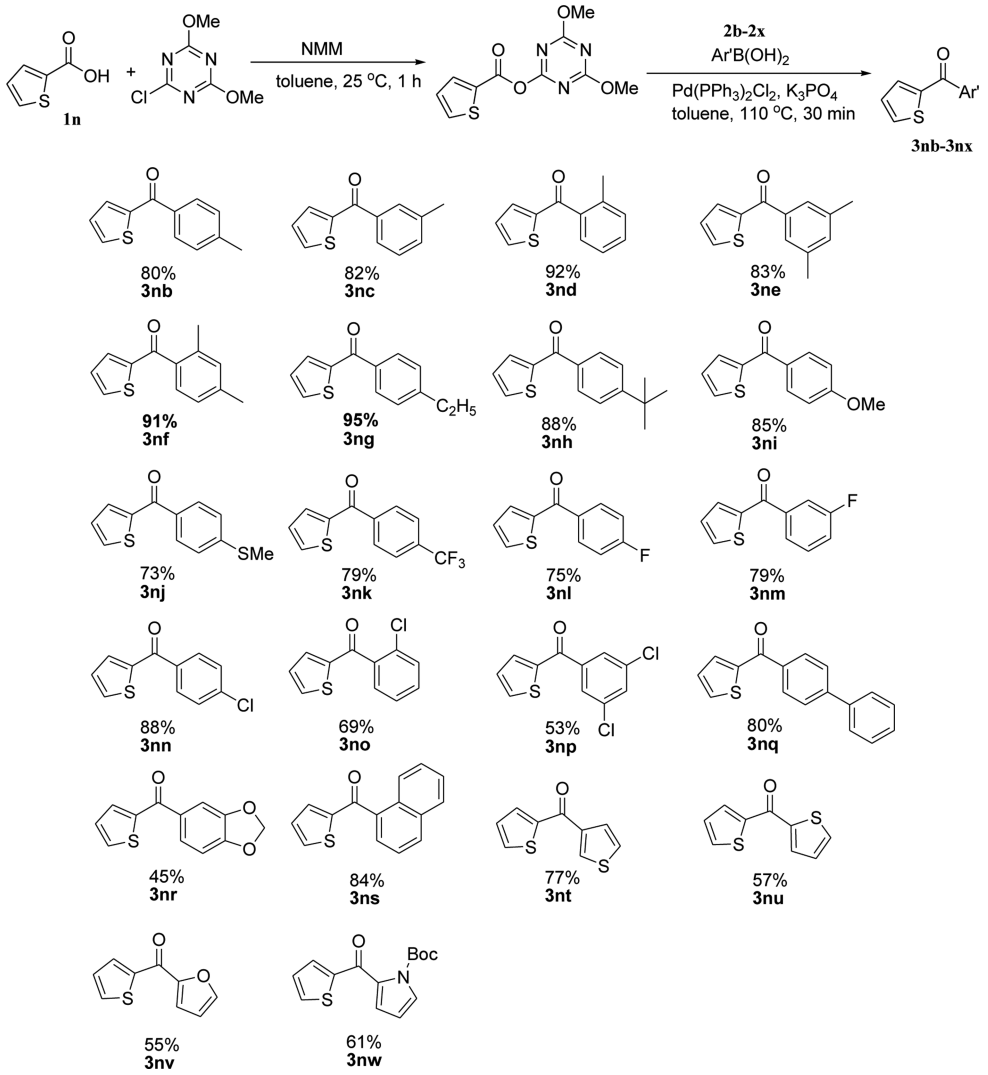
Table 3. Scope of Acylative Suzuki Coupling of Thiophene-2-carboxylic Acid 1n with Various Arylboronic Acids 2b−2x



*Adamantane-1-yl(phenyl)methanone (**3pa**).* Following the general procedure, **3pa** was isolated as a white solid (216 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 7.3 Hz, 2H), 7.43 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.3 Hz, 2H), 2.07 (s, 3H), 2.01 (s, 6H), 1.74 (q, J = 12.4 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.3, 139.6, 130.2, 128.0, 127.1, 47.0, 39.1, 36.5, 28.1. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{20}O$ 240.1514; Found 240.1517. mp 58−59 °C.

*Thiophen-2-yl(p-tolyl)methanone (**3nb**).*[10e] Following the general procedure, **3nb** was isolated as a pale yellow oil (162 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.1 Hz, 2H), 7.70 (dd, J = 5.0, 1.1 Hz, 1H), 7.65 (dd, J = 3.8, 1.1 Hz, 1H), 7.30 (d, J = 7.9 Hz, 2H), 7.16 (dd, J = 4.9, 3.8 Hz, 1H), 2.44 (s, 3H).

*Thiophen-2-yl(m-tolyl)methanone (**3nc**).*[23c] Following the general procedure, **3nc** was isolated as a pale yellow oil (165 mg, 82%). ^{1}H NMR (400 MHz, cdcl$_3$) δ 7.70 (d, J = 5.0 Hz, 1H), 7.64 (dd, J = 7.4, 4.7 Hz, 3H), 7.41−7.34 (m, 2H), 7.15 (dd, J = 6.4, 2.3 Hz, 1H), 2.42 (s, 3H).

*Thiophen-2-yl(o-tolyl)methanone (**3nd**).*[23d] Following the general procedure, **3nd** was isolated as a pale yellow oil (186 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, J = 4.9, 1.1 Hz, 1H), 7.44 (dd, J = 7.6, 1.1 Hz, 1H), 7.42 (dd, J = 3.8, 1.1 Hz, 1H), 7.38 (dd, J = 7.5, 1.3 Hz, 1H), 7.30−7.25 (m, 2H), 7.11 (dd, J = 4.9, 3.8 Hz, 1H), 2.39 (s, 3H).

*(3,5-Dimethylphenyl)(thiophen-2-yl)methanone (**3ne**).* Following the general procedure, **3ne** was isolated as a pale yellow oil (179 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 4.9 Hz, 1H), 7.62−7.60 (m, 1H), 7.44 (s, 2H), 7.19 (s, 1H), 7.13 (dd, J = 4.8, 3.9 Hz, 1H), 2.36 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 143.9, 138.3, 138.1, 134.8, 134.0, 133.9, 127.9, 126.9, 21.3. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{13}H_{12}OS$ 216.0609; Found 216.0606.

*(2,4-Dimethylphenyl)(thiophen-2-yl)methanone (**3nf**).* Following the general procedure, **3nf** was isolated as a pale yellow oil (197 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 4.9 Hz, 1H), 7.43 (d, J = 3.8 Hz, 1H), 7.38 (d, J = 7.7 Hz, 1H), 7.10 (d, J = 4.5 Hz, 2H), 7.06 (d, J = 7.8 Hz, 1H), 2.37 (d, J = 1.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3, 145.2, 140.7, 136.9, 135.6, 135.2, 134.5, 132.0, 128.6, 128.0, 125.8, 21.4, 19.8. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{13}H_{12}OS$ 216.0609; Found 216.0608.

*(4-Ethylphenyl)(thiophen-2-yl)methanone (**3ng**).* Following the general procedure, **3ng** was isolated as a pale yellow oil (205 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.1 Hz, 2H), 7.68 (d, J = 4.9 Hz, 1H), 7.64 (d, J = 3.7 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.15−7.12 (m, 1H), 2.71 (t, J = 7.6 Hz, 2H), 1.27 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.0, 149.2, 143.8, 135.7, 134.5, 133.8, 129.5, 127.9, 127.9, 29.0, 15.3. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{13}H_{12}OS$ 216.0609; Found 216.0602.

*(4-tert-Butylphenyl)(thiophen-2-yl)methanone (**3nh**).* Following the general procedure, **3nh** was isolated as a pale yellow oil (215 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.3 Hz, 2H), 7.70 (d, J = 4.9 Hz, 1H), 7.67 (d, J = 3.7 Hz, 1H), 7.51 (d, J = 8.3 Hz, 2H), 7.15 (t, J = 4.3 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9, 156.0, 143.8, 135.4, 134.6, 133.8, 129.2, 127.9, 125.4, 35.1, 31.2.

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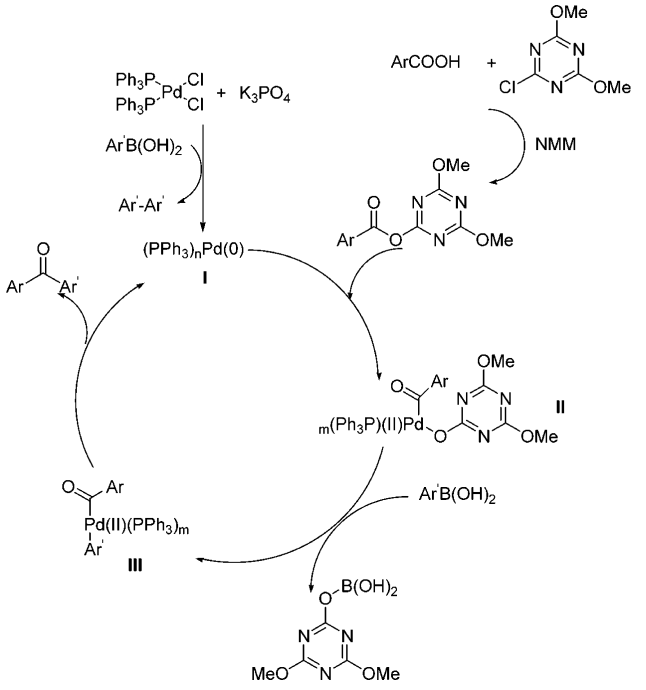
Scheme 2. Proposed Mechanism for Palladium-Catalyzed Acylative Suzuki Coupling



HRMS (EI) m/z: $[M]^+$ Calcd for $C_{15}H_{16}OS$ 244.0922; Found 244.0918.

(4-Methoxyphenyl)(thiophen-2-yl)methanone (**3ni**).[23e] Following the general procedure, **3ni** was isolated as a pale yellow oil (185 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.6 Hz, 2H), 7.66 (d, J = 4.9 Hz, 1H), 7.62 (d, J = 3.8 Hz, 1H), 7.13 (s, 1H), 6.97 (d, J = 8.7 Hz, 2H), 3.86 (s, 3H).

(4-(Methylthio)phenyl)(thiophen-2-yl)methanone (**3nj**).[23f] Following the general procedure, **3nj** was isolated as a pale yellow oil (171 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 5.0 Hz, 1H), 7.64 (d, J = 3.7 Hz, 1H), 7.31 (d, J = 8.3 Hz, 2H), 7.16 (s, 1H), 2.54 (s, 3H).

Thiophen-2-yl(4-(trifluoromethyl)phenyl)methanone (**3nk**).[23g] Following the general procedure, **3nk** was isolated as a pale yellow solid (202 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.1 Hz, 2H), 7.78 (t, J = 5.4 Hz, 3H), 7.63 (d, J = 3.8 Hz, 1H), 7.19 (t, J = 4.4 Hz, 1H). ^{19}F NMR (376 MHz, cdcl$_3$) δ −63.04.

(4-Fluorophenyl)(thiophen-2-yl)methanone (**3nl**).[10e] Following the general procedure, **3nl** was isolated as a pale yellow oil (156 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (dd, J = 8.8, 5.4 Hz, 2H), 7.73 (dd, J = 5.0, 1.1 Hz, 1H), 7.63 (dd, J = 3.8, 1.1 Hz, 1H), 7.20−7.16 (m, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ −106.21 to −106.29.

(3-Fluorophenyl)(thiophen-2-yl)methanone (**3nm**).[23h] Following the general procedure, **3nm** was isolated as a pale yellow oil (163 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 4.9 Hz, 1H), 7.65 (d, J = 4.2 Hz, 2H), 7.55 (d, J = 9.1 Hz, 1H), 7.48 (dd, J = 13.5, 7.9 Hz, 1H), 7.31−7.26 (m, 1H), 7.18 (t, J = 4.3 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.80.

(4-Chlorophenyl)(thiophen-2-yl)methanone (**3nn**).[10f] Following the general procedure, **3nn** was isolated as a pale yellow solid (196 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 4.9 Hz, 1H), 7.63 (d, J = 3.7 Hz, 1H), 7.48 (d, J = 8.3 Hz, 2H), 7.17 (s, 1H).

(2-Chlorophenyl)(thiophen-2-yl)methanone (**3no**).[10e] Following the general procedure, **3no** was isolated as a pale yellow oil (153 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 4.9 Hz, 1H), 7.48−7.40 (m, 4H), 7.35 (t, J = 7.3 Hz, 1H), 7.12 (t, J = 4.2 Hz, 1H).

(3,5-Dichlorophenyl)(thiophen-2-yl)methanone (**3np**).[23i] Following the general procedure, **3np** was isolated as a pale yellow solid (147 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 4.9 Hz, 1H), 7.72−7.69 (m, 2H), 7.64 (d, J = 3.8 Hz, 1H), 7.57 (t, J = 1.4 Hz, 1H), 7.20 (dd, J = 6.5, 2.2 Hz, 1H).

(1,1′-Biphenyl)-4-yl-2-thienyl-methanone (**3nq**). Following the general procedure, **3nq** was isolated as a pale yellow solid (211 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.1 Hz, 2H), 7.72 (dt, J = 3.6, 2.3 Hz, 4H), 7.65 (d, J = 7.8 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.42 (d, J = 7.4 Hz, 1H), 7.19 (t, J = 4.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.8, 145.1, 143.7, 140.0, 136.8, 134.7, 134.2, 129.9, 129.0, 128.2, 128.0, 127.3, 127.1. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{17}H_{12}OS$ 264.0609; Found 264.0611. mp 102−103 °C.

Benzo[d][1,3]dioxol-5-yl(thiophen-2-yl)methanone (**3nr**).[23j] Following the general procedure, **3nr** was isolated as a white solid (105 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 5.0 Hz, 1H), 7.64 (d, J = 3.8 Hz, 1H), 7.49 (s, 1H), 7.38 (s, 1H), 7.15 (s, 1H), 6.89 (d, J = 8.1 Hz, 1H), 6.07 (s, 2H).

Naphthalen-1-yl(thiophen-2-yl)methanone (**3ns**). Following the general procedure, **3ns** was isolated as a pale yellow solid (199 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19−8.11 (m, 1H), 7.98 (d, J = 8.2 Hz, 1H), 7.92−7.87 (m, 1H), 7.72 (t, J = 6.2 Hz, 2H), 7.51 (dd, J = 9.8, 5.7 Hz, 3H), 7.46 (d, J = 3.7 Hz, 1H), 7.08 (t, J = 4.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7, 145.4, 136.2, 135.7, 135.1, 133.8, 131.3, 130.6, 128.4, 128.2, 127.3, 127.1, 126.6, 125.5, 124.3. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{15}H_{10}OS$ 238.0452; Found 238.0456. mp 71−72 °C.

Thiophen-2-yl(thiophen-3-yl)methanone (**3nt**).[10f] Following the general procedure, **3nt** was isolated as a pale yellow solid (150 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.04 (m, 1H), 7.79 (d, J = 3.8 Hz, 1H), 7.69 (d, J = 4.9 Hz, 1H), 7.62 (d, J = 5.1 Hz, 1H), 7.39 (dd, J = 5.0, 2.9 Hz, 1H), 7.17 (t, J = 4.4 Hz, 1H).

Dithiophen-2-ylmethanone (**3nu**).[23k] Following the general procedure, **3nu** was isolated as a white solid (111 mg, 57%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 3.7 Hz, 2H), 7.71 (d, J = 4.9 Hz, 2H), 7.19 (t, J = 4.3 Hz, 2H).

Furan-2-yl(thiophen-2-yl)methanone (**3nv**).[23l] Following the general procedure, **3nv** was isolated as a pale yellow solid (98 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 3.7 Hz, 1H), 7.75−7.65 (m, 2H), 7.41 (d, J = 3.5 Hz, 1H), 7.20 (t, J = 4.3 Hz, 1H), 6.67−6.52 (m, 1H).

tert-Butyl 2-(Thiophene-2-carbonyl)-1H-pyrrole-1-carboxylate (**3nw**). Following the general procedure, **3nw** was isolated as a white solid (169 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (ddd, J = 4.9, 4.3, 1.1 Hz, 2H), 7.42 (dd, J = 3.1, 1.6 Hz, 1H), 7.12 (dd, J = 4.9, 3.8 Hz, 1H), 6.75 (dd, J = 3.5, 1.6 Hz, 1H), 6.22 (t, J = 3.3 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 148.4, 144.6, 133.8, 133.7, 132.1, 127.9, 126.4, 120.6, 110.3, 85.1, 27.5. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{14}H_{15}N_1O_3S$ 277.0773; Found 277.0777. mp 86−87 °C.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02667.

Copies of ^{1}H NMR, ^{19}F NMR, and ^{13}C NMR of all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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