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Note

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One-pot synthesis of arylketones from aromatic acids via palladium-catalyzed Suzuki coupling

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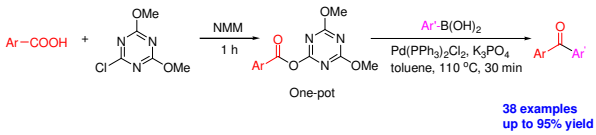


ABSTRACT: A palladium-catalyzed one-pot procedure for the synthesis of aryl ketones has been developed. Triazine esters when coupled with aryl boronic acids provided aryl ketones in moderate to excellent yields (up to 95%) in the presence of 1 mol % $Pd(PPh_3)_2Cl_2$ for 30 min.

KEYWORDS: Aromatic acid; Triazine ester; Arylketones; One-pot; Suzuki coupling

Arylketones are commonly used compounds in the preparation of pharmaceutical,[1] 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.

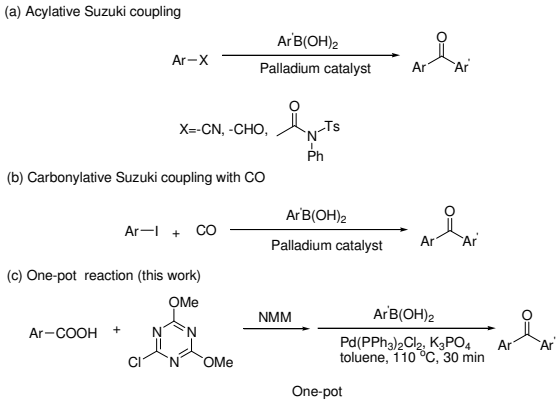
Cleavage of carbon–oxygen bonds is generally regarded as more difficult than cleavage of carbon-halogen bonds, due to the higher bond dissociation energy of C–O bond.[11] During the past few years, a series of C–O electrophiles such as pivalates,[12] acetates,[13] carbamates,[14] carbonates,[15] sulfonates,[16]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

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 makes facilitates the cleavage of the C–O bond in the ester and the oxygenated 1,3,5-triazine possesses good leaving group potential which would could accelerate the trans-metalation 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 steps procedures.

Based on 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 synthesis aryl ketones in one-pot. Firstly, 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 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).

Scheme 1. Pd-Catalyzed Carbonylative Suzuki Cross-Couplings



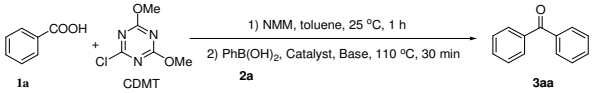
Benzoic acid **1a** and phenylboronic acid **2a** were chosen as general substrates for the one-pot synthesis of benzophenone (Table 1). We first carried out the one-pot reaction in two sequential steps, firstly reacting the aromatic acid and CDMT in toluene, using 4-methylmorpholine (NMM) as base at room temperature for 1 h, thus providing the triazine ester. Secondly 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 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 can not 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 to either K_2CO_3, Cs_2CO_3, KF, or K_3PO_4 gave rise to an increase yield in this protocol.

Through further optimization of the catalyst loading to 1 mol %, the yield of the

desire product increased to 85%.

Table 1. Effects of Catalyst, Solvent and Base



1a CDMT 2a 3aa

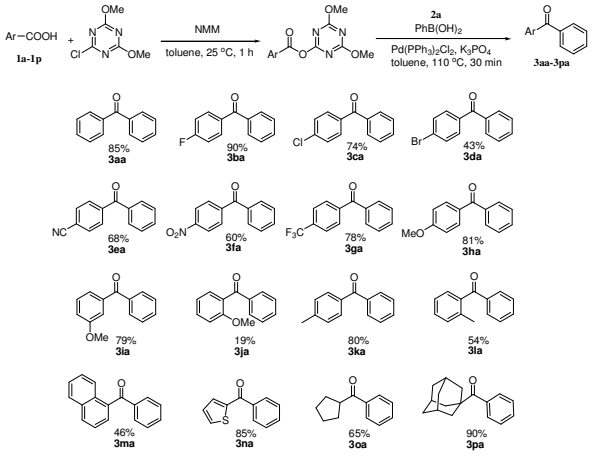
Entry	Catalyst (mol %)	Base	Solvent	yield [c] (%)
1	$Pd(OAc)_2$ (5)	Na_2CO_3	toluene	26
2	$PdCl_2$(5)	Na_2CO_3	toluene	35
3	$Pd(PPh_3)_2Cl_2$ (5)	Na_2CO_3	toluene	61
4	$Pd(PPh_3)_2Cl_2$ (5)	Na_2CO_3	DMSO	trace
5	$Pd(PPh_3)_2Cl_2$ (5)	Na_2CO_3	DMF	21
6	$Pd(PPh_3)_2Cl_2$ (5)	Na_2CO_3	1,4-dioxane	trace
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 pre-mixed in a 10 mL flask at rt. for 1h, after charging catalyst, base and **2a** (0.5 mmol), the mixture stirred and heated at 110°C for 30 min. [b]stirred and heated at 80 °C for 1h. [c]Isolated yield.

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 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 *para*-position were coupled to phenylboronic acid which providing 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 *ortho*-position on benzene result in decreasing yield, indicating that steric effects are also a factor. Other aromatic acids **1m**, **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 corresponding ketones with 65% and 90% yield respectively.

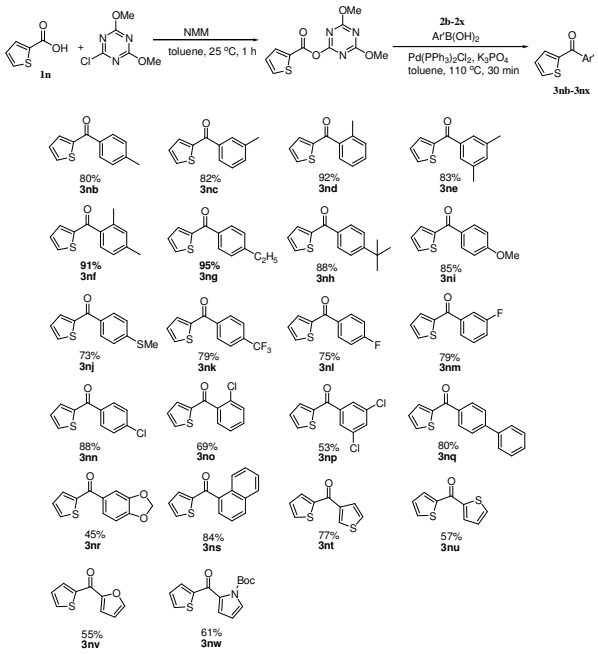
Table 2. Scope of Acylative Suzuki coupling of phenylboronic acid 2a with Various aromatic acid 1a-1p



In this catalytic system, both electron-deficient and electron-rich aryl boronic acid demonstrated good reactivity and provided the desire 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).

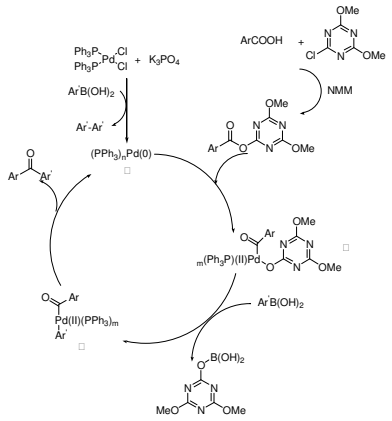
Furthermore, heteroaryl ketones **3nt** (77%), **3nu** (57%), **3vt** (55%) and **3wt** (61%) could be synthesized via this approach from 2-thiophenecarboxylic acid and heteroaryl boronic acids. To our delight, the scope of the aryl boronic acid was wide in this one-pot reaction, with high functional group compatibility and negligible steric hindrance effects.

Table 3. Scope of Acylative Suzuki coupling of thiophene-2-carboxylic acid acid 1n with Various Arylboronic Acids 2b-2x



Based on 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**; transmetallation between acylpalladium(II) and the arylboronic acid to create the complex **III**; finally, reductive elimination to form the new C-C bond and regeneration of Pd(0)-species.

Scheme 2. Proposed Mechanism for palladium-catalyzed Acylative Suzuki coupling



CONCLUSIONS

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.

EXPERIMENT 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 1h. After reaction completion monitoring by TLC, the flask was charged with $Pd(PPh_3)_2Cl_2$ (0.01mmol, 7.0mg), K_3PO_4 (2.00 mmol, 424.5 mg), phenylboronic acid (1.00mmol, 121.9mg) before standard cycles of evacuation and backfilling with dry nitrogen. The mixture was stirred and heated at 110^{o}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 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 10mmol scale to give 83% benzophenone.

Benzophenone (3aa).[5b] Following 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 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 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 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 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 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 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 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 general procedure, 3ia was isolated as a colourless 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 general procedure, 3ja was isolated as a colourless 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 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 general procedure, 3la was isolated as a colourless 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 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 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 general procedure, 3pa was isolated as a colourless 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).

Adamantane-1-yl(phenyl)methanone (3pa). Following general procedure, 3qa

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^{o}C.

Thiophen-2-yl(*p*-tolyl)methanone (3nb).[10e] Following 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 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 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 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 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 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 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. 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 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 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 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 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 –

-106.29.

(3-Fluorophenyl)(thiophen-2-yl)methanone (3nm).[23h] Following 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 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 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 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 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 ^{o}C.

Benzo[d][1,3]dioxol-5-yl(thiophen-2-yl)methanone (3nr).[23j] Following 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 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 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 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 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 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

Copies of ^{1}H NMR, ^{19}F NMR and ^{13}C NMR of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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