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Palladacycle-Catalyzed Carbonylative Suzuki–Miyaura Coupling with High Turnover Number and Turnover Frequency

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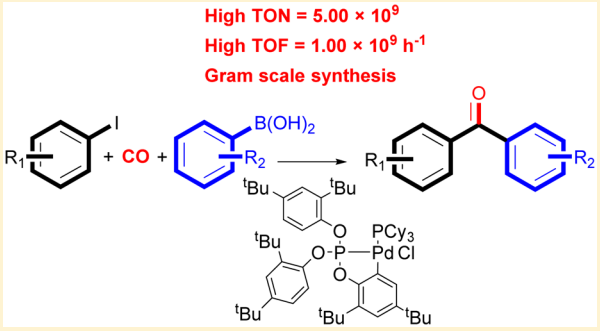
Supporting Information

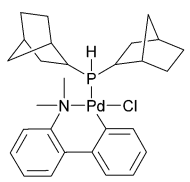
ABSTRACT: This work reports the carbonylative Suzuki–Miyaura coupling of aryl iodides catalyzed by palladacycles. More importantly, the palladacycles have been used to generate high turnover numbers (TON's) and turnover frequencies (TOF's). A range of aryl iodides can be coupled with arylboronic acids, generating TON's in the range of 10^6 to 10^7 and TOF's in the range of 10^5 to 10^6 h^{-1}. Comparison of the palladacycles with a conventional palladium source shows their superiority in generating high TON's and TOF's.



Carbonylative Suzuki–Miyaura coupling utilizing carbon monoxide as the C1 source is a pivotal reaction for the synthesis of biaryl ketones.[1] Biaryl ketones are important structural building blocks present in a wide variety of molecules, including pharmaceutical drugs, natural products, and sunscreen agents. These biaryl ketones have been synthesized through carbonylative Suzuki–Miyaura coupling using a variety of palladium catalysts, and the reaction using aryl iodides is well-documented in the literature.[2] The main drawbacks of these catalytic systems include high palladium loading, poor turnover numbers (TON's) and turnover frequencies (TOF's), and the need to handle air- and moisture-sensitive phosphine ligands. Palladacycles have been reported exhaustively for conventional cross-coupling reactions (Heck, Suzuki, Sonogashira, Buchwald–Hartwig) and have been shown to produce extremely high TON's and TOF's vis-à-vis conventional palladium sources.[3] The fact that they are air- and moisture-stable is an added advantage.

In 2002, Schnyder et al. reported a series of palladacyclic complexes with secondary phosphines[4] and showed their role as extremely active palladium sources in a series of cross-coupling reactions of aryl chlorides. It was shown that the complex of a palladacycle with secondary norbornyl phosphine **1** gave the highest catalytic activity. Almost at the same time, Bedford and co-workers reported a mixed tricyclohexylphosphine–triarylphosphite complex **2** as a highly active catalyst for the Suzuki–Miyaura coupling of aryl chlorides and thereby documented the highest TON's.[5]

A literature survey shows that palladacycles have been seldom reported for carbonylative cross-coupling reactions.[6] To the best of our knowledge, they have never been reported as a palladium source for carbonylative Suzuki–Miyaura coupling using gaseous CO under thermal conditions. The concept of low palladium loading and subsequent generation of high



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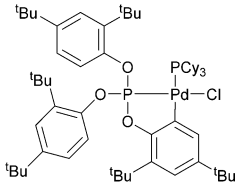

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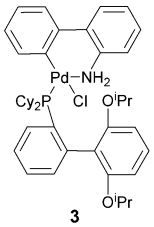

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TON's and TOF's has also not been addressed until now. Given the catalytic superiority of these palladacyclic complexes and considering our continued interest in catalyst development for carbonylation reactions,[7] we envisioned testing their activity for the carbonylative version of Suzuki–Miyaura coupling. The presence of dissolved quantities of CO, a strong π-acidic ligand, in a carbonylative coupling reaction mixture makes it difficult to achieve oxidative addition to the metal and reductive elimination. Moreover, the unusually high concentration of CO present as compared to the catalyst tends to poison the catalyst. In such a case, can such high TON's and TOF's be generated?

We initially examined the model reaction between iodobenzene **4a** and phenylboronic acid **5a** as substrates using Bedford's palladacycle **2** (Table 1). Examining the effect

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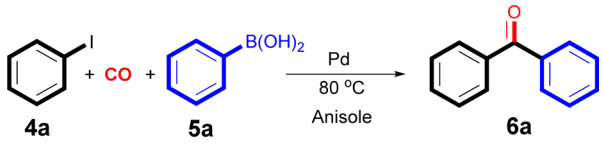
Table 1. Reaction Optimization[a]



entry	CO pressure (bar)	base	time (h)	yield[b] (%)
Effect of CO Pressure				
1	1	K_2CO_3	5	89
2	2	K_2CO_3	5	95
3	3	K_2CO_3	5	65
Effect of Base				
4	2	K_2CO_3	5	95
5	2	Na_2CO_3	5	66
6	2	Et_3N	5	74
7	2	K_3PO_4	5	70
Effect of Time				
8	2	K_2CO_3	1	41
9	2	K_2CO_3	3	79
10	2	K_2CO_3	6	95

[a]Reaction conditions: **4a** (0.5 mmol), **5a** (0.75 mmol), **2** (0.1 mol %), base (1.5 mmol), anisole (11 mL). [b]GC yield.

of CO pressure demonstrated that the reaction could be carried out at atmospheric pressure, but it gave a higher yield of benzophenone **6a** at 2 bar (Table 1, entries 1 and 2).

Further increasing the CO pressure reduces the yield. (Table 1, entry 3). A base-screening study showed that K_2CO_3 results in the highest yield of the product, as compared to that using other inorganic and organic bases (Table 1, entries 4−7). Furthermore, the reaction generated the highest yield of product in 5 h, and further increasing the duration of the reaction did not have any effect on the yield (Table 1, entries 8−10). Carbonylative Suzuki−Miyaura reactions typically proceed in nonpolar solvents like toluene and anisole;[2a,b] hence, a solvent-screening study was not performed. Anisole was used as the solvent of choice in our studies given its high boiling point. Blank experiments were carried out without the addition of phenylboronic acid and the palladium catalyst separately. In both cases, no product formation took place. Having established the optimized parameters, we focused our attention on exploring the maximum TON's and TOF's that could be generated by reducing the catalyst loading (Table 2).

Initial catalyst loading experiments showed that a complete conversion of iodobenzene could be achieved up to 10^{-3} mol % loading of palladium at 80 °C in 5 h, generating a TON of 4.75×10^4 (Table 2, entries 1−3).

At 10^{-4} mol % loading, 10% of the iodobenzene remains unreacted; nevertheless, this reaction generated a TON of 4.20×10^5 (Table 2, entry 4). To ensure complete conversion, the reaction was carried out for 12 h, which resulted in a 91% yield of the product with 3% of iodobenzene remaining unreacted (Table 2, entry 5). However, increasing the temperature to 120 °C resulted in the complete conversion of iodobenzene within 5 h, producing a TON of 4.75×10^5 (Table 2, entry 6). By further decreasing the Pd loading to 10^{-6} mol %, a TON of 4.50×10^7 could be generated (Table 2, entry 8). When the Pd loading was decreased from 10^{-7} to 10^{-9} mol %, a temperature increase to 160 °C was required to maximize the yield of the product. TON's up to 5.00×10^9 could be generated within 5 h, thus resulting in a TOF of 1.00×10^9 h^{-1} (Table 2, entries 9−11). However, in either of

Table 2. Effect of Catalyst Loading, Time, and Temperature[a]

entry	**2** mol %	BZ[f] (%)	TON[g]	TOF (h^{-1})
1	10^{-1}	98	4.90×10^2	0.98×10^2
2	10^{-2}	97	4.85×10^3	9.70×10^2
3	10^{-3}	95	4.75×10^4	9.50×10^3
4	10^{-4}	84	4.20×10^5	8.40×10^4
5[b]	10^{-4}	91	4.55×10^5	9.10×10^4
6[c]	10^{-4}	95	4.75×10^5	9.50×10^4
7[c]	10^{-5}	93	4.65×10^6	9.30×10^5
8[c]	10^{-6}	88	4.50×10^7	9.00×10^6
9[d]	10^{-7}	54	2.70×10^8	5.40×10^7
10[e]	10^{-8}	48	2.40×10^9	4.80×10^8
11[e]	10^{-9}	10	5.00×10^9	1.00×10^9

[a]Standard reaction conditions: **4a** (0.5 mmol), **5a** (0.75 mmol), K_2CO_3 (1.5 mmol), CO (2 bar), anisole (11 mL) at 80 °C for 5 h. [b]12 h. [c]120 °C. [d]140 °C. [e]160 °C. [f]GC yield (calculated as an average of triplicate measurements). [g]mol product per mol Pd. BZ, benzophenone.

these cases, the complete conversion of iodobenzene could not be achieved. To the best of our knowledge, these are the highest TON's and TOF's reported for the carbonylative Suzuki−Miyaura coupling of aryl iodides.

Having established high TON's and TOF's for the model reaction, we focused our attention on the scope of substrates. The emphasis was to briefly test whether different classes of functional groups could be tolerated, rather than carrying out an elaborate substrate study (Table 3). Aryl iodides and aryl boronic acids having electron-releasing and -withdrawing groups reacted well and were smoothly coupled to give the biaryl ketones in high yields. Aryl iodides bearing electron-withdrawing substituents are known to encourage the non-carbonylative coupling, leading to the synthesis of biaryl.[8]

However, the presence of cyano and nitro functionalities at the para and meta positions led to the synthesis of biaryl ketone/biaryl in 88/2% and 80/9% yields wherein TON's of 4.40×10^7 and 4.00×10^7 were observed, respectively (Table 3, entries 4 and 5). Electron-releasing functionalities such as methoxy and amino could also be coupled to give ketones **6b** and **6c** in 89 and 94% yields, respectively, without any biaryl formation, thus producing TON's of 4.45×10^7 and 4.70×10^7, respectively (Table 3, entries 1 and 2). However, the presence of a substituent in the ortho position brings down the yield and TON as compared to those when it is present in the para position (Table 3, entry 3). 1-Iodonaphthalene, a polyaromatic substrate, could be coupled with 4-fluorophenylboronic acid, producing **6g** in 90% yield with a TON of 4.50×10^7. Unsymmetrical ketones **6h**, **6i**, **6j**, and **6k** could be synthesized by coupling aryl iodide and aryl boronic acid, both bearing a combination of electron-releasing and -withdrawing groups. In such a case, the Pd loading had to be increased to 10^{-5} mol % to effect complete conversion of aryl iodide as well as to tolerate the increase in bulk caused by the presence of substituents on both of the substrates (Table 3, entries 7−10). Incidentally, ketones **6g**, **6i**, **6j**, and **6k** were synthesized not only with high catalytic TON's but also for the first time through carbonylative Suzuki−Miyaura coupling. 2-Iodopyridine could be successfully coupled to give **6l** in 71% yield with a TON of 3.55×10^6 with some iodopyridine remaining unreacted (Table 3, entry 11). However, on increasing the Pd loading to 10^{-3} mol %, CO pressure to 5 bar, and time to 12 h, complete conversion could be effected. An increased yield of **6l** was obtained, albeit with a

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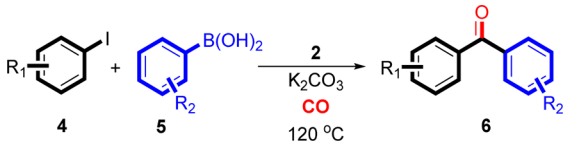
Table 3. Scope of the Palladacycle-Catalyzed Carbonylative Suzuki−Miyaura Coupling[a]



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entry	4	5	6/yield	TON[d]	TOF (h^{-1})
1	R_1 = 4-OCH_3 (**4b**)		**6b**/89	4.45×10^7	8.90×10^6
2	R_1 = 4-NH_2 (**4c**)	R_2 = H (**5a**)	**6c**/94	4.70×10^7	9.40×10^6
3	R_1 = 2-NH_2 (**4d**)		**6d**/69	3.45×10^7	6.90×10^6
4	R_1 = 3-NO_2 (**4e**)		**6e**/80	4.00×10^7	8.00×10^6
5	R_1 = 4-CN (**4f**)		**6f**/88	4.40×10^7	8.80×10^6
6	1-naphthyl (**4g**)	R_2 = 4-F (**5b**)	**6g**/90	4.50×10^7	9.00×10^6
7[b]	**4c**	R_2 = 4-Cl (**5c**)	**6h**/81	4.05×10^6	8.10×10^5
8[b]	**4f**	R_2 = 3-Me (**5d**)	**6i**/90	4.50×10^6	9.00×10^5
9[b]	**4b**	**5d**	**6j**/86	4.30×10^6	8.60×10^5
10[b]	**4e**	**5b**	**6k**/85	4.25×10^6	8.50×10^5
11[b]	2-pyridyl (**4h**)	**5a**	**6l**/71	3.55×10^6	7.10×10^5
12[c]	2-pyridyl (**4h**)	**5a**	**6l**/89	4.45×10^4	3.70×10^3
13[c]	2-thienyl (**4i**)	**5a**	**6m**/88	4.40×10^4	3.66×10^3
14[c]	**4a**	3-thienyl (**5e**)	**6n**/85	4.25×10^4	3.54×10^3
15[c]	**4i**	**5e**	**6o**/80	4.00×10^4	3.33×10^3
16[c]	**4i**	R_2 = 4-OCH_3 (**5f**)	**6p**/82	4.10×10^4	3.41×10^3
17[c]	**4i**	**5c**	**6q**/93	4.65×10^4	3.87×10^3

[a]Reaction conditions: aryl iodide (0.5 mmol), aryl boronic acid (0.75 mmol), K_2CO_3 (1.5 mmol), [Pd, **2**] (10^{-6} mol %), CO (2 bar), anisole (11 mL) at 120 °C for 5 h. [b][Pd, **2**] (10^{-5} mol %). [c][Pd, **2**] (10^{-3} mol %), CO (5 bar) for 12 h [d]mol product per mol Pd.

decrease in the TON and TOF values. (Table 3, entry 12). The thiophenyl heterocyclic moiety could also be functionalized at different positions to produce the corresponding benzoylthiophenes **6m** and **6n** with TON and TOF values of the order of 10^4 and 10^3 h^{-1}, respectively (Table 3, entries 13 and 14). Bithiophenyl ketone **6o** and benzoylthiophenes **6p** and **6q** containing electron-releasing (-OCH_3) and -withdrawing (-Cl) groups on the benzene ring could also be synthesized in good yields. The presence of the electron-withdrawing group on the benzene ring resulted in a higher yield (Table 3, entries 15−17).

Next, we screened different palladacycles and conventionally used $Pd(OAc)_2$ for the reaction between iodobenzene and phenylboronic acid and carried out a comparative study for generation of high TON's and TOF's (Table 4).

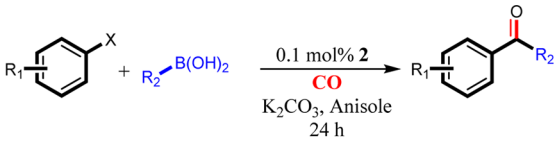
Table 4. Comparison of Palladacycles with $Pd(OAc)_2$[a]

entry	cat.	BZ[b] (%)	TON[d] ($\times 10^8$)	TOF ($\times 10^7$) (h^{-1})
1	$Pd(OAc)_2$	9	0.4	0.9
2	**1**	62	3.1	6.2
3	**2**	54	2.7	5.4
4	**3**	52	2.6	5.2
5[c]	**1**	60	3.0	6.0

[a]Reaction conditions: **4a** (0.5 mmol), **5a** (0.75 mmol), K_2CO_3 (1.5 mmol), [Pd] (10^{-7} mol %), CO (2 bar), anisole (11 mL) at 140 °C for 5 h. [b]GC yield (calculated as an average of triplicate measurements). [c]Scale up: **4a** (5 mmol), **5a** (7.5 mmol), K_2CO_3 (15 mmol), [Pd] (10^{-7} mol %), CO (2 bar), anisole (20 mL) at 140 °C for 5 h. [d]mol product per mol Pd. BZ, benzophenone.

We were delighted to observe that the palladacycles gave superior results. $Pd(OAc)_2$ gave a 9% yield of the product (Table 4, entry 1), whereas all of the palladacycles used gave >50% yield (Table 4, entries 2−4). The dinorbornyl palladacycle gave the highest yield, slightly better than Bedford's and RuPhos[9] palladacycle **3**, generating a TON of 3.10×10^8 and a TOF of 6.20×10^7 h^{-1}. Furthermore, we tested the activity of palladacycle **1** when the reaction was scaled up to gram scale (5 mmol), and the catalyst maintained its activity (Table 4, entries 2 and 5). We also tested the scope of aryl bromides, aryl chlorides, and alkylboronic acids as substrates (Scheme 1). The

Scheme 1. Carbonylative Coupling of Aryl Bromide, Aryl Chloride, and Alkylboronic Acid



4j; R_1 = 4-OMe, X = Br, R_2 = Ph, CO (3 bar), 120 °C
4k; R_1= 4-CN, X = Br, R_2 = Ph, CO (3 bar), 120 °C,
4l; R_1 = -$COCH_3$, X = Cl, R_2 = Ph, CO (5 bar) 140 °C
R_1 = H, X = I, **5f**; R_2 = *n*-butyl, CO (5 bar), 120 °C

6b; 61%
6f; 30%
6r; 0%
6s; 0%

carbonylative coupling of 4-bromoanisole **4j** and 4-bromobenzonitrile **4k** with phenylboronic acid at 0.1 mol % loading of palladacycle **2** gave only 61 and 30% yields of the respective products. Much of the aryl bromide remained unreacted and failed to undergo complete conversion. Aryl chloride **4l** and *n*-butylboronic acid **5f**, however, failed to generate any product, thus requiring a comprehensive independent investigation.

The role of active species in the case of the palladayclic catalysts may be responsible for the enhanced activity. Considering the oxidative addition of the aryl iodide to be the rate-limiting step and a Pd(0)/Pd(II) pathway to be operating, which is normally the case in carbonylative couplings, the catalyst tends to "rest" in a zero-valent state. In the case of Bedford's palladacycle **2**, deorthometalation of **I** gives **II**, which is followed by *in situ* reduction to give **III** (Scheme 2).

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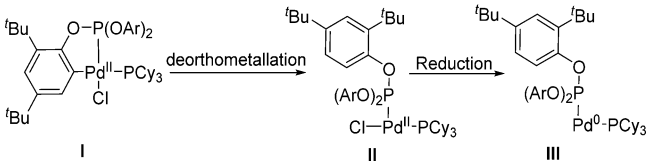
Scheme 2. Proposed Degradation of 2



Coordination of π-acidic phosphite ligand and CO will stabilize the resting state $[(PCy_3)Pd^0]$ both thermodynamically and kinetically. Moreover, the decoordination of either of them would release $[(PCy_3)Pd^0]$ into the catalytic cycle.[5a,b,6b] In the case of dinorbornyl complex **1**, which contains a secondary phosphine ligand, the mode of action and nature of the catalytically active species are unknown. However, the formation of mononuclear palladium complexes with secondary phosphine ligands as well as phosphido-bridged di- and polynuclear compounds with palladium is a possibility. Additionally, secondary phosphines react with aryl halides in the presence of palladium catalysts to form aryl phosphines.[4,10] Furthermore, we believe that the palladacyclic catalysts are not converted to Pd nanoparticles or Pd black. Even in the reaction carried out with 0.1 mol % Pd, we did not observe any particle formation or accumulation of Pd black, and the solution remained homogeneous. Similar possibility also exists for $Pd(OAc)_2$ precursor to give Pd nanoparticles and similar reaction results. However, we did not observe this under our reaction conditions.

In conclusion, we have established the first palladacycle-catalyzed carbonylative Suzuki−Miyaura coupling of aryl iodides using gaseous CO under thermal conditions for the synthesis of biaryl ketones. These palladacycles behave as robust catalysts and have been used to generate high TON's and TOF's. Comparison with a conventional palladium source shows their superiority in generating the same. Relative comparison of the palladacycles shows that they exhibit almost similar catalytic activity at concentrations as low as 10^{-7} mol %, with the dinorbornyl complex exhibiting slightly better activity.

EXPERIMENTAL SECTION

Materials and Methods. The palladacyclic complexes were commercially purchased from Sigma-Aldrich and used as received. All other chemicals and solvents were purchased from different sources and used as received without further purification. Stock solutions of the catalyst dissolved in anisole of various concentrations (10^{-1} to 10^{-10} mol %) were prepared by taking a known amount of catalyst (1 mol %) followed by successive dilutions of the initial catalyst solution. No special precautions were taken during preparation of the catalyst stock solutions, and the catalysts were weighed and handled in air. The progress of the reaction was monitored by gas chromatography and thin-layer chromatography. GC−MS was used for the mass analysis of the products. Products were purified by column chromatography on 100−200 mesh silica gel. The ^{1}H NMR spectra were recorded on 400 MHz spectrometers in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard. The ^{13}C NMR spectra were recorded on 100 MHz spectrometers in $CDCl_3$. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane as an internal standard. Coupling constant (J) values are reported in hertz (Hz). Splitting patterns of protons are described as s (singlet), d (doublet), dd (doublet of doublets), t (triplet), and m (multiplet). The products were confirmed by GC−MS, ^{1}H NMR, and ^{13}C NMR spectroscopic analysis.

General Procedure for Carbonylative Suzuki−Miyaura Coupling. Aryl iodide (0.5 mmol), aryl boronic acid (0.75 mmol), and K_2CO_3 (1.5 mmol, 207 mg) in 11 mL of anisole were added to a 100 mL stainless steel autoclave. The catalyst solution was subsequently added, and the autoclave was closed and flushed with nitrogen three times. The autoclave was then pressurized with CO at ambient temperature. The reaction mixture was stirred with a mechanical stirrer (450 rpm) at the desired temperature for the desired time. After completion of the reaction, the autoclave was cooled to room temperature and the pressure was carefully released. The reactor vessel was washed with ethyl acetate (3 × 5 mL) to remove traces of product and catalyst, if present. The ethyl acetate layer was washed with water (2 × 5 mL), dried over Na_2SO_4, and evaporated by rotary evaporation to obtain the crude product, which was either subjected to GC analysis or, in the case of the substrate study, purified by column chromatography (silica gel, 100−200 mesh size), with petroleum ether−ethyl acetate as the eluent, to afford a pure product. The products were confirmed by GC-MS, ^{1}H NMR, and ^{13}C NMR spectroscopic analysis.

Scale-Up Procedure. Iodobenzene (5 mmol, 1.02 g), phenylboronic acid (7.5 mmol, 0.91 g), and K_2CO_3 (15 mmol, 2.07 g) in 20 mL of anisole were added to a 100 mL stainless steel autoclave. The catalyst solution was subsequently added, and the autoclave was closed and flushed with nitrogen three times. The autoclave was then pressurized with CO at ambient temperature. The reaction mixture was stirred with a mechanical stirrer (450 rpm) at the desired temperature for the desired time. After cooling to room temperature, the pressure was carefully released. The reactor vessel was washed with ethyl acetate (3 × 20 mL) to remove traces of product and catalyst, if present. The ethyl acetate layer was washed with water (2 × 20 mL), dried over Na_2SO_4, and evaporated by rotary evaporation to obtain the crude product, which was subsequently subjected to GC analysis.

4-Methoxybenzophenone (6b). 94.3 mg, yield 89%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84−7.81 (m, 2H), 7.76−7.73 (m, 2H), 7.55−7.53 (m, 1H), 7.48−7.43 (m, 2H), 6.93 (m, 2H), 3.87 (s, 3H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 195.6, 163.2, 138.2, 132.5, 131.9, 130.0, 129.7, 128.1, 113.5, 55.4. GC-MS (EI, 70 eV): m/z (%): 212 (40), 135 (100), 105 (14), 77 (36).

4-Aminobenzophenone (6c). 92.5 mg, yield 94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71−7.68 (m, 4H), 7.54−7.41 (m, 3H), 6.64 (d, 2H), 4.18 (s, 2H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 195.3, 151.0, 138.8, 132.9, 131.4, 129.5, 128.0, 127.2, 113.6. GC-MS (EI, 70 eV): m/z (%): 197 (39), 120 (100), 92 (24), 65 (25).

2-Aminobenzophenone (6d). 67.9 mg, yield 69%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.61 (m, 2H), 7.53−7.42 (m, 4H), 7.30−7.24 (m, 1H), 6.73 (d, 1H), 6.61−6.56 (m, 1H), 6.10 (s, 2H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 199.0, 150.9, 140.0, 134.5, 134.2, 131.0, 129.1, 128.0, 118.0, 116.9, 115.4. GC-MS (EI, 70 eV): m/z (%): 197 (65), 196 (100), 120 (48), 92 (31), 77 (36).

3-Nitrobenzophenone (6e). 90.8 mg, yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.44−8.41 (m, 1H), 8.14−8.11 (m, 1H), 7.78 (d, 2H), 7.71−7.62 (m, 2H), 7.51 (t, 2H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 194.1, 148.0, 139.0, 136.2, 135.4, 133.3, 130.0, 129.6, 128.7, 126.7, 124.7. GC-MS (EI, 70 eV): m/z (%): 227 (23), 105 (100), 150 (11), 77 (50).

4-Cyanobenzophenone (6f). 91.0 mg, yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87−7.84 (m, 2H), 7.78−7.75 (m, 2H), 7.65−7.60 (m, 1H), 7.53−7.47 (m, 2H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 195.0, 141.1, 136.2, 133.3, 132.1, 130.2, 130.0, 128.6, 118.0, 115.6. GC-MS (EI, 70 eV): m/z (%): 207 (38), 130 (27), 105 (100), 77 (47).

(4-Fluorophenyl)(1-naphthalenyl)methanone (6g). 112.5 mg, yield 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, 2H), 8.00 (d, 2H), 7.93−7.87 (m, 3H), 7.58−7.46 (m, 4H), 7.12 (t, 2H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 196.4, 165.8 (J_{C-F} = 254 Hz), 136.0, 134.5 (2C), 133.7, 133.0 (J_{C-F} = 10 Hz, 2C), 131.3, 130.8, 128.4, 127.5, 127.3, 126.5, 125.5, 124.3, 115.6 (J_{C-F} = 21 Hz, 2C). GC-MS (EI, 70 eV): m/z (%): 250 (88), 155 (77), 127 (100), 95 (61), 75 (24).

(4-Aminophenyl)(4-chlorophenyl)methanone (6h). 93.5 mg, yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, 2H), 7.65 (d, 2H), 7.41 (d, 2H), 6.65 (d, 2H), 4.17 (s, 2H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 193.9, 151.0, 137.6, 137.0, 132.8, 130.9, 128.3, 126.9, 113.6. GC-MS (EI, 70 eV): m/z (%): 231 (10), 120 (40), 92 (8), 65 (8).

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4-(3-Methylbenzoyl)benzonitrile (6i). 99.5 mg, yield 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, 2H), 7.76 (d, 2H), 7.59−7.35 (m, 4H), 2.41 (s, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 195.2, 141.3, 138.5, 136.3, 134.1, 132.1, 130.4, 130.2, 128.4, 127.3, 118.0, 115.5, 21.3. GC-MS (EI, 70 eV): *m*/*z* (%): 221 (31), 119 (100), 91 (36), 65 (18).

(4-Methoxyphenyl)(*m*-tolyl)methanone (6j). 97.2 mg, yield 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, 2H), 7.57−7.33 (m, 4H), 6.94 (d, 2H), 3.86 (s, 3H), 2.40 (s, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 195.9, 163.1, 138.2, 138.0, 132.7, 132.5, 130.2, 130.1, 127.9, 127.0, 113.5, 55.4, 21.3. GC-MS (EI, 70 eV): *m*/*z* (%): 226 (33), 135 (100), 119 (15), 91 (17), 77 (18).

(4-Fluorophenyl)(3-nitrophenyl)methanone (6k). 104.1 mg, yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.44−8.41 (m, 1H), 8.10−8.08 (m, 1H), 7.85−7.80 (m, 2H), 7.70 (t, 1H), 7.24−7.16 (m, 2H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 192.6, 165.8 (J_{C-F} = 255 Hz), 148.03, 138.8, 135.2, 132.7 (J_{C-F} = 10 Hz), 132.4, 129.7, 126.7, 124.5, 116 (J_{C-F} = 22 Hz). GC-MS (EI, 70 eV): *m*/*z* (%): 245 (23), 123 (100), 95 (39), 75 (13).

Phenyl(2-pyridinyl)methanone (6l). 64.9 mg, yield 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, 2H), 8.04−7.98 (m, 3H), 7.87−7.82 (m, 1H), 7.57−7.52 (m, 1H), 7.46−7.41 (m, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 193.8, 154.9, 148.5, 137.0, 136.2, 132.9, 130.9, 128.1, 126.1, 124.6. GC-MS (EI, 70 eV): *m*/*z* (%): 183 (40), 155 (77), 105 (80), 77 (100), 51 (32).

2-Benzoylthiophene (6m). 82.8 mg, yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.83 (d, 2H), 7.71−7.70 (m, 1H), 7.71−7.55 (m, 2H), 7.50−7.46 (m, 2H), 7.16−7.14 (m, 1H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 188.2, 143.5, 138.0, 134.8, 134.2, 132.2, 129.1, 128.3, 127.9. GC-MS (EI, 70 eV): *m*/*z* (%): 188 (60), 111 (100), 105 (39), 77 (40), 51 (18).

3-Benzoylthiophene (6n). 80 mg, yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91−7.90 (m, 1H), 7.84−7.81 (m, 2H), 7.59−7.54 (m, 2H), 7.49−7.45 (t, 2H), 7.38−7.35 (m, 1H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 190.0, 141.2, 138.5, 133.9, 132.3, 129.3, 128.5, 128.3, 126.2. GC-MS (EI, 70 eV): *m*/*z* (%): 188 (61), 111 (100), 105 (40), 77 (39), 51 (19).

Thiophen-2-yl(thiophen-3-yl)methanone (6o). 77.7 mg, yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07−8.06 (m, 1H), 7.77−7.76 (m, 1H), 7.68−7.67 (m, 1H), 7.60−7.59 (m, 1H), 7.39−7.36 (m, 1H), 7.17−7.14 (m, 1H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 181.2, 143.9, 141.0, 133.6, 133.5, 132.2, 128.1, 127.9, 126.3. GC-MS (EI, 70 eV): *m*/*z* (%): 194 (46), 166 (6), 111 (100), 83 (20), 45 (4).

(4-Methoxyphenyl)(thiophen-2-yl)methanone (6p). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (dd, J = 8.8, 1.8 Hz, 2H), 7.71−7.58 (m, 2H), 7.27−7.11 (m, 1H), 7.03−6.89 (m, 2H), 3.87 (s, 3H). $^{13}C\{^1H\}$-NMR (100 MHz, $CDCl_3$): δ 186.9, 163.0, 143.7, 134.0, 133.4, 131.6, 130.6, 127.7, 113.6, 55.4. GC-MS (EI, 70 eV): *m*/*z* (%): 218 (57), 187 (12), 135 (100), 111 (38), 92 (13), 77 (22).

(4-Chlorophenyl)(thiophen-2-yl)methanone (6q). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87−7.76 (m, 2H), 7.72 (d, J = 5.0 Hz, 1H), 7.60 (d, *J* = 3.7 Hz, 1H), 7.51−7.39 (m, 2H), 7.15 (t, *J* = 4.4 Hz, 1H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 186.97, 143.20, 138.71, 136.38, 134.85, 134.62, 130.62, 128.79, 128.13. GC-MS (EI, 70 eV): *m*/*z* (%): 222 (32), 187 (12), 139 (25), 111 (100), 75 (14).

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of the products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01160.

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Notes

The authors declare no competing financial interest.

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