Synthesis J. Li, Z.-X. Wang Special Topic

Nickel-Catalyzed Transformation of Aryl 2-Pyridyl Ethers via Cleavage of the Carbon–Oxygen Bond: Synthesis of Mono-α-arylated Ketones

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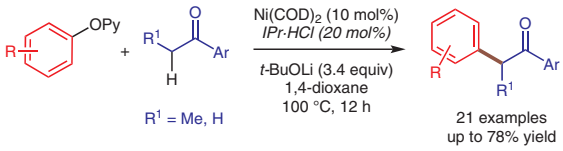

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Abstract The nickel/IPr-catalyzed reaction of aryl 2-pyridyl ethers with propiophenone and acetophenone derivatives via C–OPy bond cleavage is performed in the presence of *t*-BuOLi to give mono-α-arylated ketones in moderate yields. The method is suitable for electron-rich and electron-poor ethers as well as heteroaryl ethers and tolerates a range of active functional groups.

Key words aryl 2-pyridyl ethers, C–O activation, C–C coupling, nickel catalyst, α-arylated ketones

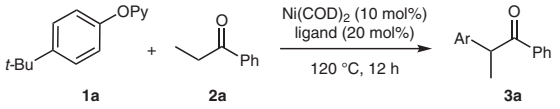
Phenol and its derivatives are inexpensive and readily available; hence, they are often used as starting materials in organic synthesis. Among phenol-based transformations, transition-metal-catalyzed cross-couplings via C–O bond cleavage has attracted significant attention in recent years.[1] A range of phenol-based electrophiles including aryl methyl ethers, carboxylates, carbamates, carbonates, phosphoramides, phosphates, sulfamates, tosylates and mesylates have been employed to construct new C–C, C–N and C–H bonds.[1] Recently, aryl 2-pyridyl ethers were demonstrated to participate in catalytic coupling with appropriate nucleophilic reagents such as $B_2(pin)_2$ and amines, and to undergo reduction to C–H via loss of the 2-pyridyloxy (OPy) group.[2] Because the OPy group in aryl 2-pyridyl ether systems is an effective directing group,[3] these reactions also provide a valuable method for subsequent conversion of the 2-pyridyloxy directing group in C–H functionalization reactions.

On the other hand, the transition-metal-catalyzed α-arylation of carbonyl compounds has attracted wide attention because α-aryl carbonyl compounds are common structural motifs in pharmaceutical and other biologically active molecules.[4] A variety of effective catalytic systems and arylation reagents have been developed.[5] Among the arylation reagents employed, aryl halides and sulfonates of phenols were predominant.[5d,6] More recently, aryl pivalates were used in the α-arylation of ketones.[7] It is therefore interesting to explore transition-metal-catalyzed reactions of aryl 2-pyridyl ethers with ketones to synthesize α-aryl ketones.

2-[4-(*tert*-Butyl)phenoxy]pyridine (**1a**) and propiophenone (**2a**) were chosen as the model substrates to screen the reaction conditions (Table 1). We first tested the reaction using a combination of $Ni(COD)_2$ (10 mol%) and a N-heterocyclic carbene (20 mol%) (IPr, IMes, SIPr, and ICy) as the catalyst, *t*-BuOLi (1.2 equiv) as the base, and 1,4-dioxane as the solvent. The combination of $Ni(COD)_2$ and IPr led to the desired product in 39% yield after the reaction was run at 120 °C for 12 hours, whilst the same reactions with IMes, SIPr, and ICy were ineffective (Table 1, entries 1–4). The combination of $Ni(COD)_2$ and phosphine ligands including dcype, BINAP, and PCy_3 also proved to be ineffective (Table 1, entries 5–7). Hence, we chose the $Ni(COD)_2$/IPr combination as the catalyst in subsequent reactions. We noticed that a higher *t*-BuOLi loading (2.4 equiv) led to a higher product yield (Table 1, entry 8). However, employing 2.4 equivalents of *t*-BuONa, NaHMDS, or LiHMDS resulted in a lower product yield than when using 1.2 equivalents of the corresponding base (Table 1, entries 9–14). This is probably due to the excess strong base causing side reactions. *t*-BuOK, MeOLi and Cs_2CO_3 were demonstrated to be ineffective in this reaction (Table 1, entries 15–17). The solvent effect was next studied with THF, *n*-Bu_2O and toluene proving to be less effective than 1,4-dioxane (Table 1, entries 18–20). Both DMF and DMAc gave comparable results to 1,4-dioxane (Table 1, entries 21 and 22). However, we were unable to further improve the yield in DMAc via optimization of the conditions (Table 1, entry 23). Increasing the propiophenone loading to 1.5 equivalents and the corresponding amount of *t*-BuOLi resulted in increased yields (Table 1, en-

tries 24 and 25). Reducing the amount of the $Ni(COD)_2$ catalyst to 5 mol% led to a decrease in the yield (Table 1, entry 26). We also found that the reaction at 100 °C gave the same yield as that at 120 °C. However, further lowering the reaction temperature led to a marked decline in the yield (Table 1, entries 27 and 28).

Table 1 Optimization of the Reaction Conditions[a]



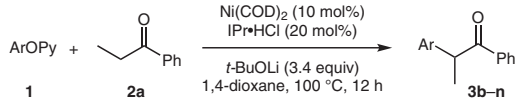
1a 2a 3a

Entry	Ligand	Base (equiv)	Solvent	Yield (%)[b]
1	IPr·HCl	*t*-BuOLi (1.2)	1,4-dioxane	39
2	IMes·HCl	*t*-BuOLi (1.2)	1,4-dioxane	trace
3	SIPr·HCl	*t*-BuOLi (1.2)	1,4-dioxane	trace
4	ICy·HCl	*t*-BuOLi (1.2)	1,4-dioxane	trace
5	dcype	*t*-BuOLi (1.2)	1,4-dioxane	trace
6	BINAP	*t*-BuOLi (1.2)	1,4-dioxane	trace
7	PCy_3	*t*-BuOLi (1.2)	1,4-dioxane	trace
8	IPr·HCl	*t*-BuOLi (2.4)	1,4-dioxane	56
9	IPr·HCl	*t*-BuONa (1.2)	1,4-dioxane	45
10	IPr·HCl	*t*-BuONa (2.4)	1,4-dioxane	33
11	IPr·HCl	NaHMDS (1.2)	1,4-dioxane	48
12	IPr·HCl	NaHMDS (2.4)	1,4-dioxane	trace
13	IPr·HCl	LiHMDS (1.2)	1,4-dioxane	60
14	IPr·HCl	LiHMDS (2.4)	1,4-dioxane	trace
15	IPr·HCl	*t*-BuOK (1.2)	1,4-dioxane	–
16	IPr·HCl	MeOLi (1.2)	1,4-dioxane	–
17	IPr·HCl	Cs_2CO_3 (1.2)	1,4-dioxane	–
18	IPr·HCl	*t*-BuOLi (1.2)	THF	20
19	IPr·HCl	*t*-BuOLi (1.2)	*n*-Bu_2O	24
20	IPr·HCl	*t*-BuOLi (1.2)	toluene	30
21	IPr·HCl	*t*-BuOLi (1.2)	DMF	38
22	IPr·HCl	*t*-BuOLi (1.2)	DMAc	43
23	IPr·HCl	*t*-BuOLi (2.4)	DMAc	43[c]
24	IPr·HCl	*t*-BuOLi (1.5)	1,4-dioxane	59[c]
25	IPr·HCl	*t*-BuOLi (3.4)	1,4-dioxane	78[c]
26	IPr·HCl	*t*-BuOLi (3.4)	1,4-dioxane	64[c,d]
27	IPr·HCl	*t*-BuOLi (3.4)	1,4-dioxane	78[c,e] (77[f])
28	IPr·HCl	*t*-BuOLi (3.4)	1,4-dioxane	52[c,g]

[a] Unless otherwise specified, the reactions were performed with 2-[4-(*tert*-butyl)phenoxy]pyridine (**1a**) (0.2 mmol) and propiophenone (**2**) (1.2 equiv) according to the conditions indicated in the above scheme.
[b] NMR yield.
[c] Propiophenone (1.5 equiv) of was employed.
[d] $Ni(COD)_2$ (5 mol%) was employed.
[e] The reaction was run at 100 °C.
[f] Yield of isolated product.
[g] The reaction was run at 80 °C.

With optimized conditions in hand (Table 1, entry 27), we next tested the scope of the aryl 2-pyridyl ethers and the results are listed in Table 2. Aryl 2-pyridyl ethers with various substituents on the phenyl rings, including electron-donating and electron-withdrawing groups, reacted smoothly with propiophenone to afford the corresponding products in 34–76% yields. It appeared that the reaction results were not controlled by the electronic effect of the substituents. 2-(Naphthalen-2-yloxy)pyridine showed similar reactivity to substituted phenyl 2-pyridyl ethers such as 2-(4-methoxyphenoxy)pyridine and 2-(4-phenoxyphenoxy)pyridine (Table 2, entries 2, 4 and 5). 6-(Pyridin-2-yloxy)quinoline also reacted smoothly with propiophenone to produce 1-phenyl-2-(quinolin-6-yl)propan-1-one in 44% yield. No products formed via C_{Py}–O cleavage were observed. Among the aryl 2-pyridyl ethers, 2-[4-(trifluoromethyl)phenoxy]pyridine gave the lowest product yield (Table 2, entry 9). This is ascribed to the existence of side reactions, and we did observe a series of by-products via TLC analysis. Common aryl, alkyl, alkoxy and amino groups and active functional groups including F, CF_3, PhC(O), *t*-BuOC(O) and CN groups were tolerated. An acetyl group was not tolerated due to the existence of active hydrogens. However, 2-[4-(2-methyl-1,3-dioxolan-2-yl)phenoxy]pyridine was able to undergo the reaction with propiophenone to yield 2-[4-(2-methyl-1,3-dioxolan-2-yl)phenyl]-1-phenylpropan-1-one (**3d**) (Table 2, entry 3). The 2-methyl-1,3-dioxolan-2-yl group in the product can be readily converted into an acetyl group via hydrolysis.

Table 2 Scope of the Aryl 2-Pyridyl Ethers[a]



1 2a 3b–n

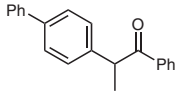
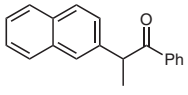
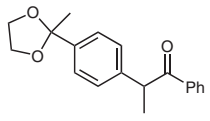
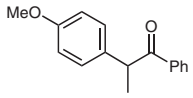
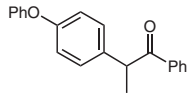
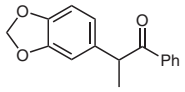
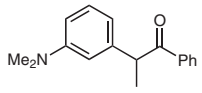
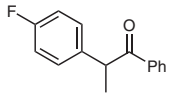
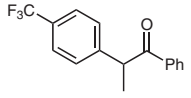
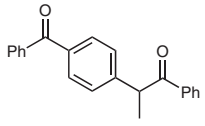
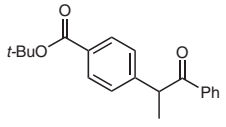
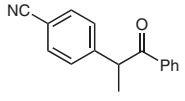
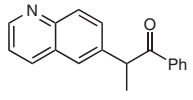
Entry	Product	Yield (%)[b]
1	 **3b**	51
2	 **3c**	64
3	 **3d**	54

Table 2 (continued)

Entry	Product	Yield (%)[b]
4	 **3e**	64
5	 **3f**	65
6	 **3g**	47
7	 **3h**	49
8	 **3i**	76
9	 **3j**	34
10	 **3k**	46
11	 **3l**	51
12	 **3m**	46
13	 **3n**	44

[a] The reactions were performed with aryl 2-pyridyl ether **1** (0.2 mmol) and propiophenone (**2a**) (1.5 equiv) according to the conditions indicated in the above scheme.
[b] Yield of isolated product.

Next, we examined the scope of the ketones and the results are listed in Table 3. 1-(4-Fluorophenyl)propan-1-one reacted smoothly with *para*-*tert*-butyl-, *para*-methoxy-, and *para*-fluoro-substituted phenyl 2-pyridyl ethers, respectively, to afford the corresponding products in 47–59% yields (Table 3, entries 1–3).

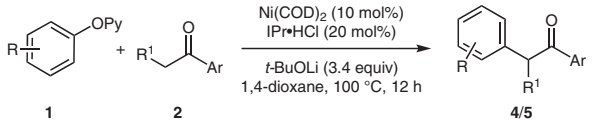
Compared with propiophenone, 1-(4-fluorophenyl)propan-1-one exhibited lower reactivity. It was expected that ketones with an electron-rich aryl group such as 1-(4-methoxyphenyl)propan-1-one would give better results. However, the reaction of 1-(4-methoxyphenyl)propan-1-one with each of the above ethers led to a mixture of products for reasons that are unclear.

It was previously reported that the catalytic α-arylation of acetophenones often results in polyarylations or aldol condensations as major side reactions.[8] Our catalyst system was demonstrated to drive only mono-α-arylation of acetophenone derivatives. The tested nucleophilic substrates included acetophenone, 1-(4-methoxyphenyl)ethan-1-one, and 1-(naphthalen-2-yl)ethan-1-one. The ethers used in the test included 2-(4-methoxyphenoxy)pyridine and 2-(*o*-tolyloxy)pyridine. 1-(4-Methoxyphenyl)ethan-1-one showed higher reactivity when it reacted with 2-(4-methoxyphenoxy)pyridine (Table 3, entries 4 and 5). 1-(Naphthalen-2-yl)ethan-1-one exhibited similar reactivity to acetophenone (Table 3, entry 7). The reaction of 2-(*o*-tolyloxy)pyridine with acetophenone gave the desired product in only 29% yield (Table 3, entry 6). This might be due to steric hindrance from the *o*-methyl group in 2-(*o*-tolyloxy)pyridine. This phenomenon is also consistent with the reaction of aryltrimethylammonium triflates with acetophenone.[5e]

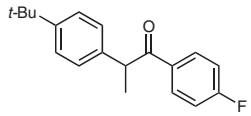
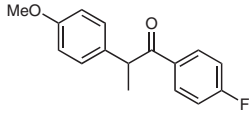
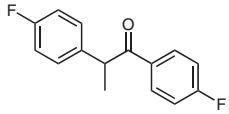
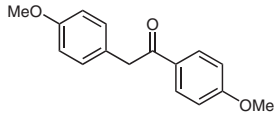
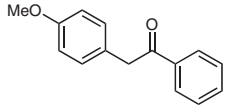
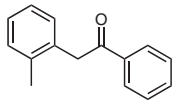
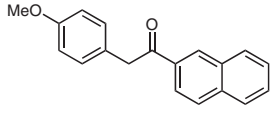
In summary, we have developed a nickel catalyst system to realize the functionalization of aryl 2-pyridyl ethers via C_{Ar}–OPy bond cleavage. A series of α-arylated ketones was synthesized in moderate yields through this reaction. The method shows a broad scope of aryl 2-pyridyl ethers, including electron-rich and electron-poor ethers as well as heteroaryl ethers. Propiophenone, acetophenone derivatives and 1-(naphthalen-2-yl)ethanone can be employed as substrates, resulting in only mono-α-arylated products. Various reactive functional groups such as fluoro, trifluoromethyl, benzoyl, *tert*-butoxycarbonyl, cyano and the β-H of the ketones were tolerated. We believe that this methodology provides a valuable complement to the current procedures for the α-arylation of ketones and should enrich the utilization of phenolic derivatives in synthetic chemistry.

All reactions were performed under a nitrogen atmosphere using standard Schlenk and vacuum line techniques. Toluene and THF were purified using JC Meyer Phoenix Solvent Systems equipment. 1,4-Dioxane was distilled under nitrogen over sodium and degassed prior to use. DMF and DMAc were dried over 4 Å molecular sieves, fractionally distilled under reduced pressure and stored under nitrogen. $Ni(COD)_2$

Table 3 Scope of the Ketones[a]



1 2 4/5

Entry	Product	Yield (%)[b]
1	 **4a**	59
2	 **4b**	47
3	 **4c**	48
4	 **5a**	58
5	 **5b**	47
6	 **5c**	29[c]
7	 **5d**	48[c]

[a] The reactions were performed with aryl 2-pyridyl ether **1** (0.2 mmol) and ketone **2** (1.5 equiv) according to the conditions indicated in the above scheme.
[b] Yield of isolated product.
[c] NMR yield.

was purchased from Alfa Aesar. NHC ligand precursors[9] and aryl 2-pyridyl ethers[2a,b] were prepared according to reported procedures. $CDCl_3$ was purchased from Cambridge Isotope Laboratories and used as received. All other chemicals were obtained from commercial vendors and used as received. Column chromatography was performed using silica gel (Yantai Chemical Industry Research Institute, 200–300 mesh) with the eluent specified in each case. NMR spectra were recorded on a Bruker Avance III 400 spectrometer at ambient temperature. The ^{1}H NMR chemical shifts are referenced to TMS and the ^{13}C NMR chemical shifts are referenced to the internal solvent resonances. The ^{19}F NMR chemical shifts are referenced to external CF_3COOH. High-resolution mass spectra (HRMS) were acquired on a Waters G2 XS-QTof mass spectrometer.

2-[4-(*tert*-Butyl)phenyl]-1-phenylpropan-1-one (3a);[10] Typical Procedure

A Schlenk tube was charged with $Ni(COD)_2$ (5.5 mg, 0.02 mmol), IPr·HCl (17 mg, 0.04 mmol), *t*-BuOLi (55 mg, 0.68 mmol), 2-[4-(*tert*-butyl)phenoxy]pyridine (45.4 mg, 0.2 mmol), propiophenone (**2a**) (40.2 mg, 0.3 mmol), and 1,4-dioxane (2 mL). The mixture was stirred at 100 °C for 12 h. The volatiles were removed by rotary evaporation. The residue was purified by column chromatography on silica gel to afford 2-[4-(*tert*-butyl)phenyl]-1-phenyl propan-1-one (**3a**).

White solid; yield: 41.6 mg (78%); eluent: petroleum ehter/EtOAc, 100:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.4 Hz, 2 H), 7.40 (t, *J* = 7.3 Hz, 1 H), 7.30 (t, *J* = 7.6 Hz, 2 H), 7.22 (d, *J* = 8.3 Hz, 2 H), 7.14 (d, *J* = 8.3 Hz, 2 H), 4.60 (q, *J* = 6.8 Hz, 1 H), 1.44 (d, *J* = 6.9 Hz, 3 H), 1.19 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.66, 149.78, 138.32, 136.66, 132.87, 128.94, 128.60, 127.49, 125.99, 47.33, 34.52, 31.43, 19.64.

2-([1,1′-Biphenyl]-4-yl)-1-phenylpropan-1-one (3b)[11]

White solid; yield: 29.2 mg (51%); eluent: toluene.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.5 Hz, 2 H), 7.59–7.46 (m, 5 H), 7.45–7.28 (m, 7 H), 4.74 (q, *J* = 6.8 Hz, 1 H), 1.58 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.41, 140.73, 140.56, 139.92, 136.56, 132.99, 128.92, 128.85, 128.65, 128.30, 127.81, 127.37, 127.11, 47.58, 19.62.

2-(Naphthalen-2-yl)-1-phenylpropan-1-one (3c)[11]

White solid; yield: 33.3 mg (64%); eluent: toluene.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 7.3 Hz, 2 H), 7.77 (t, *J* = 7.8 Hz, 3 H), 7.72 (s, 1 H), 7.51–7.38 (m, 4 H), 7.35 (t, *J* = 7.6 Hz, 2 H), 4.84 (q, *J* = 6.8 Hz, 1 H), 1.61 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.41, 139.12, 136.55, 133.78, 132.95, 132.47, 128.93, 128.62, 127.84, 127.74, 126.54, 126.30, 126.06, 125.91, 48.16, 19.66.

2-[4-(2-Methyl-1,3-dioxolan-2-yl)phenyl)]-1-phenylpropan-1-one (3d)

Colorless oil; yield: 32.0 mg (54%); eluent: petroleum ether/EtOAc, 15:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 7.2 Hz, 2 H), 7.49 (t, *J* = 6.8 Hz, 1 H), 7.43–7.36 (m, 4 H), 7.26 (d, *J* = 8.4 Hz, 2 H), 4.71 (q, *J* = 6.9 Hz, 1 H), 4.05–3.95 (m, 2 H), 3.80–3.70 (m, 2 H), 1.61 (s, 3 H), 1.53 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.42, 142.07, 140.97, 136.54, 132.97, 128.92, 128.63, 127.71, 125.98, 108.80, 64.58, 64.56, 47.45, 27.60, 19.63.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{21}O_3$: 297.1491; found: 297.1492.

2-(4-Methoxyphenyl)-1-phenylpropan-1-one (3e)[11]

White solid; yield: 30.8 mg (64%); eluent: petroleum ether/EtOAc, 20:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.92 (m, 2 H), 7.47 (t, *J* = 7.4 Hz, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 7.20 (d, *J* = 8.7 Hz, 2 H), 6.83 (d, *J* = 8.8 Hz, 2 H), 4.64 (q, *J* = 6.8 Hz, 1 H), 3.75 (s, 3 H), 1.51 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.68, 158.60, 136.64, 133.62, 132.85, 128.92, 128.89, 128.60, 114.51, 55.35, 47.11, 19.66.

2-(4-Phenoxyphenyl)-1-phenylpropan-1-one (3f)

White solid; yield: 39.3 mg (65%); eluent: petroleum ether/EtOAc, 20:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.4 Hz, 2 H), 7.49 (t, *J* = 7.4 Hz, 1 H), 7.40 (t, *J* = 7.6 Hz, 2 H), 7.35–7.27 (m, 2 H), 7.24 (d, *J* = 8.6 Hz, 2 H), 7.08 (t, *J* = 7.4 Hz, 1 H), 6.97 (d, *J* = 7.6 Hz, 2 H), 6.92 (d, *J* = 8.8 Hz, 2 H), 4.68 (q, *J* = 6.9 Hz, 1 H), 1.53 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.51, 157.06, 156.34, 136.53, 136.17, 132.98, 129.85, 129.19, 128.89, 128.65, 123.47, 119.21, 119.13, 47.10, 19.68.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{19}O_2$: 303.1385; found: 303.1383.

2-(Benzo[*d*][1,3]dioxol-5-yl)-1-phenylpropan-1-one (3g)[12]

White solid; yield: 23.9 mg (47%); eluent: petroleum ether/EtOAc, 15:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.91 (m, 2 H), 7.48 (t, *J* = 8.0 Hz, 1 H), 7.39 (t, *J* = 7.5 Hz, 2 H), 6.81–6.68 (m, 3 H), 5.89 (dd, *J* = 6.5, 1.4 Hz, 2 H), 4.60 (q, *J* = 6.8 Hz, 1 H), 1.49 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.34, 148.15, 146.61, 136.53, 135.32, 132.93, 128.86, 128.62, 128.58, 121.13, 108.78, 108.21, 101.14, 47.52, 19.66.

2-(3-(Dimethylamino)phenyl)-1-phenylpropan-1-one (3h)[6a]

Colorless oil; yield: 24.8 mg (49%); eluent: petroleum ether/EtOAc, 10:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.94 (m, 2 H), 7.45 (t, *J* = 7.4 Hz, 1 H), 7.36 (t, *J* = 7.5 Hz, 2 H), 7.15 (t, *J* = 7.9 Hz, 1 H), 6.64 (d, *J* = 7.6 Hz, 1 H), 6.61–6.54 (m, 2 H), 4.61 (q, *J* = 6.8 Hz, 1 H), 2.90 (s, 6 H), 1.53 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.63, 151.10, 142.52, 136.82, 132.73, 129.75, 128.89, 128.52, 116.22, 111.62, 111.18, 48.60, 40.65, 19.67.

2-(4-Fluorophenyl)-1-phenylpropan-1-one (3i)[11]

Colorless oil; yield: 34.7 mg (76%); eluent: toluene.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.90 (m, 2 H), 7.49 (t, *J* = 7.4 Hz, 1 H), 7.39 (t, *J* = 7.6 Hz, 2 H), 7.30–7.20 (m, 2 H), 6.97 (t, *J* = 8.7 Hz, 2 H), 4.69 (q, *J* = 6.9 Hz, 1 H), 1.51 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.35, 161.87 (d, *J* = 245.4 Hz), 137.21 (d, *J* = 6.4 Hz), 136.38, 133.06, 129.41 (d, *J* = 8.0 Hz), 128.83, 128.67, 115.93 (d, *J* = 21.5 Hz), 47.03, 19.67.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –115.79.

1-Phenyl-2-[4-(trifluoromethyl)phenyl]propan-1-one (3j)[6a]

Colorless oil; yield: 18.9 mg (34%); eluent: toluene.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.91 (m, 2 H), 7.56 (d, *J* = 8.0 Hz, 2 H), 7.51 (t, *J* = 7.4 Hz, 1 H), 7.46–7.36 (m, 4 H), 4.77 (q, *J* = 6.9 Hz, 1 H), 1.56 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 199.77, 145.49, 136.21, 133.32, 129.37 (q, *J* = 32.5 Hz), 128.85, 128.81, 128.30, 126.05 (q, *J* = 3.7 Hz), 124.20 (q, *J* = 273.0 Hz), 47.63, 19.56.

2-(4-Benzoylphenyl)-1-phenylpropan-1-one (3k)[6a]

White solid; yield: 28.9 mg (46%); eluent: petroleum ether/EtOAc, 10:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.93 (m, 2 H), 7.79–7.72 (m, 4 H), 7.57 (t, *J* = 7.4 Hz, 1 H), 7.51 (t, *J* = 7.4 Hz, 1 H), 7.49–7.36 (m, 6 H), 4.79 (q, *J* = 6.8 Hz, 1 H), 1.58 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 199.81, 196.35, 146.27, 137.63, 136.36, 136.33, 133.25, 132.54, 130.98, 130.11, 128.89, 128.77, 128.40, 127.90, 47.90, 19.51.

***tert*-Butyl 4-(1-Oxo-1-phenylpropan-2-yl)benzoate (3l)**

White solid; yield: 31.6 mg (51%); eluent: petroleum ether/EtOAc, 15:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95–7.89 (m, 4 H), 7.48 (t, *J* = 7.4 Hz, 1 H), 7.37 (t, *J* = 7.6 Hz, 2 H), 7.33 (d, *J* = 8.4 Hz, 2 H), 4.73 (q, *J* = 6.8 Hz, 1 H), 1.56 (s, 9 H), 1.54 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 199.83, 165.57, 146.24, 136.33, 133.12, 130.85, 130.28, 128.86, 128.69, 127.77, 81.11, 48.03, 28.28, 19.44.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{23}O_3$: 311.1647; found: 311.1639.

4-(1-Oxo-1-phenylpropan-2-yl)benzonitrile (3m)[13]

Colorless oil; yield: 21.6 mg (46%); eluent: petroleum ether/EtOAc, 15:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.88 (m, 2 H), 7.60 (d, *J* = 8.4 Hz, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.46–7.37 (m, 4 H), 4.77 (q, *J* = 6.9 Hz, 1 H), 1.56 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 199.36, 146.77, 136.02, 133.48, 132.87, 128.86, 128.79, 118.78, 111.06, 47.74, 19.43.

1-Phenyl-2-(quinolin-6-yl)propan-1-one (3n)[14]

Light yellow oil; yield: 23.0 mg (44%); eluent: petroleum ether/EtOAc, 2:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.86 (dd, *J* = 4.2, 1.7 Hz, 1 H), 8.11–8.04 (m, 2 H), 8.02–7.95 (m, 2 H), 7.73–7.67 (m, 2 H), 7.47 (t, *J* = 6.7 Hz, 1 H), 7.42–7.32 (m, 3 H), 4.90 (q, *J* = 6.9 Hz, 1 H), 1.63 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.13, 150.43, 147.44, 139.90, 136.34, 136.01, 133.14, 130.35, 129.90, 128.88, 128.71, 128.56, 126.23, 121.45, 47.75, 19.66.

2-[4-(*tert*-Butyl)phenyl]-1-(4-fluorophenyl)propan-1-one (4a)

Colorless oil; yield: 33.5 mg (59%); eluent: toluene.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 8.9, 5.5 Hz, 2 H), 7.30 (d, *J* = 8.4 Hz, 2 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 7.04 (t, *J* = 8.6 Hz, 2 H), 4.62 (q, *J* = 6.8 Hz, 1 H), 1.51 (d, *J* = 6.8 Hz, 3 H), 1.27 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 199.04, 165.56 (d, *J* = 255.3 Hz), 149.93, 138.21, 133.01 (d, *J* = 3.0 Hz), 131.56 (d, *J* = 9.3 Hz), 127.40, 126.08, 115.68 (d, *J* = 21.8 Hz), 47.46, 34.53, 31.42, 19.61.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{22}OF$: 285.1655; found: 285.1651.

1-(4-Fluorophenyl)-2-(4-methoxyphenyl)propan-1-one (4b)[6f]

Colorless oil; yield: 24.3 mg (47%); eluent: petroleum ether/EtOAc, 20:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (dd, *J* = 7.8, 4.4 Hz, 2 H), 7.18 (d, *J* = 8.7 Hz, 2 H), 7.04 (t, *J* = 8.6 Hz, 2 H), 6.83 (d, *J* = 8.7 Hz, 2 H), 4.58 (q, *J* = 6.8 Hz, 1 H), 3.75 (s, 3 H), 1.49 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 199.05, 165.51 (d, *J* = 255.4 Hz), 158.65, 133.45, 132.93 (d, *J* = 2.9 Hz), 131.50 (d, *J* = 9.3 Hz), 128.83, 115.67 (d, *J* = 21.8 Hz), 114.57, 55.33, 47.19, 19.63.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –105.70.

1,2-Bis(4-fluorophenyl)propan-1-one (4c)[15]

Colorless oil; yield: 23.6 mg (48%); eluent: toluene.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (dd, *J* = 8.9, 5.4 Hz, 2 H), 7.23 (dd, *J* = 8.7, 5.3 Hz, 2 H), 7.06 (t, *J* = 8.7 Hz, 2 H), 6.99 (t, *J* = 8.8 Hz, 2 H), 4.63 (q, *J* = 6.9 Hz, 1 H), 1.51 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.73, 165.67 (d, *J* = 256.0 Hz), 161.95 (d, *J* = 246.8 Hz), 137.11 (d, *J* = 3.3 Hz), 132.75 (d, *J* = 3.0 Hz), 131.50 (d, *J* = 9.3 Hz), 129.35 (d, *J* = 8.1 Hz), 116.07 (d, *J* = 21.5 Hz), 115.82 (d, *J* = 21.9 Hz), 47.16, 19.70.

1,2-Bis(4-methoxyphenyl)ethan-1-one (5a)[16]

White solid; yield: 29.7 mg (58%); eluent: petroleum ether/EtOAc, 10:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.9 Hz, 2 H), 7.18 (d, *J* = 8.6 Hz, 2 H), 6.92 (d, *J* = 8.9 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 4.17 (s, 2 H), 3.85 (s, 3 H), 3.78 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.68, 163.58, 158.56, 131.05, 130.50, 129.73, 127.05, 114.22, 113.88, 55.59, 55.36, 44.50.

2-(4-Methoxyphenyl)-1-phenylethan-1-one (5b)[17]

Colorless oil; yield: 21.2 mg (47%); eluent: petroleum ether/EtOAc, 15:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–7.98 (m, 2 H), 7.56 (t, *J* = 7.4 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 2 H), 7.19 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 4.23 (s, 2 H), 3.79 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.11, 158.89, 136.74, 133.18, 130.60, 128.83, 126.72, 114.28, 100.13, 55.40, 44.73.

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Supporting Information

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