Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c6ob01299j

Received 16th June 2016,
Accepted 18th July 2016

DOI: 10.1039/c6ob01299j

www.rsc.org/obc

Nickel catalyzed α-arylation of ketones with aryltrimethylammonium triflates†

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Nickel-catalyzed α-arylation of ketones involving aromatic C–N cleavage has been accomplished. Intermolecular coupling of aromatic ketones with a variety of aryltrimethylammonium triflates was achieved in the presence of $Ni(COD)_2$, IPr·HCl, and $LiOBu^t$, giving α-arylated ketones in reasonable to excellent yields.

Introduction

Transition metal-catalyzed α-arylation of carbonyl compounds is of high importance, as the resulting α-aryl carbonyl compounds are common structural motifs in pharmaceutical and other biologically active molecules.[1] After the pioneering studies of intermolecular palladium-catalyzed α-arylation of ketones by the groups of Miura, Buchwald, and Hartwig,[2] a variety of effective catalytic systems have been developed and the scope of carbonyl substrates has been extended to esters, amides, and aldehydes, making this reaction an efficient strategy to connect between $C(sp^2)$ and $C(sp^3)$ centers.[1d,3] Among these reactions, electrophiles were predominantly aryl halides and sulfonates of phenols.[3,4] Only recently, the Itami group has reported a challenging α-arylation of ketones with aryl pivalates under the catalysis of nickel, albeit a high temperature is required.[5a] Martin *et al.* carried out enantioselective α-arylation of 2-methyl-1-indanone with aryl pivalates catalyzed by nickel/BINAP.[5b]

In the last few years, we and other groups revealed that aryltrimethylammonium salts can be used as electrophiles in transition-metal-catalyzed C–C bond-forming reactions including reactions with Grignard reagents,[6] organozinc reagents,[7] aryl boronic acids[8] and oxazoles/thioazoles[9] and C–B bond-forming reactions with B_2pin_2.[10] It is of great interest to apply aryltrimethylammonium salts as electrophilic partners in α-arylation reaction as it can directly transform aromatic amines to α-aryl carbonyl compounds.

Although palladium-based catalysts were widely applied, the use of nickel is more ideal due to its low cost and more earth-abundance.[11] In 2002, Buchwald and co-workers initially employed $Ni(COD)_2$/BINAP to catalyze the α-arylation of γ-butyrolactones,[12] showing that nickel is an excellent palladium surrogate. Later, Chan,[13] Hartwig,[4b,14] and Martin[5b] accomplished the asymmetric arylation of ketones using nickel/diphosphine systems. Besides, nickel/NHC (N-heterocyclic carbenes) also proved to be an efficient combination[15] especially when dealing with aryl chlorides. Here we report an α-arylation of ketones with aryltrimethylammonium triflates using a nickel/NHC catalyst.

Results and discussion

We started our investigations using the reaction of 4-methoxy-*N*,*N*,*N*-trimethylbenzenaminium triflate (**1a**) with propiophenone (**2a**) as a model reaction, and the results are listed in Table 1. Inspired by previous work,[14] we first tested room temperature reaction in THF using a combination of $Ni(COD)_2$ and IPr·HCl as the catalyst precursor and LiHMDS as the base (entry 1). After 10 hours, the ^1H NMR spectrum showed that only about 5% product was formed. Then we tried to elevate the temperature (entries 2–4). To our delight, it obviously promoted the reaction, giving a 40% yield when the reaction was run at 80 °C. This positive result encouraged us to optimize other conditions to further improve the reaction. It was known that bases strongly affected enolization of ketones which was crucial to α-arylation. So we screened a series of bases besides LiHMDS (entries 5–11). The results showed that $LiOBu^t$ was superior to other bases including bis(trimethylsilyl)amide bases, sodium or potassium *tert*-butoxide, LiOMe and Cs_2CO_3. Lithium as a countercation performed better than sodium and potassium, and surprisingly, $KOBu^t$ and KHMDS did not work at all (entries 6 and 9).

Other N-heterocyclic carbenes were also used in the catalytic reactions and IPr showed the best efficiency. Switching

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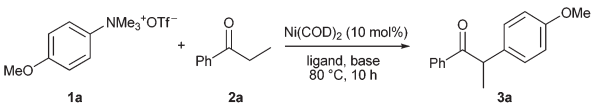
†Electronic supplementary information (ESI) available: Copies of ^1H, ^{13}C and ^{19}F NMR spectra and high-resolution mass spectra of the coupling products. See DOI: 10.1039/c6ob01299j

Table 1 The optimization of reaction conditions[a]



Entry	(Pro)ligand (20 mol%)	Base (equiv.)	Solvent	Yield[b] (%)
1[c]	IPr·HCl	LiHMDS (1.6)	THF	5
2[d]	IPr·HCl	LiHMDS (1.6)	THF	14
3[e]	IPr·HCl	LiHMDS (1.6)	THF	30
4	IPr·HCl	LiHMDS (1.6)	THF	40
5	IPr·HCl	NaHMDS (1.6)	THF	12
6	IPr·HCl	KHMDS (1.6)	THF	Trace
7	IPr·HCl	$LiOBu^t$ (1.6)	THF	52
8	IPr·HCl	$NaOBu^t$ (1.6)	THF	33
9	IPr·HCl	$KOBu^t$ (1.6)	THF	Trace
10	IPr·HCl	LiOMe (1.6 eq.)	THF	Trace
11	IPr·HCl	Cs_2CO_3 (1.6 eq.)	THF	Trace
12	SIPr·HCl	$LiOBu^t$ (1.6 eq.)	THF	16
13	IMes·HCl	$LiOBu^t$ (1.6 eq.)	THF	Trace
14	ICy·HCl	$LiOBu^t$ (1.6 eq.)	THF	—
15	PPh_3	$LiOBu^t$ (1.6 eq.)	THF	Trace
16	BINAP[f]	$LiOBu^t$ (1.6 eq.)	THF	Trace
17	Dcype[f]	$LiOBu^t$ (1.6 eq.)	THF	Trace
18	IPr·HCl	$LiOBu^t$ (1.6 eq.)	*t*-AmylOH	46
19	IPr·HCl	$LiOBu^t$ (1.6 eq.)	Toluene	42
20	IPr·HCl	$LiOBu^t$ (1.6 eq.)	DME	43
21	IPr·HCl	$LiOBu^t$ (1.6 eq.)	Dioxane	40
22[g]	IPr·HCl	$LiOBu^t$ (1.6 eq.)	THF	74
23[h]	IPr·HCl	$LiOBu^t$ (1.6 eq.)	THF	58
24	IPr·HCl	$LiOBu^t$ (2.6 eq.)	THF	62
25[g,h]	IPr·HCl	$LiOBu^t$ (3.4 eq.)	THF	84% (73%[i])

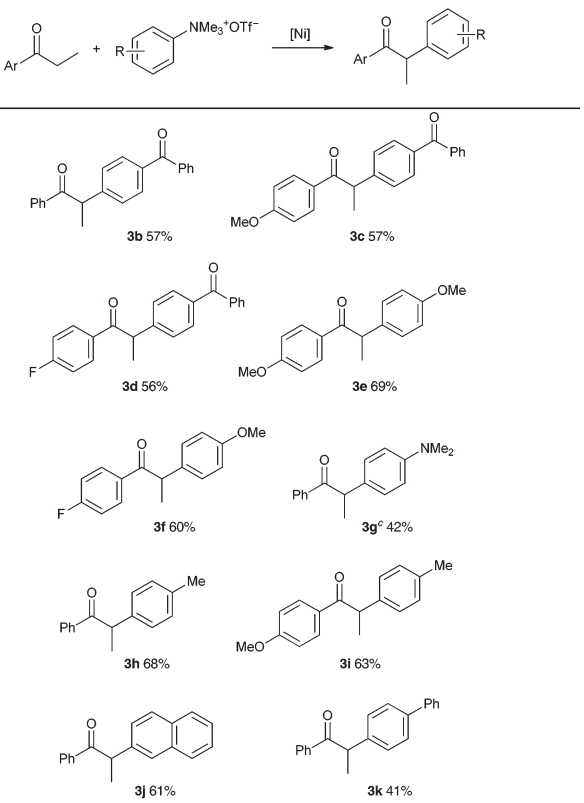
[a] Unless otherwise noted, the reaction conditions were as follows: 0.2 mmol 4-methoxy-*N*,*N*,*N*-trimethylbenzenaminium triflate, 0.24 mmol propiophenone, 10 mol% $Ni(COD)_2$, 2 cm^3 solvent, 80 °C, 10 h. [b] NMR yield. [c] Reaction was carried out at room temperature. [d] Reaction was run at 40 °C. [e] Reaction was run at 60 °C. [f] 10 mol% ligand loading. [g] 1.5 equiv. of propiophenone was used. [h] Reaction time was 24 h. [i] Isolated yield.

IPr to a few other N-heterocyclic carbene ligands led to much lower yields or even no desired product at all (entries 12–14). Mono- or bidentate phosphine ligands were also tested using $LiOBu^t$ as the base and THF as the solvent at 80 °C. Only a trace amount of the desired product was observed in each case (entries 15–17). A study on the solvent effect showed that each of *tert*-amyl alcohol, toluene, dimethoxyethane, and dioxane was less effective than THF (entries 18–21). Excess propiophenone was proven to be necessary. As the amount of propiophenone was increased to 1.5 equivalents, a dramatic improvement was observed (entry 22). A further increase of a portion of propiophenone was not helpful. In addition, increasing the loading of $LiOBu^t$ and extending the reaction time were proven to be helpful to improve the reaction results (entries 23 and 24). The use of excess $LiOBu^t$ may increase the equilibrium concentration of lithium enolate in the reaction solution. Gathering all positive conditions together we got our optimized combination (entry 25).

With the optimized reaction conditions in hand, we tested the reaction of propiophenone and its derivatives with various aryltrimethylammonium triflates, and the results are summarized in Table 2. Propiophenone, 1-(4-methoxyphenyl) propan-1-one and 1-(4-fluorophenyl)propan-1-one respectively represent nucleophilic precursors with electron-neutral, electron-rich, and electron-poor phenyl groups. Each of them reacted smoothly with aryltrimethylammonium triflates, resulting in the corresponding cross-coupling products in 41–69% yields. For the activated aryltrimethylammonium triflate, 4-benzoyl-*N*,*N*,*N*-trimethylbenzenaminium triflate, the reactivity of the three propiophenones showed no difference (**3b–3d**). For the deactivated aryltrimethylammonium triflate, 4-methoxy-*N*,*N*,*N*-trimethylbenzenaminium, 1-(4-fluorophenyl) propan-1-one showed a little lower reactivity (**3a** and **3e** *vs.* **3f**). It seems that the acidity difference of α-H of propiophenones resulting from the electron effect of the aromatic rings plays a minor role in the α-arylation reactions, especially when activated aromatic ammonium salts were used as the electrophiles.

On the other hand, both activated and deactivated aryltrimethylammonium triflates can react smoothly with propiophenones. Deactivated $p\text{-}MeOC_6H_4NMe_3{}^+OTf^-$ and $p\text{-}MeC_6H_4NMe_3{}^+OTf^-$ displayed good reactivity, whereas $p\text{-}Me_2NC_6H_4NMe_3{}^+OTf^-$ exhibited relatively low reactivity. For

Table 2 Nickel-catalyzed α-arylation of 1-arylpropan-1-ones with aryltrimethylammonium triflates[a,b]



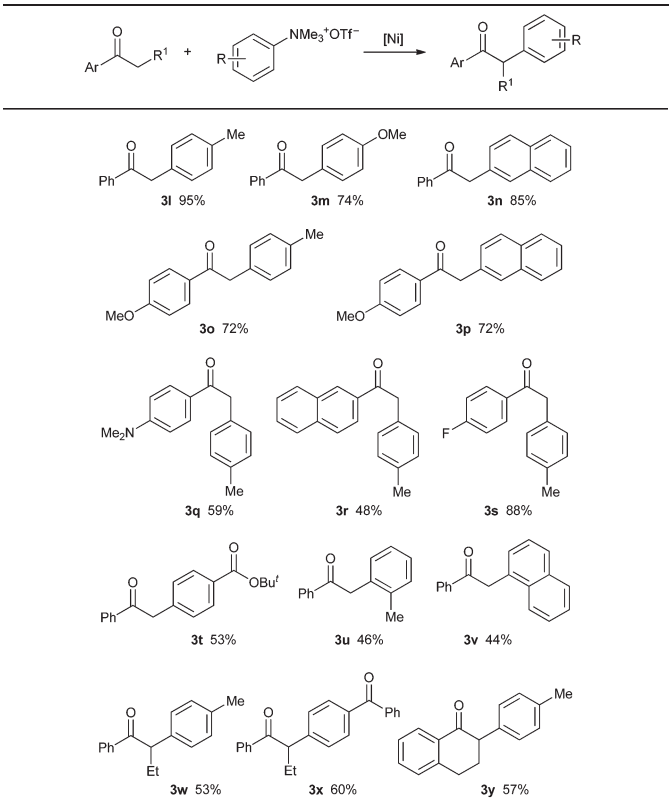
[a] Unless otherwise noted, the reaction conditions were as follows: 0.2 mmol aryltrimethylammonium triflate, 0.30 mmol 1-arylpropan-1-one, 10 mol% $Ni(COD)_2$, 20 mol% IPr·HCl, 3.4 equiv. of $LiOBu^t$, 2 cm^3 THF, 80 °C, 24 h. [b] Isolated yields. [c] 15 mol% $Ni(COD)_2$ and 30 mol% IPr·HCl were employed.

example, reaction of *p*-$Me_2NC_6H_4NMe_3^+OTf^-$ with propiophenone required a higher catalyst loading and gave only 42% product yield (**3g**). 2-Naphthyltrimethylammonium triflate showed good reactivity (**3j**). However, 1-naphthyltrimethylammonium triflate failed to give a reasonable result when reacted with propiophenone under the same conditions. This is ascribed to its steric hindrance, which may prevent its approach to the metal center of the catalyst bearing the sterically hindered ligand IPr. The electron-deficient aryltrimethylammonium salt, *p*-$Ph(CO)C_6H_4NMe_3^+OTf^-$, did not exhibit higher reactivity than *p*-$MeOC_6H_4NMe_3^+OTf^-$ and *p*-$MeC_6H_4NMe_3^+OTf^-$. As mentioned above, its reactions with propiophenones gave the corresponding coupling products in 56–57% yields (**3b–3d**). The reaction of *p*-$PhC_6H_4NMe_3^+OTf^-$ gave a lower product yield (**3k**). In the reactions studied, the N–Me cleavage of aryltrimethylammonium salts is the main side reaction. Aryldimethylamine as a side product can be observed in each reaction. This may be a key reason for relatively low product yields in some reactions. In addition, C(O)OEt, $C(O)NEt_2$ and CN functional groups in aryltrimethylammonium salts cannot be tolerated. Heteroaryl ketones such as 1-(pyridin-2-yl)ethanone and 1-(furan-2-yl)ethanone and dialkyl ketones did not suit for this transformation.

Previous studies showed that the catalytic α-arylation of acetophenones often suffers polyarylations or aldol condensations.[15] Several successful examples of monoarylation of acetone or acetophenone derivatives have been reported when palladium catalysts are employed.[1d,3,4d–f] Nickel-catalyzed monoarylation of acetophenones is still challenging.[5a,15] Delightfully, our catalyst system was demonstrated to be applicable to α-monoarylation of acetophenone derivatives (Table 3). 1-(Naphthalen-2-yl)-ethanone, acetophenone and their derivatives with a functional group at the C4 position such as 4-methoxy-, 4-dimethylamino-, and 4-fluoro- were coupled with 2-naphthalenyl-, *p*-methylphenyl-, *p*-methoxy- or *tert*-butoxycarbonylphenyltrimethylammonium triflates to furnish the expected products **3l–3t** in 48% to 95% yields. It seems that changing the nucleophilic precursors from 1-arylpropan-1-ones to acetophenone derivatives improved the performance, higher product yields being achieved in most cases. We suspected that the reduced hindrance of ketones may facilitate the transmetalation process. As mentioned above, the reaction cannot tolerate the C(O)OEt functional group. This may result from OBu^t/OEt exchange side reaction in the presence of an excess of $LiOBu^t$. We did observe that the $C(O)OBu^t$ functional group can be tolerated. The reaction of *p*-$Bu^tOOCC_6H_4NMe_3^+OTf^-$ with acetophenone resulted in the corresponding coupling product **3t** in 53% yield. Nolan *et al.* reported that [Ni(IPr*)(cin)Cl] can drive α-arylation of electron-rich acetophenones with aryl chlorides, but did not tolerate electron-neutral and electron-poor acetophenones.[15b] Our catalyst system suited for electron-rich, electron-neutral and electron-poor acetophenones. However, reaction of 1-(naphthalen-2-yl)ethanone resulted in a much lower product yield in comparison with that of acetophenone (**3l** *vs.* **3r**). The reactions were also sensitive to the steric hindrance of electrophilic substrates. For example, reaction of *o*-tolyltrimethylammonium triflate with acetophenone gave a cross-coupling product (**3u**) in 46% yield, which is much lower than that of the reaction of *p*-tolyltrimethylammonium triflate (**3l**, 95% yield). The product yield of the reaction of 1-naphthalenyltrimethylammonium triflate with acetophenone was also markedly lower than that of the reaction of 2-naphthalenyltrimethylammonium triflate with acetophenone (44% *vs.* 85%). In addition, we also tested the reaction of an acyclic ketone bulkier at the α-position of the carbonyl group, 1-phenylbutan-1-one, and a cyclic ketone, 3,4-dihydronaphthalen-1(2*H*)-one. They were catalytically α-arylated using electron-rich and electron-poor aryltrimethylammonium triflates in moderate product yields (**3w–3y**).

The detailed mechanism is not clear at this stage. Based on the previous reports for α-arylation reactions using aryl halides or phenol derivatives as the arylating reagents,[1d,15a,b] we speculate that our reaction may follow a similar process because similar conditions were employed. Thus, an active catalyst, L_2Ni, reacts with $ArNMe_3^+OTf^-$ to generate an oxidative addition species $L_2Ni(Ar)OTf$ and release NMe_3. Next, C–H nickelation of a ketone in the presence of $LiOBu^t$ forms a diorganonickel intermediate, which undergoes reductive

Table 3 Nickel-catalyzed arylation of ketones with aryltrimethylammonium triflates[a,b]



[a] Reaction conditions: 0.2 mmol aryltrimethylammonium triflate, 0.30 mmol aryl alkyl ketones, 10 mol% $Ni(COD)_2$, 20 mol% IPr·HCl, 3.4 equiv. of $LiOBu^t$, 2 cm^3 THF, 80 °C, 24 h. [b] Isolated yields.

elimination to form the C–C coupling product along with regeneration of the active nickel species L_2Ni.

Conclusions

We have developed an effective catalyst system to perform α-arylation of ketones with aryltrimethylammonium triflates as the arylating reagents. Activated, unactivated and deactivated aryltrimethylammonium triflates suited for the coupling. The ketones used in this transformation include propiophenone, butyrophenone and acetophenone derivatives as well as a cyclohexanone derivative. In the reactions monoarylation of acetophenone derivatives was successfully carried out. We believe that this methodology would provide a valuable complement to the α-arylation of ketones and enrich the utilization of aromatic amines in synthetic chemistry.

Experimental

General information

All reactions were performed under a nitrogen atmosphere using standard Schlenk and vacuum line techniques. THF, toluene, DME and 1,4-dioxane were distilled under nitrogen over sodium and degassed prior to use. Bu^{t}OH and *tert*-AmylOH were distilled under nitrogen over CaH_2 and degassed prior to use. $Ni(COD)_2$ was purchased from Alfa Aesar. Methyl triflate was purchased from Acros Organics and used as received. Aryldimethylamines were obtained from commercial vendors and purified by distillation under reduced pressure or recrystallization prior to use. $CDCl_3$ was purchased from Cambridge Isotope Laboratories and used as received. ICy·HCl was purchased from Sigma-Aldrich. Other NHC ligands were prepared according to reported procedures.[16] Aryltrimethylammonium triflates were prepared according to reported procedures.[6b,9] All other chemicals were obtained from commercial vendors and used as received. NMR spectra were recorded on a Bruker Avance III 400 spectrometer at ambient temperature. The chemical shifts of the ^{1}H NMR spectra were referenced to TMS and the chemical shifts of the ^{13}C NMR spectra were referenced to internal solvent resonances. The chemical shifts of the ^{19}F NMR spectra were referenced to external CF_3COOH. High-resolution mass spectra (HR-MS) were acquired on a Thermo Orbital XL ETD mass spectrometer.

The typical procedure for the nickel-catalyzed α-arylation of aromatic ketones with aryltrimethylammonium triflates

A Schlenk tube was charged with $Ni(COD)_2$ (5.5 mg, 0.02 mmol), IPr·HCl (17 mg, 0.04 mmol), LiOBu^t (55 mg, 0.68 mmol), 4-methoxy-*N*,*N*,*N*-trimethylbenzenaminium triflate (63 mg, 0.2 mmol), propiophenone (40.2 mg, 0.3 mmol), and THF (2 cm^3). The mixture was stirred at 80 °C for 24 hours. Volatiles were removed by rotary evaporation. The residue was purified by column chromatography on silica gel or preparative thin layer chromatography (100 : 1 mixture of petroleum ether and AcOEt) to give 2-(4-methoxyphenyl)-1-phenylpropan-1-one as a white solid (35.0 mg, 73%).

2-(4-Methoxyphenyl)-1-phenylpropan-1-one (3a).[17] White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96–7.92 (m, 2H), 7.44 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.19 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 4.63 (q, J = 6.9 Hz, 1H), 3.71 (s, 3H), 1.50 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 200.6, 158.5, 136.5, 133.5, 132.8, 128.8, 128.8, 128.5, 114.4, 55.2, 47.0, 19.6.

2-(4-Benzoylphenyl)-1-phenylpropan-1-one (3b).[15a] White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99–7.95 (m, 2H), 7.78–7.73 (m, 4H), 7.57 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.48–7.38 (m, 6H), 4.79 (q, J = 6.9 Hz, 1H), 1.58 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 199.8, 196.4, 146.3, 137.6, 136.3, 133.3, 132.5, 131.0, 130.1, 128.9, 128.8, 128.4, 127.9, 47.9, 19.5.

2-(4-Benzoylphenyl)-1-(4-methoxyphenyl)propan-1-one (3c).[15a] Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.9 Hz, 2H), 7.78–7.73 (m, 4H), 7.57 (t, J = 8.0 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.9 Hz, 2H), 4.74 (q, J = 6.8 Hz, 1H), 3.82 (s, 3H), 1.56 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.3, 196.4, 163.6, 146.7, 137.6, 136.2, 132.5, 131.2, 130.9, 130.1, 129.3, 128.4, 127.8, 113.9, 55.6, 47.5, 19.5.

2-(4-Benzoylphenyl)-1-(4-fluorophenyl)propan-1-one (3d).[15a] Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01–7.96 (m, 2H), 7.79–7.72 (m, 4H), 7.60–7.56 (m, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.39 (d, J = 8.3 Hz, 2H), 7.08 (t, J = 8.6 Hz, 2H), 4.73 (q, J = 6.9 Hz, 1H), 1.57 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.2, 196.3, 165.8 (d, J = 256.3 Hz), 146.1, 137.6, 136.5, 132.7 (d, J = 3.1 Hz), 132.6, 131.6 (d, J = 9.3 Hz), 131.1, 130.1, 128.4, 127.8, 115.9 (d, J = 21.9 Hz), 48.0, 19.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ −104.84.

1,2-Bis(4-methoxyphenyl)propan-1-one (3e).[18] Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 8.8 Hz, 2H), 7.20 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 4.60 (q, J = 6.8 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 1.49 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 199.2, 163.2, 158.5, 134.1, 131.2, 129.5, 128.8, 114.4, 113.7, 55.5, 55.3, 46.7, 19.7.

1-(4-Fluorophenyl)-2-(4-methoxyphenyl)propan-1-one (3f).[4e] Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02–7.92 (m, 2H), 7.18 (d, J = 8.7 Hz, 2H), 7.04 (t, J = 8.7 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 4.58 (q, J = 6.8 Hz, 1H), 3.75 (s, 3H), 1.50 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 199.0, 165.5 (d, J = 255.4 Hz), 158.7, 133.5, 132.9 (d, J = 2.9 Hz), 131.5 (d, J = 9.3 Hz), 128.8, 115.7 (d, J = 21.8 Hz), 114.6, 55.3, 47.2, 19.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ −105.69.

2-(4-(Dimethylamino)phenyl)-1-phenylpropan-1-one (3g).[19] Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97–7.94 (m, 2H), 7.45 (t, J = 7.3 Hz, 1H), 7.36 (t, J = 7.5 Hz, 2H), 7.14 (d, J = 8.8 Hz, 2H), 6.65 (d, J = 8.8 Hz, 2H), 4.59 (q, J = 6.8 Hz, 1H), 2.88 (s, 6H), 1.49 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 200.8, 149.6, 136.8, 132.6, 129.2, 128.9, 128.5, 128.5, 113.1, 47.0, 40.7, 19.6.

1-Phenyl-2-(*p*-tolyl)propan-1-one (3h).[17] White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98–7.95 (m, 2H), 7.47 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 4.66 (q, J = 6.8 Hz, 1H), 2.29 (s, 3H), 1.53 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 200.6, 138.6, 136.6, 132.8, 129.8, 128.9, 128.6, 127.7, 47.6, 21.1, 19.6.

1-(4-Methoxyphenyl)-2-(*p*-tolyl)propan-1-one (3i).[20] Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 9.0 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 7.9 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 4.61 (q, J = 6.8 Hz, 1H), 3.81 (s, 3H), 2.29 (s, 3H), 1.50 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 199.1, 163.2, 139.0, 136.5, 131.2, 129.7, 129.6, 127.7, 113.7, 55.5, 47.2, 21.1, 19.7.

2-(Naphthalen-2-yl)-1-phenylpropan-1-one (3j).[17] White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02–7.98 (m, 2H), 7.81–7.77 (m, 3H), 7.73 (s, 1H), 7.48–7.41 (m, 4H), 7.37 (t, J = 7.5 Hz, 2H), 4.86 (q, J = 6.8 Hz, 1H), 1.63 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 200.4, 139.1, 136.5, 133.8, 133.0, 132.5, 128.9, 128.6, 127.8, 127.8, 126.5, 126.3, 126.1, 125.9, 48.2, 19.7.

2-([1,1′-Biphenyl]-4-yl)-1-phenylpropan-1-one (3k).[15a] White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02–7.98 (m, 2H), 7.56–7.51 (m, 4H), 7.49 (d, J = 7.2 Hz, 1H), 7.44–7.39 (m, 4H), 7.37 (d, J = 8.4 Hz, 2H), 7.32 (t, J = 7.4 Hz, 1H), 4.75 (q, J = 6.8 Hz, 1H), 1.58 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 200.4, 140.8, 140.6, 139.9, 136.6, 133.0, 128.9, 128.9, 128.7, 128.3, 127.8, 127.4, 127.1, 47.6, 19.6.

1-Phenyl-2-(*p*-tolyl)ethan-1-one (3l).[21] Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, J = 8.2 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.20–7.13 (m, 4H), 4.26 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.9, 136.7, 136.6, 133.2, 131.5, 129.5, 129.4, 128.7, 45.2, 21.2.

2-(4-Methoxyphenyl)-1-phenylethan-1-one (3m).[22] White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 7.3 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.19 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.23 (s, 2H), 3.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.1, 158.7, 136.7, 133.2, 130.6, 128.8, 128.7, 126.6, 114.3, 55.4, 44.8.

2-(Naphthalen-2-yl)-1-phenylethan-1-one (3n).[23] White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09–8.03 (2H, m), 7.85–7.77 (m, 3H), 7.73 (s, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.50–7.38 (m, 5H), 4.46 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.6, 136.5, 133.5, 133.2, 132.3, 132.0, 128.6, 128.6, 128.3, 128.0, 127.6, 127.6, 127.5, 126.1, 125.7, 45.7.

1-(4-Methoxyphenyl)-2-(*p*-tolyl)ethan-1-one (3o).[21] Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 4.20 (s, 2H), 3.85 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.6, 163.5, 136.4, 131.9, 131.0, 129.7, 129.5, 129.3, 113.8, 55.5, 45.0, 21.2.

1-(4-Methoxyphenyl)-2-(naphthalen-2-yl)ethan-1-one (3p).[24] White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.8 Hz, 2H), 7.83–7.76 (m, 3H), 7.73 (s, 1H), 7.48–7.39 (m, 3H), 6.93 (d, J = 8.8 Hz, 2H), 4.40 (s, 2H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.4, 163.7, 133.7, 132.7, 132.5, 131.1, 129.7, 128.4, 128.1, 127.8, 127.8, 127.7, 126.2, 125.8, 114.0, 55.6, 45.6.

1-(4-(Dimethylamino)phenyl)-2-(*p*-tolyl)ethan-1-one (3q). Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 9.1 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.64 (d, J = 9.1 Hz, 2H), 4.15 (s, 2H), 3.04 (s, 6H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.1, 153.4, 136.1, 132.8, 131.0, 129.4, 129.3, 124.6, 110.8, 44.7, 40.1, 21.2. HR-MS: m/z 254.15360 $[M + H]^+$, calcd for $C_{17}H_{20}NO$ 254.15448.

1-(Naphthalen-2-yl)-2-(*p*-tolyl)ethan-1-one (3r). White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.06 (dd, J = 1.7, 8.7 Hz, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.88 (t, J = 7.6 Hz, 2H), 7.63–7.53 (m, 2H), 7.21 (d, J = 7.9 Hz, 2H), 7.15 (d, J = 7.9 Hz, 2H), 4.38 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.0, 136.6, 135.7, 134.1, 132.6, 131.7, 130.5, 129.8, 129.6, 129.5, 128.6, 128.6, 127.9, 126.9, 124.5, 45.3, 21.2. HR-MS: m/z 261.12709 $[M + H]^+$, calcd for $C_{19}H_{17}O$ 261.12793.

1-(4-Fluorophenyl)-2-(*p*-tolyl)ethan-1-one (3s).[21] Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06–8.00 (m, 2H), 7.16–7.09 (m, 6H), 4.22 (s, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.4, 165.8 (d, J = 255.8 Hz), 136.8, 133.1 (d, J = 3.0 Hz), 131.4 (d, J = 9.4 Hz), 131.3, 129.6, 129.3, 115.8 (d, J = 21.9 Hz), 45.3, 21.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ −105.12.

***tert*-Butyl 4-(2-oxo-2-phenylethyl)benzoate (3t).** White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01–7.98 (m, 2H), 7.95 (d, J = 8.3 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 4.33 (s, 2H), 1.58 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.1, 165.7, 139.3, 136.5, 133.5, 130.8, 129.9, 129.5, 128.8, 128.7, 81.1, 45.6, 28.3. HR-MS: m/z 297.14899 $[M + H]^+$, calcd for $C_{19}H_{21}O_3$ 297.14906.

1-Phenyl-2-(*o*-tolyl)ethanone (3u).[25] Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 6.9 Hz, 2H), 7.46–7.58 (m, 3H), 7.13–7.24 (m, 4H), 4.31 (s, 2H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.6, 137.0, 137.0, 133.6, 133.3, 130.5, 130.4, 128.8, 128.5, 127.4, 126.2, 43.6, 19.9.

2-(Naphthalen-1-yl)-1-phenylethanone (3v).[25] Light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 6.8 Hz, 2H), 7.86 (s, 2H), 7.78 (d, J = 7.6 Hz, 1H), 7.35–7.57 (m, 7H), 4.72 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.7, 136.8, 134.0, 133.4, 132.4, 131.5, 128.9, 128.8, 128.6, 128.1, 128.0, 126.4, 125.9, 125.6, 124.0, 43.2.

1-Phenyl-2-(*p*-tolyl)butan-1-one (3w). Colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00–7.95 (m, 2H), 7.48 (t, J = 7.3 Hz, 1H), 7.39 (t, J = 7.5 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 7.9 Hz, 2H), 4.42 (t, J = 7.3 Hz, 1H), 2.29 (s, 3H), 2.25–2.12 (m, 1H), 1.90–1.80 (m, 1H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 200.3, 137.2, 136.7, 136.7, 132.8, 129.7, 128.8, 128.6, 128.2, 55.2, 27.2, 21.1, 12.4. HR-MS: m/z 239.14293 $[M + H]^+$, calcd for $C_{17}H_{19}O$ 239.14358.

2-(4-Benzoylphenyl)-1-phenylbutan-1-one (3x). Colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01–7.96 (m, 2H), 7.79–7.72 (m, 4H), 7.57 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.38–7.38 (m, 6H), 4.57 (t, J = 7.3 Hz, 1H), 2.31–2.19 (m, 1H), 1.96–1.84 (m, 1H), 0.94 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 199.6, 196.4, 144.5, 137.6, 136.9, 136.4, 133.2, 132.5, 130.8, 130.1, 128.8, 128.4, 128.4, 55.4, 27.3, 12.4. HR-MS: m/z 329.15348 $[M + H]^+$, calcd for $C_{23}H_{21}O_2$ 329.15415.

2-(*p*-Tolyl)-3,4-dihydronaphthalen-1(2*H*)-one (3y).[26] White solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 7.8 Hz, 1H), 7.51 (dt, J = 1.2, 7.5 Hz, 1H), 7.35 (t, J = 7.4 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 3.81–3.75 (m, 1H), 3.16–3.02 (m, 2H), 2.47–2.39 (m, 2H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.5, 144.2, 136.8, 136.6, 133.5, 133.0, 129.4, 128.9, 128.4, 127.9, 126.8, 54.1, 31.3, 28.9, 21.2.

Acknowledgements

Financial support from the National Natural Science Foundation of China (grant no. 21372212) and the National Basic Research Program of China (grant no. 2015CB856600) is greatly acknowledged.

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