Chemoselective Transfer Hydrogenation of α,β-Unsaturated Ketones Catalyzed by Iridium Complexes

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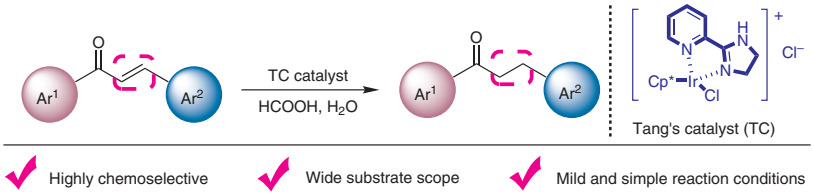

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Abstract Efficient chemoselective transfer hydrogenation of the C=C bond of α,β-unsaturated ketones has been developed, using the iridium complexes containing pyridine-imidazolidinyl ligands as catalysts and formic acid as a hydrogen source. In comparison with organic solvents or H_2O as solvent, the mixed solvents of H_2O and MeOH are critical for a high catalytic chemoselective transformation. This chemoselective transfer hydrogenation can be carried out in air, which is operationally simple, allowing a wide variety of α,β-unsaturated substrates with different functional groups (electron-donating and electron-withdrawing substituents) leading to chemoselective transfer hydrogenation in excellent yields. The practical application of this protocol is demonstrated by a gram-scale transformation.

Key words transfer hydrogenation, iridium complex, α,β-unsaturated ketones, formic acid, chemoselective reduction

Saturated carbonyl compounds are ubiquitous, and many pharmaceutically active molecules contain 1,3-diaryl ketones (Figure 1).[1]

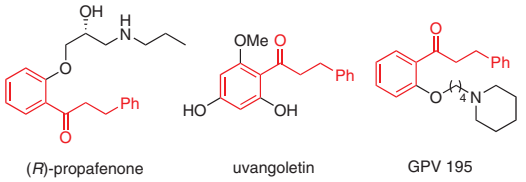
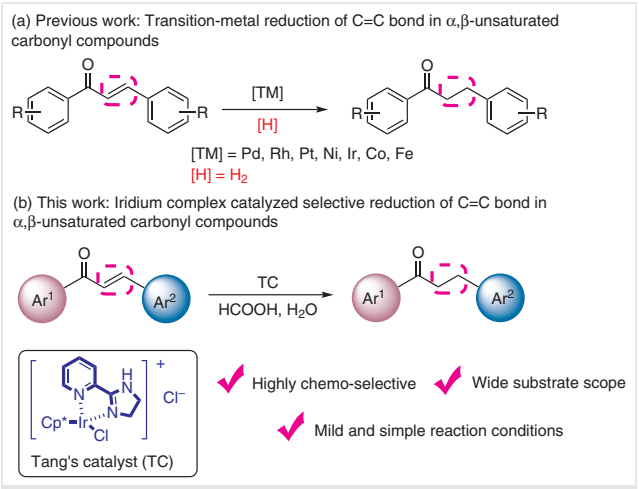


Figure 1 Examples of pharmaceutically active molecules containing 1,3-diaryl ketones

Among the methodologies for the synthesis of saturated carbonyl compounds, one of the best ways is the selective reduction of carbon–carbon double bonds on α,β-unsaturated carbonyl compounds.[2] However, chemoselective reduction of carbon–carbon double bonds of α,β-unsaturated carbonyl compounds wherein the carbon–oxygen double bond is not affected,[3] is a challenge with a significant role in organic synthesis.[4]

Traditional transformation of chemoselective reduction of C=C bonds of α,β-unsaturated carbonyl compounds include hydrogenation with hydrogen over a Pd/C catalyst.[5] It is well known that transition metals are not only good electron donors, but also electron acceptors due to the availability of vacant d-orbitals that possess specific electronic and spatial effects when coordinated with organic ligands.[6] Therefore, much effort has been devoted to the development of highly chemoselective reduction of C=C bonds for α,β-unsaturated carbonyl compounds catalyzed by transition-metal catalysts, such as Pd,[2d,7] Rh,[8] Ru, [2c,e,f] Ni,[2b,9] Ir,[10] Co,[11] and Fe (Scheme 1a).[12] At the same time, nontransition-metal hydrides such as Sn, Se, Te, B, [13]and others[14] have



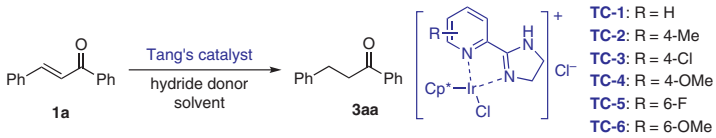
Scheme 1 Selective reduction of the C=C bond of α,β-unsaturated carbonyl compounds

also been employed for the selective reduction of C=C bonds in α,β-unsaturated carbonyl compounds. Furthermore, enzymic reduction is receiving increasing attention due to the potential for high chemoselectivity.

However, most of transition metals and their metal complexes are expensive, and the methodology is difficult to realize at industrial scale. Meanwhile, hydrogen is usually employed as the reductant, often under high pressures.[15] Besides these drawbacks, other disadvantages of these methodologies may include harsh reaction conditions, long reaction time, low yields, and low functional group selectivity, limiting their applications in organic synthesis. Therefore, more general, practical, mild, and efficient methods for the selective reduction of the C=C bond in α,β-unsaturated carbonyl compounds without affecting the C=O bond remain highly desirable.

Transfer hydrogenation is a well-established and efficient protocol that has the advantage of not requiring special equipment or hydrogen gas. Recently, our group developed iridium complex catalyzed transfer hydrogenation of C=O and C=N bonds by using formic acid or formate as the hydride source.[16] As far as we know, reports on iridium complex catalyzed transfer hydrogenation of C=C bonds remain limited.[17] Therefore, we examined the iridium complex catalyzed chemoselective transfer hydrogenation of the C=C bond of α,β-unsaturated carbonyl compounds by

Table 1 Optimization of Reaction Conditions[a]



TC-1: R = H
TC-2: R = 4-Me
TC-3: R = 4-Cl
TC-4: R = 4-OMe
TC-5: R = 6-F
TC-6: R = 6-OMe

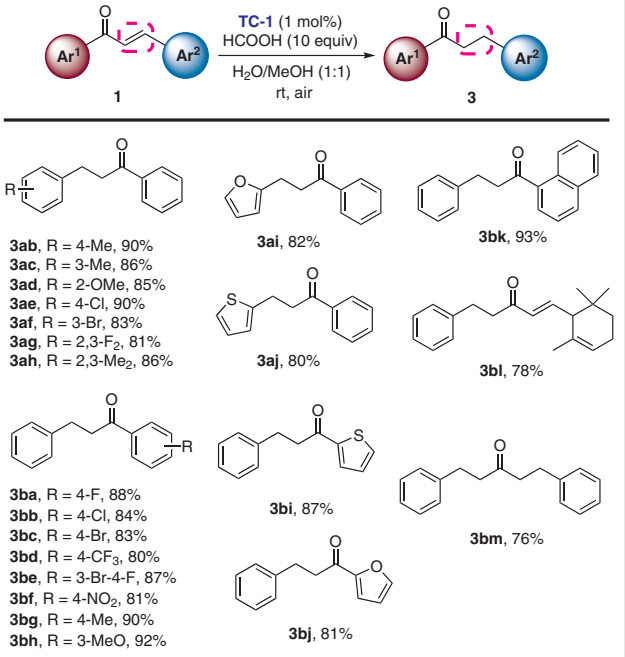
Entry	Catalyst	Hydrogen donor	Solvent	Yield (%)[b]
1	**TC-1**	HCOOH	H_2O	60
2	**TC-2**	HCOOH	H_2O	45
3	**TC-3**	HCOOH	H_2O	49
4	**TC-4**	HCOOH	H_2O	55
5	**TC-5**	HCOOH	H_2O	52
6	**TC-6**	HCOOH	H_2O	57
7	**TC-1**	HCOONa	H_2O	48
8[c]	**TC-1**	HCOOH/Et_3N	H_2O	42
9[d]	**TC-1**	HCOOH	H_2O	63
10	**TC-1**	HCOOH	DMF	43
11	**TC-1**	HCOOH	toluene	51
12	**TC-1**	HCOOH	THF	46
13	**TC-1**	HCOOH	CH_2Cl_2	57
14	**TC-1**	HCOOH	MeCN	48
15	**TC-1**	HCOOH	MeOH	57
16[e]	**TC-1**	HCOOH	H_2O	69
17[f]	**TC-1**	HCOOH	H_2O/CH_2Cl_2	80
18[g]	**TC-1**	HCOOH	H_2O/MeOH	90
19[h]	**TC-1**	HCOOH	H_2O/MeOH	93(90)
20[i]	**TC-1**	HCOOH	H_2O	12
21[j]	**TC-1**	HCOOH	–	5

[a] Reaction conditions: **1a** (0.5 mmol), solvent (2 mL), catalyst (1 mol%), hydrogen donor (10 equiv) at room temperature under air for 12 h.
[b] Determined by GC–MS using dodecane as the internal standard. The number in parentheses is the isolated yield.
[c] The reaction was carried out with 5.0 equiv of HCOOH, 2.0 equiv of Et_3N.
[d] The reaction was carried out under N_2 atmosphere.
[e] The reaction was carried out at 80 °C.
[f] CH_2Cl_2 (1 mL) was added in the reaction.
[g] MeOH (1.0 mL) was added in the reaction.
[h] MeOH (2mL) was added in the reaction.
[i] 2 equiv $(n\text{-Bu})_4NBr$.
[j] This reaction in only formic acid.

adjusting the structures of the catalysts and hydrogen source. To achieve this goal, two problems needed to be settled: the effective catalytic system to realize C=C bond reduction and the suppression of side reactions. Herein, we describe an efficient and practical iridium complex catalyzed chemoselective transfer hydrogenation of the C=C bond of α,β-unsaturated carbonyl compounds.

In the initial attempts at selective reduction of α,β-unsaturated ketones, chalcone was used as model substrate, iridium complexes as catalysts, and HCOOH as hydrogen source at room temperature under air (Table 1). Interestingly, the desired product **3aa** was afforded in a yield of 60% with the **TC-1** catalyst (entry 1). To explore better catalytic system, several other of Tang's catalysts with different substituted functional groups were also screened (entries 2–6). Disappointedly, lower catalytic activities were obtained. As different hydride sources have important effects on transfer hydrogenation, other candidates were employed in this catalytic system. However, lower yields were obtained by using HCOONa and HCOOH/NEt_3 as hydride sources (entries 7 and 8). We also performed the reaction under N_2 under standard conditions, but this showed no obvious improvement (entry 9). During our study, we observed that the substrate did not dissolve in the water. Therefore, a screening of organic solvents was performed. As shown (Table 1, entries 10–15), only moderate yields were achieved in organic solvents. However, at the same time, we also found that the solubility of **1a** in organic solvents was different. For example, MeOH and CH_2Cl_2 can dissolve **1a** completely, while it did not dissolve in DMF. Furthermore, when the reaction was performed in water, a white suspension was observed on the water surface, which was characterized by NMR spectroscopy and found to be unreacted starting material **1a**. A higher reaction temperature led to slightly better conversion (entry 16). In our previous study, we knew that the catalysts had the features of excellent water solubility. Based on our previous research and above results, we envisaged that mixed solvents could help to improve catalytic activity. With this in mind, mixed solvents were next tested. To our satisfaction, high yields of **3aa** were achieved in a mixture of H_2O and MeOH under the standard conditions (entries 17–19). A phase-transfer catalyst such as quaternary ammonium salt ((*n*-Bu)$_4$NBr) was used in just water, but only 12% of desired product was detected (entry 20). When using formic acid as hydrogen source and solvent, only a 5% yield of **3aa** was obtained (entry 21).

Intrigued by this simple and efficient procedure for the selective reduction of **1a**, we then explored the substrate scope under the optimized transfer hydrogenation conditions (Scheme 2). In general, electron-donating and electron-withdrawing substituents on the phenyl ring (β to carbonyl group) and benzoyl rings are well tolerated and furnished the desired products in good yields (Scheme 2). For example, the substrate with a phenyl ring β to the carbonyl



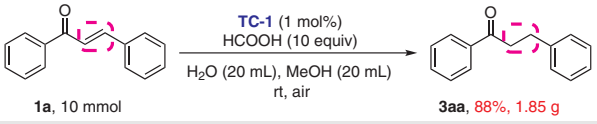
Scheme 2 Substrate scope. *Reagents and conditions*: **1** (0.5 mmol), **TC-1** (1.0 mol%), and HCOOH (10.0 equiv) in H_2O (2.0 mL) and MeOH (2.0 mL), room temperature, air, 12 h. Yield of isolated product.

group contains substituents such as *p*-methyl, methoxy, chloride, fluoride, and bromide provided good to excellent yields of the corresponding products under standard conditions (**3ab–ah**). Notably, substrates with heterocyclic rings such as furyl, thiophenyl, and naphthyl also reacted smoothly and gave the desired products in high yields (**3ai**,**aj**).

To explore the utility of this iridium-catalyzed chemoselective transfer hydrogenation further, we also examined substrates with different substituents on the benzoyl ring. A variety of chalcones with halogen substituents on the benzoyl ring were selectively reduced in good yields (**3ba–bc**,**be**). Substrates with strongly electron-drawing groups on the benzoyl ring, such as trifluoromethyl and nitryl, were selectively reduced to give the desired substituted ketones in yields of 80% and 81%, respectively (**3bd**,**bf**). Substrates possessing methyl and methoxy groups on the benzoyl ring also reacted under the optimized conditions (**3bg**,**bh**). Of note, heterocyclic acyl substrates were also observed to be well-tolerated under the standard conditions, giving **3bi** and **3bj** in 87% and 81% yields, respectively. In addition, the sterically hindered 1-naphthoyl substrate (**2bk**) led to the successful synthesis of **3bk**. In addition, the doubly unsaturated substrate **2bl** with a β-aryl and β-cylcohexenyl substituent gave **3bl** efficiently, which demonstrates that unsaturated double bonds contiguous with a β-aryl group can also be reduced selectively. In keeping with this

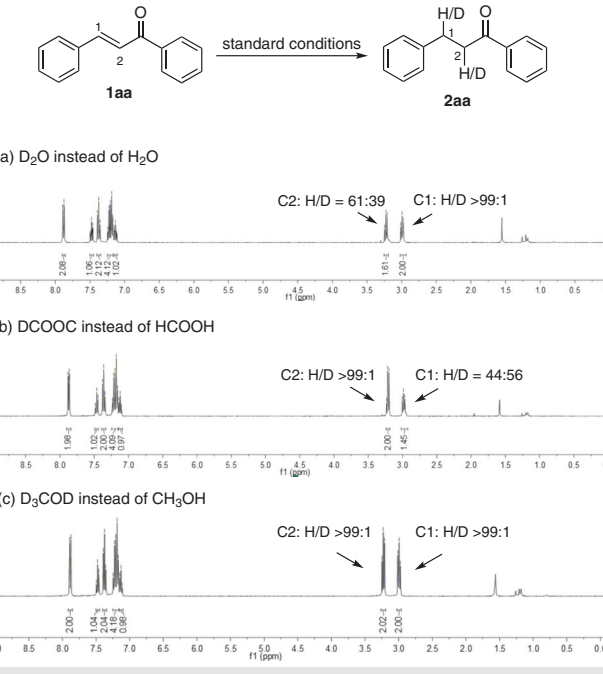
observation, when dibenzylideneacetone was employed as the substrate, the corresponding doubly reduced product **3bm** could be obtained in a yield of 76%.

In order to verify the practical synthetic application of this chemoselective transfer hydrogenation reduction of α,β-unsaturated ketones, a scaled-up experiment was conducted. When **1a** (10 mmol) was carried out under above established conditions, **3aa** was isolated by flash chromatography in a yield of 88% (Scheme 3).



Scheme 3 Gram-scale experiment

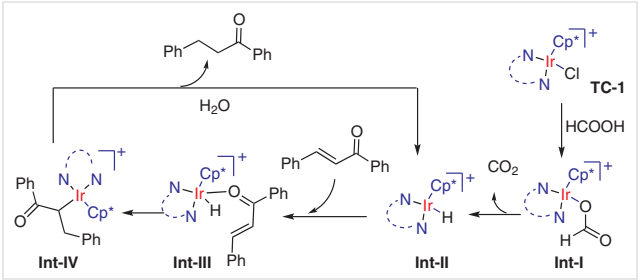
Alcohols are usually employed as the proton source for transfer hydrogenation reduction[18] and are preferred as a convenient, economical, and environmentally relatively benign choice. In this catalytic system, the hydride and proton sources are derived from formic acid and methanol. To gain more insight into this catalytic system, deuterium-labeling experiments were performed (Scheme 4). By using D_2O as solvent, the ratio of H/D at C2 was found to be 61:39 and C1 was not deuterated. The deuterium incorporation at C2 may be caused by H–D exchange between [Ir]–H and D_2O. However, the outcome was quite different when DCO_2D was employed. By using DCO_2D instead of HCOOH under standard reaction conditions, product **3aa** was afforded in 90% yield with a C1 ratio of H/D of 44:56, with no deuteration at C2.



Scheme 4 Mechanistic studies

Again, the incomplete deuterium incorporation at C1 may be caused by H–D exchange between [Ir]–D and H_2O. When D_3COD was employed, efficient preparation of **3aa** was observed without deuterium incorporation.

Based on the above control experiments, we propose the following mechanism (Scheme 5). Initially, the Ir hydride (**Int-II**) complex is formed by ligand exchange from **Tc-1** with HCOOH followed by release of carbon dioxide.[19] Then, the Ir hydride species coordinates with substrate **1a** to generate **Int-III**, followed by the insertion of the polar C=C bond to generate **Int-IV**.[20] Finally, the desired product **3aa** is achieved by ligand exchange of **Int-IV**, from which **Int-II** is released for the next catalytic cycle.



Scheme 5 Proposed mechanism

In conclusion, we have developed an iridium-catalyzed chemoselective transfer hydrogenation of the C=C bond of chalcones to prepare 1,4-diaryl ketones in good to excellent yields by using formic acid as hydrogen source.[21] The broad substrates scope, simple operation, and high chemoselectivity are the attractive features of this transformation. Further investigations as well as exploration of asymmetric transfer hydrogenation are in progress.

Funding Information

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1706022.

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(21) **Procedure for the Preparation of 3**

To a 25.0 mL dried Schlenk tube was added the α,β-unsaturated ketone (**2**, 0.5 mmol), Ir catalyst (1.0 mol %), HCOOH (10.0 equiv), water (2.0 mL), and MeOH (2.0 mL) successively. The mixture was stirred at room temperature for 12 h under air. After reaction was complete, the mixture was diluted with H_2O (15.0 mL), neutralized with saturated aq. $NaHCO_3$, and extracted with EtOAc (3 × 10.0 mL). The combined organic layers were washed with brine (3 × 10.0 mL) and dried over anhydrous $MgSO_4$. After filtration and removal of the EtOAc under vacuum, the crude product was purified by column chromatography on silica gel, eluting with hexane or petroleum ether/ethyl acetate (10:1 to 50:1) to achieve the desired products.

1,3-Diphenylpropan-1-one (3aa)[12b]

Yield 90% (94.5 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 7.8 Hz, 2 H), 7.59 (t, *J* = 7.3 Hz, 1 H), 7.49 (t, *J* = 7.7 Hz, 2 H), 7.37–7.22 (m, 5 H), 3.37–3.30 (m, 2 H), 3.14–3.07 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.3, 141.3, 136.9, 133.1, 128.6, 128.6, 128.5, 128.1, 126.2, 40.5, 30.2.

1-Phenyl-3-(*p*-tolyl)propan-1-one (3ab)[14]

Yield 90% (96.3 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.92 (m, 2 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.13 (q, *J* = 8.1 Hz, 4 H), 3.31–3.24 (m, 2 H), 3.06–3.00 (m, 2 H), 2.32 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.4, 138.2, 136.9, 135.7, 133.1, 129.2, 128.6, 128.3, 128.1, 40.6, 29.7, 21.0.

1-Phenyl-3-(*m*-tolyl)propan-1-one (3ac)[2d]

Yield 86% (95.2 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.5 Hz, 2 H), 7.55 (t, *J* = 7.3 Hz, 1 H), 7.45 (t, *J* = 7.6 Hz, 2 H), 7.19 (t, *J* = 7.5 Hz, 1 H), 7.04 (dd, *J* = 13.2, 9.1 Hz, 3 H), 3.33–3.26 (m, 2 H), 3.06–2.99 (m, 2 H), 2.33 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.4, 141.3, 138.1, 136.9, 133.1, 129.3, 128.6, 128.5, 128.1, 126.9, 125.4, 40.6, 30.1, 21.4.

3-(2-Methoxyphenyl)-1-phenylpropan-1-one (3ad)[14]

Yield 85% (102 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$):

δ = 7.97 (d, *J* = 7.8 Hz, 2 H), 7.53 (t, *J* = 7.3 Hz, 1 H), 7.43 (t, *J* = 7.6 Hz, 2 H), 7.23–7.16 (m, 2 H), 6.92–6.81 (m, 2 H), 3.81 (s, 3 H), 3.29–3.22 (m, 2 H), 3.08–3.01 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.0, 157.6, 137.0, 132.9, 130.2, 129.6, 128.6, 128.2, 127.6, 120.6, 110.3, 55.2, 39.0, 25.8.

3-(4-Chlorophenyl)-1-phenylpropan-1-one (3ae)[14]

Yield 90% (109.8 mg), colorless oil (88.5–90 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.91 (m, 2 H), 7.56 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.28–7.24 (m, 2 H), 7.18 (d, *J* = 8.4 Hz, 2 H), 3.28 (t, *J* = 7.5 Hz, 2 H), 3.04 (t, *J* = 7.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 139.7, 136.8, 133.2, 131.9, 129.8, 128.7, 128.6, 128.0, 40.2, 29.4.

3-(4-Bromophenyl)-1-phenylpropan-1-one (3af)[14]

Yield 83% (119.5 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–7.95 (m, 2 H), 7.58 (dd, *J* = 10.7, 4.0 Hz, 2 H), 7.48 (t, *J* = 7.6 Hz, 2 H), 7.35 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.27 (td, *J* = 7.5, 1.1 Hz, 1 H), 7.10 (td, *J* = 7.7, 1.7 Hz, 1 H), 3.37–3.32 (m, 2 H), 3.24–3.19 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 140.6, 136.8, 133.2, 132.9, 130.8, 128.6, 128.1, 128.0, 127.7, 124.4, 38.6, 30.8.

3-(2,3-Difluorophenyl)-1-phenylpropan-1-one (3ag)

Yield 81% (99.6 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.95 (m, 2 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.48 (t, *J* = 7.7 Hz, 2 H), 7.08–6.98 (m, 3 H), 3.34 (t, *J* = 7.5 Hz, 2 H), 3.15 (t, *J* = 7.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.6, 149.9 (dd, *J* = 243, 13 Hz), 136.6, 133.2, 130.6 (d, *J* = 12 Hz), 128.7, 128.0, 125.6 (t, *J* = 4 Hz), 123.9 (dd, *J* = 6, 4 Hz), 115.2 (d, *J* = 17 Hz), 38.6, 23.6.

3-(2,3-Dimethylphenyl)-1-phenylpropan-1-one (3ah)

Yield 86% (102.3 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 7.6 Hz, 2 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.49 (t, *J* = 7.6 Hz, 2 H), 7.11–7.05 (m, 3 H), 3.27 (dd, *J* = 9.3, 6.5 Hz, 2 H), 3.15–3.08 (m, 2 H), 2.33 (s, 3 H), 2.28 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.5, 139.3, 137.1, 136.9, 134.6, 133.1, 128.6, 128.1, 128.1, 126.9, 125.6, 39.6, 28.3, 20.7, 15.1. ESI-HRMS: *m/z* calcd for $C_{17}H_{19}O$ $[M + H]^+$: 239.1436; found: 239.1433.

3-(Furan-2-yl)-1-phenylpropan-1-one (3ai)[22a]

Yield 82% (82 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.95 (m, 2 H), 7.56 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.33–7.28 (m, 1 H), 6.30–6.25 (m, 1 H), 6.05 (d, *J* = 3.1 Hz, 1 H), 3.35–3.31 (m, 2 H), 3.11–3.07 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.7, 154.8, 141.1, 136.8, 133.2, 128.6, 128.1, 110.3, 105.3, 36.9, 22.5.

1-Phenyl-3-(thiophen-2-yl)propan-1-one (3aj)[22b]

Yield 80% (86.4 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.93 (m, 2 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.6 Hz, 2 H), 7.11 (dd, *J* = 5.1, 0.9 Hz, 1 H), 6.91 (dd, *J* = 5.0, 3.5 Hz, 1 H), 6.85 (d, *J* = 3.1 Hz, 1 H), 3.38–3.33 (m, 2 H), 3.31–3.26 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.6, 143.9, 136.8, 133.2, 128.7, 128.1, 126.9, 124.7, 123.4, 40.6, 24.2.

1-(4-Fluorophenyl)-3-phenylpropan-1-one (3ba)[2d]

Yield 88% (100.3 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.93 (m, 2 H), 7.32–7.18 (m, 5 H), 7.09 (t, *J* = 8.6 Hz, 2 H), 3.25 (t, *J* = 7.7 Hz, 2 H), 3.05 (t, *J* = 7.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 165.7 (d, *J* = 253 Hz), 141.2, 133.3 (d, *J* = 2 Hz), 130.7 (d, *J* = 9 Hz), 128.60, 128.5 (d, *J* = 14 Hz), 126.2, 115.7 (d, *J* = 22 Hz), 40.4, 30.1. ESI-HRMS: *m/z* calcd for $C_{15}H_{14}OF$ $[M + H]^+$: 229.1029; found: 229.1030.

1-(4-Chlorophenyl)-3-phenylpropan-1-one (3bb)[2d]

Yield 84% (102.5 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.86 (m, 2 H), 7.42 (d, *J* = 8.5 Hz, 2 H), 7.31–7.20 (m, 5 H), 3.26 (dd, *J* = 10.0, 5.3 Hz, 2 H), 3.06 (dd, *J* = 10.0, 5.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0, 141.1, 139.5, 135.2, 129.5, 128.9, 128.,6 128.4, 126.2, 40.4, 30.1.

1-(4-Bromophenyl)-3-phenylpropan-1-one (3bc)[2d]

Yield 83% (119.5 mg), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.5 Hz, 2 H), 7.61 (d, *J* = 8.5 Hz, 2 H), 7.36–7.22 (m, 5 H), 3.29 (t, *J* = 7.7 Hz, 2 H), 3.09 (t, *J* = 7.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.2, 141.1, 135.6, 131.9, 129.6, 128.6, 128.4, 128.3, 126.3, 40.4, 30.1.

3-Phenyl-1-[4-(trifluoromethyl)phenyl]propan-1-one (3bd)[2d]

Yield 80% (111.2 mg), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.2 Hz, 2 H), 7.74 (d, *J* = 8.3 Hz, 2 H), 7.36–7.22 (m, 5 H), 3.35 (t, *J* = 7.6 Hz, 2 H), 3.11 (t, *J* = 7.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.2, 140.9, 139.5, 134.6 (q, *J* = 33 Hz), 128.6, 128.4, 128.4, 126.3, 125.7 (q, *J* = 4 Hz), 123.5 (q, *J* = 258 Hz), 40.8, 29.9.

1-(3-Bromo-4-fluorophenyl)-3-phenylpropan-1-one (3be)

Yield 87% (133.1 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (dd, *J* = 6.6, 2.1 Hz, 1 H), 7.92 (ddd, *J* = 8.5, 4.7, 2.1 Hz, 1 H), 7.36–7.30 (m, 2 H), 7.28–7.18 (m, 4 H), 3.28 (t, *J* = 7.6 Hz, 2 H), 3.09 (t, *J* = 7.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 162.0 (d, *J* = 244 Hz), 140.9, 134.4 (d, *J* = 3 Hz), 134.0 (d, *J* = 1 Hz), 129.2 (d, *J* = 8 Hz), 128.6, 128.4, 126.3, 116.7 (d, *J* = 23 Hz), 109.9 (d, *J* = 22 Hz), 40.4, 30.0. ESI-HRMS *m/z* calcd for $C_{15}H_{13}OBrF$ $[M + H]^+$: 307.0134; found: 307.0135.

1-(4-Nitrophenyl)-3-phenylpropan-1-one (3bf)[22c]

Yield 81% (103.3 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 8.8 Hz, 2 H), 8.11 (d, *J* = 8.8 Hz, 2 H), 7.36–7.30 (m, 2 H), 7.27 (dd, *J* = 11.1, 4.1 Hz, 3 H), 3.37 (t, *J* = 7.6 Hz, 2 H), 3.12 (t, *J* = 7.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.7, 150.3, 141.3, 140.6, 129.1, 128.7, 128.4, 126.4, 123.9, 41.0, 29.9.

3-Phenyl-1-(*p*-tolyl)propan-1-one (3bg)[2d]

Yield 90% (100.8 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.2 Hz, 2 H), 7.36–7.23 (m, 7 H), 3.34–3.28 (m, 2 H), 3.13–3.07 (m, 2 H), 2.44 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 143.9, 141.4, 134.4, 129.3, 128.6, 128.5, 128.2, 126.1, 40.4, 30.3, 21.7.

1-(4-Methoxyphenyl)-3-phenylpropan-1-one (3bh)[14]

Yield 92% (110.4 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 7.7, 1.7 Hz, 1 H), 7.51–7.46 (m, 1 H), 7.28 (dq, *J* = 21.7, 7.4 Hz, 5 H), 7.06–6.97 (m, 2 H), 3.91 (s, 3 H), 3.37–3.31 (m, 2 H), 3.09–3.03 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.8, 158.6, 141.8, 133.5, 130.4, 128.5, 128.4, 128.3, 125.9, 120.7, 111.5, 55.5, 45.5, 30.5.

3-Phenyl-1-(thiophen-2-yl)propan-1-one (3bi)[12b]

Yield 87% (94.0 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 3.8 Hz, 1 H), 7.65 (d, *J* = 4.9 Hz, 1 H), 7.36–7.27 (m, 4 H), 7.24 (t, *J* = 7.5 Hz, 1 H), 7.14 (t, *J* = 4.3 Hz, 1 H), 3.29–3.24 (m, 2 H), 3.13–3.08 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.2, 144.2, 141.0, 133.6, 131.9, 128.6, 128.5, 128.1, 126.3, 41.2, 30.4.

1-(Furan-2-yl)-3-phenylpropan-1-one (3bj)[12b]

Yield 81% (89.1 mg), pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 0.9 Hz, 1 H), 7.34–7.19 (m, 6 H), 6.54 (dd, *J* = 3.5, 1.6 Hz, 1 H), 3.21–3.16 (m, 2 H), 3.07 (dd, *J* = 9.7, 5.3 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.5, 152.7, 146.4, 141.0, 128.5, 128.4, 126.2, 117.1, 112.2, 40.2, 30.0.

1-(Naphthalen-1-yl)-3-phenylpropan-1-one (3bk)[14]

Yield 93% (120.9 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60 (d, *J* = 8.5 Hz, 1 H), 8.01 (d, *J* = 8.2 Hz, 1 H), 7.91 (d, *J* = 7.9 Hz, 1 H), 7.85 (d, *J* = 7.2 Hz, 1 H), 7.64–7.55 (m, 2 H), 7.50 (t, *J* = 7.7 Hz, 1 H), 7.31 (dq, *J* = 12.0, 7.3 Hz, 5 H), 3.42 (t, *J* = 7.7 Hz, 2 H), 3.18 (t, *J* = 7.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.6, 141.2, 136.0, 134.0, 132.6, 130.2, 128.6, 128.5, 128.5, 127.9, 127.5, 126.5, 126.2, 125.8, 124.4, 43.9, 30.6.

(*E*)-5-Phenyl-1-(2,6,6-trimethylcyclohex-2-en-1-yl)pent-1-en-3-one (3bl)

Yield 78% (110.0 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.18 (m, 7 H), 6.15 (d, *J* = 16.3 Hz, 1 H), 2.96 (td, *J* = 14.1, 6.9 Hz, 4 H), 2.08 (t, *J* = 6.0 Hz, 2 H), 1.76 (s, 3 H), 1.65 (d, *J* = 2.8 Hz, 1 H), 1.49 (d, *J* = 5.6 Hz, 2 H), 1.07 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.7, 142.5, 141.4, 136.2, 136.0, 130.5, 128.5, 128.4, 126.1, 42.2, 39.7, 34.1, 33.6, 30.4, 28.8, 21.8, 18.9. ESI-HRMS *m/z* calcd for $C_{20}H_{27}O$ [M + H]$^+$: 283.2062; found: 283.2064.

1,5-Diphenylpentan-3-one (3bm)[22d]

Yield 76% (90.4 mg), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (t, *J* = 7.4 Hz, 4 H), 7.22 (dd, *J* = 17.0, 7.3 Hz, 6 H), 2.93 (t, *J* = 7.6 Hz, 4 H), 2.75 (dd, *J* = 9.7, 5.5 Hz, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.2, 141.0, 128.5, 128.3, 126.1, 44.5, 29.8

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