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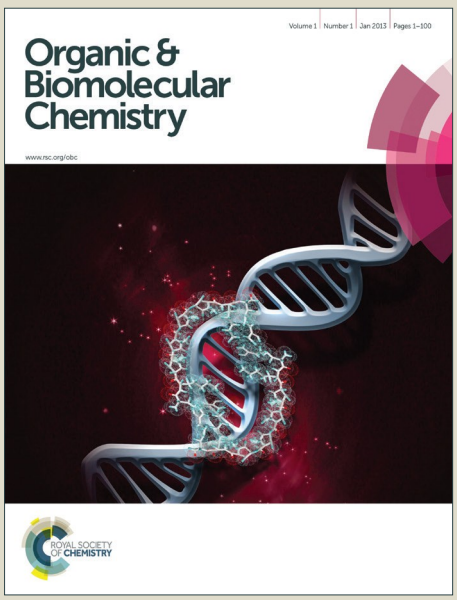

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ARTICLE

Decarboxylative Substitution of β-Keto Acids to Benzylic Alcohols Catalyzed by Molecular Iodine

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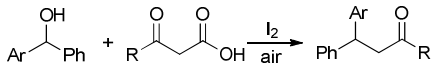
An efficient method for the molecular iodine catalyzed decarboxylative substitution of β-keto acids with benzylic alcohols under mild conditions has been dedcribed and the valuable α-functionalized ketones were obtained in good to excellent yields.

Introduction

The development of catalytic and mild carbon-carbon bond formations is of a paramount importance in the synthesis of fine chemicals, natural products and pharmaceuticals.[1] Recently, decarboxylative carbon allylation processes have been widely used for organic synthesis.[2] Among the myriad of reports devoted to this reaction, an important type of such reactions involves decarboxylative substitution of β-keto acids to benzyl alcohols or benzyl derivatives.[3] Indeed, benzyl alcohols are superior to benzyl derivatives since no modified substrates are involved.[4] In particular, the direct reaction between β-keto acids and benzyl alcohols are noteworthy, because only the water and CO_2 are generated as byproducts. As we know, only $FeCl_3$ has been reported so far to catalyze decarboxylative substitution to assemble the valuable α-functionalized ketones efficiently. [5-7] However, $FeCl_3$ as the catalyst often results in the residue of heavy metals in the products such as pharmaceuticals. Therefore, the development of a metal-free that could catalyze the decarboxylative substitution in broad substrate spectrum is highly desirable.

In the past decade, molecular iodine has attracted much attention in organic synthesis due to its high tolerance to air and moisture, as well as its inexpensive, less toxic, and environmentally friend characteristics.[8] Furthermore, recent developments on carbon-carbon bond forming reaction has demonstrated that molecular iodine would hold promise as an efficient Lewis acid catalyst.[9] We therefore believe that molecular iodine should be also a suitable catalyst for the decarboxylative substitution of β-keto acids to benzylic alcohols. Herein, we describe a concise decarboxylative substitution process of various β-keto acids with benzylic alcohols in the presence of catalytic amount iodine that proceeded in good to excellent yields (up to 96%) under mild conditions (Scheme 1).

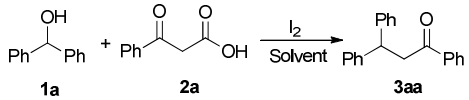


Scheme 1 Molecular iodine catalyzed decarboxylative substitution of β-keto acids with benzylic alcohols.

Results and discussion

We initiated our investigation by reacting benzhydrol **1a** with benzoylacetic acid **2a** catalyzed by I_2 at 60 °C. To determine the optimized reaction conditions, the effects of reaction solvent, temperature and catalyst loading on the reaction were examined (Table 1).

Table 1 Optimization of reaction conditions[a]



1a **2a** **3aa**

Entry	Solvent	Temp (°C)	Cat. (mol %)	Yield (%)[b]
1	CH_3CN	60	10	23
2	DCE	60	10	50
3	CH_3NO_2	60	10	76
4	THF	60	10	-
5	Toluene	60	10	-
6	CH_3NO_2	70	10	92
7	CH_3NO_2	80	10	92
8	CH_3NO_2	70	5	65
9	CH_3NO_2	70	-	-

[a] Reactions were carried out with **1a** (0.5 mmol), **2a** (0.6 mmol), I_2 (10 mol%) in 3 mL solvent for 2 h. [b] Isolated yield based on the amount of benzhydrol.

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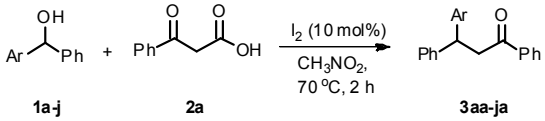
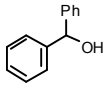
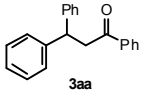
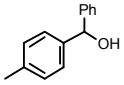
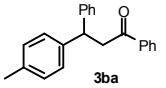
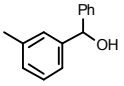
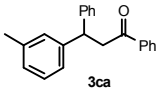
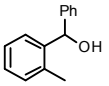
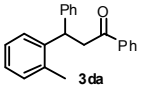
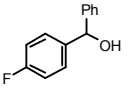
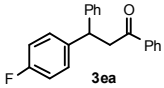
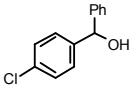
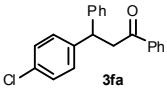
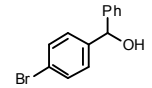
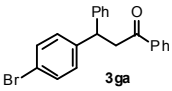
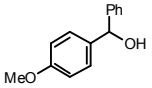
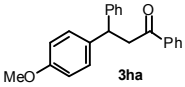
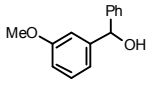
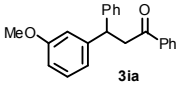
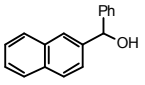
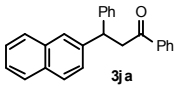
Table 2 Iodine-catalyzed decarboxylative substitution of benzoylacetic acid **2a** with benzhydryl alcohols **1a-j**[a]



1a-j **2a** **3aa-ja**

Entry	**1a-j**: Ar	**3aa-ja**	Yield (%)[b]
1		 **3aa**	92
2		 **3ba**	94
3		 **3ca**	91
4		 **3da**	94
5		 **3ea**	90
6		 **3fa**	93
7		 **3ga**	90
8		 **3ha**	96
9		 **3ia**	90
10		 **3ja**	93

[a] Reactions were carried out with **1a-j** (0.5 mmol), **2a** (0.6 mmol), I_2 (10 mol%) in 3 mL CH_3NO_2 at 70 °C for 2 h. [b] Isolated yield based on the amount of benzylic alcohol.

The results in Table 1 disclosed that the solvent showed a significant effect on the reaction. When CH_3CN, DCE and CH_3NO_2 were used as the solvent, the reaction proceeded smoothly (Table 1, entries 1, 2 and 3). And no decarboxylative substitution product was separated by use of THF or toluene as the solvent (Table 1, entries 4 and 5). It was found that CH_3NO_2 could offer the reaction in the highest yield (Table 1, entry 3). Thus, CH_3NO_2 was selected as an optimal reaction medium for subsequent condition optimization. To our satisfaction, product **3aa** was obtained in excellent yield (92%) by increasing the temperature to 70 °C (Table 1, entry 6). However, further promoting the reaction temperature didn't improve the reaction performance (Table 1, entry 7). Finally, lower product yield of 65% was obtained on decreasing the I_2 loading from 10 to 5 mol% under similar conditions and no reaction took place in the absence of I_2 (Table 1, entries 8 and 9).

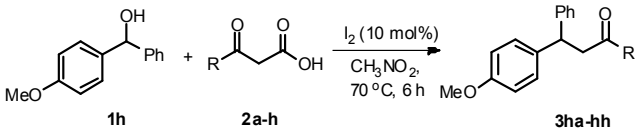
With the optimized conditions in hand, we carried out the investigation on the scope of the process with respect to benzylic alcohols (Table 2). We were pleased to find that the reaction worked efficiently for all benzylic alcohols substrates tested, with the desired products being obtained in excellent yields (up to 96%). The aromatic ring bearing electron-neutral groups with different substitution patterns were well tolerated (Table 2, entries 2-4). And the presence of F, Cl or Br at the para-position of the phenyl ring had no influence on the reactivity, affording the products in excellent yields (Table 2, entries 5-7). Indeed, it is noteworthy that a 4-methoxy group on aryl ring led to the best yield (Table 2, entry 8). Also, 2-naphthyl substituted substrate presented a suitable substrate for the reaction (Table 2, entry 10).

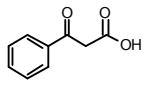
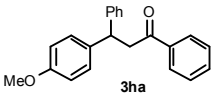
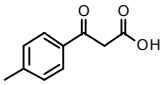
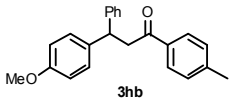
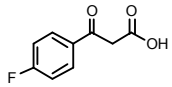
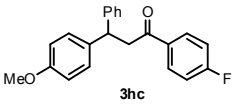
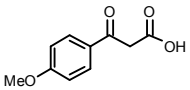
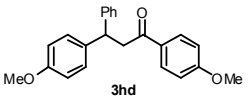
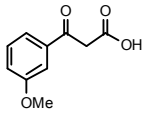
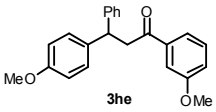
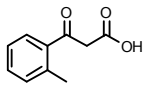
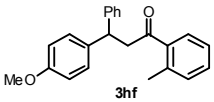
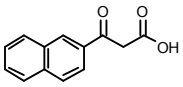
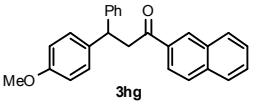
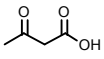
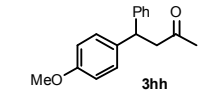
Encouraged by the success of benzylic alcohols, we next conducted the reactions of various β-keto acids with *p*-methoxy substituted substrate **1h**. The results are summarized in Table 3. Studies showed that the substituents in the phenyl ring of β-keto acids have a significant influence on the reactivity. The electron-rich groups still gave the desired product in excellent yields (Table 3, entries 4-5). However, an electron-withdrawing substituent such as fluorine was detrimental to the catalytic reaction with moderate reactivity (Table 3, entry 3). 2-naphthyl substituted **2g** presented a suitable substrate for the reaction (Table 3, entry 7). Furthermore, aliphatic substrate β-keto acid **2g** worked well, leading to the desired decarboxylative substitution product in excellent yield (Table 3, entry 8).

In addition, more benzylic alcohols and β-keto acids were employed to investigate of the present method for extension of the substrate scope. The results are summarized in Scheme 2. To our delight, cyclohexanone carboxylic acid **2i**, tetralone carboxylic acid **2j** and 2-thienone carboxylic acid **2k** gave the products **3ai**, **3aj** and **3ak** in very high yields (88%, 92% and 93%, respectively). And allylic benzylic alcohol **1k** underwent the reaction at room temperature to give the corresponding product **3kh** in high yield (90%). However, in comparison with allylic benzylic alcohol, the reaction with propargylic-benzylic alcohol **1l** gave lower yield. Unfortunately, the reaction failed when 2-cyclohexenol was employed in the system.

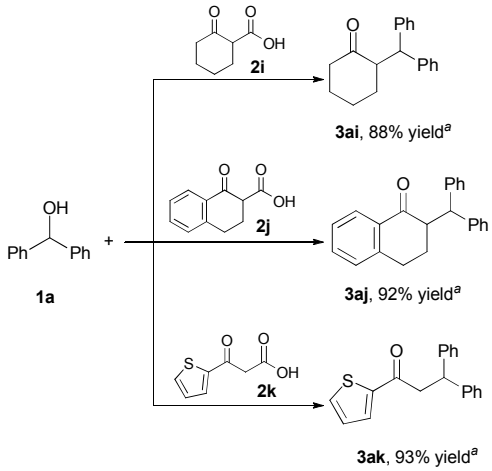
Based on the above experimental results, a possible reaction mechanism was proposed for this molecular iodine-catalyzed decarboxylative substitution, as depicted in Scheme 2. Benzhydrol **1a** is subjected to iodine-catalyzed carbon-oxygen bond cleavage to provide benzhydryl carbocation **A**.[10] Then, benzhydryl carbocation **A** could be attacked by benzoylacetic acid **2a** to afford β-keto acid intermediate **B** via carbon-carbon bond-formation. Consequent ketone product **3aa** was generated undergoes decarboxylation (Scheme 3).

Table 3 Iodine-catalyzed decarboxylative substitution of benzhydryl alcohol **1h** with benzoylacetic acids **2a-h** [a]

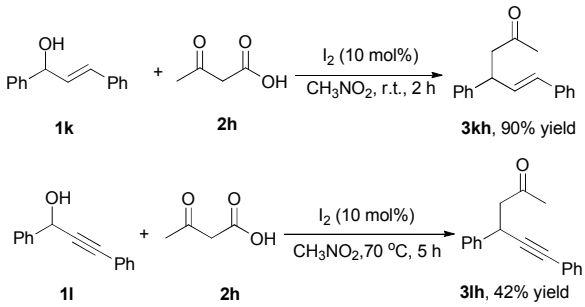


Entry	β-keto acid	Product	Yield (%)[b]
1		 3ha	96
2		 3hb	84
3		 3hc	75
4		 3hd	92
5		 3he	90
6		 3hf	86
7		 3hg	91
8		 3hh	87

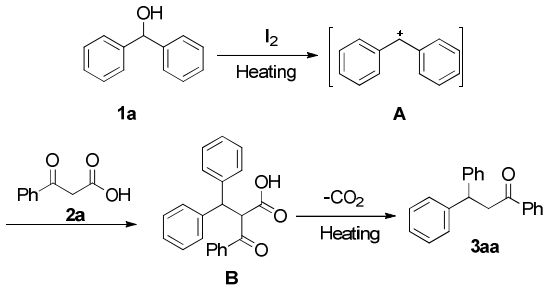
[a] Reactions were carried out with **1h** (0.5 mmol), **2a-h** (0.6 mmol), I_2 (10 mol%) in 3 mL CH_3NO_2 at 70 °C for 6 h. [b] Isolated yield based on the amount of benzylic alcohol.



[a] Reaction conditions: I_2 (10 mol%), CH_3NO_2,70 °C, 2 h.



Scheme 2 Substrate scope of benzylic alcohols and β-keto acids.



Scheme 3 Proposed reaction mechanism.

Conclusions

In summary, we have documented a molecular iodine-catalyzed decarboxylative substitution of β-keto acids with benzylic alcohols at 70 °C under atmospheric and moisture conditions that proceeded in good to excellent yields. The results have disclosed that the present catalytic system showed broad generality with regard to β-keto acids nucleophiles, in which benzylic alcohols containing electron-withdrawing and donating, and sterically demanding group also proved to be suitable substrates. Studies on mechanistic investigations as well as the extension of the protocol to other carbon nucleophiles are in progress.

Experimental

General Information

All reactions were carried out under air. Solvents were purified by standard procedure before use. Commercial solvents were used without further purification. Flash chromatography was performed on silica gel 60 (40-63μm, 60Å). Thin layer chromatography (TLC) was performed on glass plates coated with silica gel 60 with F254 indicator. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker 600 MHz spectrometer. Chemical shifts for protons are reported in

parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.26). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker 151 MHz spectrometer. Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$ = δ 77.07). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. Benzhydryl alcohols [11] and β-keto acids [12] were synthesized according to reported procedures. Electrospray ionization high-resolution mass spectra (ESI-HRMS) were recorded on a Bruke P-SIMS-Gly FT-ICR mass spectrometer.

Typical procedure for I_2-catalyzed decarboxylative substitution of β-keto acids with benzylic alcohols.

A 25 mL Schlenk flask, fitted with a reflux condenser, I_2 (0.05 mmol, 10 mol %), benzylic alcohol **1** (0.5 mmol), β-keto acid **2** (0.6 mmol) and 3 mL CH_3NO_2. The mixture was heated at 70 °C for 2-6 h, cooled down, and treated with aqueous $Na_2S_2O_3$, then extracted three times with ethyl acetate. The combined organic extracts were dried with anhydrous Na_2SO_4. After concentration under reduced pressure, the resulting residue was purified by column chromatography (SiO_2; Hexane/EtOAc, 20:1) to give propargylic alkylation product **3**.

1,3,3-triphenylpropan-1-one (3aa).[13] White solid, 92% yield, m.p. = 93.2-94.2 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.8 Hz, 2 H), 7.55 (t, *J* = 7.3 Hz, 1 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.28 (s, 4 H), 7.27 (s, 4 H),7.18 (m, 2 H), 4.84 (t, *J* = 7.2 Hz, 1 H), 3.75 (d, *J* = 7.3 Hz, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.0, 144.2, 137.1, 133.1, 128.7, 128.6, 128.1, 127.9, 126.4, 46.0, 44.8.

1,3-diphenyl-3-(*p*-tolyl)propan-1-one (3ba).[13] White solid, 94% yield, m.p. = 95.5-96.5 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.7 Hz, 2 H), 7.55 (t, *J* = 7.0 Hz, 1 H), 7.44 (t, *J* = 7.2 Hz, 2 H), 7.27-7.26 (m, 4 H), 7.16 (d, *J* = 5.8 Hz, 3 H), 7.09 (d, *J* = 6.9 Hz, 2 H), 4.80 (t, *J* = 6.9 Hz, 1 H), 3.73 (d, *J* = 7.1 Hz, 2 H), 2.29 (s, 3 H). 13C NMR (151 MHz, CDCl3) δ 198.1, 144.5, 141.2, 137.2, 135.9, 133.1, 129.3, 128.6, 128.6, 128.1, 127.9, 127.8,126.4, 45.6, 44.9, 21.1.

1,3-diphenyl-3-(*m*-tolyl)propan-1-one (3ca).[14] White solid, 91% yield, m.p. = 72.5-73.2 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.7 Hz, 2 H), 7.55 (t, *J* = 7.0 Hz, 1 H), 7.44 (t, *J* = 7.2 Hz, 2 H), ^1H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.5 Hz, 2 H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.26-7.25 (m, 4 H), 7.15 (t, *J* = 7.3 Hz, 2 H), 7.06 (d, *J* = 7.8 Hz, 2 H), 6.98 (d, *J* = 7.3 Hz, 1 H), 4.78 (t, *J* = 7.2 Hz, 1 H), 3.72 (dd, *J* = 7.2, 2.1 Hz, 2 H), 2.29 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.1, 144.3, 144.2, 138.2, 137.2, 133.1, 128.8, 128.6, 128.6,128.5, 128.1, 127.9, 127.3, 126.4, 124.8, 45.99, 44.81, 21.58.

1,3-diphenyl-3-(*o*-tolyl)propan-1-one (3da).[13] White solid, 94% yield, m.p. = 89.2-90.2 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.4 Hz, 2 H), 7.54 (t, *J* = 7.4 Hz, 1 H), 7.43 (t, *J* = 7.7 Hz, 2 H), 7.26-7.20 (m, 5 H), 7.17-7.10 (m, 4 H), 5.02 (t, *J* = 7.2 Hz, 1 H), 3.71 (qd, *J* = 17.2, 7.3 Hz, 2 H), 2.33 (s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.1, 143.8, 141.9, 137.2, 136.5, 133.1, 130.8, 128.6, 128.5, 128.1, 128.1, 126.4, 126.3, 126.1, 45.1, 41.9, 20.0.

3-(4-fluorophenyl)-1,3-diphenylpropan-1-one (3ea).[13] White solid, 90% yield, m.p. = 95.3-97.2 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.4, 1.2 Hz, 2 H), 7.58-7.55 (m, 1 H), 7.47-7.44 (m, 2 H), 7.29 -7.22 (m, 7 H), 6.98- 6.95 (m, 2 H), 4.83 (t, *J* = 7.3 Hz, 1 H), 3.76-3.69 (m, 2 H).^{13}C NMR (151 MHz, $CDCl_3$) δ 197.9, 161.4 (d, *J* = 244.7 Hz), 144.1, 139.9, 137.1, 133.2, 129.4, 128.7, 128.1 (d, *J* = 2.9 Hz), 127.8, 127.7, 126.6, 115.4 (d, *J* = 21.3 Hz), 45.2, 44.8.

3-(4-chlorophenyl)-1,3-diphenylpropan-1-one (3fa).[14] White solid, 93% yield, m.p. = 85.2-86.0 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.6 Hz, 2 H), 7.55 (t, *J* = 7.3 Hz, 1 H), 7.44 (t, *J* = 7.7 Hz, 2 H), 7.29-7.17 (m, 9H), 4.80 (t, *J* = 7.2 Hz, 1 H), 3.70 (dd, *J* = 7.2, 4.4 Hz, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.7, 143.8, 142.7, 137.0, 133.3, 132.2, 129.3, 128.7, 128.7, 128.1, 127.8, 126.7, 45.3, 44.6.

3-(4-bromophenyl)-1,3-diphenylpropan-1-one (3ga).[15] White solid, 90% yield, m.p. = 101.1-102.1 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.9 Hz, 2 H), 7.56 (t, *J* = 7.1 Hz, 1 H), 7.45 (t, *J* = 7.6 Hz, 2 H), 7.38 (d, *J* = 8.1 Hz, 2 H), 7.28 (t, *J* = 7.4 Hz, 2 H), 7.23 (d, *J* = 7.7 Hz, 2 H), 7.19 (t, *J* = 7.3 Hz, 1 H), 7.14 (d, *J* = 8.1 Hz, 2 H), 4.79 (t, *J* = 7.2 Hz, 1 H), 3.72-3.70 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.7, 143.7, 143.27, 136.97, 133.3, 131.7, 129.7, 128.7, 128.7, 128.1, 127.8, 126.7, 120.3, 45.4, 44.5.

3-(4-methoxyphenyl)-1,3-diphenylpropan-1-one(3ha).[13] White solid, 96% yield, m.p. = 91.5-92.5 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.3, 1.1 Hz, 2 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.44 (t, *J* = 7.8 Hz, 2 H), 7.28-7.25 (m, 4 H), 7.19-7.17 (m, 3 H), 6.82-6.81 (m, 2 H), 4.79 (t, *J* = 7.3 Hz, 1 H), 3.76 (s, 3 H), 3.71 (dd, *J* = 7.3, 1.7 Hz, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.2, 158.1, 144.6, 137.2, 136.3, 133.1, 128.8, 128.7, 128.6, 128.1, 127.8, 126.4, 114.0, 55.3, 45.2, 45.0.

3-(3-methoxyphenyl)-1,3-diphenylpropan-1-one (3ia).[14] White solid, 90% yield, m.p. = 85.1-86.5 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.2 Hz, 2 H), 7.53 (d, *J* = 6.8 Hz, 1 H), 7.43 (t, *J* = 7.1 Hz, 2 H), 7.26 (s, 4H), 7.20-7.17 (m, 2H), 6.86 (d, *J* = 7.0 Hz, 1 H), 6.81 (s, 1 H), 6.71 (d, *J* = 7.4 Hz, 1H), 4.80 (t, *J* = 6.5 Hz, 1H), 3.74-3.71 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.0, 159.8, 145.9, 144.1, 137.1, 133.1, 129.6, 128.7, 128.1, 127.9, 126.5, 120.3, 114.2, 111.4, 55.2, 46.0, 44.7.

3-(naphthalen-2-yl)-1,3-diphenylpropan-1-one (3ja).[14] White solid, 93% yield, m.p. = 125.1-126.1 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.4 Hz, 2 H), 7.76-7.71 (m, 4 H), 7.54 (t, *J* = 7.4 Hz, 1 H), 7.45-7.42 (m, 5H), 7.30-7.25 (m, 4 H), 7.17 (t, *J* = 7.2 Hz, 1 H), 5.00 (t, *J* = 7.2 Hz, 1H), 3.88-3.79 (m, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.0, 144.0, 141.6, 137.1, 133.5, 133.1, 132.2, 128.6, 128.6, 128.3, 128.1, 128.0, 127.8, 127.6, 126.8, 126.5, 126.0, 125.8, 125.6, 46.0, 44.6.

3-(4-methoxyphenyl)-3-phenyl-1-(*p*-tolyl)propan-1-one (3hb). White solid, 84% yield, m.p. = 80.7-81.7 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2 H), 7.26-7.22 (m, 6 H), 7.18-7.15 (m, 3 H), 6.80 (d, *J* = 8.7 Hz, 2 H), 4.77 (t, *J* = 7.3 Hz, 1 H), 3.75 (s, 3 H), 3.67 (dd, *J* = 7.3, 2.0 Hz, 2 H), 2.40 (s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.8, 158.0, 144.6, 143.9, 136.4, 134.7, 129.3, 128.8, 128.5, 128.2, 127.8, 126.3, 113.9, 55.2, 45.2, 44.8, 21.6. HRMS calc. for $[M-H]^-$ $C_{23}H_{21}O_2$: 329.1542, found: 329.1532.

1-(4-fluorophenyl)-3-(4-methoxyphenyl)-3-phenylpropan-1-one (3hc). White solid, 75% yield, m.p. = 75.5-76.5 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.8, 5.4 Hz, 2 H), 7.28-7.23 (m, 2

H), 7.24 (d, *J* = 6.8 Hz, 2 H), 7.18-7.08 (m, 3 H), 7.10 (t, *J* = 8.6 Hz, 2 H), 6.80 (d, *J* = 8.7 Hz, 2 H), 4.75 (t, *J* = 7.3 Hz, 1 H), 3.75 (s, 3 H), 3.66 (dd, *J* = 7.3, 1.3 Hz, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.6, 165.7 (d, *J* = 254.6 Hz), 158.1, 144.4, 136.1, 133.5, 130.7 (d, *J* = 9.3 Hz), 128.75, 128.59, 127.72, 126.38, 115.7 (d, *J* = 21.9 Hz), 113.98, 55.23, 45.25, 44.85. HRMS calc. for $[M+H]^+$ $C_{22}H_{20}FO_2$: 335.1447, found: 335.1451.

1,3-bis(4-methoxyphenyl)-3-phenylpropan-1-one(3hd).[14] White solid, 92% yield, m.p. = 88.4-89.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 2 H), 7.27-7.24 (m, 4 H), 7.17-7.14 (m, 3 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 6.80 (d, *J* = 8.6 Hz, 2 H), 4.76 (t, *J* = 7.3 Hz, 1 H), 3.85 (s, 3 H), 3.75 (s, 3 H), 3.64 (dd, *J* = 7.3, 2.0 Hz, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.7, 163.5, 158.0, 144.7, 136.4, 130.4, 130.2, 128.8, 128.5, 127.8, 126.3, 113.9, 113.7, 55.5, 55.2, 45.3.

1-(3-methoxyphenyl)-3-(4-methoxyphenyl)-3-phenylpropan-1-one (3he). White solid, 90% yield, m.p. = 66.5-68.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 1 H), 7.43 (s, 1 H), 7.34 (t, *J* = 7.9 Hz, 1 H), 7.28- 7.24 (m, 4 H), 7.18-7.15 (m, 3 H), 7.09 (dd, *J* = 8.1, 2.2 Hz, 1 H), 6.81 (d, *J* = 8.6 Hz, 2 H), 4.77 (t, *J* = 7.3 Hz, 1 H), 3.82 (s, 3 H), 3.75 (s, 3 H), 3.69 (dd, *J* = 7.3, 1.4 Hz, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.0, 159.9, 158.1, 144.6, 138.5, 136.3, 129.6, 128.8, 128.6, 127.8), 126.3, 120.7, 119.7, 114.0, 112.3, 55.5, 55.2, 45.3, 45.1. HRMS calc. for $[M+Na]^+$ $C_{23}H_{22}NaO_3$: 369.1467, found: 369.1458.

3-(4-methoxyphenyl)-3-phenyl-1-(*o*-tolyl)propan-1-one (3hf). White solid, 86% yield, m.p. = 75.2-76.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.7, 1.0 Hz, 1 H), 7.34 (td, *J* = 7.5, 1.2 Hz, 1 H), 7.27-7.14 (m, 9 H), 6.81-6.79 (m, 2 H), 4.68 (t, *J* = 7.7 Hz, 1 H), 3.76 (s, 3 H), 3.60 (d, *J* = 7.7 Hz, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 202.8, 158.1, 144.3, 138.5, 137.9, 136.0, 131.8, 131.1, 128.8, 128.6, 127.9, 127.8, 126.4, 125.6, 114.0, 55.3, 48.1, 45.8, 20.7. HRMS calc. for $[M+Na]^+$ $C_{23}H_{22}NaO_2$: 353.1517，found: 353.1524.

3-(4-methoxyphenyl)-1-(naphthalen-2-yl)-3-phenylpropan-1-one (3hg).[14] White solid, 91% yield, m.p. = 111.3-112.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 1 H), 7.94 (d, *J* = 8.1 Hz, 1 H), 7.87 (d, *J* = 8.5 Hz, 2 H), 7.59 (t, *J* = 7.2 Hz, 1 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.28 (s, 4 H), 7.21 (d, *J* = 8.3 Hz, 2 H), 7.17 (s, 1 H), 6.82 (d, *J* = 8.1 Hz, 2 H), 4.84 (t, *J* = 7.1 Hz, 1 H), 3.84 (d, *J* = 7.1 Hz, 2 H), 3.75 (s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.1, 158.1, 144.6, 136.3, 135.6, 134.5, 132.5, 129.7, 129.6, 128.8, 128.6, 128.5, 127.8, 126.8, 126.4, 123.9, 114.0, 55.23, 45.36, 45.05.

4-(4-methoxyphenyl)-4-phenylbutan-2-one (3hh).[5a] White solid, 87% yield, m.p. = 58.0-59.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27-7.24 (m, 2 H), 7.20 (d, *J* = 7.1 Hz, 2 H), 7.18-7.11 (m, 3 H), 6.82-6.80(m, 2 H), 4.53 (t, *J* = 7.6 Hz, 1 H), 3.75 (s, 3 H), 3.14 (d, *J* = 7.6 Hz, 2 H), 2.06 (s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 207.1, 158.1, 144.3, 136.0, 128.7, 128.6, 127.6, 126.4, 114.0, 55.2, 49.9, 45.3, 30.7.

2-benzhydrylcyclohexanone (3ai).[5a] White solid, 88% yield, m.p. = 104.0-105.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28-7.20 (m, 8 H), 7.16-7.10 (m, 2 H), 4.31 (d, *J* = 10.8 Hz, 1 H), 3.35 (td, *J* = 10.5, 3.9 Hz, 1 H), 2.42-2.34 (m, 2 H), 2.04-2.02 (m, 1 H), 1.85-1.82 (m, 2 H), 1.78-1.73(m, 1 H), 1.68-1.62 (m, 1 H), 1.43-1.36 (m, 1 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.8, 143.4, 142.6, 128.1, 127.9, 127.9, 127.1, 125.9, 125.6, 54.4, 50.5, 42.1, 33.0, 28.7, 24.1.

2-benzhydryl-3,4-dihydronaphthalen-1(2H)-one (3aj).[5a] White solid, 92% yield, m.p. = 129.7-130.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.9 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 1 H), 7.29-7.26 (m, 9 H), 7.22 (d, *J* = 7.7 Hz, 1 H), 7.19-7.16 (m, 2 H), 4.69-4.67 (m, 1 H), 3.50-3.46 (m, 1 H), 3.05-2.94 (m, 2 H), 2.17-2.14(m, 1 H), 1.90-1.84(m, 1 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.5, 142.9, 132.7, 128.3, 128.2, 128.0, 127.9, 127.5, 127.2, 126.2, 125.9, 125.8, 50.9, 49.5, 27.4, 26.4.

3,3-diphenyl-1-(thiophen-2-yl)propan-1-one (3ak).[5a] White solid, 93% yield, m.p. = 148.0-149.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (d, *J* = 3.8 Hz, 1 H), 7.59 (d, *J* = 4.9 Hz, 1 H), 7.26 (dd, *J* = 8.1, 4.0 Hz, 8 H), 7.18-7.15 (m, 2 H), 7.10-7.08 (m, 1 H), 4.81 (t, *J* = 7.4 Hz, 1 H), 3.65 (dd, *J* = 7.4, 1.1 Hz, 2 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.4, 143.4, 133.2, 131.3, 128.1, 127.6, 127.4, 126.0, 45.6, 45.0.

(*E*)-4,6-diphenylhex-5-en-2-one (3kh).[5a] Colorless oil, 90% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32-7.30 (m, 4 H), 7.28-7.24 (m, 4 H), 7.23-7.17 (m, 2 H), 6.38 (d, *J* = 15.9 Hz, 1 H), 6.32 (ddd, *J* = 15.9, 6.8, 1.9 Hz, 1 H), 4.08 (q, *J* = 7.1 Hz, 1 H), 2.98-2.90 (m, 2 H), 2.10 (s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.4, 142.5, 136.6, 131.9, 129.5, 128.2, 128.0, 127.2, 126.8, 126.2, 125.8, 48.9, 43.5, 30.3.

4,6-diphenylhex-5-yn-2-one (3lh).[5a] Yellow oil, 42% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 1.2 Hz, 1 H), 7.44 (d, *J* = 0.6 Hz, 1 H), 7.43-7.40 (m, 2 H), 7.35-7.33 (m, 2 H), 7.29-7.27 (m, 3H), 7.26-7.24 (m, 1 H), 4.41 (dd, *J* = 8.1, 6.3 Hz, 1 H), 3.07 (dd, *J* = 16.4, 8.2 Hz, 1 H), 2.89 (dd, *J* = 16.4, 6.2 Hz, 1 H), 2.17 (s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 205.3, 131.2, 128.2, 127.7, 127.5, 127.0, 126.6, 89.9, 82.8, 51.4, 33.1, 30.2.

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