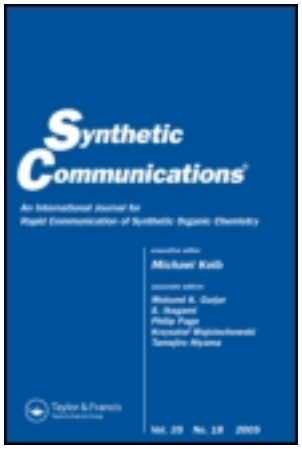

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Highly Efficient One-Pot, Three-Component Synthesis of β-Aminoketones Catalyzed by $Fe(O_2CCF_3)_3$

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HIGHLY EFFICIENT ONE-POT, THREE-COMPONENT SYNTHESIS OF β-AMINOKETONES CATALYZED BY $Fe(O_2CCF_3)_3$

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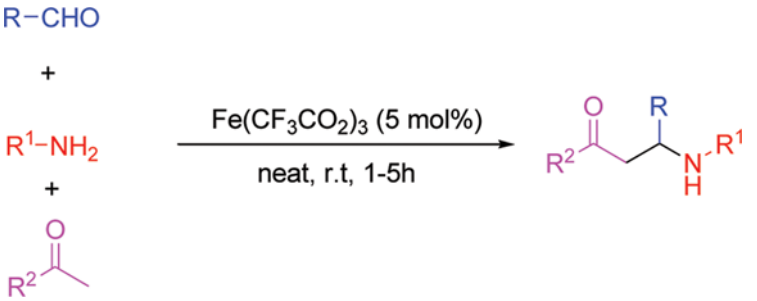
GRAPHICAL ABSTRACT



Abstract *A highly efficient one-pot, three-component synthesis of* β*-aminoketones was demonstrated using the cost-effective, noncorrosive, and easily available* $Fe(O_2CCF_3)_3$ *as a catalyst for the first time. The method can be employed to synthesize a wide range of target compounds and to introduce different functional groups into the* β*-aminoketone skeleton. Additionally, the method consistently has the advantages of good yields, short reaction time, and simply experimental workup procedure, which makes it a useful process for the synthesis of functionalized* β*-aminoketones.*

Keywords β-Aminoketones; iron(III) trifluoroacetate; three-component reaction

INTRODUCTION

β-Aminoketones represent an important class of compounds because of their significant applications in of biological activities[1] and as key intermediates for manufacturing pharmaceuticals and natural products including β-amino alcohols, β-amino acids, β-lactams, and aminocyclopropanols.[2,3] Owing to these significant properties and functions, the development of effective methods to construct this type of compound has been attracting considerable attention. Generally, β-aminoketones

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can be prepared by Mannich reaction in the presence of a suitable catalyst such as organobismuth(III) perfluorooctanesulfonate,[4] $BiCl_3$,[5] sulfamic acid,[6] functionalized ionic liquid,[7] $ZrOCl_2$,[8] polymer-supported $Yb(OTf)_3$,[9] and K_2CO_3,[10] Moreover, the modified Mannich-type reactions from imines and ketones,[11,12] imines and enolate derivatives,[13] or coupling reactions of amides and vinyl Grinard reagents provide new access to functionalized β-aminoketones.[14] However, many of these reported methods suffer from the drawbacks such as unsatisfactory yields, prolonged reaction time, the use of not readily available starting materials, or expensive or toxic catalysts. Therefore, the search for an effective catalytic process along with eco-compatible merit for the availability of β-aminoketones is of great importance. In recent years, iron, a rising star in catalysis, has attracted much attention. It was associated with sustainable chemistry and has notable advantages such as high abundance in nature, easy availability, and environmental friendliness.[15,16] Iron(III) trifluoroacetate was found to be a cost-effective, noncorrosive, crystalline Lews acid with outstanding physical stability.[17,18] We therefore investigate its new catalytic applications in the formation of carbon–carbon and carbon–heteroatom bonds. Hereby, we report a highly efficient one-pot, direct, three-component synthesis of β-aminoketone **4** and **5** via iron(III) trifluoroacetate–catalyzed coupling reaction of aldehyde **1**, amine **2**, and ketone **3** under mild reaction conditions [Eq. (1)].

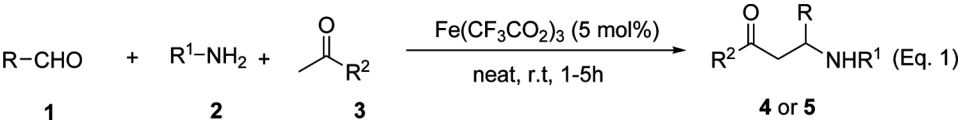
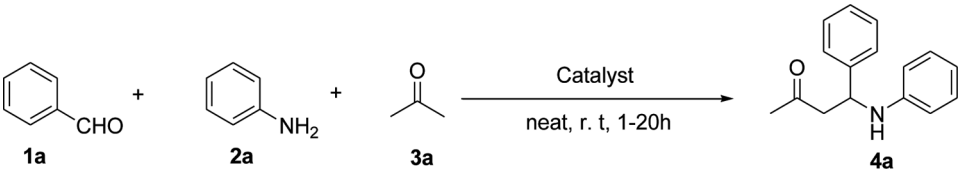


Table 1. Screening suitable catalyst and catalytic loading for the synthesis of **4a**[a]

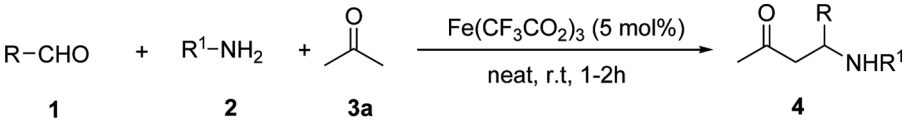


Entry	Catalyst	Reaction time (h)	Catalyst loading (mol%)	**4a** yields (%)[b]
1	$FeCl_3$	20	10	17
2	$Fe_2(SO_4)_3$	20	10	10
3	$ZnCl_2$	20	10	47
4	NH_2SO_3H	2	10	90
5	$Fe(O_2CCF_3)_3$	1	10	93
6	$Fe(O_2CCF_3)_3$	1	5	90
7	$Fe(O_2CCF_3)_3$	20	0	0

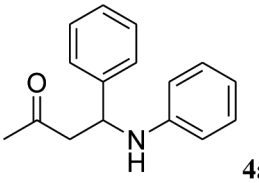
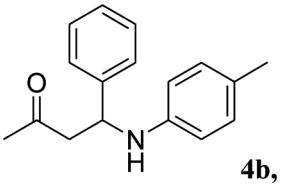
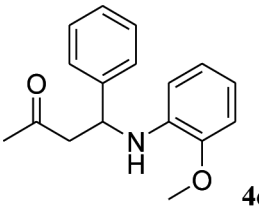
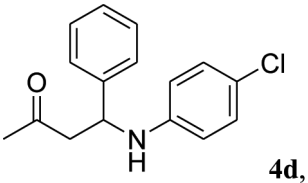
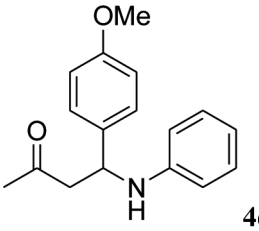
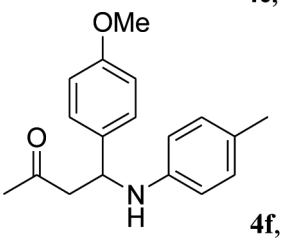
[a]Reaction conditions: Unless otherwise stated, benzaldehyde **1a** (1.1 mmol, 106 mg), aniline **2a** (1 mmol, 93 mg), and **3a** (1 mL) along with different catalysts were stirred in a Schlenk tube at room temperature for the appropriate reaction time according to Table 1.

[b]Isolated yields.

Table 2. $Fe(O_2CCF_3)_3$-catalyzed one-pot, three-component synthesis of 1-methy-β-aminoketones[a]

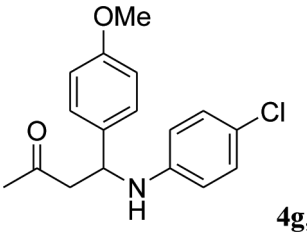
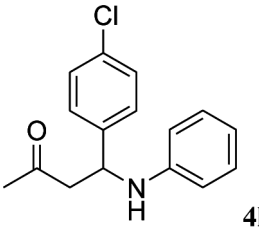
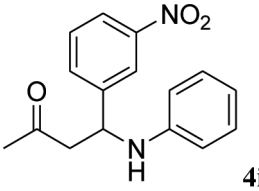
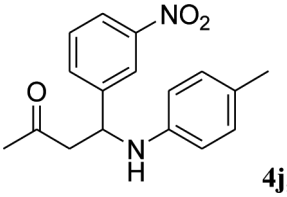
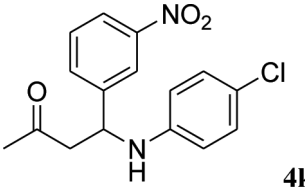
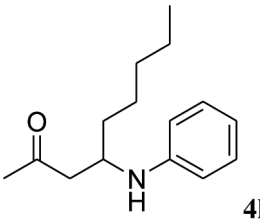


1 2 3a 4

Entry	Aldehyde **1**	Amine **2**	Time (h)	**4** yields (%)[b]
1	**1a:** R=Ph	**2a:** R^1 = Ph	2	 **4a,** 90
2	**1a:** R=Ph	**2b:** R^1 = 4-CH_3 C_6H_4	1.5	 **4b,** 92
3	**1a:** R=Ph	**2c:** R^1 = 2-OCH_3 C_6H_4	1.5	 **4c,** 86
4	**1a:** R=Ph	**2d:** R^1 = 4-Cl C_6H_4	2	 **4d**, 90
5	**1b:** R = 4-OCH_3 C_6H_4	**2a:** R^1 = Ph	2	 **4e**, 93
6	**1b:** R = 4-OCH_3 C_6H_4	**2b:** R^1 = 4-CH_3 C_6H_4	1.5	 **4f**, 96

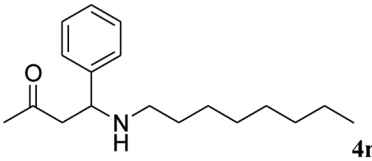
(*Continued*)

Table 2. Continued

Entry	Aldehyde **1**	Amine **2**	Time (h)	**4** yields (%)[b]
7	**1b:** R = 4-OCH_3 C_6H_4	**2d:** R^1 = 4-Cl C_6H_4	2	 **4g**, 96
8	**1c:** R = 4-ClC_6H_4	**2a:** R^1 = Ph	1.5	 **4h**, 86
9	**1d:** R = 3-NO_2 C_6H_4	**2a:** R^1 = Ph	1	 **4i**, 80
10	**1d:** R = 3-NO_2 C_6H_4	**2b:** R^1 = 4-$CH_3C_6H_4$	1	 **4j**, 85
11	**1d:** R = 3-NO_2 C_6H_4	**2d:** R^1 = 4-Cl C_6H_4	1.5	 **4k**, 82
12	**1e:** R=$CH_3(CH_2)_4$	**2a:** R^1 = Ph	2	 **4l**, 71

(*Continued*)

Table 2. Continued

Entry	Aldehyde **1**	Amine **2**	Time (h)	**4** yields (%)[b]
13	**1a:** R=Ph	**2e:** R=$CH_3(CH_2)_7$	2	 **4m**, 73
14	**1e:** R=$CH_3(CH_2)_4$	**2e:** R=$CH_3(CH_2)_7$	2	—

[a]Reaction conditions: The mixture of $Fe(O_2CCF_3)_3$ (0.05 mmol, 19.8 mg), aldehyde **1** (1.1 mmol), amine **2** (1 mmol), and acetone **3a** (1 mL) was stirred in a schlenk tube at room temperature for appropriate reaction time according to Table 2.

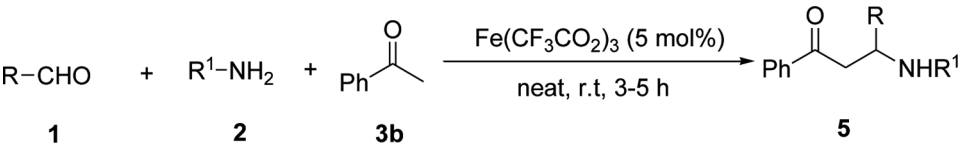
[b]Isolated yields.

[c]Expected product was not found.

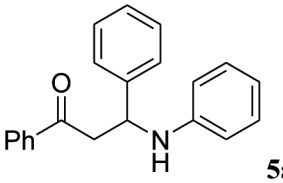
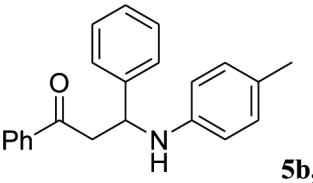
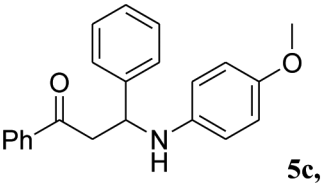
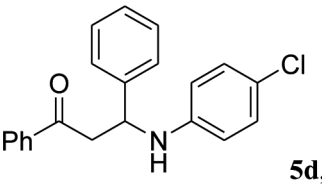
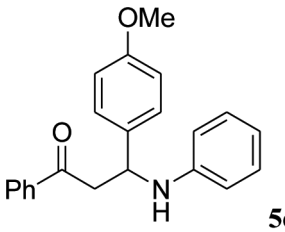
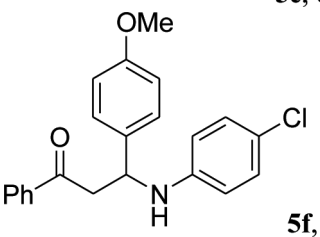
To establish an effective conversion system, the synthesis of 4-phenyl-4-(phenylamino)butan-2-one **4a** from benzaldehyde **1a** (1.1 mmol), aniline **2a** (1 mmol), and acetone **3a** (1 mL) was chosen as a model reaction to evaluate the catalytic activities of several Lewis acids and sulfamic acid. Initially, we carried out the reaction at room temperature (rt) for 20 h by using 10 mol% of $FeCl_3$ as the catalyst, and a 17% isolated yield of **4a** was obtained (Table 1, entry 1). Using 10 mol% of $Fe_2(SO_4)_3$, $ZnCl_2$, NH_2SO_3H, and $Fe(O_2CCF_3)_3$ resulted in 10%, 47%, 90%, and 93% isolated yields, respectively (Table 1, entries 2–5). Clearly, $Fe(O_2CCF_3)_3$ showed the best activity for the formation of **4a** in the shortest reaction time. Decreasing the catalyst loading from 10 mol% to 5 mol% did not lead to a significantly decreased yield (Table 1, entry 6). Thus, 5 mol% of $Fe(O_2CCF_3)_3$ is sufficient to promote the reaction. The reaction under catalyst-free conditions failed to afford the expected product even after prolonged reaction time (20 h) (Table 1, entry 7). Based on these results, the optimized reaction conditions can be summarized as 5 mol% of $Fe(O_2CCF_3)_3$ catalyst, neat reaction conditions, and room temperature.

With the best reaction conditions in hand, we then investigated the generality of this synthetic protocol. A variety of aldehydes **1**, amines **2**, and acetone **3a** were employed for the formation of 1-methly-β-aminoketone **4**. As shown in Table 2, all the reactions proceeded smoothly and afforded the expected products in good to excellent isolated yields (Table 1, from 71% to 96%). It was found that electronic effects of substituents on the benzene ring of arylaldehydes and arylamines were quite effective on the reactions. The arylaldehyde **1** tolerating an electron-withdrawing group (such as $-Cl$, $-NO_2$) or arylamine **2** bearing an electron-releasing groups (such as $-OCH_3$, $-CH_3$) resulted in relatively faster reaction and completed the conversion of starting materials in 1.5 h (Table 2, entries 2, 3, 6, and 8–11), which could be attributed to easy formation of imine intermediates according to the Mannich reaction mechanism.[10–12] It is noteworthy that substrate of 4-methoxybenzaldehyde (Table 2, entries 5–7) gave greater product yields compared to 3-nitrobenzaldehyde (Table 2, entries 9–11), and the result can be explained as follows: An arylaldehyde bearing an electron-withdrawing group ($-NO_2$) could decrease the stability of the final coupling product,

Table 3. $Fe(O_2CCF_3)_3$-catalyzed one-pot, three-component synthesis of 1-phenyl-β-aminoketones[a]

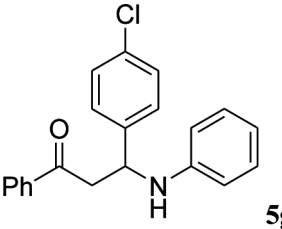
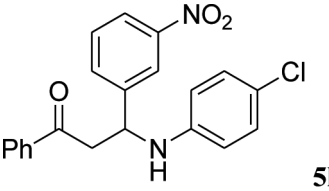
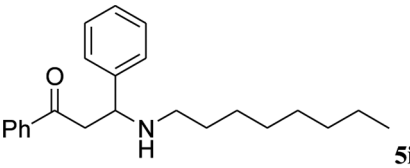
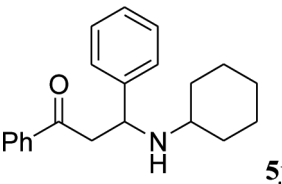
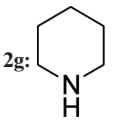
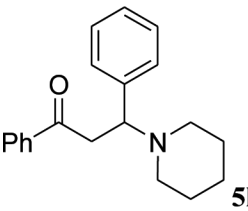


1 2 3b 5

Entry	Aldehyde **1**	Amine **2**	Time (h)	**4** yields (%)[b]
1	**1a:** R=Ph	**2a:** R^1 = Ph	3	 **5a,** 86
2	**1a:** R=Ph	**2b:** R^1 = 4-CH_3 C_6H_4	3	 **5b,** 80
3	**1a:** R=Ph	**2c:** R^1 = 4-O $CH_3C_6H_4$	3	 **5c,** 85
4	**1a:** R=Ph	**2d:** R^1 = 4-Cl C_6H_4	5	 **5d**, 95
5	**1b:** R = 4-OCH_3 C_6H_4	**2a:** R^1 = Ph	3	 **5e**, 83
6	**1b:** R = 4-OCH_3 C_6H_4	**2d:** R^1 = 4-Cl C_6H_4	4	 **5f**, 90

(*Continued*)

Table 3. Continued

Entry	Aldehyde **1**	Amine **2**	Time (h)	**4** yields (%)[b]
7	**1c:** R = 4-ClC_6H_4	**2a:** R^1 = Ph	3	 **5g**, 86
8	**1d:** R = 3-NO_2 C_6H_4	**2d:** R^1 = 4-Cl C_6H_4	4	 **5h**, 70
9	**1a:** R=Ph	**2e:** R=CH_3 $(CH_2)_7$	3	 **5i**, 79
10	**1a:** R=Ph	**2f:** R=C_6H_{11}	3	 **5j**, 71
11	**1a:** R=Ph	**2g:** 	3	 **5k**, 67

[a]Reaction conditions: The mixture of $Fe(O_2CCF_3)_3$ (0.05 mmol, 19.8 mg), aldehyde **1** (1.1 mmol), amine **2** (1 mmol), and acetophenone **3b** (1 mL) was stirred in a Schlenk tube at room temperature for the appropriate reaction time according to Table 3.

[b]Isolated yields.

and $Fe(O_2CCF_3)_3$ catalyst could promote aniline elimination and lead to the enone formation.[1] This speculation was further confirmed by gas chromatography–mass spectrometry (GC-MS) analysis. The three-component reactions for the coupling of alkylaldehyde **1d** with aniline **2a** and acetone **3a**, or alkylamine **2d** with benzaldehyde **1a** and **3a**, also worked well and provided β-carbon alkylated product **4j** and *N*-alkylated product **4k** respectively in good yields (Table 2, entries 12 and 13). However, the extension for coupling reaction of **1d, 2d**, and ketone failed to give the expected

product and resulted in a complex reaction system (Table 2, entry 14). The highly reactive alkylaldehyde and alkylamine along with $Fe(O_2CCF_3)_3$ catalyst could lead to some side reactions prior to the formation of β-aminoketones.

The reactions of acetophenone **3b** with different arylaldehydes **1** and arylamines **2** were subsequently surveyed to form 1-phenyl-β-aminoketone **5** under the optimized reaction conditions; the results are outlined in Table 3. The electronic effects of substituents in the arylaldehydes and arylamines are similar to the results obtained in Table 3. Compared to the substrate of acetone **3a**, applying acetophenone **3b** for the synthesis of product **5** requires a longer reaction time to complete the conversion of benchmark substrate of amine (Table 3, entries 1–8), and thus acetophenone was considered to be less reactive than acetone under the same employed reaction conditions. Notably, alkylamines such as *n*-octylamine **2d**, cyclohexanamine **2e,** and piperidine **2f** were also proved to be effective substrates for the synthesis of *N*-alkylated β-aminoketones (Table 2, entries 9–11).

In conclusion, we have developed a highly efficient, simple, general, and straightforward method for the synthesis of β-aminoketones by using the cost-effective, noncorrosive, and easily available $Fe(O_2CCF_3)_3$ as a catalyst for the first time.[19] The represented protocol allows assembly of a wide range of target compounds and introduction of different functional groups into the β-aminoketone skeleton by employing a variety of readily available aldehydes, amines, and ketones. In addition, the method consistently has the advantages of good yields, short reaction times, and simple experimental workup procedure, which make it a highly practical process for the synthesis of functionalized β-aminoketones. Further applications on this type of compound are ongoing in our laboratory and will be published in due course.

EXPERIMENTAL

All the known products were characterized by melting points (mp), ^{1}H NMR, and infrared (IR) spectra, and the new compounds **4c, 4g, 4j 4l**, and **4m** were additionally characterized by ^{13}C NMR and high-resolution mass spectra (HRMS). Melting points were measured on an Electrothemal SGW-X4 microscopy digital melting-point apparatus and are uncorrected, IR spectra were recorded on a FTLA2000 spectrometer, and ^{1}HNMR spectra were obtained on a Bruker-200 instrument. Chemical shifts are reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). LRMS and HRMS were measured on Finnigan MAT 95 spectrometer; TLC was performed using commercially prepared 100 to 400-mesh silica gel plates (GF254), and visualization is effected at 254 nm. All the reagents were purchased from commercial sources (Alfa, Acros, Aldrich) and used without further purification.

General Procedure for the Preparation of 4a–4k and 5a–5f

The catalyst $Fe(O_2CCF_3)_3$ (0.05 mmol, 19.8 mg) was added to the solution of arylaldehyde (1.1 mmol) and aniline (1 mmol) in acetone or acetophenone (1 mL). The resulting mixture was stirred at room temperature for an appropriate reaction time (determined by thin-layer chromatography, TLC), filtered, and washed with

diethyl ether. The combined organic solvent was evaporated under vacuum to afforded the crude product, which was purified on preparative TLC eluting with petroleum ether: Ethyl–acetate (10:1). Desired products **4a–4i** were afforded in 80% to 96% yields. Products **5a–5i** were obtained via recrystallization of the crude products in ethanol solution.

All the new compounds were characterized by their spectral (^{1}H NMR, ^{13}C NMR, IR, MS, and HRMS) and physical data. Known compounds were characterized by ^{1}H NMR and IR. Wherever literature examples were available, the data were compared and were found to be identical with authentic samples.

Spectral Data

4-Phenyl-4-(phenylamino)butan-2-one (4a)[20]. Yield: 90%; white solid; mp: 85–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.11 (s, 3H), 2.93 (d, $J = 6.8$ Hz, 2H), 4.46 (br, 1H), 4.85 (t, $J = 6.8$ Hz, 1H), 6.55 (dd, $J = 7.6$ Hz, 2H), 6.66–6.70 (m, 1H), 7.08–7.12 (m, 3H), 7.24–7.39 (m, 4H); IR (neat): 3370, 1708, 1602, 1509, 1489,1282, 1092, 816 cm^{-1}.

4-Phenyl-4-(p-tolylamino)butan-2-one (4b)[12]. Yield: 92%; yellow solid; mp: 92–94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.13 (s, 3H), 2.21 (s, 3H), 2.94 (d, $J = 6.4$ Hz, 2H), 4.35 (br, 1H), 4.84 (t, $J = 6.8$ Hz, 1H), 6.50 (dd, $J = 8.4$ Hz, 2H), 6.94 (d, $J = 8.0$ Hz, 2H), 7.25–7.27(m, 1H), 7.32–7.40 (m, 4H); IR (neat): 3380, 2917, 1708, 1617, 1519, 1452, 1264, 1163, 808 cm^{-1}.

4-(2-Methoxyphenylamino)-4-phenylbutan-2-one (4c). Yield: 86%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.02 (s, 3H), 2.87 (d, $J = 6.8$ Hz, 2H), 3.78 (s, 3H), 4.79 (br, 1H), 4.80 (t, $J = 6.8$ Hz, 1H), 6.33–6.36 (m, 1H), 6.54–6.69 (m, 3H), 7.13–7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.83, 147.00, 142.79, 136.68, 128.83, 127.36, 126.35, 121.16, 117.02, 111.29, 109.48, 55.54, 54.09, 51.78, 30.70; IR (neat): 3395, 2956, 1710, 1600, 1511, 1464, 1358, 1753 cm^{-1}; MS (EI, m/z): 269 $[M]^+$; HRMS (EI, m/z) calcd. for $C_{17}H_{19}NO_2[M+H]^+$: 269.1416; found 269.1406.

4-(4-Chlorophenylamino)-4-phenylbutan-2-one (4d)[12]. Yield: 90%; yellow solid; mp: 76–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.94 (d, $J = 6.4$ Hz, 2H), 4.55 (br, 1H), 4.81 (t, $J = 6.4$ Hz, 1H), 6.48 (dd, $J = 8.8$ Hz, 2H), 7.03–7.07 (m, 2H), 7.27–7.37 (m, 5H); IR (neat): 3370, 1707, 1602, 1508, 1489, 1455, 1281, 1092, 816 cm^{-1}.

4-(4-Methoxyphenyl)-4-(phenylamino)butan-2-one (4e)[20]. Yield: 93%; yellow solid; mp: 89–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.93 (d, $J = 6.8$ Hz, 2H), 3.80 (s, 3H), 4.36 (br, 1H), 4.82 (t, $J = 6.8$ Hz, 1H), 6.52–6.59 (m, 2H), 6.65–6.72 (m, 1H), 6.85–6.89 (m, 2H), 7.09–7.32 (m, 4H); IR (neat): 3394, 2956, 2836, 1710, 1602, 1511, 1438, 1359, 1247, 1175, 831 cm^{-1}.

4-(4-Methoxyphenyl)-4-(p-tolylamino)butan-2-one (4f)[20]. Yield: 96%; yellow solid; mp: 55–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.16 (s, 3H), 2.37 (dd, $J = 9.2$ Hz, 3H), 2.86 (d, $J = 6.4$ Hz, 2H), 3.74 (s, 3H), 4.20 (br, 1H), 4.75 (t, $J = 6.4$ Hz, 1H), 6.45 (dd, $J = 6.4$ Hz, 2H), 6.80-6.90 (m, 4H), 7.11–7.26 (m, 2H); IR

(neat): 3388, 2956, 2917, 2836, 1710, 1613, 1512, 1422, 1358, 1249, 1173, 1032, 809 cm^{-1}.

4-(4-Chlorophenylamino)-4-(4-methoxyphenyl)butan-2-one (4g). Yield: 96%; yellow solid; mp 123–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.92 (d, $J = 6.4$ Hz, 2H), 3.81 (s, 3H), 4.50 (br, 1H), 4.75 (t, $J = 6.4$ Hz, 1H), 6.45–6.50 (m, 2H), 6.86–7.08 (m, 4H), 7.24–7.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.73, 159.31, 145.82, 134.33, 129.39, 127.74, 122.82, 115.31, 114.64, 78.10, 77.46, 76.83, 55.67, 54.32, 51.50, 31.34; IR (neat): 3395, 2956, 1710, 1600, 1511, 1464, 1358, 11753 cm^{-1}; MS (EI, m/z): 303 $[M]^+$. HRMS (EI, m/z) calcd. for $C_{17}H_{19}ClNO_2[M+H]^+$: 304.1104, found 304.1096.

4-(4-Chlorophenyl)-4-(phenylamino)butan-2-one (4h)[20]. Yield: 86%; yellow solid; mp 123–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.93 (d, $J = 6.4$ Hz, 2H), 4.55 (br, 1H), 4.88 (t, $J = 6.4$ Hz, 1H), 6.45–6.50 (m, 2H), 6.66–6.72 (m, 1H), 7.08–7.12 (m, 2H), 7.48–7.61 (m, 4H); IR (neat): 3382, 2931, 1706, 1622, 1381, 1176, 820 cm^{-1}.

4-(3-Nitrophenyl)-4-(phenylamino)butan-2-one (4i)[20]. Yield: 80%; Yellow solid; mp: 97–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.18 (s, 3H), 3.02 (d, $J = 6.4$ Hz, 2H), 4.58 (br, 1H), 4.97 (t, $J = 6.4$ Hz, 1H), 6.54 (dd, $J = 8.4$ Hz, 2H), 6.69–6.76 (m, 1H), 7.09–7.17 (m, 2H), 7.28–7.80 (m, 2H), 8.10–8.28 (m, 2H); IR (neat): 3398, 2919, 1714, 1672, 1602, 1527, 1440, 1350, 1318, 1265, 1164, 1123, 808 cm^{-1}.

4-(3-Nitrophenyl)-4-(p-tolylamino)butan-2-one (4j). Yield: 85%; yellow solid; mp: 71–73 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.18 (s, 3H), 2.19 (s, 3H), 3.02 (d, $J = 6.4$ Hz, 2H), 4.45 (br, 1H), 4.97 (t, $J = 6.4$ Hz, 1H), 6.47 (dd, $J = 8.0$ Hz, 2H), 6.92–6.96 (m, 2H), 7.51–7.79 (m, 2H), 8.10–8.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.53, 145.79, 144.21, 133.34, 130.20, 128.25, 122.89, 121.81, 114.46, 78.12, 77.45, 76.84, 54.32, 51.23, 31.08, 20.80; IR (neat): 3399, 2919, 2867, 1714, 1618, 1584, 1524, 1406, 1350, 1369, 1263, 1164, 1129, 809 cm^{-1}; MS (EI, m/z): 298 $[M]^+$; HRMS (EI, m/z) calcd. for $C_{17}H_{19}N_2O_3[M+H]^+$: 299.1396; found 299.1389.

4-(4-Chlorophenylamino)-4-(3-nitrophenyl)butan-2-one (4k)[7]. Yield: 82%; yellow solid; M.P: 86–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.18 (s, 3H), 3.02 (d, $J = 6.4$ Hz, 2H), 4.65 (br, 1H), 4.91 (t, $J = 6.4$ Hz, 1H), 6.46 (m, 2H), 7.05–7.09 (m, 2H), 7.48–7.76 (m, 2H), 8.11–8.25 (m, 2H); IR (neat): 3400, 2950, 1714, 1600, 1529, 1402, 1350, 1314, 1262, 1164, 818 cm^{-1}.

4-(Phenylamino)nonan-2-one (4l). Yield: 71%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80–0.94 (m, 3H), 1.18–1.49 (m, 8H), 2.07 s, 3H), 2.51–2.84 (m, 3H), 3.66 (br, 1H), 6.51–7.18 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.21, 144.64, 134.65, 129.44, 117.46, 47.97, 32.42, 31.95, 25.98, 23.30, 22.90, 14.12; IR (neat): 3387, 2966, 2862, 1701, 1628, 1544, 1406, 1385, 1362, 1261, 1161, 1129, 811 cm^{-1}; MS (EI, m/z): 233 $[M]^+$; HRMS (EI, m/z) calcd. for $C_{15}H_{23}NO$ $[M+H]^+$: 233.1780; found 233.1776.

4-(Octylamino)-4-phenylbutan-2-one (4m). Yield: 73%; yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.74–0.82 (m, 3H), 1.17–1.22 (m, 12H), 2.32 (s, 3H),

2.74 (m, 3H), 3.16–3.18 (m, 2H), 4.29–4.31 (m, 1H); 7.19–7.47 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.12, 143.50, 131.01, 130.59, 127.18, 47.69, 45.32, 30.12, 29.40, 27.58, 14.16; IR (neat): 3382, 2972, 1704, 1632, 1382, 1264, 1163, 1131, 821 cm^{-1}; MS (EI, m/z): 275 $[M]^+$; HRMS (EI, m/z) calcd. for $C_{18}H_{29}NO$ $[M+H]^+$: 275.2249; found 275.2201.

1,3-Diphenyl-3-(phenylamino)propan-1-one (5a)[7]. Yield: 86%; white solid; mp: 167–168 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.50 (m, 2H), 4.62 (br, 1H), 5.02 (t, $J=6.8$ Hz, 1H), 6.56–6.72 (m, 5H), 7.07–7.39 (m, 4H), 7.43–7.60 (m, 4H), 7.91–7.95 (m, 2H); IR (neat): 3386, 3024, 2875, 2364, 1673, 1603, 1515, 1454, 1371, 1227, 1000, 865 cm^{-1}.

1,3-Diphenyl-3-(p-tolylamino)propan-1-one (5b)[7]. Yield: 80%; white solid; mp: 167–168 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.20 (s, 3H), 3.48 (m, 2H), 4.38 (br, 1H), 5.00 (t, $J=7.2$ Hz, 1H), 6.51 (dd, $J=8.0$ Hz, 2H), 6.92 (dd, $J=8.0$, 2H), 7.25–7.38 (m, 4H), 7.45–7.59 (m, 4H), 7.93 (m, 2H); IR (neat): 3403, 3025, 2916,,2358, 1681, 1621, 1527, 1449, 1370, 1321, 1292, 1215, 1002, 803 cm^{-1}.

3-(4-Methoxyphenylamino)-1,3-diphenylpropan-1-one (5c)[21]. Yield: 85%; white solid; mp: 163–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.52–3.40 (m, 2H), 3.70 (s, 3H), 4.30 (br, 1H), 4.96 (t, $J=6.8$ Hz, 1H), 6.52 (d, $J=8.4$ Hz, 2H), 6.68 (d, $J=8.2$, 2H), 7.25 (s, 1H), 7.32 (t, $J=7.2$ Hz, 2H), 7.45 (t, $J=6.8$ Hz, 4H), 7.56 (t, $J=7.2$ Hz, 1H), 7.92 (d, $J=7.6$ Hz, 2H); IR (neat): 3397, 2976,,2358, 1679, 1597, 1381, 1115, 803 cm^{-1}.

3-(4-Chlorophenylamino)-1,3-diphenylpropan-1-one (5d)[7]. Yield: 95%; white solid; mp: 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (m, 2H), 4.67 (br, 1H), 4.96 (t, $J=6.8$ Hz, 1H), 6.50 (dd, $J=6.8$ Hz, 2H), 7.05 (dd, $J=6.8$ Hz, 2H), 7.26–7.60 (m, 8H), 7.90–7.95 (m, 2H); IR (neat): 3373, 3021, 2900, 2364, 1666, 1602, 1508, 1489, 1448, 1400, 1371, 1285, 1220, 1175, 1004, 806 cm^{-1}.

3-(4-Methoxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one (5e)[7]. Yield: 83%; White solid; mp: 148–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.47 (m, 2H), 3.80 (s, 3H), 4.57 (br, 1H), 4.99 (t, $J=6.8$ Hz, 1H), 6.57–6.72 (m, 3H), 6.87 (m, 2H), 7.12 (m, 2H), 7.36–7.59 (m, 5H), 7.93 (m, 2H); IR (neat): 3376, 2917, 2849, 1666, 1606, 1510, 1447, 1287, 1248, 1175, 1028, 833 cm^{-1}.

3-(4-Chlorophenylamino)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (5f)[7]. Yield: 90%; yellow solid; mp: 156–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.96 (d, $J=6.8$ Hz, 2H), 3.81 (s, 3H), 4.45 (br, 1H), 4.88 (t, $J=6.8$ Hz, 1H), 6.56–6.74 (m, 4H), 7.10–7.42 (m, 9H); IR (neat): 3384, 2929, 1670, 1604, 1595, 1447, 1289, 1251, 1106, 1029, 812 cm^{-1}.

3-(4-Chlorophenyl)-1-phenyl-3-(phenylamino)propan-1-one (5g)[22]. Yield: 86%; yellow solid; mp: 130–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.41–3.52 (m, 2H), 4.56 (br, 1H), 4.98 (t, $J=6.8$ Hz, 1H), 6.32 (t, $J=7.6$ Hz, 2H), 6.53 (d, $J=7.6$ Hz, 2H), 6.92 (t, $J=6.8$ Hz, 2H), 7.05 (d, $J=8.4$ Hz, 2H), 7.42–7.51 (m, 2H), 7.62 (d, $J=7.6$ Hz, 2H), 7.92–7.94 (m, 2H); IR (neat): 3378, 2992, 1667, 1442, 1112, cm^{-1}.

3-(4-Chlorophenylamino)-3-(3-nitrophenyl)-1-phenylpropan-1-one (5h)[8]. Yield: 70%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.11 (s, 3H), 2.93 (d, $J = 6.8$ Hz, 2H), 4.13 (br, 1H), 4.08 (br, 2H), 4.85 (t, $J = 6.8$ Hz, 1H), 6.55 (dd, $J = 7.6$ Hz, 2H), 6.68–6.69 (m, 1H), 7.10–7.12 (m, 1H), 7.24–7.39 (m, 4H); IR (neat): 3400, 3070, 2878, 2352, 1709, 1614, 1537, 1446, 1350, 1202, 1121, 1009, 933, 810 cm^{-1}.

3-(Octylamino)-1,3-diphenylpropan-1-one (5i)[23]. Yield: 79%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84–0.89 (m, 3H), 1.14–1.42 (m, 12H), 1.85 (brs, 1H), 2.36–2.49 (m, 2H), 3.24–3.42 (m, 2H), 4.28 (q, $J = 4.8$ Hz, 1H), 7.23–8.12 (m, 10H); IR (neat): 3321, 2916, 1681, 1343, 1245, 1002, 821 cm^{-1}.

3-(Cyclohexylamino)-1,3-diphenylpropan-1-one (5j)[23]. Yield: 71%; colorless solid; mp: 37–39 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07–1.70 (br, 10H), 2.06 (s, 1H), 2.25–2.30 (m, 1H), 3.24–3.28 (m, 2H), 4.50 (q, $J = 5.0$ Hz, 1H), 7.21–8.13 (m, 10H); IR (neat): 3403, 2923, 1675, 1378, 1326, 1076, 831 cm^{-1};

1,3-Diphenyl-3-(piperidin-1-yl)propan-1-one (5k)[23]. Yield: 67%; white solid; M.P: 90–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23–1.52 (br, 6H), 2.25–2.48 (m, 4H), 3.34–3.60 (m, 2H), 4.23 (t, $J = 6.8$ Hz, 1H), 7.20–8.00 (m, 10H); IR (neat): 2983, 2879, 1676, 1544, 1481, 1379, 1032, 862 cm^{-1}.

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