Iodine Promoted Conversion of Esters to Nitriles and Ketones under Metal-Free Conditions

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ABSTRACT: We report a novel strategy to prepare valuable nitriles and ketones through the conversion of esters under metal-free conditions. By using the I_2/PCl_3 system, various substrates including aliphatic and aromatic esters could react with acetonitrile and arenes to afford the desired products in good to excellent yields. This method is compatible with a number of functional groups and provides a simple and practical approach for the synthesis of nitrile compounds and aryl ketones.

R^1, R^2 = Alkyl, Aryl, Alkenyl
45 examples; Up to 98%!
Wide substrate scope!
Practical and simple conditions!
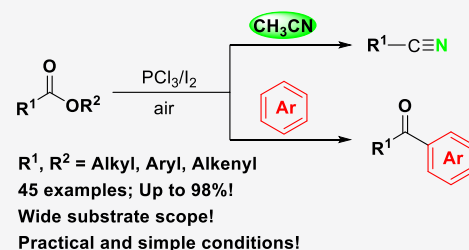
Nitriles and ketones are two important kinds of organic intermediates which have played an important role in organic synthesis, pharmaceuticals, agrochemicals, and materials.[1] Typical methods for the synthesis of nitriles include Kolbe nitrile synthesis,[2] Sandmeyer reactions,[3] Rosenmund−von Braun reactions,[4] and the dehydration of amides with various dehydration systems.[5] Alternatively, the preparation of nitriles from carboxylic acids,[6] aldehydes,[7] and alcohols[8] has also been reported. However, these methods usually require equivalent toxic metal cyanides, harsh reaction conditions, or two or more reaction steps. Esters are common chemicals that widely exist in nature. The development of practical and efficient transformations of esters to nitriles is highly demanded. To the best of our knowledge, only a few examples of direct conversion of esters to nitriles were reported. Unfortunately, these methods require two reaction steps and at least 1 equiv of metallic reagents such as dimethylaluminum amide and diisobutylaluminum hydride or $NaN(SiMe_3)_2$.[9] With respect to the synthesis of ketones, the Friedel−Craft acylation reaction is the main route to prepare aromatic ketones.[10] However, the acylated reagents are usually limited to carboxylic acids, acyl chlorides, and anhydrides. In 2000, Olah demonstrated the only example where ester was used as the acylated reagent for preparing aromatic ketones.[11] Nevertheless, this method was limited because of the large excess of trifluoromethanesulfonic acid (5.0 equiv) and narrow substrate scope. Therefore, seeking a simple, general, and practical way to synthesize various nitriles and ketones from esters is attractive.

Molecular iodine is a simple and readily available chemical which was used in various oxidation reactions, deprotecting reactions, and other transformations.[12] Recently, we are interested in the applications of phosphorus compounds and iodine in organic synthesis.[13] As a part of our ongoing research, we envisioned that, if nitriles and ketones could be prepared from esters in the presence of I_2 and PCl_3, a cheap, simple, and metal-free reaction for the synthesis of these products will be

developed. Herein, we report an iodine-promoted protocol, which provides access to nitriles and ketones from esters in the presence of air. Thus, by using the I_2/PCl_3 system, virous nitriles including aliphatic and aromatic nitriles were generated from the reaction of esters with acetonitrile (Scheme 1a). On the other hand, acylation reactions also took place with arenes to give the corresponding ketones in high yields (Scheme 1b).

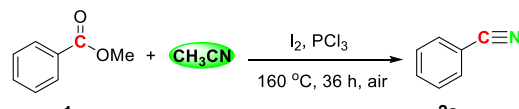**Scheme 1. Conversion of Esters to Nitriles and Ketones**
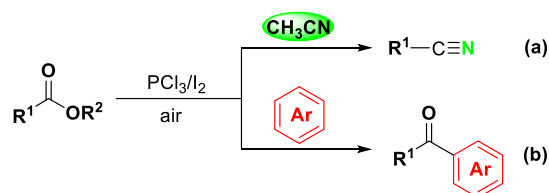
We started our investigations using methyl benzoate (**1a**) and acetonitrile as model substrates (Table 1). Thus, **1a** (0.3 mmol), molecular iodine (0.15 mmol), PCl_3 (0.3 mmol), and CH_3CN (0.6 mL) in a closed sealed tube were treated at 160 °C for 36 h. We were encouraged to observe 63% GC yield of the product **2a** was generated (entry 1). Further shortening the reaction time gave slightly lower yield (entry 2). Interestingly, only 38% yield of **2a** was obtained when the reaction was performed under a N_2 atmosphere, which indicates that the water in the air may have played an important role in this
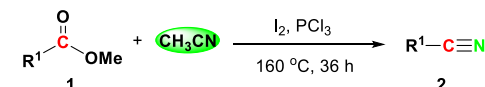
Table 1. Optimization of the Reaction Conditions[a]

entry	PCl₃ (equiv)	I₂ (equiv)	CH₃CN (mL)	yield (%)[b]
1	1.0	0.5	0.6	63
2	1.0	0.5	0.6	59[c]
3	1.0	0.5	0.6	38[c,d]
4	1.0	0.1	0.6	24
5	1.0	1.0	0.6	66
6	1.0	0.7	0.6	62
7	0.8	0.5	0.6	42
8	**0.8**	**0.7**	**0.6**	**65 (62)**
9	0.5	0.7	0.6	60
10	0.8	0.7	0.3	52
11	0.8	0.7	1.2	66
12	0.8	0.7	0.6	39[e]
13	none	0.7	0.6	N.D.
14	1.0	none	0.6	trace
15	none	0.7	0.6	48[f]
16	none	0.7	0.6	22[g]
17	0.8	0.7	0.6	75[h]

[a]Reaction conditions: **1a** (0.3 mmol), CH₃CN, PCl₃, and I₂ stirred in a 25 mL sealed tube at 160 °C for 36 h. N.D. = Not detected. Isolated yield in parentheses. [b]GC yield based on **1a** using *n*-dodecane as an internal standard. [c]22 h. [d]Under N₂. [e]130 °C. [f]PCl₅ was used instead of PCl₃. [g]P₂O₅ was used instead of PCl₃. [h]H₂O (0.6 mmol) was added additionally under N₂.

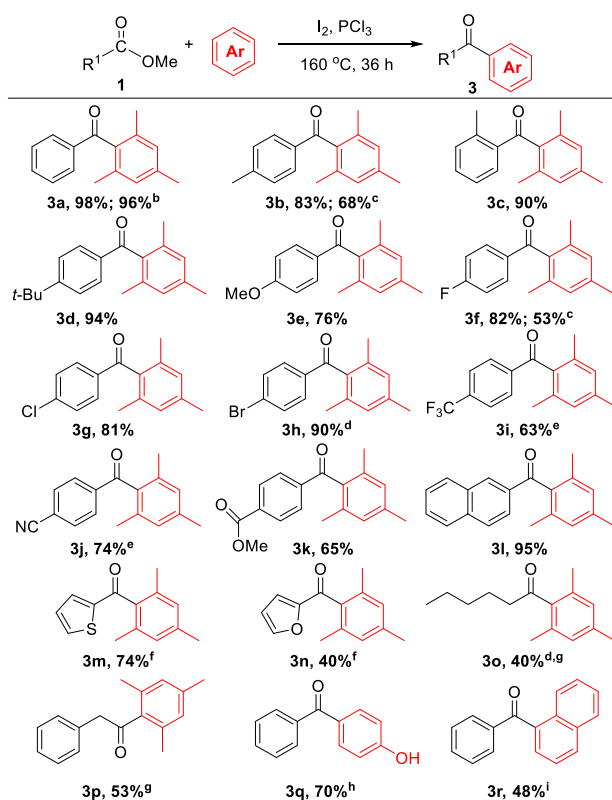**Table 2. Conversion of Methyl Esters to Nitriles**[a]

[a]Reaction conditions: **1** (0.3 mmol), CH₃CN (0.6 mL), PCl₃ (0.24 mmol), and I₂ (0.21 mmol) stirred in a sealed tube with air at 160 °C for 36 h. Yield based on ester. [b]Reactions were conducted under N₂, and H₂O (0.6 mmol) was added additionally. [c]PCl₃ (0.3 mmol) was used. [d]120 °C. [e]I₂ (0.3 mmol) was used.

transformation (entry 3). After an extensive screening the amount of PCl₃ and I₂, we found that PCl₃ (0.8 equiv) and I₂ (0.7 equiv) was the best choice (entries 4−9). Considering CH₃CN was used as both reagent and solvent, we further optimized the amount of CH₃CN. The results obtained showed that neither decreasing nor increasing CH₃CN could significantly enhance the reaction efficiency (entries 10 and 11). Lower temperature dramatically reduced the desired product (entry 12). As anticipated, no product or only a trace amount of **2a** was detected when the reaction was conducted in the absence of PCl₃ or I₂ (entries 13 and 14). When PCl₅ and P₂O₅ were used instead of PCl₃, lower yields of **2a** were obtained (entries 15 and 16). Moderate amounts of water are beneficial to the reaction (see entry 17 and Supporting Information (SI)).

With optimized conditions in hand, we turned our attention to examine the substrate scope. As shown in Table 2, methyl benzoate derivatives bearing whether electron-rich or electron-deficient substituent groups such as methyl, *tert*-butyl, methoxy, fluoro, chloro, bromo, and trifluoromethyl groups were well tolerated in these metal-free conditions (**2b−2i**). Interestingly, the skeleton of herbicide cyhalofop-butyl **2j** and herbicide 2,6-dichlorobenzonitrile **2k** were synthesized successfully from the corresponding esters in good yields.[14] Moreover, the scope of this reaction could be expanded to methyl 2-naphthoate and heterocyclic substrate as exemplified by **2l** and **2m**. To our delight, when alkyl esters methyl dodecanoate and methyl 2-phenylacetate were subjected into the reaction, the desired products were isolated in 78% and 47% yields, respectively (**2n** and **2p**). In the case of cyclic alkyl ester, the reaction proceeded smoothly, providing **2o** in 74%

yield. Surprisingly, secondary ester methyl 2-phenylpropanoate was also amenable under this system (**2q**).

To demonstrate the generality of this reaction, the conversion of esters to ketones was tested under the similar reaction conditions. As shown in Table 3, the reaction of methyl benzoate with mesitylene occurred smoothly whether mesitylene was used as solvent or in equivalent (**3a**). Substrates containing methyl, *tert*-butyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, and cyano groups gave the corresponding ketones in good to excellent yields (**3b−3j**). One ester group could survive in this system when dimethyl terephthalate was used (**3k**). Moreover, methyl 2-naphthoate was also suitable under this system (**3l**). Notably, thiophene- and furan-derived esters also reacted with mesitylene to afford **3m** and **3n** in 74% and 40% yields, respectively. Alkyl esters such as methyl 2-phenylacetate and hexanoyl chloride led to the desired products in moderate yields (**3o** and **3p**). When an equivalent of phenol was used as arene, 70% yield of *para*-substituted product was obtained (**3q**). Naphthalene also reacted with methyl benzoate to give product **3r** in high regioselectivity.

Encouraged by the above results, *n*-hexyl, cyclohexyl, phenyl, cinnamyl, and benzyl esters were subjected to the reaction. As demonstrated in Table 4, under the optimized reaction conditions, all the substrates were converted to the corresponding nitrile **2a** and ketone **3a** in good to excellent yields. These results indicated that this reaction has good substrate compatibility.

To probe the practicality of this transformation, two gram-scale reactions were performed. As shown in Scheme 2, methyl benzoate **1a** (6.0 mmol), I₂ (3.0 mmol), and PCl₃ (6.0 mmol)

Table 3. Conversion of Methyl Esters to Ketones[a]

3a, 98%; 96%[b]   3b, 83%; 68%[c]   3c, 90%

3d, 94%   3e, 76%   3f, 82%; 53%[c]

3g, 81%   3h, 90%[d]   3i, 63%[e]

3j, 74%[e]   3k, 65%   3l, 95%

3m, 74%[f]   3n, 40%[f]   3o, 40%[d,g]

3p, 53%[g]   3q, 70%[h]   3r, 48%[i]

[a]Reaction conditions: **1** (0.3 mmol), arene (0.6 mL), PCl$_3$ (0.3 mmol), and I$_2$ (0.15 mmol) were stirred in a sealed tube with air at 160 °C for 36 h. Yield based on ester. [b]Mesitylene (1.2 mmol) and DCE (0.3 mL) were used. [c]Reactions were conducted under N$_2$, and H$_2$O (0.6 mmol) was added additionally. [d]PCl$_3$ (0.21 mmol) was used. [e]PCl$_3$ (0.45 mmol), mesitylene (0.1 mL), 48 h. [f]24 h. [g]130 °C. [h]Phenol (1.2 mmol) and DCE (0.6 mL) were used. [i]Naphthalene (1.8 mmol) and DCE (0.6 mL) was used.

**Table 4. Substrate Applicability of Different Esters**[a]
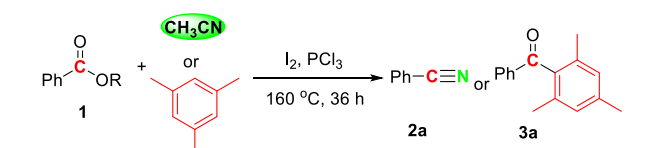
entry	R =	yield of 2a (%)	yield of 3a (%)[b]
1	n-hexyl	58	70
2	cyclohexyl	41	74
3	phenyl	55	94
4	cinnamyl	62	88
5	Bn	68	98

[a]Reaction conditions: for nitriles: **1** (0.3 mmol), CH$_3$CN or arene (0.6 mL), PCl$_3$ (0.3 mmol), and I$_2$ (0.15 mmol) were stirred in a sealed tube at 160 °C for 36 h. Yield based on esters. [b]PCl$_3$ (0.24 mmol) and I$_2$ (0.21 mmol) were used.

were stirred in mesitylene (12 mL) at 160 °C for 70 h. As anticipated, 96% yield of product **3a** was generated (eq 1). Under the similar reaction conditions, the reaction of **1a** with acetonitrile produced the corresponding product **2a** in 51% yield (eq 2).
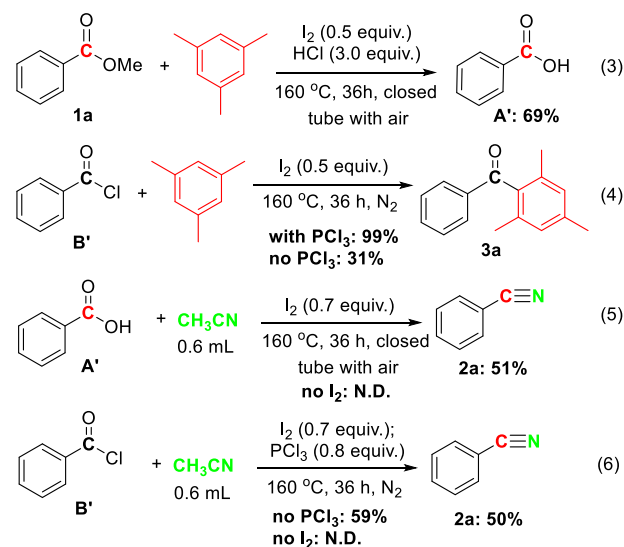
Some control experiments were performed to elucidate the mechanism of this reaction. When HCl was used instead of

Scheme 2. Gram-Scale Reactions
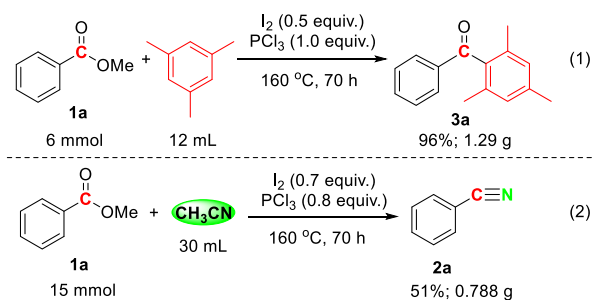
PCl$_3$, 69% yield of benzoic acid was observed (eq 3) (Scheme 3). When we considered the reaction of benzoic acid with

Scheme 3. Control Experiments

PCl$_3$, acid chloride may be the highly active species in the acylation of arenes. We then subjected benzoyl chloride to the reaction, and 99% (with 0.5 equiv of PCl$_3$) and 31% (no PCl$_3$) yields of **3a** were obtained, respectively (eq 4). To confirm the carboxylic acid could directly react with acetonitrile to afford the corresponding nitriles, benzoic acid was used instead of methyl benzoate, and the product **2a** was generated in 51% yield (eq 5). However, whether benzoic acid or benzoyl chloride was used, no product was detected in the absence of I$_2$. Conversely, moderate yields of **2a** were observed in the presence of I$_2$ (eqs 5 and 6). These results indicated that molecule I$_2$ plays an important role in this transformation.

Although the detailed mechanism was unclear, on the basis of the above results and previous reports,[13,15] plausible reaction pathways were proposed in Scheme 4. First, PCl$_3$ reacted with H$_2$O which existed in the air or solvent to give HCl. In the presence of I$_2$, HCl, and HI, methyl ester **1** then could be converted to intermediate carboxylic acid **A** and acid chloride **B** in situ, which were also detected by GC−MS. Finally, the reaction of **B** with CH$_3$CN or arene produced nitrile **2** (see SI) or ketone **3** with the aid of I$_2$. On the other hand, molecular I$_2$ reacts with CH$_3$CN to form intermediate **C**. Nucleophilic attacks of **C** from carboxylic acid **A** generated intermediate **D**, which undergoes the rearrangement to form intermediate **E**. Mumm rearrangement[16] of **E** yielded intermediate **F**. Further Mumm rearrangement of **F** gives the

Scheme 4. Plausible Reaction Pathways
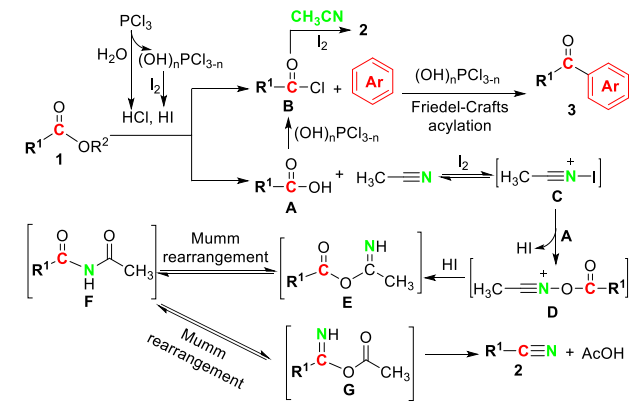
intermediate **G**. Elimination of acetic acid from **G** afforded the corresponding product **2**. Therefore, the carbon atom of CN originated from the carbonyl carbon of ester.

In summary, we have successfully demonstrated an iodine promoted conversion of esters to valuable nitriles and ketones under metal-free conditions. By using the I_2/PCl_3 system, a variety of esters including aliphatic esters and aromatic esters could react with acetonitrile or arenes to afford the corresponding products in good to excellent yields. This method is practical and easily scaled-up, which provides a simple and efficient way for the preparation of nitriles and ketones.

■ EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all reactions were carried out in closed sealed oven-dried Schlenk tubes under air. Reagents and solvents were obtained from commercial suppliers and used without purification. Flash column chromatography was performed using 200−300 mesh silica gel. Visualization on TLC was achieved by the use of UV light (254 nm). A FULI GC-9790II equipped with an FID detector was used to analyze the reaction mixtures. ^{1}H NMR and ^{13}C{^{1}H} NMR spectroscopies were recorded on a Bruker AV-II 500 MHz NMR spectrometer (^{1}H 500 MHz, ^{13}C{^{1}H} 125.76 MHz) in CDCl$_3$. The coupling constants J are given in Hz. Chemical shifts for ^{1}H NMR are referred to internal Me$_4$Si (0 ppm). GC−MS was conducted on a Shimadzu GCMS-QP2010 plus equipped with an EI ion source. High resolution mass spectra (HRMS) (TOF) were measured using an electrospray ionization (ESI) mass spectrometry.

Typical Procedure for Conversion of Methyl Esters to Nitriles. Under air, a mixture of aryl ester **1** (0.3 mmol), CH$_3$CN (0.6 mL), I$_2$ (53.3 mg, 0.21 mmol), and PCl$_3$ (21 μL, 0.24 mmol) was stirred in a 25 mL closed sealed tube in an oil bath at 160 °C for the indicated time. After the mixture was cooled down to the room temperature, the mixture was quenched with Na$_2$S$_2$O$_3$ aqueous solution and was extracted with EtOAc three times. Then the combined the organic layer was dried over MgSO$_4$ and filtrated. The filtrate was concentrated, and the residue was further purified by column chromatography on silica gel to give the product nitriles **2**.

Procedure for the Preparation of 2a on Gram Scale. Under air, a mixture of aryl ester **1a** (1.874 mL, 15.0 mmol), CH$_3$CN (30 mL), I$_2$ (2664.9 mg, 10.5 mmol), and PCl$_3$ (1.05 mL, 12.0 mmol) was stirred in a 100 mL closed sealed tube in an oil bath at 160 °C for 70 h. After the mixture was cooled down to the room temperature, the mixture was quenched with Na$_2$S$_2$O$_3$ aqueous solution and was extracted with EtOAc three times. Then the combined organic layer was dried over MgSO$_4$ and filtrated. The filtrate was concentrated, and the residue was further purified by column chromatography on silica gel to give the product **2a** in 0.788 g.

Yields were based on two parallel reactions, and the mass of the product is the total mass of two parallel reactions!

Benzonitrile (2a).[17] Colorless oil, yield 62% (38.3 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.64−7.61 (m, 2H), 7.59−7.57 (m, 1H), 7.47−7.44 (m, 2H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 132.8, 132.1, 129.2, 118.9, 112.4. GC−MS (EI, 70 eV) m/z = 103 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_7$H$_6$N 104.0500, found 104.0490.

4-Methylbenzonitrile (2b).[17] Colorless oil, yield 67% (47.0 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.57−7.53 (m, 2H), 7.28−7.26 (m, 2H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 143.7, 132.1, 129.8, 119.2, 109.3, 21.9. GC−MS (EI, 70 eV) m/z = 117 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_8$H$_8$N 118.0657, found 118.0747.

2-Methylbenzonitrile (2c).[18] Yellow oil, yield 63% (44.2 mg). Eluent: Petroleum ether/EtOAc = 30/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.59 (d, J = 10.0 Hz, 1H), 7.49−7.46 (m, 1H), 7.32−7.31 (d, J = 5.0 Hz, 1H), 7.27−7.25 (m, 1H), 2.54 (s, 3H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 141.9, 132.7, 132.5, 130.2, 126.2, 118.1, 112.8, 20.5. GC−MS (EI, 70 eV) m/z = 117 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_8$H$_8$N 118.0657, found 118.0732.

4-(tert-Butyl)benzonitrile (2d).[19] Yellow oil, yield 82% (78.2 mg). Eluent: Petroleum ether/EtOAc = 30/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.59 (d, J = 5.0 Hz, 2H), 7.48 (d, J = 10.0 Hz, 2H), 1.33 (s, 9H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 156.7, 132.0, 126.2, 119.2, 109.3, 35.3, 31.0. GC−MS (EI, 70 eV) m/z = 159 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_{11}$H$_{14}$N 160.1126, found 160.1169.

4-Methoxybenzonitrile (2e).[17] White solid, yield 31% (24.8 mg). Eluent: Petroleum ether/EtOAc = 30/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.59 (d, J = 10.0 Hz, 2H), 6.96 (d, J = 5.0 Hz, 2H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 162.9, 134.0, 119.3, 114.8, 104.0, 55.6. GC−MS (EI, 70 eV) m/z = 133 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_8$H$_8$NO 134.0606, found 134.0774.

4-Fluorobenzonitrile (2f).[17] White solid, yield 53% (38.4 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.73−7.69 (m, 2H), 7.22−7.18 (m, 2H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 165.1 (d, 1J_{C-F} = 256.6 Hz), 134.7 (d, 3J_{C-F} = 10.1 Hz), 118.1, 116.9 (d, 2J_{C-F} = 22.6 Hz), 108.6 (d, 4J_{C-F} = 3.8 Hz). GC−MS (EI, 70 eV) m/z = 121 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_7$H$_5$FN 122.0406, found 122.0970.

4-Chlorobenzonitrile (2g).[17] Colorless oil, yield 47% (39.0 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.64 (m, 2H), 7.53 (m, 2H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 139.6, 133.4, 129.7, 118.0, 110.8. GC−MS (EI, 70 eV) m/z = 138 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_7$H$_5$ClN 138.0111, found 138.0657.

4-Bromobenzonitrile(2h).[17] White solid, yield 52% (56.8 mg). Eluent: Petroleum ether/EtOAc = 30/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.64 (d, J = 15.0 Hz, 2H), 7.53 (d, J = 10.0 Hz, 2H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 133.4, 132.7, 128.0, 118.1, 111.3. GC−MS (EI, 70 eV) m/z = 182 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_7$H$_5$BrN 181.9605, found 181.9818.

4-(Trifluoromethyl)benzonitrile (2i).[20] Colorless oil, yield 56% (57.4 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.83−7.81 (m, 2H), 7.78−7.76 (m, 2H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 134.6 (q, 2J_{C-F} = 34.0 Hz), 132.7, 126.2 (q, 3J_{C-F} = 3.8 Hz), 123.1 (d, 1J_{C-F} = 272.9 Hz), 117.5, 116.1. GC−MS (EI, 70 eV) m/z = 171 (M+). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_8$H$_5$F$_3$N 172.0374, found 172.1027.

3,4-Difluorobenzonitrile (2j).[21] White solid, yield 46% (38.4 mg). Eluent: Petroleum ether/EtOAc = 30/1. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54−7.46 (m, 2H), 7.34−7.27 (m, 1H). ^{13}C{^{1}H} NMR (125.76 MHz, CDCl$_3$) δ 154.6−152.4 (dd, J_{C-F} = 12.6 Hz, 259.1 Hz), 151.4−149.3 (dd, J_{C-F} = 13.8 Hz, 254.0 Hz), 129.7−129.6 (m), 121.6 (d, J_{C-F} = 20.1 Hz), 118.9 (d, J_{C-F} = 18.9 Hz), 116.9, 109.0−109.0 (m). GC−MS (EI, 70 eV) m/z = 139 (M+). HRMS (ESI-TOF) m/z: [M]$^+$ Calcd for C$_7$H$_3$F$_2$N 139.0234, found 139.0400.

2,6-Dichlorobenzonitrile (2k).[22] White solid, yield 65% (67.0 mg). Eluent: Petroleum ether/EtOAc = 30/1. ¹H NMR (500 MHz, CDCl₃) δ 7.51−7.43 (m, 3H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 138.5, 133.9, 128.2, 114.4, 113.3. GC−MS (EI, 70 eV) m/z = 172 (M+). HRMS (ESI-TOF) m/z: [M]⁺ Calcd for C₇H₃Cl₂N 170.9643, found 170.9635.

2-Naphthonitrile (2l).[17] White solid, yield 54% (49.6 mg). Eluent: Petroleum ether/EtOAc = 30/1. ¹H NMR (500 MHz, CDCl₃) δ 8.22(s, 1H), 7.92−7.88 (m, 3H), 7.66−7.59 (m, 3H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 134.7, 134.2, 132.3, 129.2, 129.1, 128.4, 128.1, 127.7, 126.4, 119.3, 109.4. GC−MS (EI, 70 eV) m/z = 153 (M+). HRMS (ESI-TOF) m/z: [M]⁺ Calcd for C₁₁H₇N 153.0578, found 153.0898.

Thiophene-2-carbonitrile (2m).[17] Colorless oil, yield 42% (27.4 mg). Eluent: Petroleum ether/EtOAc = 30/1. ¹H NMR (500 MHz, CDCl₃) δ 7.63−7.61 (m, 2H), 7.14−7.12 (m, 1H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 137.5, 132.6, 127.7, 114.3, 109.9. GC−MS (EI, 70 eV) m/z = 109 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₅H₄NS 110.0064, found 110.0234.

Dodecanenitrile (2n).[22] Colorless oil, yield 78% (84.4 mg). Eluent: Petroleum ether/EtOAc = 30/1. ¹H NMR (500 MHz, CDCl₃) δ 2.33 (t, J = 7.1 Hz, 2H), 1.68−1.62 (m, 2H), 1.47−1.41 (m, 2H), 1.31−1.26 (m, 14H), 0.88 (t, J = 7.1 Hz, 3H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 119.9, 31.9, 29.6, 29.5, 29.3, 28.8, 28.7, 25.4, 22.7, 17.1, 14.1. GC−MS (EI, 70 eV) m/z = 181 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₁₂H₂₄N 182.1909, found 182.1959.

Cyclohexanecarbonitrile (2o).[23] Colorless oil, yield 74% (48.4 mg). Eluent: Petroleum ether/EtOAc = 50/1. ¹H NMR (500 MHz, CDCl₃) δ 2.65−2.61 (m, 1H), 1.88−1.83 (m, 2H), 1.76−1.66 (m, 4H), 1.54−1.41 (m, 4H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 122.7, 29.5, 28.0, 25.2, 24.1. GC−MS (EI, 70 eV) m/z = 109 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₇H₁₂N 110.0970, found 110.0929.

2-Phenylacetonitrile (2p).[24] Colorless oil, yield 47% (33.0 mg). Eluent: Petroleum ether/EtOAc = 30/1. ¹H NMR (500 MHz, CDCl₃) δ 7.38−7.35 (m, 2H), 7.33−7.30 (m, 3H), 3.72 (s, 2H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 130.0, 129.2, 128.1, 128.0, 118.0, 23.6. GC−MS (EI, 70 eV) m/z = 117 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₈H₈N 118.0657, found 118.0700.

2-Phenylpropanenitrile (2q).[25] Yellow oil, yield 44% (34.6 mg). Eluent: Petroleum ether/EtOAc = 30/1. ¹H NMR (500 MHz, CDCl₃) δ 7.40−7.31 (m, 5H), 3.90 (q, J = 7.3 Hz, 1H), 1.64 (d, J = 7.3 Hz, 3H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 137.1, 129.2, 128.1, 126.7, 121.6, 31.3, 21.5. GC−MS (EI, 70 eV) m/z = 131 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₉H₁₀N 132.0813, found 132.0799.

Typical Procedure for Conversion of Methyl Esters to Ketones. Under air, a mixture of aryl ester **1** (0.3 mmol), arene (0.6 mL), I₂ (38.1 mg, 0.15 mmol), and PCl₃ (27 μL, 0.3 mmol) was stirred in a 25 mL closed sealed tube in an oil bath at 160 °C for the indicated time. After the mixture was cooled down to the room temperature, the mixture was quenched with Na₂S₂O₃ aqueous solution and was extracted with EtOAc three times. Then the combined organic layer was dried over MgSO₄ and filtrated. The filtrate was concentrated, and the residue was further purified by column chromatography on silica gel to give the product **3**.

Procedure for the Preparation of 3a on Gram Scale. Under air, a mixture of aryl ester **1a** (0.75 mL, 6.0 mmol), mesitylene (12 mL), I₂ (761.4 mg, 3.0 mmol), and PCl₃ (0.525 mL, 6.0 mmol) was stirred in a 50 mL closed sealed tube in oil bath at 160 °C for 70 h. After the mixture was cooled down to the room temperature, the mixture was quenched with Na₂S₂O₃ aqueous solution and was extracted with EtOAc three times. Then the combined organic layer was dried over MgSO₄ and filtrated. The filtrate was concentrated, and the residue was further purified by column chromatography on silica gel to give the product **3a** in 1.29 g.

Yields were based on two parallel reactions, and the mass of the product is the total mass of two parallel reactions!

Mesityl(phenyl)methanone (3a).[26] Yellow oil, yield 98% (131.8 mg). Eluent: Petroleum ether/EtOAc = 50/1. ¹H NMR (500 MHz, CDCl₃) δ 7.80 (d, J = 7.7 Hz, 2H), 7.58−7.55 (m, 1H), 7.45−7.42 (m, 2H), 6.89 (s, 2H), 2.33 (s, 3H), 2.08 (s, 6H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 200.8, 138.5, 137.4, 136.9, 134.2, 133.6, 129.4, 128.8, 128.4, 21.2, 19.4. GC−MS (EI, 70 eV) m/z = 224 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₁₆H₁₇O 225.1279, found 225.1283.

Mesityl(p-tolyl)methanone (3b).[27] Yellow oil, yield 83% (118.6 mg). Eluent: Petroleum ether/EtOAc = 50/1. ¹H NMR (500 MHz, CDCl₃) δ 7.70 (d, J = 7.7 Hz, 2H), 7.24 (d, J = 7.9 Hz, 2H), 6.89 (s, 2H), 2.41 (s, 3H), 2.33 (s, 3H), 2.08 (s, 6H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 200.4, 144.5, 138.3, 137.2, 135.0, 134.2, 129.6, 129.5, 128.3, 21.8, 21.2, 19.3. GC−MS (EI, 70 eV) m/z = 238 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₁₇H₁₉O 239.1436, found 239.1452.

Mesityl(o-tolyl)methanone (3c).[26] Yellow solid, yield 90% (128.6 mg). Eluent: Petroleum ether/EtOAc = 40/1. ¹H NMR (500 MHz, CDCl₃) δ 7.41−7.35 (m, 2H), 7.32−7.30 (m, 1H), 7.16 (t, J = 7.4 Hz, 1H), 6.88 (s, 2H), 2.70 (s, 3H), 2.33 (s, 3H), 2.10 (s, 6H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 202.7, 140.0, 138.5, 138.5, 137.0, 134.4, 132.2, 132.2, 131.9, 128.5, 125.9, 21.8, 21.2, 19.4. GC−MS (EI, 70 eV) m/z = 238 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₁₇H₁₉O 239.1436, found 239.1513.

(4-(tert-Butyl)phenyl)(mesityl)methanone (3d).[28] Yellow oil, yield 94% (158.0 mg). Eluent: Petroleum ether/EtOAc = 40/1. ¹H NMR (500 MHz, CDCl₃) δ 7.74 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 6.89 (s, 2H), 2.33 (s, 3H), 2.09 (s, 6H), 1.34 (s, 9H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 200.5, 157.4, 138.3, 137.2, 134.8, 134.2, 129.4, 128.3, 125.7, 35.2, 31.1, 21.2, 19.4. GC−MS (EI, 70 eV) m/z = 280 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₂₀H₂₅O 281.1905, found 281.1907.

Mesityl(4-methoxyphenyl)methanone (3e).[26] Yellow oil, yield 76% (115.8 mg). Eluent: Petroleum ether/EtOAc = 30/1. ¹H NMR (500 MHz, CDCl₃) δ 7.66−7.61 (m, 2H), 6.78−6.71 (m, 4H), 3.70 (s, 3H), 2.19 (s, 3H), 1.96 (s, 6H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 199.2, 164.0, 138.2, 137.2, 134.1, 131.8, 130.5, 128.3, 114.0, 55.5, 21.2, 19.3. GC−MS (EI, 70 eV) m/z = 254 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₁₇H₁₉O₂ 225.1385, found 225.1390.

Fluorophenyl)(mesityl)methanone (3f).[29] Yellow oil, yield 82% (119.0 mg). Eluent: Petroleum ether/EtOAc = 50/1. ¹H NMR (500 MHz, CDCl₃) δ 7.84−7.81 (m, 2H), 7.13−7.09 (m, 2H), 6.90 (s, 2H), 2.33 (s, 3H), 2.08 (s, 6H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 199.2, 166.1 (d, 1J_{C-F} = 255.3 Hz), 138.7, 136.5, 134.1, 133.1 (d, 4J_{C-F} = 2.7 Hz), 132.1 (d, 3J_{C-F} = 9.5 Hz), 128.4, 116.0 (d, 2J_{C-F} = 22.0 Hz), 21.2, 19.4. GC−MS (EI, 70 eV) m/z = 242 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₁₆H₁₆FO 243.1185, found 243.1259.

Chlorophenyl)(mesityl)methanone (3g).[30] Yellow oil, yield 81% (125.8 mg). Eluent: Petroleum ether/EtOAc = 50/1. ¹H NMR (500 MHz, CDCl₃) δ 7.63 (d, J = 10.0 Hz, 2H), 7.29 (d, J = 10.0 Hz, 2H), 6.78 (s, 2H), 2.21 (s, 3H), 1.96 (s, 6H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 198.3, 139.0, 137.7, 135.3, 134.7, 133.1, 129.7, 128.1, 127.4, 20.1, 18.3. GC−MS (EI, 70 eV) m/z = 259 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₁₆H₁₆ClO 259.0890, found 259.0907.

Bromophenyl)(mesityl)methanone (3h).[31] Yellow oil, yield 90% (163.6 mg). Eluent: Petroleum ether/EtOAc = 50/1. ¹H NMR (500 MHz, CDCl₃) δ 7.57 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.8 Hz, 2H), 6.80 (s, 2H), 2.23 (s, 3H), 1.98 (s, 6H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 199.7, 138.8, 136.3, 136.1, 134.2, 132.2, 130.9, 129.0, 128.5, 21.2, 19.4. GC−MS (EI, 70 eV) m/z = 303 (M+). HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₁₆H₁₄BrO 303.0385, found 303.0379.

Mesityl(4-(trifluoromethyl)phenyl)methanone (3i).[26] Yellow solid, yield 63% (110.4 mg). Eluent: Petroleum ether/EtOAc = 50/1. ¹H NMR (500 MHz, CDCl₃) δ 7.91 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H), 6.92 (s, 2H), 2.35 (s, 3H), 2.07 (s, 6H). ¹³C{¹H} NMR (125.76 MHz, CDCl₃) δ 199.7, 139.9, 139.1, 136.0, 134.8 (d, 2J_{C-F} = 32.7 Hz), 134.3, 129.7, 128.6, 125.9 (q, 3J_{C-F} = 3.8 Hz), 123.6 (d, 1J_{C-F} = 272.9 Hz), 21.2, 19.4. GC−MS (EI, 70 eV) m/z = 292 (M

+). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}F_3O$ 293.1153, found 293.0990.

4-(2,4,6-Trimethylbenzoyl)benzonitrile (3j).[32] White solid, yield 74% (110.6 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^1H NMR (500 MHz, CDCl$_3$) δ 7.89 (d, J = 7.9 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 6.92 (s, 2H), 2.34 (s, 3H), 2.06 (s, 6H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 199.3, 140.2, 139.4, 135.6, 134.27, 132.8, 129.7, 128.6, 118.0, 116.7, 21.2, 19.4. GC−MS (EI, 70 eV) m/z = 249 (M+). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}NO$ 250.1232, found 250.1795.

Methyl 4-(2,4,6-trimethylbenzoyl) benzoate (3k).[33] White solid, yield 65% (110.0 mg). Eluent: Petroleum ether/EtOAc = 30/1. ^1H NMR (500 MHz, CDCl$_3$) δ 8.11 (d, J = 8.6 Hz, 2H), 7.86 (d, J = 8.2 Hz, 2H), 6.91 (m, 2H), 3.95 (s, 3H), 2.34 (s, 3H), 2.07 (s, 6H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 200.2, 166.3, 140.5, 139.0, 136.3, 134.3, 130.1, 129.7, 129.3, 128.5, 52.5, 21.2, 19.4. GC−MS (EI, 70 eV) m/z = 282 (M+). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}O_3$ 283.1334, found 283.1333.

Mesityl(naphthalen-2-yl)methanone (3l).[34] White solid, yield 95% (156.2 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^1H NMR (500 MHz, CDCl$_3$) δ 8.17 (s, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.93− 7.86 (m, 3H), 7.62−7.59 (m, 1H), 7.54−7.51 (m, 1H), 6.95 (s, 2H), 2.38 (s, 3H), 2.12 (s, 6H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 200.8, 138.6, 137.0, 136.0, 134.8, 134.4, 132.7, 132.1, 129.8, 128.8, 128.7, 128.4, 127.9, 126.8, 124.3, 21.2, 19.5. GC−MS (EI, 70 eV) m/z = 274 (M+). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{19}O$ 275.1436, found 275.1441.

Mesityl(thiophen-2-yl)methanone (3m).[26] Yellow oil, yield 74% (102.4 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^1H NMR (500 MHz, CDCl$_3$) δ 7.71 (d, J = 4.9 Hz, 1H), 7.34 (d, J = 3.2 Hz, 1H), 7.09−7.07 (m, 1H), 6.88 (s, 2H), 2.32 (s, 3H), 2.16 (s, 6H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 192.9, 145.1, 138.7, 137.0, 135.0, 134.7, 134.2, 128.4, 128.3, 21.2, 19.3. GC−MS (EI, 70 eV) m/z = 230 (M+). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}OS$ 231.0844, found 231.0847.

Furan-2-yl(mesityl)methanone (3n).[35] White solid, yield 40% (51.4 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^1H NMR (500 MHz, CDCl$_3$) δ 7.65 (s, 1H), 6.94−6.93 (m, 1H), 6.88 (s, 2H), 6.53−6.52 (s, 1H), 2.32 (s, 3H), 2.16 (s, 6H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 187.8, 153.3, 147.6, 139.0, 135.9, 134.6, 128.4, 120.3, 112.5, 21.2, 19.2. GC−MS (EI, 70 eV) m/z = 214 (M+). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}O_2$ 215.1072, found 215.1081.

1-Mesitylhexan-1-one (3o).[36] Yellow oil, yield 40% (52.4 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^1H NMR (500 MHz, CDCl$_3$) δ 6.82 (s, 2H), 2.68 (t, J = 7.5 Hz, 2H), 2.27 (s, 3H), 2.18 (s, 6H), 1.73−1.67 (m, 2H), 1.36−1.34 (m, 4H), 0.92−0.89 (m, 3H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 211.0, 139.9, 138.2, 132.5, 128.5, 44.9, 31.5, 23.1, 22.6, 21.0, 19.1, 14.0. GC−MS (EI, 70 eV) m/z = 218 (M+). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{23}O$ 219.1749, found 219.1832.

1-Mesityl-2-phenylethan-1-one (3p).[37] Yellow oil, yield 53% (75.6 mg). Eluent: Petroleum ether/EtOAc = 50/1. ^1H NMR (500 MHz, CDCl$_3$) δ 7.33−7.30 (m, 2H), 7.28−7.25 (m, 1H), 7.21−7.20 (m, 2H), 6.82 (s, 2H), 4.00 (s, 2H), 2.28 (s, 3H), 2.13 (s, 6H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 207.6, 139.2, 138.5, 133.3, 132.8, 129.9, 128.6, 128.5, 127.1, 51.8, 21.1, 19.2. GC−MS (EI, 70 eV) m/z = 238 (M+). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{18}NaO$ 261.1255, found 261.1313.

(4-Hydroxyphenyl)(phenyl)methanone (3q).[38] White solid, yield 70% (83.2 mg). Eluent: Petroleum ether/EtOAc = 40/1. ^1H NMR (500 MHz, CDCl$_3$) δ 8.22−8.20 (m, 2H), 7.64−7.61 (m, 1H), 7.52− 7.49 (m, 2H), 7.44−7.40 (m, 2H), 7.28−7.25 (m, 1H), 7.24−7.20 (m, 2H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 165.2, 151.0, 133.6, 130.2, 129.3, 129.5, 128.6, 125.9, 121.8. GC−MS (EI, 70 eV) m/z = 198 (M+). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{11}O_2$ 199.0759, found 199.0946.

Naphthalen-1-yl(phenyl)methanone (3r).[39] White solid, yield 48% (66.8 mg). Eluent: Petroleum ether/EtOAc = 40/1. ^1H NMR (500 MHz, CDCl$_3$) δ 8.11−8.09 (m, 1H), 8.02−8.00 (m, 1H), 7.94−

7.92 (m, 1H), 9.89−7.87 (m, 2H), 7.62−7.58 (m, 2H), 7.56−7.49 (m, 3H), 7.48−7.45 (m, 2H). $^{13}C\{^1H\}$ NMR (125.76 MHz, CDCl$_3$) δ 198.0, 138.4, 136.4, 133.8, 133.2, 131.3, 131.0, 130.4, 128.5, 128.4, 127.8, 127.3, 126.5, 125.7, 124.4. GC−MS (EI, 70 eV) m/z = 232 (M +). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{13}O$ 233.0966, found 233.1073.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02794.

Copies of ^1H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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