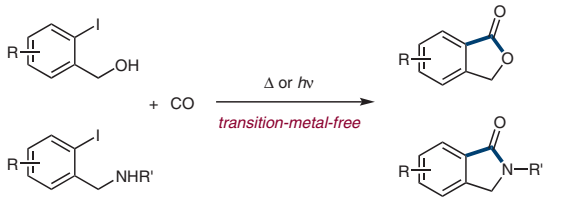
Synthesis T. Fukuyama et al. Special Topic

Electron-Transfer-Induced Intramolecular Heck Carbonylation Reactions Leading to Benzolactones and Benzolactams

Takahide Fukuyama[a]
Takanobu Bando[a]
Ilhyong Ryu *[a,b]

[a] Department of Chemistry, Graduate School of Science, Osaka Prefecture University, 1-1 Gakuen-cho, Sakai, Osaka, 599-8531, Japan
ryu@c.s.osakafu-u.ac.jp
[b] Department of Applied Chemistry, National Chiao Tung University, 1001 University Road, Hsinchu, Taiwan

Published as part of the Special Topic *Modern Radical Methods and their Strategic Applications in Synthesis*



up to 95% yield, 20 examples

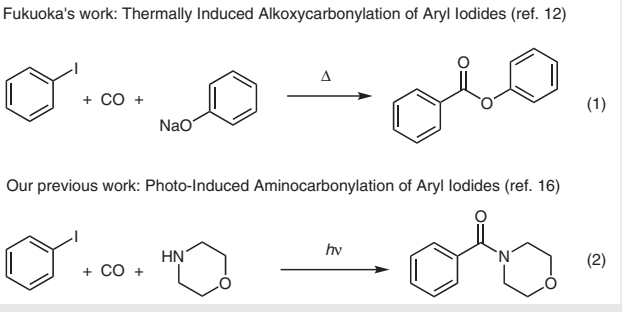
Received: 07.03.2018
Accepted after revision: 18.04.2018
Published online: 29.05.2018
DOI: 10.1055/s-0037-1609964; Art ID: ss-2018-c0146-st

Abstract A metal-catalyst-free intramolecular Heck carbonylation reaction of benzyl alcohols and benzyl amines with carbon monoxide under heating at 250 °C affords the corresponding benzolactones and benzolactams in good to excellent yields. A hybrid radical/ionic chain mechanism, involving electron transfer from radical anions generated by nucleophilic attack of alcohols or amines on intermediate acyl radicals, is proposed.

Key words carbonylation, electron transfer, radical reactions, metal-free, lactones, lactams

Carbonylation using CO is a fundamental synthetic method for the construction of carbonyl compounds.[1] Since the pioneering work by Heck and co-workers in the 1970s,[2] both Pd-catalyzed alkoxy- and amino-carbonylation of aryl halides with CO have been used in numerous applications for the synthesis of aromatic esters and amides. Carbonylative cyclization of haloarenes containing either an amino or hydroxy moiety, an intramolecular variant, affords benzolactones and benzolactams.[3]

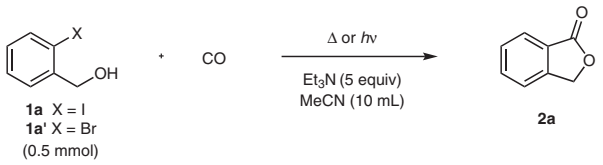
Our group has been fascinated by radical carbonylation methods[4,5] that employ the addition of a variety of carbon-centered alkyl, vinyl, and aryl radicals to CO. Recent topics have involved metal-free carbonylation reactions of *aryl* halides and related substrates based on the novel concept of using an 'electron' as a catalyst.[6,7] In the general scheme of these reactions, one electron transfer to aryl halides triggers the generation of aryl radicals and a radical carbonylation of aryl radicals[8] then follows to generate acyl radicals,[5] the carbonyl function of which is then attacked by alkoxide anions and amines to give esters and amides,[9,10] respectively, with the delivery of one electron to the substrates from radical anion intermediates. Lei and co-workers reported that aryl iodides react with CO and *t*-BuOK as a radical mediator in the presence of 1,10-phenanthroline to give *t*-Bu esters in good yields.[11] Fukuoka reported that aryl iodides react with CO and alkali metal aryloxides under heating (250 °C, 2 h) to give high yields of esters (Scheme 1, eq 1).[12] The groups of Xiao[13] and von Wangelin[14] concurrently reported that arene diazonium salts also participate in alkoxycarbonylation with CO and alcohols under photoredox-catalyzed conditions using eosin Y. More recently, von Wangelin and Koziakov reported that alkoxycarbonylation of aryl diazonium salts was affected by the use of mild bases such as HCO_2Na.[15] All these efforts represent the development of transition-metal-catalyst-free Heck carbonylations. We previously reported the aminocarbonylation of aryl iodides with CO and amines by employing photoirradiation with a Xe lamp (Scheme 1, eq 2).[16] In this paper, we report the intramolecular variation of a metal-catalyst-free carbonylation reaction to synthesize benzolactones and benzolactams using aryl iodides that possess nucleophilic hydroxy and amino substituents.



Scheme 1 Thermally induced alkoxycarbonylation (ref. 12) and photo-induced aminocarbonylation of aryl iodides (ref. 16)

Initially, we examined the cyclative carbonylation using 2-iodobenzyl alcohol (**1a**) as a model substrate, and Fukuoka's heating conditions were tested. When **1a** was treated with pressurized CO (65 atm) in the presence of five equivalents of Et_3N in MeCN (10 mL) at 230 °C for 16 hours, to our delight, the anticipated reaction proceeded to give benzolactone **2a** in 58% yield (Table 1, entry 1). Since a significant amount of **1a** remained intact, we instead used an elevated temperature of 250 °C, which resulted in full conversion of **1a** to give **2a** in 91% yield (entry 2). Lowering the CO pressure to 40 atm led to a decreased yield of **2a** (entry 3). The use of 2-bromobenzyl alcohol (**1a′**) was unsuccessful (entry 4). We also examined photoirradiation conditions using a 500 W Xe lamp and a quartz tube, which worked well, but required a longer reaction time (entries 5 and 6).

Table 1 Optimization of the Reaction Conditions for the Synthesis of Benzolactone **2a**

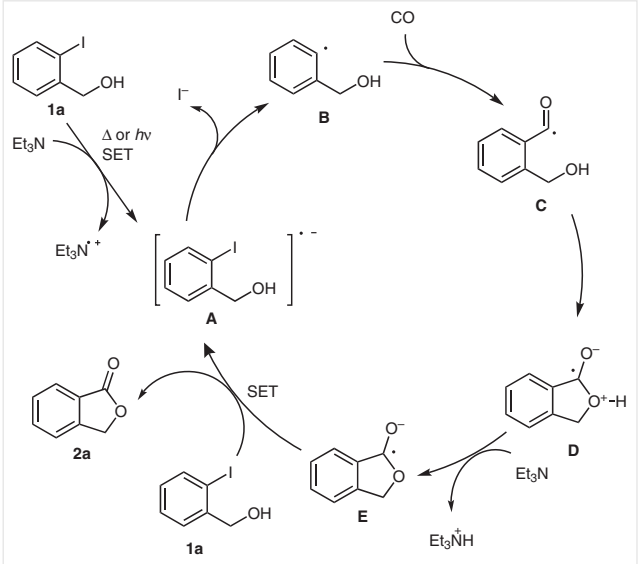


Entry	Substrate	CO (atm)[a]	Conditions	Time (h)	Yield (%)[b]
1	**1a**	65	230 °C	16	58 (40)
2	**1a**	65	250 °C	16	91 (0)
3	**1a**	40	250 °C	16	79[c] (3)
4	**1a′**	65	250 °C	16	0 (100)
5[d]	**1a**	75	Xe	22	60[c] (22)
6[e]	**1a**	70	Xe	48	85 (7)

[a] Initial CO pressure.
[b] Yield of isolated product after silica gel chromatography. NMR yield of unreacted substrate is shown in parentheses.
[c] NMR yield.
[d] Xe lamp (500 W, quartz), Et_3N (2.5 equiv).
[e] Xe lamp (500 W, quartz), Et_3N (2 equiv).

With the optimized thermal conditions in hand (Table 1, entry 2), we next examined the substrate scope of the present intramolecular Heck carbonylation leading to benzolactones (Table 2). The reaction proceeded regardless of the class of alcohol, and secondary (**1b** and **1c**) and tertiary (**1d**) alcohols gave the corresponding benzolactones **2b–d** in good yields (entries 2–4). Substituted iodoarenes **1e–i** participated in the present benzolactone synthesis: the reactions of 2-iodo-3-methylbenzyl alcohol (**1e**), 2-iodo-4-methylbenzyl alcohol (**1f**), 4-chloro-2-iodobenzyl alcohol (**1g**), 2-iodo-5-methylbenzyl alcohol (**1h**), and 5-chloro-2-iodobenzyl alcohol (**1i**) gave good yields of products **2e–i** (entries 5–9). The reaction of 3-hydroxymethyl-2-iodonaphthalene (**1j**) gave naphtholactone **2j** in a 95% yield. The protocol was successfully extended to the synthesis of six-membered benzolactone **2k** as well (entry 11), whereas seven-membered benzolactone **2l** was obtained in a low yield (entry 12). Benzolactone **2k** was also obtained under photoirradiation conditions, albeit in an inferior yield (entry 11). We also tested 2-iodoacetoamide **1m**, which was converted into 2-methyl-4-oxo-3,1-benzoxazine (**2m**) in a 36% yield. The result of the reaction of 5-bromo-2-iodobenzyl alcohol (**1n**) was intriguing since the less reactive bromoarene portion also underwent aminocarbonylation (entry 14). The formation of **2n′** would have been caused by intramolecular electron transfer, and, indeed, a similar result was observed in a photo-induced aminocarbonylation reaction.[16]

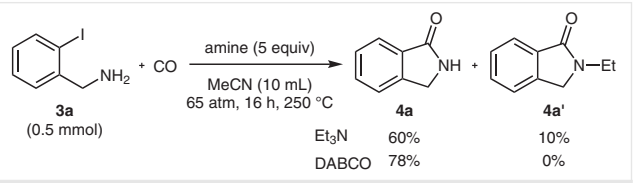
We propose an electron-transfer-based pathway for the present carbonylation leading to lactones (Scheme 2). A single-electron transfer (SET) between Et_3N and the aryl iodide **1a** generates radical anion **A**, which is followed by the elimination of an iodide anion to generate aryl radical **B**. The aryl radical **B** would then react with CO to give acyl radical **C**. Nucleophilic addition of the hydroxy group to the acyl radical moiety would give a zwitterionic radical intermediate **D**.[10] Deprotonation followed by a single-electron transfer (SET) from radical anion **E** to another molecule of starting substrate **1a** would then give **2a** and regenerate radical anion **A**.



Scheme 2 Proposed mechanism for the cyclative carbonylation of iodoarenes with an electron as the catalyst

We next investigated the reaction of 2-iodobenzyl amines (Scheme 3). The reaction of 2-iodobenzyl amine (**3a**) with CO at 250 °C gave the corresponding benzolactam **4a** in a 60% yield along with a 10% yield of ethyl-substituted benzolactam (**4a′**). The by-product **4a′** would be formed by the reaction of **4a** with EtI, which would be generated by the reaction of Et_3N with HI·Et_3N at 250 °C.[17] We found that

the formation of **4a′** was suppressed by the use of DABCO (1,4-diazabicyclo[2.2.2]octane) as the base, and benzolactam **4a** was obtained as the sole product in a 78% yield.

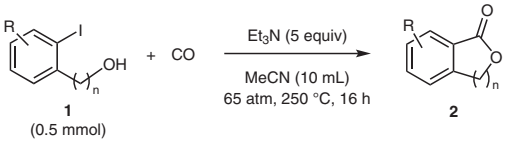


Scheme 3 Synthesis of benzolactam **4a** from benzyl amine **3a** and CO

Next, we examined the substrate scope of the intramolecular aminocarbonylation (Table 3). The reaction of secondary amine **3b** gave the corresponding benzolactam **4b** in good yield (entry 2). Halogen-substituted benzolactams **4c** and **4d** were also obtained in good yields (entries 3 and 4). The reaction of benzyl amine **3e** having a CF_3 substituent proceeded well to give CF_3-substituted benzolactam **4e** in an 85% yield (entry 5). In a similar manner, the reaction of 2-iodobenzamide **3f** gave phthalimide **4f** in a 73% yield (entry 6).

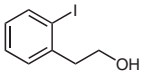
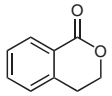
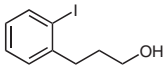
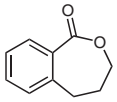
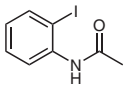
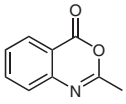
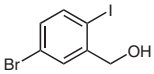
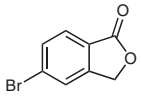
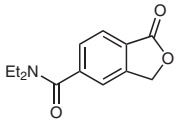
In summary, we have found that a transition-metal-free synthesis of benzolactones and benzolactams by carbonylation can be achieved using an electron as the catalyst. Further applications of metal-free carbonylation reactions based on the same concept are currently being investigated in our laboratory.

Table 2 Synthesis of Benzolactones **2** from Substrates **1** and CO



Entry	Substrate	Product	Yield (%)[a]
1	**1a**	**2a**	91 (85)[b]
2 3	**1b**, R = Me **1c**, R = Pr	**2b** **2c**	59 73
4	**1d**	**2d**	79
5[c]	**1e**	**2e**	75
6[c] 7	**1f**, R = Me **1g**, R = Cl	**2f** **2g**	75 81
8[c] 9	**1h**, R = Me **1i**, R = Cl	**2h** **2i**	71 87
10	**1j**	**2j**	95

Table 2 (continued)

Entry	Substrate		Product		Yield (%)[a]
11[c]	**1k**		**2k**		93 (51)[b]
12	**1l**		**2l**		25
13	**1m**		**2m**		36
14	**1n**		**2n**		3[d]
			2n′		34

[a] Yield of isolated product after silica gel column chromatography.
[b] Xe lamp irradiation, quartz tube, Et_3N (2 equiv), CO (70 atm), 48 h.
[c] Reaction time: 24 h.
[d] NMR yield.

Photoirradiation reactions were carried out using a stainless autoclave with quartz windows lined with a 30 mmϕ quartz glass liner and employing a 500 W Xenon short arc lamp (Using Co. Ltd., lamp house: SX-UI500XQ, Xenon short arc lamp: UXL-500SX, power supply: BA-X500). Thin-layer chromatography (TLC) was performed on Merck precoated plates (silica gel 60 F254, Art 5715, 0.25 nm). The products were purified by flash chromatography on silica gel [Kanto Chem. Co. Silica Gel 60N (spherical, neutral, 40–50 µm)] and, if necessary, were further purified by recycling preparative HPLC (Japan Analytical Industry Co. Ltd., LC-918) equipped with GPC columns (JAIGEL-1H + JAIGEL-2H columns) using $CHCl_3$ as the eluent. Melting points were measured in capillary tubes using a BÜCHI Melting Point B-540 instrument. Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer and are reported as wavenumbers (cm^{-1}). ^1H, ^{13}C and ^{19}F NMR spectra were recorded with JEOL JNM-ECS400 and Varian MR400 spectrometers. ^1H NMR spectra were recorded at 400 MHz and referenced to the residual solvent peak at 7.26 ppm. ^{13}C NMR spectra were recorded at 100 MHz and referenced to the solvent peak at 77.00 ppm. ^{19}F NMR spectra were recorded at 378 MHz. Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Low-resolution El mass spectra (EIMS) were recorded with a JEOL MS700 spectrometer. High-resolution mass spectra (HRMS) were recorded with a JEOL MS700 spectrometer and ESI-QTOF (compact-NPC, Bruker).

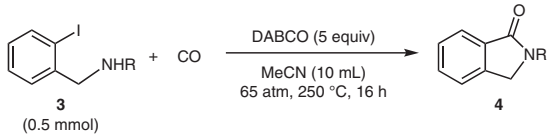
Reaction of 2-Iodobenzyl Alcohol (1a) with CO under Thermal Conditions; Typical Procedure

A magnetic stir bar, 2-iodobenzyl alcohol (**1a**) (116.0 mg, 0.5 mmol), Et_3N (251.6 mg, 2.5 mmol), and MeCN (10 mL) were placed in a stainless steel autoclave equipped with an inserted Pyrex glass liner. The autoclave was closed, purged three times with CO, pressurized with 65 atm of CO and then heated at 250 °C in a salt bath with stirring for 16 h. After the reaction was complete, excess CO was discharged at room temperature. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, 3:1) to give **2a** (60.4 mg, 91%) as a white solid.

Reaction of 2-Iodobenzyl Alcohol (1a) with CO under Photoirradiation Conditions; Typical Procedure

A magnetic stir bar, 2-iodobenzyl alcohol (**1a**) (117.7 mg, 0.5 mmol), Et_3N (101.2 mg, 1.0 mmol), and MeCN (10 mL) were placed in a stainless steel autoclave for photoreactions equipped with an inserted quartz glass liner. The autoclave was closed, purged three times with carbon monoxide, pressurized with 70 atm of CO and then irradiated with a Xenon arc lamp (500 W) with stirring for 48 h. After the reaction was complete, excess CO was discharged at room temperature. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, 5:1) to give **2a** (57 mg, 85%) as a white solid.

Table 3 Synthesis of Benzolactams **4** via Carbonylation of Substrates **3**



3 (0.5 mmol) **4**

Entry	Substrate	Product	Yield (%)[a]
1	**3a**	**4a**	78
2	**3b**	**4b**	66
3	**3c**	**4c**	72
4	**3d**	**4d**	66
5	**3e**	**4e**	85
6	**3f**	**4f**	73

[a] Yield of isolated product after silica gel column chromatography.

Phthalide (2a)[18a]

Yield: 60 mg (91%); white solid; mp 72.2–73.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 6.2 Hz, 1 H), 7.70 (t, *J* = 7.6 Hz, 1 H), 7.57–7.50 (m, 2H), 5.32 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 146.6, 134.1, 129.1, 125.7, 122.2, 69.8.

3-Methylphthalide (2b)[18b]

Yield: 60 mg (59%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 7.6 Hz, 1 H), 7.70–7.66 (m, *J* = 7.6 Hz, 1 H), 7.55 (t, *J* = 7.6 Hz, 1 H), 7.45 (d, *J* = 7.6 Hz, 1 H), 5.58 (q, *J* = 6.8 Hz, 1 H), 1.64 (d, *J* = 4.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 151.1, 134.0, 129.0, 125.6, 121.5, 77.7, 20.3.

3-*n*-Propylphthalide (2c)[18c]

Yield: 68 mg (73%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.6 Hz, 1 H), 7.67 (t, *J* = 7.6 Hz, 1 H), 7.53 (t, *J* = 7.2 Hz, 1 H), 7.44 (d, *J* = 6.8 Hz, 1 H), 5.49 (dd, *J* = 8.0 Hz, 4.0 Hz, 1 H), 2.06–1.98 (m, 1 H), 1.80–1.71 (m, 1 H), 1.62–1.45 (m, 2 H), 0.99 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 150.1, 133.8, 129.0, 126.1, 125.6, 121.7, 82.2, 36.8, 18.2, 13.8.

3,3-Dimethyl-3*H*-isobenzofuran-1-one (2d)[18d]

Yield: 62 mg; colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.0 Hz, 1 H), 7.67 (dd, *J* = 7.6 Hz, 7.2 Hz, 1 H), 7.51 (dd, *J* = 7.6 Hz, 7.0 Hz, 1 H), 7.40 (d, *J* = 7.2 Hz, 1 H), 1.67 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.7, 154.9, 134.1, 128.8, 125.6, 125.2, 120.6, 85.3, 27.2.

7-Methylphthalide (2e)[18e]

Yield: 60 mg (75%); white solid; mp 87.1–87.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (t, *J* = 7.6 Hz, 1 H), 7.30–7.26 (m, 2 H), 5.26 (s, 2 H), 2.69 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 147.0, 139.7, 133.7, 130.5, 123.1, 119.3, 68.8, 17.2.

6-Methylphthalide (2f)[18d]

Yield: 56 mg (75%); yellow solid; mp 118.0–118.7 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (s, 1 H), 7.50 (d, *J* = 8.0 Hz, 1 H), 7.36 (d, *J* = 7.6 Hz, 1 H), 5.29 (s, 2 H), 2.47 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 143.8, 139.2, 135.1, 125.8, 125.6, 121.7, 69.5, 21.2.

6-Chlorophthalide (2g)[18f]

Yield: 69 mg (81%); white solid; mp 108.3–109.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 2.0 Hz, 1 H), 7.66 (d, *J* = 8.4 Hz, 1 H), 7.47 (d, *J* = 8.0 Hz, 1 H), 5.32 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.5, 144.6, 135.3, 134.3, 127.5, 125.6, 123.3, 69.4.

5-Methylphthalide (2h)[18f]

Yield: 52 mg (71%); white solid; mp 117.7–119.1 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.0 Hz, 1 H), 7.34 (d, *J* = 8.4 Hz, 1 H), 7.28 (s, 1 H), 5.27 (s, 2 H), 2.50 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 147.1, 145.2, 130.2, 125.5, 123.2, 122.3, 69.4, 22.0.

5-Chlorophthalide (2i)[18g]

Yield: 75 mg (87%); white solid; mp 154.7–155.3 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.84 (m, 1 H), 7.55–7.51 (m, 2 H), 5.31 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 148.1, 140.7, 129.8, 126.8, 124.2, 122.5, 68.9.

Naphtho[2,3-*c*]furan-1(3*H*)-one (2j)[18h]

Yield: 86 mg (95%); white solid; mp 210.2–211.3 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (s, 1 H), 8.04 (d, *J* = 8.4 Hz, 1 H), 7.94 (d, *J* = 8.4 Hz, 1 H), 7.90 (s, 1 H), 7.58–7.68 (m, 2 H), 5.50 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 139.9, 136.2, 133.1, 129.9, 129.0, 128.1, 127.0, 126.9, 123.4, 120.9, 69.6.

Isochroman-1-one (2k)[18e]

Yield: 70 mg (93%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 7.6 Hz, 1 H), 7.55 (td, *J* = 12.0 Hz, 1.2 Hz, 1 H), 7.41 (t, *J* = 7.2 Hz, 1 H), 7.27 (d, *J* = 6.4 Hz, 1 H), 4.55 (t, *J* = 5.6 Hz, 2 H), 3.07 (t, *J* = 6.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.1, 139.5, 133.6, 130.2, 127.6, 127.2, 125.1, 67.2, 27.7.

4,5-Dihydro-2-benzoxepin-1(3*H*)-one (2l)[18i]

Yield: 20 mg (25%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 8.0 Hz, 1.2 Hz, 1 H), 7.49 (td, *J* = 7.2 Hz, 1.6 Hz, 1 H), 7.37 (td, *J* = 8.0 Hz, 0.8 Hz, 1 H), 7.22 (d, *J* = 8.0 Hz, 1 H), 4.16 (t, *J* = 6.4 Hz, 2 H), 2.91 (t, *J* = 7.2 Hz, 2 H), 2.13 (quin, *J* = 7.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 137.5, 132.6, 131.6, 130.1, 128.6, 127.3, 66.5, 29.4, 27.7.

2-Methyl-3,1-benzoxazin-4-one (2m)[18j]

Yield: 29 mg (36%); white solid; mp 73.6–76.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 8.0 Hz, 1.6 Hz, 1 H), 7.82–7.78 (m, 1 H), 7.56–7.49 (m, 2 H), 2.48 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 159.7, 146.4, 135.5, 128.4, 128.2, 126.4, 116.6, 21.4.

***N*,*N*-Diethyl-1,3-dihydro-1-oxo-5-isobenzofurancarboxamide (2n′)**

Yield: 39 mg (34%); yellow solid; mp 105.0–109.0 °C.

IR (neat): 3486, 3225, 2979, 2877, 2520, 2370, 2130, 1752, 1637, 1449, 1278, 1159, 1065, 1005, 867, 784, 706, 579 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.93 (m, 1 H), 7.52–7.51 (m, 2 H), 5.36 (s, 2 H), 3.59–3.48 (m, 2 H), 3.32–3.23 (m, 2 H), 1.29–1.26 (m, 3 H), 1.20–1.11 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 169.5, 146.8, 143.0, 127.0, 126.1, 126.0, 120.1, 69.5, 43.2, 39.4, 14.1, 12.8.

EIMS: *m*/*z* (%) = 233 (18) $[M]^+$, 232 (47), 161 (100), 133 (19), 103 (10), 83 (13).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{15}NO_3$: 233.1052; found: 233.1056.

Isoindoline-1-one (4a)[18k]

Yield: 50 mg (78%); white solid; mp 151.3–151.7 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (br s, 1 H), 7.88 (d, *J* = 7.6 Hz, 1 H), 7.60–7.56 (m, 1 H), 7.50–7.47 (m, 2 H), 4.49 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 143.8, 132.3, 131.8, 128.1, 123.8, 123.3, 45.9.

2-Methylisoindoline-1-one (4b)[18l]

Yield: 44 mg (66%); white solid; mp 112.6–113.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.2 Hz, 1 H), 7.52–7.50 (m, 1 H), 7.46–7.42 (m, 2 H), 4.37 (s, 2 H), 3.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 140.9, 132.8, 131.1, 127.9, 123.5, 122.5, 51.9, 29.4.

5-Chloro-2-methylisoindoline-1-one (4c)

Yield: 71 mg (72%); yellow solid; mp 113.3–114.0 °C.

IR (neat): 3337, 3067, 2917, 2867, 2366, 1920, 1673, 1613, 1423, 1396, 1280, 1173, 1063, 940, 877, 842, 766, 674, 636, 547, 527, 418 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76–7.74 (m, 1 H), 7.44–7.43 (m, 2 H), 4.36 (s, 2 H), 3.19 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.5, 142.5, 137.4, 131.4, 128.6, 124.7, 123.0, 51.5, 29.5.

EIMS: *m*/*z* (%) = 183 (39) $[M]^+$, 181 (94), 146 (100), 125 (36), 89 (35), 75 (18).

HRMS (EI): *m*/*z* $[M]^+$ calcd for C_9H_8ClNO: 181.0294; found: 181.0302.

5-Fluoro-2-methylisoindoline-1-one (4d)

Yield: 54 mg (66%); white solid; mp 78.4–79.3 °C.

IR (neat): 3448, 3071, 2864, 1686, 1619, 1473, 1251, 1090, 770, 678, 570 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 8.2 Hz, 4.8 Hz, 1 H), 7.17–7.12 (m, 2 H), 4.36 (s, 2 H), 3.19 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.6, 164.9 (d, J_{C-F} = 248.2 Hz), 143.2 (d, J_{C-F} = 9.6 Hz), 128.9, 125.4 (d, J_{C-F} = 9.5 Hz), 115.7 (d, J_{C-F} = 22.9 Hz), 110.0 (d, J_{C-F} = 23.9 Hz), 51.6, 29.4.

^{19}F NMR (378 MHz, $CDCl_3$): δ = –108.2 (s, 1 F).

EIMS: *m*/*z* (%) = 165 (100) $[M]^+$, 164 (59), 136 (57), 109 (44), 69 (81).

HRMS (EI): *m*/*z* $[M]^+$ calcd for C_9H_8FNO: 165.0590; found: 165.0590.

2-Methyl-6-(trifluoromethyl)isoindoline-1-one (4e)

Yield: 90 mg (85%); brown solid; mp 103.5–106.1 °C.

IR (neat): 3354, 2970, 2918, 1819, 1686, 1483, 1328, 1166, 1132, 1050, 960, 912, 846, 768, 635, 607, 509 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1 H), 7.79 (d, *J* = 7.6 Hz, 1 H), 7.58 (d, *J* = 8.0 Hz, 1 H), 4.45 (s, 2 H), 3.23 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.1, 144.3, 133.6, 130.8 (q, J_{C-F} = 32.5 Hz), 127.9 (q, J_{C-F} = 3.8 Hz), 123.8 (q, J_{C-F} = 270.2 Hz), 123.2, 120.7 (q, J_{C-F} = 3.8 Hz), 51.8, 29.5.

^{19}F NMR (378 MHz, $CDCl_3$): δ = –62.2 (s, 3 F).

EIMS: *m*/*z* (%) = 215 (100) $[M]^+$, 214 (53), 196 (21), 186 (37), 159 (32), 146 (57), 83 (22).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{10}H_8F_3NO$: 215.0558; found: 215.0560.

***N*-Methylphthalimide (4f)**[18m]

Yield: 73 mg (73%); white solid; mp 134.0–134.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.83 (m, 2 H), 7.74–7.69 (m, 2 H), 3.19 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 133.8, 132.2, 133.1, 23.9.

Funding Information

This work was supported by Grants-in-Aid for Scientific Research (A) (no. 26248031) from JSPS and Scientific Research on Innovative Areas 2707 Middle molecular strategy (no. 15H05850) from MEXT.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1609964.

References

(1) (a) Beller, M. *Catalytic Carbonylation Reactions*, In *Topics in Organometallic Chemistry*; Springer: Berlin, **2006**. (b) *Modern Carbonylation Methods*; Kollár, L., Ed.; Wiley-VCH: Weinheim, **2008**. (c) Fukuyama, T.; Maetani, S.; Ryu, I. *Carbonylation and Decarbonylation Reactions*, In *Comprehensive Organic Synthesis*, 2nd ed., Vol. 3; Molander, G. A.; Knochel, P., Eds.; Elsevier: Oxford, **2014**, 1073–1100. (d) Wu, X.-F.; Beller, M. *Transition Metal Catalyzed Carbonylative Synthesis of Heterocycles*, In *Topics in Heterocyclic Chemistry*; Springer International: Cham, **2016**.

(2) (a) Schoenberg, A.; Bartoletti, I.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3318. (b) Schoenberg, A.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3327.

(3) (a) Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4193. (b) Mori, M.; Chiba, K.; Ban, Y. *J. Org. Chem.* **1978**, *43*, 1684.

(4) For reviews on radical carbonylation, see: (a) Ryu, I.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1050. (b) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177. (c) Ryu, I. *Chem. Soc. Rev.* **2001**, *30*, 16. (d) Ryu, I. *Chem. Rec.* **2002**, *2*, 249. (e) Ryu, I.; Uenoyama, Y.; Matsubara, H. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1476. (f) Schiesser, C. H.; Wille, U.; Matsubara, H.; Ryu, I. *Acc. Chem. Res.* **2007**, *40*, 303. (g) Sumino, S.; Fusano, A.; Fukuyama, T.; Ryu, I. *Acc. Chem. Res.* **2014**, *47*, 1563.

(5) For a review of acyl radicals, see: Chatgilialoglu, C.; Crich, D.; Komatsu, M.; Ryu, I. *Chem. Rev.* **1999**, *99*, 1991.

(6) For reviews, see: (a) Studer, A.; Curran, D. P. *Nat. Chem.* **2014**, *6*, 765. (b) Studer, A.; Curran, D. P. *Angew. Chem. Int. Ed.* **2016**, *55*, 58.

(7) Shirakawa, E.; Hayashi, T. *Chem. Lett.* **2012**, *41*, 130.

(8) (a) Ryu, I.; Kusano, K.; Masumi, N.; Yamazaki, H.; Ogawa, A.; Sonoda, N. *Tetrahedron Lett.* **1990**, *31*, 6887. (b) Ryu, I.; Yamazaki, H.; Ogawa, A.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1993**, *115*, 1187. (c) Kawamoto, T.; Okada, T.; Curran, D. P.; Ryu, I. *Org. Lett.* **2013**, *15*, 2144.

(9) For carbonylative synthesis of amides and lactams including trapping of acyl radicals by amines, see: (a) Uenoyama, Y.; Fukuyama, T.; Nobuta, O.; Matsubara, H.; Ryu, I. *Angew. Chem. Int. Ed.* **2005**, *44*, 1075. (b) Uenoyama, Y.; Fukuyama, T.; Ryu, I. *Org. Lett.* **2007**, *9*, 935. (c) Ryu, I.; Fukuyama, T.; Tojino, M.; Uenoyama, Y.; Yonamine, Y.; Terasoma, N.; Matsubara, H. *Org. Biomol. Chem.* **2011**, *9*, 3780. (d) Fukuyama, T.; Nakashima, N.; Okada, T.; Ryu, I. *J. Am. Chem. Soc.* **2013**, *135*, 1006.

(10) For a related lactone synthesis, see: Ryu, I.; Fukuyama, T.; Nobuta, O.; Uenoyama, Y. *Bull. Korean Chem. Soc.* **2010**, *31*, 545.

(11) Zhang, H.; Shi, R.; Ding, A.; Lu, L.; Chen, B.; Lei, A. *Angew. Chem. Int. Ed.* **2012**, *51*, 12542.

(12) Fukuoka, S. *Ind. Eng. Chem. Res.* **2016**, *55*, 4830.

(13) Guo, W.; Lu, L.-Q.; Wang, Y.-N.; Chen, J.-R.; Xiao, W. J. *Angew. Chem. Int. Ed.* **2015**, *54*, 2265.

(14) Majek, M.; von Wangelin, A. J. *Angew. Chem. Int. Ed.* **2015**, *54*, 2270.

(15) Koziakov, D.; von Wangelin, A. J. *Org. Biomol. Chem.* **2017**, *15*, 6715.

(16) Kawamoto, T.; Sato, A.; Ryu, I. *Chem. Eur. J.* **2015**, *21*, 14764.

(17) In a separate experiment we confirmed that 1-iodooctane was formed from trioctylamine and NH_4I at 250 °C.

(18) (a) Jiang, X.; Zhang, J.; Ma, S. *J. Am. Chem. Soc.* **2016**, *138*, 8344. (b) Gerbino, D. C.; Augner, D.; Slavov, N.; Schmalz, H.-G. *Org. Lett.* **2012**, *14*, 2338. (c) Ranade, V. S.; Consiglio, G.; Prins, R. *J. Org. Chem.* **2000**, *62*, 1132. (d) Lodi, M.; Gedu, S. *J. Org. Chem.* **2015**, *80*, 7089. (e) Hattori, T.; Ueda, S.; Takakura, R.; Sawama, Y.; Monguchi, Y.; Sajiki, H. *Chem. Eur. J.* **2017**, *23*, 8196. (f) Nguyen, T. Q.; Rodriguez-Santamaria, J. A.; Yoo, W.-J.; Kobayashi, S. *Green Chem.* **2017**, *19*, 2501. (g) Gonzalez-de-Castro, A.; Robertson, C. M.; Xiao, J. *J. Am. Chem. Soc.* **2014**, *136*, 8350. (h) Bhavani, S. C.; Beeraiah, B. *Eur. J. Org. Chem.* **2017**, 3381. (i) Morimoto, T.; Fujioka, M.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Organomet. Chem.* **2007**, *692*, 625. (j) Verma, A.; Kumar, S. *Org. Lett.* **2016**, *18*, 4388. (k) Lopez-Valdez, G.; Olguin-Uribe, S.; Millan-Orriz, A.; Gamez-Montano, R.; Miranda, L. *Tetrahedron* **2011**, *67*, 2693. (l) Adachi, S.; Onozuka, M.; Yoshida, Y.; Ide, M.; Saikawa, Y.; Nakata, M. *Org. Lett.* **2014**, *16*, 358. (m) Wang, L.; Fu, H.; Jiang, Y.; Zhao, Y. *Chem. Eur. J.* **2008**, *14*, 10722.