Supporting Information

Copper-catalyzed aerobic double functionalization of benzylic C(sp³)−H bonds
for the synthesis of 3-hydroxyisoindolinones

Kanako Nozawa-Kumada,* Yuta Matsuzawa, Kanako Ono, Masanori Shigeno and Yoshinori Kondo*

Graduate School of Pharmaceutical Sciences, Tohoku University, 6-3, Aoba, Aramaki, Aoba-ku,
Sendai 980-8578, Japan

*E-mail: kanako.kumada.d1@tohoku.ac.jp, yoshinori.kondo.a7@tohoku.ac.jp
# Table of Contents

1. General comments .................................................. S3
2. Materials .......................................................... S3
3. Preparation of starting materials ............................... S3
4. General procedure for the intramolecular C(sp$^3$)–H amidation of 1a .............................. S15
5. General procedure for the intramolecular C(sp$^3$)–H amidation of 2-alkyl-N-phenylbenzamide .......................................................... S25
6. Procedure for gram-scale synthesis of the 3-hydroxyisoindolinone 2a .............................. S31
7. Mechanistic study .................................................. S32
8. References .......................................................... S32
9. $^1$H-, $^{13}$C-, and $^{19}$F-NMR spectra ............................. S34
1. General comments

Unless otherwise noted, reactions were carried out under N₂ atmosphere. Melting points were measured with a Yazawa micro melting point apparatus and uncorrected. IR spectra were recorded on a SHIMADZU IRAffinity. ¹H-NMR spectra were recorded on a JEOL JNM-AL400 (400 MHz) spectrometer or a JEOL ECA600 (600 MHz) spectrometer. Chemical shifts are expressed in δ (parts per million, ppm) values and coupling constants are expressed in hertz (Hz). ¹H NMR spectra were referenced to tetramethylsilane as an internal standard or to a solvent signal (CDCl₃: 7.26 ppm, DMSO-d₆: 2.49 ppm, CD₃OD: 3.30 ppm). ¹³C NMR spectra were referenced to a solvent signal (CDCl₃: 77.0 ppm, DMSO-d₆: 39.5 ppm, CD₃OD: 49.0 ppm, acetone-d₆: 29.8 ppm). ¹⁹F NMR spectra were referenced to 4-fluorotoluene as an internal standard (−118.0 ppm). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, dd, = double doublet, dt = double triplet, td = triple doublet, m = multiplet. Low and high resolution mass spectra (LRMS and HRMS) were obtained from Mass Spectrometry Resource, Graduate School of Pharmaceutical Sciences, Tohoku University, on a JEOL JMS-DX 303 and JMS-700/JMS-T 100 GC spectrometer. Gel permeation chromatography (GPC) was conducted with a Recycling Preparative HPLC LC-9210 (Japan Analytical Industry, Co. Ltd.).

2. Materials

Materials were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used as received. Flash column chromatography was performed with Kanto silica gel 60 N (spherical, neutral, 70−230 mesh).

3. Preparation of starting materials

1r was prepared according to the literature procedure. Other starting materials were prepared according to the following methods.

Method A

To a solution of 2-alkylbenzoic acid (1.0 equiv.) in dry DCM (0.25 M) was added (COCl)₂ (1.2 equiv.) dropwise at 0 °C, followed by a catalytic amount of DMF (3 drops). The reaction mixture was allowed to stir at rt until completion. The solvent was then removed to afford the corresponding crude acid chloride. To a solution of acid chloride in dry DCM (0.25 M) were added aniline derivative (1.2 equiv.) and triethylamine (1.2 equiv.) dropwise at 0 °C, and the mixture was stirred at rt overnight. The reaction was diluted with 1M HCl aq. (10 mL) and extracted with DCM (2 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried over Na₂SO₄ and concentrated under reduced pressure. The residue was then purified by recrystallization to afford the corresponding amide.
compound.

**Method B**

Step 1: A solution of aryl bromide **A** (1.2 equiv.) in THF (0.25 M) was added slowly to the mixture of Mg (1.0 equiv.) with small amount of I₂ (0.01 equiv.), and the mixture was stirred for 1 h. Then, a solution of substrate **B** (1.0 equiv.) in THF (0.10 M) was added to the reaction mixture slowly. The resultant mixture was stirred at rt until the reaction was completed as monitored by TLC. The reaction mixture was slowly diluted with sat. NH₄Cl aq. (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by SiO₂ column chromatography to give the alcohol **C**.

Step 2: To a solution of the substrate **C** (1.0 equiv.) in DCM (0.20 M) was added CF₃CO₂H (4.0 equiv.) dropwise at 0 °C. After stirred for 10 min, Et₃SiH (2.0 equiv.) was added dropwise, and the resulting mixture was stirred at rt overnight. The solvent was concentrated under reduced pressure, and the residue was purified by SiO₂ column chromatography to give the substrate **D**.

Step 3: To a solution of compound **D** (1.0 equiv.) in THF (0.20 M) was added n-BuLi (1.5 equiv.) dropwise at −78 °C. The reaction mixture was stirred at −78 °C for 1 h. Then anhydrous CO₂ was bubbled through the mixture for 30 min. The reaction mixture was allowed to warm to rt for 30 min. The reaction was quenched with H₂O (10 mL), alkalized with 1M NaOH aq. to pH 12–14, and washed with Et₂O (10 mL). The resulting aqueous layer was acidified with HCl aq. to pH 1–2, and extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), then dried over Na₂SO₄ and concentrated under reduced pressure to give the crude carboxylic acid **E**, which was used in the next step without further purification.

Step 4: To a solution of compound **E** (1.0 equiv.) in dry DCM (0.25 M) was added (COCl)₂ (1.2 equiv.) dropwise at 0 °C, followed by a catalytic amount of DMF (3 drops). The reaction was allowed to stir at rt until completion. The solvent was then removed to afford the corresponding crude acid
chloride. To a solution of acid chloride in dry DCM (0.25 M) were added aniline (1.2 equiv.) and triethylamine (1.2 equiv.) dropwise at 0 °C, and stirred at rt overnight. The reaction was diluted with 1M HCl aq. (10 mL) and extracted with DCM (2 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The crude material was then purified by recrystallization to afford the corresponding amide compound.

**Method C**

To a solution of 2-benzylbenzoic acid (1.0 equiv.) in dry DCM (0.25 M) was added (COCl)$_2$ (1.2 equiv.) dropwise at 0 °C, followed by a catalytic amount of DMF (3 drops). The reaction was allowed to stir at rt until completion. The solvent was then removed to afford the corresponding crude acid chloride. A solution of the acid chloride in EtOAc (1.0 M) was added dropwise to the mixture of NH$_2$OR·HCl (1.2 equiv.) and K$_2$CO$_3$ (2.0 equiv.) in EtOAc (0.25 M) and H$_2$O (0.50 M) at 0 °C, and stirred at rt overnight. The reaction mixture was extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was then purified by SiO$_2$ column chromatography to afford the corresponding amide.

**2-Benzyl-N-phenylbenzamide (1a)**

\[
\begin{array}{c}
\text{Ph} \\
\text{Ph} \\
\text{N} \\
\text{O} \\
\end{array}
\]

Prepared according to Method A, 1054.7 mg (74%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 123–125 °C.

$^1$H NMR (400 MHz, CDCl$_3$/TMS) δ (ppm): 7.54 (1H, d, $J = 7.8$ Hz), 7.43–7.37 (3H, m), 7.33–7.29 (4H, m), 7.27–7.23 (3H, m), 7.20–7.16 (3H, m), 7.12 (1H, t, $J = 7.3$ Hz), 4.24 (2H, s); $^{13}$C($^1$H) NMR (100 MHz, CDCl$_3$/TMS) δ (ppm): 167.9, 140.5, 138.6, 137.7, 136.8, 131.2, 130.3, 128.9, 128.8, 128.6, 127.4, 126.6, 126.3, 124.4, 119.9, 38.9; LRMS (EI) $m/z$: 287 ($M^+$); HRMS (EI-EB) Calcd. for C$_{20}$H$_{17}$NO: 287.1310, found: 287.1323; IR (neat): 3328, 3026, 1654, 1597, 1525, 1495, 1436, 1320, 744, 722 cm$^{-1}$.

**2-Benzyl-5-methyl-N-phenylbenzamide (1b)**

\[
\begin{array}{c}
\text{Me} \\
\text{Ph} \\
\text{N} \\
\text{O} \\
\end{array}
\]

Prepared according to Method B, 843.9 mg (31% over 4 steps, 10.0 mmol scale), recrystallized from
DCM/hexane, colorless needles, mp. 164–165 °C.

\(^1\)H NMR (600 MHz, CDCl\(_3/\)TMS) \(\delta\) (ppm): 7.37–7.34 (3H, m), 7.31–7.28 (3H, m), 7.25–7.21 (3H, m), 7.18–7.15 (4H, m), 7.10 (1H, t, \(J = 7.6\) Hz), 4.18 (2H, s), 2.36 (3H, s); \(^{13}\)C\(^{1}\)H) NMR (150 MHz, CDCl\(_3/\)TMS) \(\delta\) (ppm): 168.0, 140.8, 137.7, 136.7, 136.4, 135.3, 131.2, 131.1, 128.9, 128.7, 128.6, 128.1, 126.2, 124.4, 119.8, 38.6, 20.9; LRMS (EI) \(m/\ell\): 301 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{21}\)H\(_{19}\)NO: 301.1467, found: 301.1470; IR (neat): 3247, 3028, 1652, 1593, 1501, 1436, 1326, 752, 731 cm\(^{-1}\).

### 2-Benzyl-5-fluoro-N-phenylbenzamide (1c)

\(\text{ Prepared according to Method B, 689.6 mg (23% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 133–135 °C.} \)

\(^1\)H NMR (600 MHz, CDCl\(_3/\)TMS) \(\delta\) (ppm): 7.47 (1H, s), 7.34 (2H, d, \(J = 8.0\) Hz), 7.28 (2H, t, \(J = 7.7\) Hz), 7.24–7.16 (5H, m), 7.12–7.05 (4H, m), 4.14 (2H, s); \(^{13}\)C\(^{1}\)H) NMR (150 MHz, CDCl\(_3/\)TMS) \(\delta\) (ppm): 166.5, 161.0 (C–F, \(\J_{C-F} = 247.7\) Hz), 140.3, 138.2 (C–F, \(\J_{C-F} = 5.8\) Hz), 137.4, 134.2 (C–F, \(\J_{C-F} = 2.9\) Hz), 132.9, 132.8, 128.9, 128.7 (C–F, \(\J_{C-F} = 5.8\) Hz), 126.4, 124.7, 120.0, 117.2 (C–F, \(\J_{C-F} = 2.9\) Hz), 114.5 (C–F, \(\J_{C-F} = 23.0\) Hz), 38.2; \(^{19}\)F NMR (565 MHz, CDCl\(_3/\)TMS) \(\delta\) (ppm): -114.6; LRMS (EI) \(m/\ell\): 305 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{20}\)H\(_{16}\)FNO: 305.1216, found: 305.1194; IR (neat): 3239, 3072, 1653, 1595, 1493, 1442, 1328, 751, 731 cm\(^{-1}\).

### 2-Benzyl-5-chloro-N-phenylbenzamide (1d)

\(\text{ Prepared according to Method B, 81.4 mg (3% over 4 steps, 7.5 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 145–147 °C.} \)

\(^1\)H NMR (600 MHz, CDCl\(_3/\)TMS) \(\delta\) (ppm): 7.49 (1H, s), 7.37–7.35 (3H, m), 7.30 (2H, t, \(J = 7.8\) Hz), 7.25–7.17 (5H, m), 7.14–7.11 (3H, m), 4.17 (2H, s); \(^{13}\)C\(^{1}\)H) NMR (150 MHz, CDCl\(_3/\)TMS) \(\delta\) (ppm): 166.4, 140.0, 138.3, 137.4, 137.2, 132.6, 132.5, 130.4, 129.0, 128.8, 128.7, 127.5, 126.5, 124.8, 120.0, 38.5; LRMS (EI) \(m/\ell\): 321 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{20}\)H\(_{16}\)ClNO: 321.0920, found: 321.0924; IR (neat): 3247, 2962, 1650, 1595, 1495, 1442, 1327, 749, 731 cm\(^{-1}\).
2-Benzyl-4-methoxy-N-phenylbenzamide (1e)

Prepared according to Method B, 602.6 mg (19% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 165–167 °C.

$^1$H NMR (600 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 7.51 (1H, d, $J = 8.3$ Hz), 7.36–7.25 (7H, m), 7.20–7.18 (3H, m), 7.10 (1H, t, $J = 7.3$ Hz), 6.81–6.78 (2H, m), 4.23 (2H, s), 3.80 (3H, s); $^{13}$C {$^1$H} NMR (150 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 167.6, 161.0, 140.9, 140.4, 137.9, 129.4, 129.3, 128.9, 128.8, 128.7, 126.3, 124.3, 119.8, 117.0, 111.5, 55.3, 39.2; LRMS (EI) $m$/z: 317 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{21}$H$_{19}$NO$_2$: 317.1416, found: 317.1407; IR (neat): 3291, 3030, 1645, 1595, 1521, 1494, 1436, 1244, 753, 721 cm$^{-1}$.

2-Benzyl-N-phenyl-4-(trifluoromethyl)benzamide (1f)

Prepared according to Method B, 334.6 mg (9% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 188–192 °C.

$^1$H NMR (600 MHz, CD$_3$OD) $\delta$ (ppm): 7.64–7.60 (2H, m), 7.57–7.53 (3H, m), 7.32 (2H, t, $J = 7.9$ Hz), 7.21–7.12 (6H, m), 4.24 (2H, s); $^{13}$C {$^1$H} NMR (150 MHz, CD$_3$OD) $\delta$ (ppm): 169.6, 142.0, 141.9, 141.0, 139.5, 132.9 (C–F, $^3$J$_{C-F} = 32.5$ Hz), 130.2, 129.8, 129.6, 129.2, 128.2 (C–F, $^3$J$_{C-F} = 3.8$ Hz), 127.5, 125.8, 125.3 (C–F, $^3$J$_{C-F} = 271.2$ Hz), 124.3 (C–F, $^3$J$_{C-F} = 3.8$ Hz), 121.9, 39.6; $^{19}$F NMR (565 MHz, CD$_3$OD): $-61.5$; LRMS (EI) $m$/z: 355 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{21}$H$_{16}$F$_3$NO: 355.1184, found: 355.1178; IR (neat): 3290, 3042, 1651, 1598, 1528, 1322, 1152, 1097, 752, 732 cm$^{-1}$.

6-Benzyl-N-phenylbenzo[d][1,3]dioxole-5-carboxamide (1g)

Prepared according to Method B, 666.5 mg (27% over 4 steps, 7.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 180–185 °C.

$^1$H NMR (600 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 7.34–7.26 (7H, m), 7.21 (1H, t, $J = 7.2$ Hz), 7.18 (2H, d, $J = 6.8$ Hz), 7.10 (1H, t, $J = 7.2$ Hz), 7.04 (1H, s), 6.73 (1H, s), 6.00 (2H, s), 4.15 (2H, s); $^{13}$C {$^1$H} NMR (150 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 167.2, 149.3, 146.2, 140.6, 137.7, 133.2, 130.1, 129.0, 128.7,
128.6, 126.4, 124.4, 119.7, 111.2, 107.8, 101.6, 38.8; LRMS (EI) m/z: 331 (M⁺); HRMS (EI-EB) Calcd. for C₂₁H₁₇NO₃: 331.1208, found: 331.1204; IR (neat): 3236, 3056, 1639, 1594, 1494, 1446, 1035, 751, 731 cm⁻¹.

**2-Benzyl-N-(p-tolyl)benzamide (1h)**

![2-Benzyl-N-(p-tolyl)benzamide (1h) structure]

Prepared according to Method A, 458.0 mg (51%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 149–151 °C.

¹H NMR (600 MHz, CDCl₃/TMS) δ (ppm): 7.51 (1H, d, J = 7.4 Hz), 7.40 (1H, t, J = 7.4 Hz), 7.30–7.23 (7H, m), 7.19–7.16 (3H, m), 7.11 (2H, d, J = 8.2 Hz), 4.22 (2H, s), 2.31 (3H, s); ¹³C(¹H) NMR (150 MHz, CDCl₃/TMS) δ (ppm): 167.8, 140.6, 138.5, 137.0, 135.1, 134.1, 131.2, 130.3, 129.4, 128.8, 128.6, 127.4, 126.6, 126.3, 119.9, 39.0, 20.9; LRMS (EI) m/z: 301 (M⁺); HRMS (EI-EB) Calcd. for C₂₁H₁₉NO: 301.1467, found: 301.1476; IR (neat): 3230, 3027, 1643, 1599, 1510, 1325, 1090, 810, 738 cm⁻¹.

**2-Benzyl-N-(4-methoxyphenyl)benzamide (1i)**

![2-Benzyl-N-(4-methoxyphenyl)benzamide (1i) structure]

Prepared according to Method A, 782.0 mg (84%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 148–150 °C.

¹H NMR (600 MHz, CDCl₃/TMS) δ (ppm): 7.52 (1H, d, J = 7.3 Hz), 7.40 (1H, t, J = 7.3 Hz), 7.31–7.16 (10H, m), 6.85 (2H, d, J = 9.2 Hz), 4.23 (2H, s), 3.80 (3H, s); ¹³C(¹H) NMR (150 MHz, CDCl₃/TMS) δ (ppm): 167.7, 156.5, 140.7, 138.6, 136.9, 131.2, 130.8, 130.3, 128.8, 128.6, 127.4, 126.6, 126.3, 121.7, 114.1, 55.5, 39.0; LRMS (EI) m/z: 317 (M⁺); HRMS (EI-EB) Calcd. for C₂₁H₁₉NO₂: 317.1416, found: 317.1424; IR (neat): 3276, 3025, 1647, 1592, 1325, 1090, 810, 734 cm⁻¹.

**2-Benzyl-N-(4-fluorophenyl)benzamide (1j)**

![2-Benzyl-N-(4-fluorophenyl)benzamide (1j) structure]
Prepared according to Method A, 733.7 mg (87%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 124–126 °C.

$^1$H NMR (600 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 7.53 (1H, d, $J = 7.6$ Hz), 7.43 (1H, t, $J = 7.6$ Hz), 7.33–7.30 (4H, m), 7.26–7.24 (2H, m), 7.20–7.15 (4H, m), 7.00 (2H, t, $J = 8.6$ Hz), 4.23 (2H, s); $^{13}$C {$^1$H} NMR (150 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 167.9, 159.4 (C–F, $^1J_{C-F} = 244.8$ Hz), 140.5, 138.5, 136.6, 133.7 (C–F, $^2J_{C-F} = 2.9$ Hz), 131.2, 130.4, 128.8, 128.5, 127.3, 126.5, 126.2, 121.7 (C–F, $^3J_{C-F} = 7.2$ Hz), 115.5 (C–F, $^2J_{C-F} = 23.0$ Hz), 38.9; $^{19}$F NMR (565 MHz, CDCl$_3$/TMS) $\delta$ (ppm): $-119.0$; LRMS (EI) m/z: 305 (M$^+$); HRMS (EI-EB) Calcd. for C$_{20}$H$_{16}$FNO: 305.1216, found: 305.1223; IR (neat): 3286, 1650, 1403, 1210, 834, 741 cm$^{-1}$.

2-Benzyl-$N$-(4-chlorophenyl)benzamide (1k)

Prepared according to Method A, 540.9 mg (55%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 143–145 °C.

$^1$H NMR (600 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 7.50 (1H, d, $J = 6.4$ Hz), 7.42 (1H, t, $J = 7.4$ Hz), 7.30–7.23 (9H, m), 7.18 (1H, t, $J = 7.4$ Hz), 7.12 (2H, d, $J = 7.3$ Hz), 4.20 (2H, s); $^{13}$C {$^1$H} NMR (150 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 167.8, 140.5, 138.4, 136.6, 136.2, 131.4, 130.6, 129.4, 128.9, 128.8, 128.7, 127.5, 126.7, 126.4, 121.0, 39.0; LRMS (EI) m/z: 321 (M$^+$); HRMS (EI-EB) Calcd. for C$_{20}$H$_{16}$FNO: 321.0920, found: 321.0916; IR (neat): 3301, 1651, 1590, 1505, 1396, 1308, 820, 745 cm$^{-1}$.

2-Benzyl-$N$-(4-bromophenyl)benzamide (1l)

Prepared according to Method A, 1010.2 mg (90%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 136–138 °C.

$^1$H NMR (600 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 7.51 (1H, d, $J = 6.4$ Hz), 7.44–7.39 (3H, m), 7.32–7.24 (7H, m), 7.19–7.17 (1H, m), 7.14 (2H, d, $J = 6.4$ Hz), 4.21 (2H, s); $^{13}$C {$^1$H} NMR (150 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 167.8, 140.5, 138.4, 136.7, 136.6, 131.9, 131.4, 130.6, 128.8, 128.4, 127.5, 126.7, 126.4, 121.3, 117.0, 39.1; LRMS (EI) m/z: 365 (M$^+$); HRMS (EI-EB) Calcd. for C$_{20}$H$_{16}$BrNO: 365.0415, found: 365.0423; IR (neat): 3301, 1653, 1586, 1506, 1391, 817, 745, 703 cm$^{-1}$.
2-Benzyl-N-(4-iodophenyl)benzamide (1m)

![Chemical Structure Image]

Prepared according to Method A, 977.2 mg (82%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 163–165 °C.

$^1$H NMR (600 MHz, CDCl₃/TMS) δ (ppm): 7.59 (2H, d, $J = 6.4$ Hz), 7.51 (1H, d, $J = 7.3$ Hz), 7.43 (1H, t, $J = 7.3$ Hz), 7.31 (2H, t, $J = 7.3$ Hz), 7.25–7.24 (3H, m), 7.19–7.17 (1H, m), 7.15–7.12 (4H, m), 4.21 (2H, s); $^{13}$C{$^1$H} NMR (150 MHz, CDCl₃/TMS) δ (ppm): 167.8, 140.5, 138.4, 137.9, 137.4, 136.6, 131.4, 130.6, 128.74, 128.68, 127.5, 126.7, 126.4, 121.6, 87.6, 39.1; LRMS (EI) m/z: 413 (M⁺); HRMS (EI-EB) Calcd. for C₂₀H₁₆INO: 413.0277, found: 413.0304; IR (neat): 3296, 3021, 1647, 1584, 1506, 1388, 817, 739 cm⁻¹.

2-Benzyl-N-(4-cyanophenyl)benzamide (1n)

![Chemical Structure Image]

Prepared according to Method A, 653.1 mg (70%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 149–152 °C.

$^1$H NMR (600 MHz, CDCl₃/TMS) δ (ppm): 7.59–7.43 (7H, m), 7.33 (2H, t, $J = 6.9$ Hz), 7.26–7.17 (3H, m), 7.12 (2H, d, $J = 7.3$ Hz), 4.20 (2H, s); $^{13}$C{$^1$H} NMR (150 MHz, CDCl₃/TMS) δ (ppm): 168.1, 141.7, 140.3, 138.4, 136.0, 133.1, 131.5, 130.9, 128.70, 128.68, 127.6, 126.8, 126.5, 119.5, 118.7, 107.2, 39.1; LRMS (EI) m/z: 312 (M⁺); HRMS (EI-EB) Calcd. for C₂₁H₁₆N₂O: 312.1263, found: 312.1257; IR (neat): 3280, 2226, 1657, 1592, 1508, 1405, 1322, 838, 731 cm⁻¹.

tert-Butyl 4-(2-benzylbenzamido)benzoate (1o)

![Chemical Structure Image]

Prepared according to Method A, 555.6 mg (60%, 2.5 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 174–176 °C.

$^1$H NMR (600 MHz, CDCl₃/TMS) δ (ppm): 7.92 (2H, d, $J = 8.3$ Hz), 7.54 (1H, d, $J = 7.4$ Hz), 7.44
-7.32 (6H, m), 7.26–7.14 (5H, m), 4.22 (2H, s), 1.59 (9H, s); $^{13}$C{^1H} NMR (150 MHz, CDCl$_3$/TMS) δ (ppm): 167.9, 165.2, 141.3, 140.5, 138.4, 136.6, 131.5, 130.7, 130.5, 128.74, 128.71, 127.7, 127.5, 126.8, 126.4, 118.7, 80.9, 39.1, 28.2; LRMS (EI) m/z: 387 (M$^+$); HRMS (EI-EB) Calcd. for C$_{25}$H$_{25}$NO$_3$: 387.1834, found: 387.1846; IR (neat): 3276, 2975, 1702, 1655, 1531, 1295, 1161, 854, 746 cm$^{-1}$.

2-Benzyl-N-(1-methyl-1H-indol-5-yl)benzamide (1p)

Prepared according to Method A, 394.8 mg (35%, 3.3 mmol scale), recrystallized from DCM/hexane, colorless blocks, mp. 205–208 °C. $^1$H NMR (600 MHz, CDCl$_3$/TMS) δ (ppm): 7.78 (1H, s), 7.56 (1H, d, $J$ = 7.6 Hz), 7.39 (1H, t, $J$ = 7.6 Hz), 7.32–7.17 (9H, m), 7.10 (1H, d, $J$ = 8.9 Hz), 7.05 (1H, d, $J$ = 2.8 Hz), 6.44 (1H, d, $J$ = 3.4 Hz), 4.26 (2H, s), 3.77 (3H, s); $^{13}$C{^1H} NMR (150 MHz, CDCl$_3$/TMS) δ (ppm): 167.9, 140.8, 138.7, 137.3, 134.3, 131.1, 130.1, 129.7, 128.9, 128.6, 128.5, 127.4, 126.5, 126.2, 115.7, 112.7, 109.2, 101.1, 39.0, 32.9; LRMS (EI) m/z: 340 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{23}$H$_{20}$N$_2$O: 340.1576, found: 340.1559; IR (neat): 3065, 1635, 1547, 1484, 1439, 1337, 875, 750, 718, 706 cm$^{-1}$.

2-Benzyl-N-(thiophen-3-yl)benzamide (1q)

Prepared according to Method A, 503.9 mg (84%, 2.0 mmol scale), recrystallized from DCM/hexane, colorless plates, mp. 118–120 °C. $^1$H NMR (400 MHz, CDCl$_3$/TMS) δ (ppm): 7.60 (1H, d, $J$ = 2.0 Hz), 7.55–7.51 (2H, m), 7.42 (1H, t, $J$ = 7.6 Hz), 7.34–7.25 (4H, m), 7.22–7.16 (4H, m), 6.74 (1H, d, $J$ = 3.9 Hz), 4.23 (2H, s); $^{13}$C{^1H} NMR (100 MHz, CDCl$_3$/TMS) δ (ppm): 167.0, 140.5, 138.5, 136.3, 135.3, 131.2, 130.4, 128.8, 128.6, 127.6, 126.6, 126.3, 124.4, 121.0, 110.5, 39.0; LRMS (EI) m/z: 293 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{18}$H$_{13}$NOS: 293.0874, found: 293.0852; IR (neat): 3047, 1641, 1581, 1538, 1307, 967, 835, 779, 738, 701 cm$^{-1}$.
2-Benzyl-N-(tert-butoxy)benzamide (1s)

![Structure of 2-Benzyl-N-(tert-butoxy)benzamide (1s)](image)

Prepared according to Method C, 1015.5 mg (70%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless plates, mp. 96–98 °C.

$^1$H NMR (400 MHz, CDCl$_3$/TMS) δ (ppm): 7.90 (1H, s), 7.39–7.33 (2H, m), 7.27–7.15 (7H, m), 4.17 (2H, s), 1.24 (9H, s); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$/TMS) δ (ppm): 168.8, 140.4, 139.4, 133.5, 131.0, 130.5, 128.9, 128.5, 127.5, 126.2, 126.1, 82.3, 38.5, 26.2; LRMS (EI) m/z: 283 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{18}$H$_{21}$NO$_2$: 283.1572, found: 283.1581; IR (neat): 3222, 2982, 1645, 1510, 901, 738, 702 cm$^{-1}$.

2-Benzyl-N-(benzyloxy)benzamide (1t)

![Structure of 2-Benzyl-N-(benzyloxy)benzamide (1t)](image)

Prepared according to Method C, 827.3 mg (86%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 88–89 °C.

$^1$H NMR (600 MHz, CDCl$_3$/TMS) δ (ppm): 8.50 (1H, br.s), 7.32–7.25 (6H, m), 7.21 (3H, t, $J = 7.6$ Hz), 7.16–7.09 (5H, m), 4.82 (2H, s), 4.10 (2H, s); $^{13}$C{$^1$H} NMR (150 MHz, CDCl$_3$/TMS) δ (ppm): 167.4, 140.3, 139.8, 135.1, 132.7, 130.9, 130.6, 129.1, 129.0, 128.6, 128.4, 128.3, 127.5, 126.1, 126.0, 78.0, 38.4; LRMS (EI) m/z: 317 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{21}$H$_{19}$NO$_2$: 317.1416, found: 317.1411; IR (neat): 3194, 1647, 1597, 1496, 1306, 1027, 739, 700 cm$^{-1}$.

2-(4-Methoxybenzyl)-N-phenylbenzamide (1u)

![Structure of 2-(4-Methoxybenzyl)-N-phenylbenzamide (1u)](image)

Prepared according to Method B, 516.1 mg (16% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 154–157 °C.

$^1$H NMR (600 MHz, CDCl$_3$/TMS) δ (ppm): 7.52 (1H, d, $J = 7.6$ Hz), 7.42–7.39 (3H, m), 7.33–7.27 (5H, m), 7.12 (1H, t, $J = 7.6$ Hz), 7.08 (2H, d, $J = 8.9$ Hz), 6.78 (2H, d, $J = 8.2$ Hz), 4.16 (2H, s), 3.74 (3H, s); $^{13}$C{$^1$H} NMR (150 MHz, CDCl$_3$/TMS) δ (ppm): 167.9, 158.1, 139.0, 137.8, 136.8, 132.6,
131.1, 130.4, 129.8, 127.4, 126.5, 124.4, 119.8, 114.0, 55.2, 38.1; LRMS (EI) \( m/z \) 317 (M⁺);
HRMS (EI-TOF) Calcd. for \( \text{C}_{21}\text{H}_{19}\text{NO}_2 \): 317.1416, found: 317.1428; IR (neat): 3277, 1645, 1595, 1509, 1436, 1245, 1032, 754 cm⁻¹.

2-(4-Chlorobenzyl)-N-phenylbenzamide (1v)

![Structure of 2-(4-Chlorobenzyl)-N-phenylbenzamide](image)

Prepared according to Method B, 435.1 mg (13% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 170–172 °C.

\(^1\)H NMR (600 MHz, \( \text{CDCl}_3/\text{TMS} \)) \( \delta \) (ppm): 7.50 (1H, d, \( J = 7.6 \) Hz), 7.45 (2H, d, \( J = 8.2 \) Hz), 7.40 (1H, t, \( J = 7.2 \) Hz), 7.35–7.29 (4H, m), 7.26–7.25 (1H, m), 7.19–7.18 (2H, m), 7.15–7.10 (3H, m), 4.18 (2H, s); \(^{13}\)C\(^{\text{(1H)}}\) NMR (150 MHz, \( \text{CDCl}_3/\text{TMS} \)) \( \delta \) (ppm): 167.8, 139.1, 138.8, 137.6, 136.6, 132.0, 131.1, 130.5, 130.3, 129.1, 128.6, 127.1, 126.8, 124.7, 119.9, 38.2; LRMS (EI) \( m/z \) 321 (M⁺);
HRMS (EI-TOF) Calcd. for \( \text{C}_{20}\text{H}_{16}\text{NO}_2\text{Cl} \): 321.0920, found: 321.0940; IR (neat): 3237, 3072, 1647, 1595, 1490, 1325, 1087, 751, 719 cm⁻¹.

2-Ethyl-N-phenylbenzamide (1w)

![Structure of 2-Ethyl-N-phenylbenzamide](image)

Prepared according to Method A, 897.0 mg (80%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 140–142 °C.

\(^1\)H NMR (400 MHz, \( \text{CDCl}_3/\text{TMS} \)) \( \delta \) (ppm): 7.62 (2H, d, \( J = 7.8 \) Hz), 7.47–7.24 (7H, m), 7.15 (1H, t, \( J = 7.6 \) Hz), 2.87 (2H, q, \( J = 7.6 \) Hz), 1.27 (3H, t, \( J = 7.6 \) Hz); \(^{13}\)C\(^{\text{(1H)}}\) NMR (100 MHz, \( \text{CDCl}_3/\text{TMS} \)) \( \delta \) (ppm): 168.2, 142.5, 138.0, 136.2, 130.3, 129.6, 129.1, 126.6, 125.8, 124.5, 119.9, 26.3, 15.9; LRMS (EI) \( m/z \) 225 (M⁺);
HRMS (EI-EB) Calcd. for \( \text{C}_{15}\text{H}_{15}\text{NO} \): 225.1154, found: 225.1162; IR (neat): 3270, 2967, 1639, 1596, 1491, 1441, 1324, 892, 758 cm⁻¹.

N-Phenyl-2-propylbenzamide (1x)

![Structure of N-Phenyl-2-propylbenzamide](image)
Prepared according to Method A, 436.6 mg (62%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 100–102 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 7.81 (1H, br.s), 7.56 (2H, d, \(J = 7.3\) Hz), 7.35–7.09 (7H, m), 2.74 (2H, t, \(J = 7.6\) Hz), 1.62 (2H, sext, \(J = 7.6\) Hz), 0.91 (3H, t, \(J = 7.6\) Hz); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 168.3, 140.8, 138.0, 136.3, 130.1, 130.0, 128.9, 126.6, 125.7, 124.3, 119.9, 35.1, 24.6, 14.0; LRMS (EI) \(m/\zeta\): 239 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{16}\)H\(_{17}\)NO: 239.1310, found: 239.1306; IR (neat): 3237, 2966, 1641, 1596, 1539, 1492, 1442, 1325, 760 cm\(^{-1}\).

2-Butyl-N-phenylbenzamide (1y)

Prepared according to Method A, 485.2 mg (38%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp 73–76 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 7.60–7.58 (3H, m), 7.41–7.32 (4H, m), 7.27 (1H, d, \(J = 7.8\) Hz), 7.24–7.19 (1H, m), 7.14 (1H, t, \(J = 7.6\) Hz), 2.80 (2H, t, \(J = 7.7\) Hz), 1.61 (2H, quin, \(J = 7.7\) Hz), 1.34 (2H, sext, \(J = 7.7\) Hz), 0.89 (3H, t, \(J = 7.7\) Hz); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 168.2, 141.2, 138.0, 136.4, 130.2, 130.1, 129.0, 126.6, 125.8, 124.5, 119.9, 33.8, 32.9, 22.6, 13.9; LRMS (EI) \(m/\zeta\): 253 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{17}\)H\(_{19}\)NO: 253.1467, found: 253.1462; IR (neat): 3306, 2929, 1652, 1597, 1521, 1501, 1436, 1320, 749 cm\(^{-1}\).

2-(Cyclopropylmethyl)-N-phenylbenzamide (1z)

Prepared according to Method A, 170.4 mg (67%, 1.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp 109–111 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 7.61 (2H, d, \(J = 8.3\) Hz), 7.49–7.35 (6H, m), 7.30–7.26 (1H, m), 7.15 (1H, t, \(J = 7.6\) Hz), 2.79 (2H, d, \(J = 6.8\) Hz), 1.09–0.99 (1H, m), 0.53–0.49 (2H, m), 0.22 (2H, q, \(J = 5.0\) Hz); \(^{13}\)C\{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 168.3, 140.4, 137.9, 136.3, 130.2, 130.0, 129.0, 126.5, 126.0, 124.5, 119.8, 37.2, 11.8, 4.8; LRMS (EI) \(m/\zeta\): 251 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{17}\)H\(_{18}\)NO: 251.1310, found: 251.1304; IR (neat): 3293, 1651, 1598, 1519, 1501, 1438, 1322, 746 cm\(^{-1}\).
4. General procedure for the intramolecular C(sp^3)–H amidation of 1a (Table 1, entry 1)

Under O_2 atmosphere, a mixture of 2-alkylbenzamide (1a–v, 0.20 mmol), Cu_2O (0.010 mmol, 1.4 mg) and DMAP (0.020 mmol, 2.4 mg) in 1,2-dichloroethane (1.0 mL) was stirred at 80 °C for 24 h in a sealed tube (Maruemu Corporation, NR-10, φ16.5×105×φ10.0 mm, 12 mL volume). The reaction mixture was diluted with water (10 mL) and extracted with DCM (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by SiO_2 column chromatography to give the corresponding desired compound 2a–v.

Table S1. Effect of copper sources

<table>
<thead>
<tr>
<th>entry</th>
<th>copper source</th>
<th>yield (%)^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>CuCl</td>
<td>(89)</td>
</tr>
<tr>
<td>3</td>
<td>CuBr</td>
<td>(74)</td>
</tr>
<tr>
<td>4</td>
<td>CuI</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>CuCN</td>
<td>79</td>
</tr>
<tr>
<td>6</td>
<td>CuOAc</td>
<td>(91)</td>
</tr>
<tr>
<td>7b</td>
<td>Cu_2O</td>
<td>(92)</td>
</tr>
<tr>
<td>8</td>
<td>[(MeCN)_4Cu]PF_6</td>
<td>67</td>
</tr>
<tr>
<td>9</td>
<td>[(MeCN)_4Cu]OTf</td>
<td>65</td>
</tr>
<tr>
<td>10</td>
<td>CuCl_2</td>
<td>37</td>
</tr>
<tr>
<td>11</td>
<td>CuBr_2</td>
<td>59</td>
</tr>
<tr>
<td>12</td>
<td>Cu(OH)_2</td>
<td>88</td>
</tr>
</tbody>
</table>

^a Determined by ^1H-NMR using 1,1,2-trichloroethane as an internal standard. Isolated yields in parentheses. ^b Cu_2O (5 mol%) was used.
Table S2. Effect of additives

<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>yield (%)</th>
<th>entry</th>
<th>base</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>0</td>
<td>2</td>
<td>DMAP</td>
<td>(92)</td>
</tr>
<tr>
<td>3</td>
<td>pyridine</td>
<td>(85)</td>
<td>4</td>
<td>4-aminopyridine</td>
<td>48</td>
</tr>
<tr>
<td>5</td>
<td>4-methoxypyridine</td>
<td>(80)</td>
<td>6</td>
<td>4-tert-butylypyridine</td>
<td>(91)</td>
</tr>
<tr>
<td>7</td>
<td>3-cyanopyridine</td>
<td>0</td>
<td>8</td>
<td>2,6-di-tert-butylypyridine</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>bipyridine</td>
<td>0</td>
<td>10</td>
<td>1,10-phenanthroline</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>NEt₃</td>
<td>66</td>
<td>12</td>
<td>DBU</td>
<td>(81)</td>
</tr>
<tr>
<td>13</td>
<td>TBD</td>
<td>40</td>
<td>14</td>
<td>proron sponge</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>K₂CO₃</td>
<td>0</td>
<td>16</td>
<td>KOt-Bu</td>
<td>0</td>
</tr>
<tr>
<td>17</td>
<td>NaH</td>
<td>0</td>
<td>18</td>
<td>LiHMDS</td>
<td>0</td>
</tr>
</tbody>
</table>

* Determined by ¹H-NMR using 1,1,2-trichloroethane as an internal standard. Isolated yields in parentheses.
Table S3. Effect of solvents

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DCE</td>
<td>(92)</td>
</tr>
<tr>
<td>2</td>
<td>DCM</td>
<td>28</td>
</tr>
<tr>
<td>3</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Et₂O</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>DME</td>
<td>trace</td>
</tr>
<tr>
<td>6</td>
<td>MeCN</td>
<td>33</td>
</tr>
<tr>
<td>7</td>
<td>benzene</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>toluene</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>PhCl</td>
<td>11</td>
</tr>
<tr>
<td>10</td>
<td>DMSO</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>DMF</td>
<td>0</td>
</tr>
</tbody>
</table>

* Determined by ¹H-NMR using 1,1,2-trichloroethane as an internal standard. An isolated yield in parentheses.

Figure S1. Unsuccessful substrates in copper-catalyzed aerobic double C(sp³)−H functionalization

3-Hydroxy-2,3-diphenylisoindolin-1-one (2a)

Purified by SiO₂ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless prisms, mp. 202–204 °C, 52.5 mg (92%).

¹H NMR (400 MHz, CDCl₃/TMS) δ (ppm): 7.74 (1H, d, J = 7.3 Hz), 7.51 (1H, t, J = 7.6 Hz), 7.44–7.36 (5H, m), 7.30 (1H, d, J = 7.8 Hz), 7.26–7.17 (5H, m), 7.11 (1H, t, J = 7.6 Hz), 3.87 (1H, br.s); ¹³C{¹H}
NMR (100 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 167.4, 148.6, 138.6, 135.8, 133.2, 129.8, 129.7, 128.5, 128.4, 128.3, 126.2, 126.1, 125.4, 123.9, 122.7, 93.0; LRMS (EI) $m/z$: 301 (M$^+$); HRMS (EI-EB) Calcd. for C$_{20}$H$_{15}$NO$_2$: 301.1103, found: 301.1106; IR (neat): 3193, 1674, 1593, 1495, 1370, 1207, 1045, 939, 861, 756, 707 cm$^{-1}$.

3-Hydroxy-6-methyl-2,3-diphenylisoindolin-1-one (2b)

Purified by SiO$_2$ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless prisms, mp 204–207 °C, 52.7 mg (87%).

$^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ (ppm): 7.62 (1H, s), 7.58 (1H, s), 7.48 (2H, d, $J = 8.2$ Hz), 7.41 (1H, d, $J = 7.9$ Hz), 7.32 (2H, d, $J = 7.9$ Hz), 7.26–7.09 (7H, m), 2.40 (3H, s); $^{13}$C {$^1$H} NMR (150 MHz, DMSO-$d_6$) $\delta$ (ppm): 166.6, 147.0, 140.2, 139.3, 136.7, 134.0, 129.9, 128.4, 128.3, 125.9, 125.7, 125.4, 123.1, 122.6, 92.3, 20.9; LRMS (EI) $m/z$: 315 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{21}$H$_{17}$NO$_2$: 315.1259, found: 315.1288; IR (neat): 3231, 1674, 1498, 1359, 1055, 843 cm$^{-1}$.

6-Fluoro-3-hydroxy-2,3-diphenylisoindolin-1-one (2c)

Purified by SiO$_2$ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless needles, mp. 189–191 °C, 61.5 mg (95%).

$^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ (ppm): 7.72 (1H, s), 7.62 (1H, d, $J = 5.5$ Hz), 7.47–7.43 (3H, m), 7.35–7.20 (8H, m), 7.13 (1H, t, $J = 7.1$ Hz); $^{13}$C {$^1$H} NMR (150 MHz, DMSO-$d_6$) $\delta$ (ppm): 165.3, 162.8 (C–F, $^1$J$_{C-F}$ = 246.2 Hz), 145.5 (C–F, $^4$J$_{C-F}$ = 2.9 Hz), 139.6, 136.3, 132.1 (C–F, $^3$J$_{C-F}$ = 8.6 Hz), 128.5, 128.4, 128.1, 126.0, 125.6, 125.2 (C–F, $^3$J$_{C-F}$ = 8.6 Hz), 120.6 (C–F, $^2$J$_{C-F}$ = 23.0 Hz), 109.8 (C–F, $^2$J$_{C-F}$ = 24.5 Hz), 92.1; $^{19}$F NMR (565 MHz, DMSO-$d_6$) $\delta$ (ppm): $-111.5$; LRMS (EI) $m/z$: 319 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{20}$H$_{14}$FNO$_2$: 319.1009, found: 319.0994; IR (neat): 3260, 2929, 1674, 1615, 1496, 1363, 1056, 832 cm$^{-1}$.

6-Chloro-3-hydroxy-2,3-diphenylisoindolin-1-one (2d)
Purified by SiO$_2$ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless needles, mp. 207–209 °C, 52.6 mg (87%).

$^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ (ppm): 7.82 (1H, d, $J = 2.1$ Hz), 7.71 (1H, s), 7.63 (1H, dd, $J = 8.3$, 2.1 Hz), 7.45 (2H, d, $J = 7.6$ Hz), 7.33 (2H, d, $J = 7.5$ Hz), 7.27–7.23 (5H, m), 7.19 (1H, t, $J = 7.6$ Hz), 7.11 (1H, t, $J = 7.6$ Hz); $^{13}$C($^1$H) NMR (150 MHz, DMSO-$d_6$) $\delta$ (ppm): 164.9, 148.0, 139.3, 136.1, 134.1, 133.1, 131.8, 128.4, 128.3, 128.0, 125.94, 125.89, 125.4, 124.8, 122.7, 92.0; LRMS (EI) $m/z$: 335 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{20}$H$_{14}$ClNO$_2$: 335.0713, found: 335.0743; IR (neat): 3313, 1687, 1493, 1358, 1048, 824, 767 cm$^{-1}$.

3-Hydroxy-5-methoxy-2,3-diphenylisoindolin-1-one (2e)

Purified by SiO$_2$ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 202–203 °C, 63.3 mg (98%).

$^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ (ppm): 7.75 (1H, d, $J = 8.6$ Hz), 7.65 (1H, s), 7.47 (2H, d, $J = 8.5$ Hz), 7.33 (2H, d, $J = 7.9$ Hz), 7.27–7.19 (5H, m), 7.10–7.07 (2H, m), 6.71 (1H, d, $J = 2.2$ Hz), 3.75 (3H, s); $^{13}$C($^1$H) NMR (150 MHz, DMSO-$d_6$) $\delta$ (ppm): 166.2, 163.5, 152.0, 140.1, 136.8, 128.4, 128.3, 128.0, 125.9, 125.5, 124.9, 115.9, 107.4, 91.9, 55.9; LRMS (EI) $m/z$: 331 (M$^+$); HRMS (EI-EB) Calcd. for C$_{21}$H$_{17}$NO$_3$: 331.1208, found: 331.1204; IR (neat): 3262, 1669, 1605, 1497, 1359, 1284, 1284, 1020, 751, 740 cm$^{-1}$.

3-Hydroxy-2,3-diphenyl-5-(trifluoromethyl)isoindolin-1-one (2f)

Purified by SiO$_2$ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 208–210 °C, 67.7 mg (93%).

$^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ (ppm): 8.07 (1H, d, $J = 7.9$ Hz), 7.96 (1H, d, $J = 7.9$ Hz), 7.87 (1H, s), 7.56 (1H, s), 7.49–7.48 (2H, m), 7.40 (2H, d, $J = 7.2$ Hz), 7.29–7.22 (5H, m), 7.15 (1H, t, $J = 7.5$ Hz); $^{13}$C($^1$H) NMR (150 MHz, DMSO-$d_6$) $\delta$ (ppm): 164.9, 150.1, 138.9, 136.0, 133.5, 133.1 (C–F, $^2$J$_{C-F}$ = 32.2 Hz), 128.5, 128.4, 128.3, 126.8 (C–F, $^3$J$_{C-F}$ = 3.6 Hz), 126.2, 126.0, 125.6, 124.5, 123.6 (C–F, $^1$J$_{C-F}$ = 274.3 Hz), 119.6 (C–F, $^3$J$_{C-F}$ = 3.8 Hz), 92.2; $^{19}$F NMR (565 MHz, DMSO-$d_6$) $\delta$ (ppm): –60.7; LRMS (EI) $m/z$: 369 (M$^+$); HRMS (EI-EB) Calcd. for C$_{21}$H$_{14}$F$_3$NO$_2$: 369.0977, found: 369.0980; IR (neat): 3317, 1691, 1499, 1367, 1321, 1135, 1060, 756, 746 cm$^{-1}$.
7-Hydroxy-6,7-diphenyl-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]isoindol-5-one (2g)

Purified by SiO₂ column chromatography (elucent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 242–243 °C, 64.5 mg (89%).

¹H NMR (600 MHz, DMSO-d₆) δ (ppm): 7.59 (1H, s), 7.47 (2H, d, J = 8.2 Hz), 7.32 (2H, d, J = 8.2 Hz), 7.26–7.19 (6H, m), 7.08 (1H, t, J = 7.4 Hz), 6.73 (1H, s), 6.14 (1H, s), 6.09 (1H, s); ¹³C{¹H} NMR (150 MHz, DMSO-d₆) δ (ppm): 166.1, 152.0, 148.8, 145.5, 140.1, 136.8, 128.4, 128.3, 127.9, 125.9, 125.4, 125.0, 123.5, 103.0, 102.5, 102.4, 91.7; LRMS (EI) m/z: 345 (M⁺); HRMS (EI-TOF) Calcd. for C₂₁H₁₅NO₄: 345.1001, found: 345.0989; IR (neat): 3268, 2901, 1684, 1609, 1498, 1356, 1309, 940, 831, 745 cm⁻¹.

3-Hydroxy-3-phenyl-2-(p-tolyl)isoindolin-1-one (2h)

Purified by SiO₂ column chromatography (elucent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 195–198 °C, 58.9 mg (97%).

¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 7.81 (1H, d, J = 7.3 Hz), 7.61–7.53 (3H, m), 7.34–7.32 (4H, m), 7.05 (2H, d, J = 8.3 Hz), 2.20 (3H, s); ¹³C{¹H} NMR (100 MHz, DMSO-d₆) δ (ppm): 166.4, 149.6, 140.0, 135.2, 133.8, 133.2, 129.9, 129.4, 128.4, 128.4, 127.9, 126.0, 125.8, 123.0, 122.9, 92.2, 20.6; LRMS (EI) m/z: 315 (M⁺); HRMS (EI-TOF) Calcd. for C₂₁H₁₇NO₂: 315.1259, found: 315.1255; IR (neat): 3224, 1674, 1614, 1511, 1358, 1205, 940, 813 cm⁻¹.

3-Hydroxy-2-(4-methoxyphenyl)-3-phenylisoindolin-1-one (2i)

Purified by SiO₂ column chromatography (elucent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 206–209 °C, 66.7 mg (99%).

¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 7.80 (1H, d, J = 6.8 Hz), 7.61–7.51 (3H, m), 7.32–7.18 (8H, m), 6.82 (2H, d, J = 8.8 Hz), 3.68 (3H, s); ¹³C{¹H} NMR (100 MHz, DMSO-d₆) δ (ppm): 166.4, 157.4, 149.6, 140.0, 133.1, 130.0, 129.4, 128.9, 128.3, 127.94, 127.85, 126.1, 123.0, 122.9, 113.6, 92.1, 55.2; LRMS (EI) m/z: 331 (M⁺); HRMS (EI-TOF) Calcd. for C₂₁H₁₇NO₃: 331.1208, found: 331.1204; IR
(neat): 3200, 2956, 1669, 1512, 1368, 1253, 1028, 858, 782 cm⁻¹.

2-(4-Fluorophenyl)-3-hydroxy-3-phenylisoindolin-1-one (2j)

![Chemical structure of 2j]

Purified by SiO₂ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless prisms, mp. 187–189 °C, 60.9 mg (96%).

¹H NMR (600 MHz, DMSO-d₆) δ (ppm): 7.83 (1H, d, J = 7.2 Hz), 7.65 (1H, s), 7.62 (1H, td, J = 7.6, 1.2 Hz), 7.57 (1H, td, J = 7.6, 1.0 Hz), 7.48–7.46 (2H, m), 7.34–7.32 (2H, m), 7.28–7.25 (3H, m), 7.22–7.20 (1H, m), 7.13–7.10 (2H, m); 

¹³C {¹H} NMR (150 MHz, DMSO-d₆) δ (ppm): 166.5, 160.0 (C–F, ¹J_C–F = 242.1 Hz), 149.5, 139.8, 133.4, 132.7 (C–F, ²J_C–F = 2.9 Hz), 129.7, 129.6, 128.5, 128.1, 127.9 (C–F, ³J_C–F = 8.6 Hz), 126.0, 123.2, 123.0, 115.2 (C–F, ²J_C–F = 22.9 Hz), 92.3; 

¹⁹F NMR (565 MHz, DMSO-d₆) δ (ppm): −115.8; LRMS (EI) m/z: 319 (M⁺); HRMS (EI-TOF) Calcd. for C₂₀H₁₄FNO₂: 319.1009, found: 319.0988; IR (neat): 3205, 1674, 1496, 1359, 1206, 941, 859, 756 cm⁻¹.

2-(4-Chlorophenyl)-3-hydroxy-3-phenylisoindolin-1-one (2k)

![Chemical structure of 2k]

Purified by SiO₂ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 216–220 °C, 56.0 mg (86%).

¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 7.84 (1H, d, J = 6.8 Hz), 7.74 (1H, br.s), 7.64–7.55 (4H, m), 7.36–7.32 (4H, m), 7.29–7.19 (4H, m); 

¹³C {¹H} NMR (100 MHz, DMSO-d₆) δ (ppm): 166.4, 149.4, 139.7, 135.6, 133.5, 129.8, 129.6, 129.4, 128.6, 128.4, 128.1, 126.5, 125.9, 123.2, 122.9, 92.4; LRMS (EI) m/z: 335 (M⁺); HRMS (EI-TOF) Calcd. for C₂₀H₁₄ClNO₂: 335.0713, found: 335.0725; IR (neat): 3205, 1674, 1496, 1359, 1206, 941, 859, 756 cm⁻¹.

2-(4-Bromophenyl)-3-hydroxy-3-phenylisoindolin-1-one (2l)

![Chemical structure of 2l]

Purified by SiO₂ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 235–238 °C, 67.9 mg (87%).
\(^{1}\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) (ppm): 7.83 (1H, d, \(J = 7.3\) Hz), 7.74 (1H, s), 7.64–7.53 (4H, m), 7.46 (2H, d, \(J = 8.8\) Hz), 7.35 (2H, d, \(J = 7.3\) Hz), 7.29–7.25 (3H, m), 7.23–7.20 (1H, m); \(^{13}\)C\{\(^{1}\)H\} NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) (ppm): 166.3, 149.3, 139.7, 136.0, 133.4, 131.2, 129.5, 129.3, 128.5, 128.0, 126.6, 125.8, 123.1, 122.8, 117.9, 92.3; LRMS (EI) \(m/z\): 379 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{20}\)H\(_{14}\)BrNO\(_2\): 379.0208, found: 379.0187; IR (neat): 3295, 1674, 1494, 1357, 942, 821, 754 cm\(^{-1}\).

3-Hydroxy-2-(4-iodophenyl)-3-phenylisoindolin-1-one (2m)

Purified by SiO\(_2\) column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless plates, mp. 236–239 °C, 76.0 mg (91%).

\(^{1}\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) (ppm): 7.84 (1H, d, \(J = 7.3\) Hz), 7.75 (1H, s), 7.63–7.54 (4H, m), 7.42 (2H, d, \(J = 8.8\) Hz), 7.36 (2H, d, \(J = 7.3\) Hz), 7.29–7.19 (4H, m); \(^{13}\)C\{\(^{1}\)H\} NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) (ppm): 166.4, 149.4, 139.7, 137.2, 136.6, 133.5, 129.6, 129.4, 128.6, 128.1, 126.9, 125.9, 123.2, 122.9, 92.4, 90.6; LRMS (EI) \(m/z\): 427 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{20}\)H\(_{14}\)INO\(_2\): 427.0069, found: 427.0055; IR (neat): 3318, 1675, 1607, 1490, 1354, 1057, 943, 818 cm\(^{-1}\).

4-(1-Hydroxy-3-oxo-1-phenylisoindolin-2-yl)benzonitrile (2n)

Purified by SiO\(_2\) column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 197–198 °C, 52.9 mg (83%).

\(^{1}\)H NMR (600 MHz, DMSO-\(d_6\)) \(\delta\) (ppm): 7.96–7.94 (3H, m), 7.87 (1H, d, \(J = 7.4\) Hz), 7.75–7.72 (2H, m), 7.61 (1H, td, \(J = 7.6, 1.2\) Hz), 7.58 (1H, t, \(J = 7.5\) Hz), 7.40 (2H, d, \(J = 7.4\) Hz), 7.31–7.28 (3H, m), 7.23 (1H, t, \(J = 7.4\) Hz); \(^{13}\)C\{\(^{1}\)H\} NMR (150 MHz, DMSO-\(d_6\)) \(\delta\) (ppm): 166.6, 149.2, 141.2, 139.5, 133.9, 132.5, 129.7, 128.70, 128.67, 128.2, 125.6, 123.4, 123.0, 122.8, 118.7, 106.6, 92.7; LRMS (EI) \(m/z\): 326 (M\(^+\)); HRMS (EI-TOF) Calcd. for C\(_{21}\)H\(_{14}\)N\(_2\)O\(_2\): 326.1055, found: 326.1085; IR (neat): 3247, 2225, 1679, 1602, 1506, 1057, 943, 818 cm\(^{-1}\).

\(\textit{tert}\)-Butyl 4-(1-hydroxy-3-oxo-1-phenylisoindolin-2-yl)benzoate (2o)

Purified by SiO\(_2\) column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 197–198 °C, 52.9 mg (83%).
Purified by SiO₂ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 219–222 °C, 78.5 mg (96%).

1H NMR (400 MHz, DMSO-d₆) δ (ppm): 7.87–7.83 (4H, m), 7.79–7.77 (2H, m), 7.63 (1H, t, J = 7.1 Hz), 7.57 (1H, t, J = 7.6 Hz), 7.38 (2H, d, J = 7.3 Hz), 7.30–7.24 (3H, m), 7.20 (1H, t, J = 7.3 Hz), 1.49 (9H, s);

13C{¹H} NMR (100 MHz, DMSO-d₆) δ (ppm): 166.5, 164.5, 149.3, 141.0, 139.7, 133.6, 129.6, 129.1, 128.5, 127.4, 123.2, 123.0, 122.8, 92.6, 80.5, 27.7; LRMS (EI) m/z: 401 (M⁺); HRMS (EI-TOF) Calcd. for C₂₅H₂₃NO₄: 401.1627, found: 401.1623; IR (neat): 3236, 2974, 1708, 1679, 1605, 1355, 1284, 1114, 856 cm⁻¹.

3-Hydroxy-2-(1-methyl-1H-indol-5-yl)-3-phenylisoindolin-1-one (2p)

\[
\begin{align*}
\text{O} & \quad \text{N} \\
\text{Ph} \quad \text{OH} & \quad \text{N} \\
\text{Me} & \quad \text{Ph}
\end{align*}
\]

Purified by SiO₂ column chromatography (eluent; hexane/AcOEt = 4/1 to AcOEt), recrystallized from DCM/hexane colorless needles, mp. 205–206 °C, 70.3 mg (>99%).

1H NMR (400 MHz, CDCl₃/TMS) δ (ppm): 7.86 (1H, d, J = 7.3 Hz), 7.55–7.48 (3H, m), 7.38–7.36 (2H, m), 7.33 (1H, d, J = 7.3 Hz), 7.26–7.21 (3H, m), 7.14 (1H, d, J = 8.8 Hz), 7.04 (1H, dd, J = 8.3, 2.0 Hz), 6.98 (1H, d, J = 2.9 Hz), 6.34 (1H, d, J = 2.9 Hz), 3.71 (3H, s), 3.46 (1H, br.s);

13C{¹H} NMR (150 MHz, CDCl₃/TMS) δ (ppm): 167.7, 148.7, 139.0, 135.6, 132.8, 130.7, 129.6, 129.2, 128.4, 128.22, 128.18, 126.8, 126.3, 123.8, 122.8, 121.5, 120.2, 109.2, 101.5, 92.7, 32.8; LRMS (EI) m/z: 354 (M⁺); HRMS (EI-TOF) Calcd. for C₂₃H₁₈N₂O₂: 354.1368, found: 354.1403; IR (neat): 3263, 1694, 1494, 1451, 1357, 1200, 1050, 768, 755, 745 cm⁻¹.

3-Hydroxy-3-phenyl-2-(thiophen-3-yl)isoindolin-1-one (2q)

\[
\begin{align*}
\text{O} & \quad \text{N} \\
\text{Ph} \quad \text{OH} & \quad \text{S}
\end{align*}
\]

Purified by SiO₂ column chromatography (eluent; hexane/AcOEt = 2/1 to AcOEt), recrystallized from DCM/hexane, colorless needles, mp. 246–248 °C, 48.9 mg (79%).

1H NMR (400 MHz, DMSO-d₆) δ (ppm): 7.81 (1H, d, J = 7.8 Hz), 7.66 (1H, s), 7.60–7.54 (3H, m), 7.39–7.36 (3H, m), 7.34–7.28 (4H, m), 7.25–7.24 (1H, m); 13C{¹H} NMR (100 MHz, DMSO-d₆) δ (ppm): 165.3, 149.2, 140.1, 134.4, 133.2, 129.4, 129.1, 128.6, 128.0, 125.5, 124.0, 123.0, 122.8, 122.6, 112.5, 91.9; LRMS (EI) m/z: 307 (M⁺); HRMS (EI-TOF) Calcd. for C₁₈H₁₃NO₂S: 307.0667, found: 307.0676; IR (neat): 3263, 1682, 1541, 1426, 1356, 1201, 1049, 768, 756, 745 cm⁻¹.

S23
3-Hydroxy-2-methoxy-3-phenylisoindolin-1-one (2r)

Purified by SiO\textsubscript{2} column chromatography (eluuent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless needles, mp. 162–164 °C, 32.8 mg (61%).

\textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}/TMS) \(\delta\) (ppm): 7.76 (1H, d, \(J = 7.7\) Hz), 7.52 (1H, td, \(J = 7.7, 1.1\) Hz), 7.49–7.45 (3H, m), 7.38–7.32 (3H, m), 7.29 (1H, d, \(J = 7.7\) Hz), 3.88–3.87 (4H, m);

\textsuperscript{13}C\{\textsuperscript{1}H\} NMR (150 MHz, CDCl\textsubscript{3}/TMS) \(\delta\) (ppm): 164.8, 145.9, 137.7, 133.4, 129.8, 128.8, 128.5, 127.9, 126.2, 123.7, 122.7, 90.8, 65.5; LRMS (EI) \(m/z\): 255 (M\textsuperscript{+}); HRMS (EI-EB) Calcd. for C\textsubscript{15}H\textsubscript{13}NO\textsubscript{3}: 255.0895, found: 255.0897; IR (neat): 3217, 2944, 1711, 1681, 1613, 1469, 1365, 1201, 1048, 1000, 770, 704 cm\textsuperscript{-1}.

2-(\textit{tert}-Butoxy)-3-hydroxy-3-phenylisoindolin-1-one (2s)

Purified by SiO\textsubscript{2} column chromatography (eluuent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless needles, mp 157–159 °C, 35.4 mg (62%).

\textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) (ppm): 7.75 (1H, d, \(J = 7.8\) Hz), 7.62 (1H, t, \(J = 7.6\) Hz), 7.54 (1H, t, \(J = 7.3\) Hz), 7.41 (1H, s), 7.34–7.19 (6H, m), 1.23 (9H, s);

\textsuperscript{13}C\{\textsuperscript{1}H\} NMR (100 MHz, DMSO-\textit{d}\textsubscript{6}) \(\delta\) (ppm): 167.1, 147.5, 139.5, 133.4, 129.4, 128.01, 127.98, 127.7, 126.2, 123.1, 122.6, 90.8, 82.3, 27.7; LRMS (FAB) \(m/z\): 298 (M\textsuperscript{+}); HRMS (FAB-EB) Calcd. for C\textsubscript{18}H\textsubscript{20}NO\textsubscript{3}: 298.1443, found: 298.1428; IR (neat): 3327, 2971, 1689, 1468, 1369, 1174, 1062, 959, 772 cm\textsuperscript{-1}.

2-(Benzyloxy)-3-hydroxy-3-phenylisoindolin-1-one (2t)

Purified by SiO\textsubscript{2} column chromatography (eluuent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless needles, mp. 173–175 °C, 48.7 mg (76%).

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}/TMS) \(\delta\) (ppm): 7.79 (1H, d, \(J = 7.3\) Hz), 7.51 (1H, td, \(J = 7.6, 1.3\) Hz), 7.47–7.43 (3H, m), 7.36–7.25 (9H, m), 5.16 (1H, d, \(J = 10.8\) Hz), 4.89 (1H, d, \(J = 10.8\) Hz), 3.42 (1H, br.s);

\textsuperscript{13}C\{\textsuperscript{1}H\} NMR (100 MHz, CDCl\textsubscript{3}/TMS) \(\delta\) (ppm): 165.1, 146.1, 137.8, 135.3, 133.3, 129.7, 129.4, 128.69, 128.66, 128.5, 128.3, 127.9, 126.3, 123.6, 122.8, 90.8, 79.1; LRMS (EI) \(m/z\): 331 (M\textsuperscript{+}); HRMS (EI-EB) Calcd. for C\textsubscript{21}H\textsubscript{17}NO\textsubscript{3}: 331.1208, found: 331.1196; IR (neat): 3292, 2889, 1705, 1695,
3-Hydroxy-3-(4-methoxyphenyl)-2-phenylisoindolin-1-one (2u)

![Chemical structure of 2u]

Purified by SiO$_2$ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless needles, mp. 199–200 °C, 56.6 mg (88%).

$^1$H NMR (400 MHz, CDCl$_3$/TMS) δ (ppm): 7.65 (1H, d, J = 7.8 Hz), 7.49 (1H, t, J = 7.6 Hz), 7.42 (2H, d, J = 7.8 Hz), 7.35 (1H, t, J = 7.3 Hz), 7.30–7.25 (3H, m), 7.18 (2H, t, J = 7.8 Hz), 7.10 (1H, t, J = 7.3 Hz), 6.74 (2H, d, J = 8.8 Hz), 4.12 (1H, br.s), 3.72 (3H, s); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$/TMS) δ (ppm): 167.4, 159.4, 148.8, 135.8, 133.1, 130.6, 129.6, 129.5, 128.5, 127.4, 126.1, 125.4, 123.7, 122.6, 113.7, 93.0, 55.1; LRMS (EI) m/z: 331 (M$^+$); HRMS (EI-EB) Calcd. for C$_{21}$H$_{17}$NO$_3$: 331.1208, found: 331.1212; IR (neat): 3236, 1674, 1607, 1495, 1363, 1250, 1172, 1028, 828, 758 cm$^{-1}$.

3-(4-Chlorophenyl)-3-hydroxy-2-phenylisoindolin-1-one (2v)

![Chemical structure of 2v]

Purified by SiO$_2$ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless prisms, mp. 236–238 °C, 59.4 mg (91%).

$^1$H NMR (600 MHz, CDCl$_3$/TMS) δ (ppm): 7.80 (1H, d, J = 7.6 Hz), 7.54 (1H, t, J = 7.3 Hz), 7.47–7.42 (3H, m), 7.31–7.28 (3H, m), 7.25–7.20 (4H, m), 7.13 (1H, t, J = 7.6 Hz), 3.57 (1H, s); $^{13}$C{$^1$H} NMR (150 MHz, CDCl$_3$/TMS) δ (ppm): 167.0, 148.2, 137.3, 135.7, 134.4, 133.4, 130.1, 130.0, 128.72, 128.70, 127.7, 126.4, 125.5, 124.1, 122.6, 92.5; LRMS (EI) m/z: 335 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{20}$H$_{14}$ClNO$_2$: 335.0713, found: 335.0716; IR (neat): 3172, 1679, 1598, 1491, 1366, 1250, 1172, 1028, 816, 755 cm$^{-1}$.

5. General procedure for the intramolecular C(sp$^3$)–H amidation of 2-alkyl-N-phenylbenzamide (Scheme 1, 2w–z)

A mixture of 2-alkyl-N-phenylbenzamide (1w–z, 0.40 mmol), Cu$_2$O (0.020 mmol, 2.9 mg) and DMAP (0.040 mmol, 4.9 mg) in 1,2-dichloroethane (2.0 mL) was placed in a high-pressure vessel (Taiatsu...
Glass Industry, Co., Ltd., TVS-1, 50 mL volume) and stirred under 2 atm of O\textsubscript{2} at 80 °C for 24 h. The reaction mixture was diluted with water (10 mL) and extracted with DCM (3 × 20 mL). The combined organic layers were washed with brine (10 mL) and dried over Na\textsubscript{2}SO\textsubscript{4}. The solvent was removed under reduced pressure and the residue was purified by SiO\textsubscript{2} column chromatography to give the corresponding desired compound 2w–z.

3-Hydroxy-3-methyl-2-phenylisoindolin-1-one (2w)

\[
\text{N} \quad \text{O} \quad \text{Ph} \\
\text{Me} \quad \text{OH}
\]

Purified by SiO\textsubscript{2} column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless prisms, mp. 190–193 °C, 57.1 mg (62%).

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}/TMS) \(\delta\) (ppm): 7.59–7.58 (2H, m), 7.53 (1H, d, \(J = 7.8\) Hz), 7.47 (2H, d, \(J = 7.8\) Hz), 7.40–7.26 (4H, m), 3.74 (1H, br.s), 1.60 (3H, s); \textsuperscript{13}C\{\textsuperscript{1}H\} NMR (100 MHz, CDCl\textsubscript{3}/TMS) \(\delta\) (ppm): 166.6, 147.9, 135.4, 132.8, 130.0, 129.6, 128.9, 127.1, 127.0, 121.6, 90.4, 24.3; LRMS (EI) \(m/z\): 239 (M\textsuperscript{+}); HRMS (EI-EB) Calcd. for C\textsubscript{15}H\textsubscript{13}NO\textsubscript{2}: 239.0946, found: 239.0936; IR (neat): 3355, 2993, 1674, 1612, 1495, 1466, 1387, 1148, 947, 760, 700 cm\textsuperscript{-1}.

3-Ethyl-3-hydroxy-2-phenylisoindolin-1-one (2x)

\[
\text{N} \quad \text{O} \quad \text{Ph} \\
\text{Et} \quad \text{OH}
\]

Purified by SiO\textsubscript{2} column chromatography (eluent; hexane/AcOEt = 2/1) and GPC (eluent; THF), recrystallized from DCM/hexane, colorless prisms, mp. 166–168 °C, 66.7 mg (68%).

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}/TMS) \(\delta\) (ppm): 7.57–7.50 (4H, m), 7.42 (1H, d, \(J = 7.3\) Hz), 7.35–7.24 (4H, m), 4.28 (1H, br.s), 2.09–1.93 (2H, m), 0.41 (3H, t, \(J = 7.6\) Hz); \textsuperscript{13}C\{\textsuperscript{1}H\} NMR (100 MHz, CDCl\textsubscript{3}/TMS) \(\delta\) (ppm): 167.1, 146.1, 135.4, 132.7, 130.8, 129.5, 128.7, 126.6, 126.1, 123.5, 121.7, 93.9, 28.7, 7.7; LRMS (EI) \(m/z\): 253 (M\textsuperscript{+}); HRMS (EI-TOF) Calcd. for C\textsubscript{16}H\textsubscript{15}NO\textsubscript{2}: 253.1103, found: 253.1105; IR (neat): 3269, 2968, 1680, 1615, 1494, 1370, 1092, 1035, 751, 699 cm\textsuperscript{-1}.

3-Hydroxy-2-phenyl-3-propylisoindolin-1-one (2y)

\[
\text{N} \quad \text{O} \quad \text{Ph} \\
n-\text{Pr} \quad \text{OH}
\]

Purified by SiO\textsubscript{2} column chromatography (eluent; hexane/AcOEt = 2/1) and GPC (eluent; THF),
recrystallized from DCM/hexane, colorless needles, mp. 151–153 ºC, 67.9 mg (65%).

$^1$H NMR (400 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 7.77 (1H, d, $J = 7.8$ Hz), 7.65–7.56 (4H, m), 7.49 (1H, t, $J = 7.6$ Hz), 7.41 (2H, t, $J = 7.8$ Hz), 7.31 (1H, t, $J = 7.3$ Hz), 3.09 (1H, s), 2.05 (1H, td, $J = 12.0, 4.7$ Hz), 1.96 (1H, td, $J = 12.0, 4.7$ Hz), 1.08–1.05 (1H, m), 0.76–0.66 (4H, m); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 167.0, 146.4, 135.4, 132.7, 130.8, 129.5, 128.8, 126.7, 126.3, 123.6, 121.7, 93.2, 38.0, 16.7, 13.6; LRMS (EI) $m/z$: 267 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{17}$H$_{17}$NO$_2$: 267.1259, found: 267.1265; IR (neat): 3276, 2964, 1678, 1604, 1494, 1374, 1075, 761, 701 cm$^{-1}$.

3-Cyclopropyl-3-hydroxy-2-phenylisoindolin-1-one (2z)

![Structure](image)

Purified by SiO$_2$ column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless prisms, mp. 132–133 ºC, 76.8 mg (65%).

$^1$H NMR (400 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 7.75 (1H, d, $J = 7.3$ Hz), 7.63–7.58 (2H, m), 7.50–7.45 (3H, m), 7.40 (2H, t, $J = 7.6$ Hz), 7.36–7.34 (1H, m), 2.94 (1H, br.s), 1.09–1.02 (1H, m), 0.60–0.47 (2H, m), 0.46–0.39 (1H, m), 0.34–0.28 (1H, m); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 166.7, 147.3, 135.6, 132.2, 130.5, 129.4, 128.5, 128.2, 127.1, 123.3, 122.4, 91.0, 17.9, 1.7; LRMS (EI) $m/z$: 265 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{17}$H$_{15}$NO$_2$: 265.1103, found: 265.1128; IR (neat): 3300, 3014, 1684, 1595, 1505, 1348, 1146, 1023, 848, 756, 702 cm$^{-1}$.

3-Methoxy-2,3-diphenylisoindolin-1-one (3)

![Structure](image)

To a solution of 2a (46.6 mg, 0.15 mmol) in MeOH (5.0 mL) was added 1M HCl aq. (1.0 mL). The reaction mixture was stirred at 40 ºC for 4 h, and then diluted with sat. K$_2$CO$_3$ aq. (10 mL). The resulting mixture was extracted with DCM (3 × 10 mL), and the combined organic layers were washed with brine (10 mL) and dried over Na$_2$SO$_4$, and then concentrated under reduced pressure. The residue was purified by SiO$_2$ column chromatography (eluent; hexane/EtOAc = 4/1) to afford 3 (47.9 mg, 98%).

Recrystallized from DCM/hexane, colorless prisms, mp. 151–153 ºC.

$^1$H NMR (400 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 7.99–7.97 (1H, m), 7.58–7.52 (4H, m), 7.39 (2H, dd, $J = 7.6, 1.7$ Hz), 7.27–7.20 (6H, m), 7.11 (1H, t, $J = 7.6$ Hz), 3.15 (3H, s); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$/TMS) $\delta$ (ppm): 167.6, 145.1, 138.9, 136.3, 133.1, 131.4, 129.8, 128.6, 128.3, 128.2, 126.1,
125.7, 124.0, 123.9, 123.0, 97.1, 50.3; LRMS (El) m/z: 315 (M+); HRMS (El-TOF) Calcd. for C\textsubscript{21}H\textsubscript{17}NO\textsubscript{2}: 315.1259, found: 315.1251; IR (neat): 2933, 2849, 1715, 1596, 1490, 1349, 1073, 863, 754, 705 cm\textsuperscript{-1}.

3-(1H-imidazol-1-yl)-2,3-diphenylisoindolin-1-one (4)

![Structural formula of 3-(1H-imidazol-1-yl)-2,3-diphenylisoindolin-1-one (4)](image)

To a solution of imidazole (386.4 mg, 5.6 mmol) in DCM (4.0 mL) was added SOCl\textsubscript{2} (120 μL, 1.6 mmol) at 0 °C. After the reaction mixture was stirred for 5 min at 0 °C, 2a (211.7 mg, 0.70 mmol) was added with stirring. After 10 min, the reaction mixture was diluted with H\textsubscript{2}O and extracted with DCM (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na\textsubscript{2}SO\textsubscript{4}, and then concentrated under reduced pressure. The residue was purified by SiO\textsubscript{2} column chromatography (eluent; EtOAc) to afford 4 (249.6 mg, >99%). Recrystallized from MeOH, colorless prisms, mp 165–168 °C.

\(^1\)H NMR (400 MHz, CD\textsubscript{3}OD) δ (ppm): 8.00–7.98 (1H, m), 7.74–7.67 (2H, m), 7.50–7.44 (7H, m), 7.34–7.26 (3H, m), 6.97 (1H, s), 6.93–6.91 (2H, m), 6.82 (1H, s); \(^{13}\)C\textsubscript{1H} NMR (100 MHz, CD\textsubscript{3}OD) δ (ppm): 169.8, 147.7, 139.1, 137.7, 136.1, 135.2, 131.9, 130.9, 130.5, 130.4, 130.3, 129.9, 129.8, 129.4, 128.3, 125.6, 125.0, 120.8, 86.0; LRMS (El) m/z: 351 (M+); HRMS (El-EB) Calcd. for C\textsubscript{23}H\textsubscript{17}N\textsubscript{3}O: 351.1372, found: 351.1364; IR (neat): 1711, 1600, 1493, 1344, 1218, 761, 703 cm\textsuperscript{-1}.

2,3-Diphenylisoindoline-1-thione (5)

![Structural formula of 2,3-Diphenylisoindoline-1-thione (5)](image)

A mixture of 2a (148.3 mg, 0.50 mmol) and Lawesson’s reagent (227.7 mg, 0.55 mmol) in toluene (5.0 mL) was stirred at 120 °C for 10 min and then concentrated under reduced pressure. The residue was purified by SiO\textsubscript{2} column chromatography (eluent; EtOAc) to afford 5 (141.2 mg, 95%). Recrystallized from MeOH, colorless prisms, mp 165–168 °C.

\(^1\)H NMR (600 MHz, DMSO-\textsubscript{d}\textsubscript{6}) δ (ppm): 8.02 (1H, d, J = 7.6 Hz), 7.64 (1H, t, J = 7.3 Hz), 7.61–7.57 (3H, m), 7.37 (2H, t, J = 7.9 Hz), 7.31 (1H, d, J = 7.6 Hz), 7.26–7.20 (4H, m), 7.12 (2H, d, J = 6.8 Hz), 6.78 (1H, s); \(^{13}\)C\textsubscript{1H} NMR (150 MHz, DMSO-\textsubscript{d}\textsubscript{6}) δ (ppm): 192.7, 144.9, 138.3, 138.1, 136.1, 132.5, 128.9, 128.8, 128.6, 128.4, 127.5, 127.3, 127.0, 125.3, 122.8, 73.4; LRMS (El) m/z: 301 (M+); HRMS (El-TOF) Calcd. for C\textsubscript{20}H\textsubscript{15}NS: 301.0925, found: 301.0922; IR (neat): 2892, 1597, 1490, 1472,
4-Phenylphthalazin-1(2H)-one (6)\(^6\)

To a solution of 2a (127.9 mg, 0.42 mmol) in 1-propanol (5.0 mL) was added \(\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}\) (300 \(\mu\)L, 6.2 mmol) and the reaction mixture was stirred at 100 °C for 16 h. Then, the mixture was cooled to 0 °C and added \(\text{H}_2\text{O}\) (5.0 mL). The residue was diluted with EtOAc (10 mL), washed with brine (10 mL), dried over \(\text{Na}_2\text{SO}_4\), and concentrated under reduced pressure. The residue was purified by SiO\(_2\) column chromatography (eluent; hexane/EtOAc = 2/1) to afford 6 (86.3 mg, 91%).

Recrystallized from DCM/hexane, colorless prisms, mp. 219–222 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 10.53 (1H, br.s), 8.55–8.53 (1H, m), 7.84–7.75 (3H, m), 7.61–7.52 (5H, m); \(^{13}\)C\({}^1\)H NMR (100 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 160.5, 148.2, 135.0, 133.4, 131.5, 129.7, 129.4, 129.2, 128.6, 128.3, 127.0, 126.9; LRMS (El) \(m/\text{z}: 222\ (\text{M}^+)\); HRMS (El-TOF) Calcd. for C\(_{14}\)H\(_{10}\)N\(_2\)O: 222.0793, found: 222.0772; IR (neat): 2869, 1665, 1607, 1486, 1337, 1153, 896, 781, 749 cm\(^{-1}\).  

2,3-Diphenylisoindolin-1-one (7)\(^7\)

To a solution of 2-benzoyl-N-phenylbenzamide (724.8 mg, 2.4 mmol) in CH\(_3\)CN (10 mL) was added Et\(_3\)SiH (800 \(\mu\)L, 5.0 mmol) and TiCl\(_4\) (1.0 M in DCM, 5.0 mL, 5.0 mmol). The reaction mixture was stirred at reflux for 4 h and then concentrated under reduced pressure. The mixture was diluted with EtOAc (10 mL), washed with brine (10 mL), dried over \(\text{Na}_2\text{SO}_4\), and concentrated reduced pressure. The residue was purified by SiO\(_2\) column chromatography (eluent; hexane/EtOAc = 2/1) to afford 7 (504.3 mg, 73%).

Recrystallized from DCM/hexane, colorless needles, mp. 190–192 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 7.97 (1H, d, \(J = 6.4\) Hz), 7.61 (2H, d, \(J = 7.8\) Hz), 7.52–7.46 (2H, m), 7.31–7.20 (8H, m), 7.08 (1H, t, \(J = 7.1\) Hz), 6.08 (1H, s); \(^{13}\)C\({}^1\)H NMR (100 MHz, CDCl\(_3\)/TMS) \(\delta\) (ppm): 167.9, 145.6, 137.63, 137.58, 132.4, 131.1, 129.1, 128.8, 128.5, 128.3, 126.9, 124.9, 124.1, 123.0, 122.5, 122.4, 65.6; LRMS (El) \(m/\text{z}: 285\ (\text{M}^+)\); HRMS (El-TOF) Calcd. for C\(_{20}\)H\(_{15}\)NO: 285.1154, found: 285.1134; IR (neat): 3042, 1684, 1599, 1493, 1368, 1143, 753, 737 cm\(^{-1}\).
2-Benzoyl-N-phenylbenzamide (8)

Prepared according to Method A, 305.7 mg (20%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 199–201 °C.

$^1$H NMR (400 MHz, CDCl$_3$/TMS) δ (ppm): 7.90 (1H, d, $J = 7.3$ Hz), 7.70–7.63 (3H, m), 7.57–7.52 (2H, m), 7.38–7.32 (3H, m), 7.07 (2H, t, $J = 8.0$ Hz) 6.83 (1H, t, $J = 7.3$ Hz), 6.68 (2H, d, $J = 7.8$ Hz), 4.96 (1H, br.s); $^{13}$C{$^1$H} NMR (150 MHz, acetone-$d_6$) δ (ppm): 169.6, 152.1, 144.5, 141.0, 135.6, 131.1, 129.9, 129.5, 129.3, 126.6, 126.5, 126.1, 124.3, 120.7, 118.8, 118.7; LRMS (EI) $m/z$: 301 (M$^+$); HRMS (EI-TOF) Calcd. for C$_{20}$H$_{15}$NO$_2$: 301.1103, found: 301.1124; IR (neat): 3347, 3062, 1736, 1599, 1517, 1451, 1271, 1108, 871, 749 cm$^{-1}$.

3-Hydroperoxy-2,3-diphenylisoindolin-1-one (9)

To a solution of 2a (309.4 mg, 1.0 mmol) and H$_2$SO$_4$ (200 μL) in DCM (5.0 mL) was added H$_2$O$_2$ (30% in H$_2$O, 250 μL) dropwise at 0 °C. The mixture became homogeneous after 5 min and was gradually warmed to rt. After stirring for 24 h at rt, the solution was washed with sat. Na$_2$CO$_3$ aq. (3 × 10 mL) and brine (10 mL), dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was then purified by recrystallization from DCM/hexane to afford 9 (290.3 mg, 89%) as colorless prisms, mp. 201–204 °C.

$^1$H NMR (600 MHz, CDCl$_3$/TMS) δ (ppm): 7.97 (1H, d, $J = 7.3$ Hz), 7.89 (1H, s), 7.62–7.56 (2H, m), 7.42 (2H, d, $J = 7.3$ Hz), 7.37 (1H, d, $J = 7.3$ Hz), 7.31–7.26 (6H, m), 7.19 (1H, t, $J = 6.9$ Hz), 5.30 (1H, s); $^{13}$C{$^1$H} NMR (150 MHz, CDCl$_3$/TMS) δ (ppm): 168.0, 144.5, 135.6, 135.5, 133.0, 131.8, 130.1, 129.1, 128.9, 128.6, 126.8, 126.2, 126.1, 124.0, 122.7, 100.7; LRMS (EI) $m/z$: 317 (M$^+$); HRMS (EI-EB) Calcd. for C$_{20}$H$_{15}$NO$_3$: 317.1052, found: 317.1067; IR (neat): 3347, 3062, 1736, 1599, 1517, 1451, 1271, 1108, 871, 749 cm$^{-1}$.

(Z)-N,3-diphenylisobenzofuran-1(3H)-imine (10)

$^{(Z)}$N,3-diphenylisobenzofuran-1(3H)-imine (10)

S30
To a solution of N-phenylthiobenzamide (1.3 g, 6.2 mmol) in THF (40 mL) was added n-BuLi (1.6 M in hexane, 8.4 mL, 13.4 mmol) dropwise at −78 °C and the mixture was gradually warmed to 0 °C. After stirring for 1.5 h at the same temperature, the mixture was cooled to −78 °C and treated with benzaldehyde (689.2 mg, 6.7 mmol), then temperature was gradually warmed to 0 °C and H₂O (1.3 mL) was added. After stirring for 2 days at rt, the reaction mixture was diluted with sat. NH₄Cl aq. (30 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried over Na₂SO₄ and concentrated under reduced pressure. The residue was then purified by SiO₂ column chromatography (eluent; hexane/EtOAc = 20/1) to afford 10 (717.3 mg, 41%).

Recrystallized from DCM/hexane, colorless needles, mp. 145–148 °C.

¹H NMR (400 MHz, CDCl₃/TMS) δ (ppm): 8.04–8.01 (1H, m), 7.53–7.51 (2H, m), 7.37–7.22 (10H, m), 7.08 (1H, t, J = 7.1 Hz), 6.46 (1H, s); ¹³C{¹H} NMR (100 MHz, CDCl₃/TMS) δ (ppm): 158.3, 146.5, 146.4, 138.0, 132.1, 130.6, 129.02, 128.99, 128.9, 128.6, 126.9, 124.0, 124.1, 123.6, 122.3, 85.8; LRMS (EI) m/z: 285 (M⁺); HRMS (EI-TOF) Calcd. for C₂₀H₁₅NO: 285.1154, found: 285.1151; IR (neat): 3025, 1737, 1683, 1592, 1489, 1201, 1059, 952, 764, 736 cm⁻¹.

**Preparation of ethereal H₂O₂¹⁰**

Et₂O (50 mL) was placed in a separatory funnel and washed with four portions (30 mL each) of NaCl-saturated H₂O₂ (prepared by stirring the commercially available 30% aqueous hydrogen peroxide with an excess of powdered NaCl at ambient temperature until the initially cloudy liquid phase became a clear solution; the supernatant was used). The ethereal layer was then dried over MgSO₄. The supernatant (ca. 1.7 M in H₂O₂ as titrated with 0.1 M KMnO₄) was used directly in the transformation from the iminolactone 10 to 2a.

**6. Procedure for gram-scale synthesis of the 3-hydroxyisoindolinone 2a**

**Scheme S1.** Gram-scale synthesis of 3-hydroxyisoindolinone 2a

A mixture of 2-benzyl-N-phenylbenzamide (1a, 5.0 mmol, 1.44 g), Cu₂O (0.25 mmol, 35.3 mg) and DMAP (0.50 mmol, 61.0 mg) in 1,2-dichloroethane (25 mL) was stirred at 80 °C for 24 h in a two-necked flask with a balloon filled with O₂. The reaction mixture was diluted with water (30 mL) and extracted with DCM (3 × 50 mL). The combined organic layers were washed with brine (30 mL) and
dried over Na$_2$SO$_4$. The solvent was removed under reduced pressure and the residue was purified by SiO$_2$ column chromatography to give the corresponding desired compound 2a (1.39 g, 91%).

7. Mechanistic study

The reaction was carried out in the presence of 1.5 equiv. radical scavenger (BHT or 9,10-dihydroanthracene). The reaction was completely inhibited, indicating that it proceeded via a radical process. (Scheme S2).

**Scheme S2.** Radical scavenging experiment of 1a

When the reaction of 1a was conducted for 3h, the peroxide 9 or B was detected by FAB-HRMS of the crude reaction mixture (Scheme S3). The result suggests that it is an intermediate in this reaction.

**Scheme S3.** HRMS experiment on the reaction mixture

8. References

9. $^1$H-, $^{13}$C-, and $^{19}$F-NMR spectra

$^1$H-NMR spectrum of 1a (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 1a (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 1b (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of 1b (CDCl$_3$, 150 MHz)
\(^1\)H-NMR spectrum of 1c (CDCl\(_3\), 600 MHz)
$^{13}$C-NMR spectrum of 1c (CDCl$_3$, 150 MHz)

$^{19}$F-NMR spectrum of 1c (CDCl$_3$, 565 MHz)
$^1$H-NMR spectrum of 1d (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of 1d (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1e (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of 1e (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1f (CD$_3$OD, 600 MHz)

$^{13}$C-NMR spectrum of 1f (CD$_3$OD, 150 MHz)
\textsuperscript{19}F-NMR spectrum of 1f (CD$_2$OD, 565 MHz)
$^{1}$H-NMR spectrum of 1g (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of 1g (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1h (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of 1h (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1i (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of 1i (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1j (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of 1j (CDCl$_3$, 150 MHz)

$^{19}$F-NMR spectrum of 1j (CDCl$_3$, 565 MHz)
$^1$H-NMR spectrum of 1k (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of 1k (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 11 (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of II (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1m (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of 1m (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1n (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of 1n (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1o (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of 1o (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1p (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of 1p (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of $1q$ (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of $1q$ (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 1s (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 1s (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 1t (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of 1t (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of $1u$ (CDCl$_3$, 600 MHz)

$^{13}$C-NMR spectrum of $1u$ (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 1v (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of 1v (CDCl$_3$, 150 MHz)
\[ \text{H-NMR spectrum of } 1w \text{ (CDCl}_3, 400 \text{ MHz)} \]

\[ \text{C-NMR spectrum of } 1w \text{ (CDCl}_3, 100 \text{ MHz)} \]
$^1$H-NMR spectrum of 1x (CDCl$_3$, 400 MHz)
$^{13}\text{C-NMR}$ spectrum of $1\text{x}$ (CDCl$_3$, 100 MHz)

$^1\text{H-NMR}$ spectrum of $1\text{y}$ (CDCl$_3$, 400 MHz)
$^{13}$C-NMR spectrum of 1y (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 1z (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 1z (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 2a (CDCl$_3$, 400 MHz)
$^{13}$C-NMR spectrum of 2a (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 2b (DMSO-$d_6$, 600 MHz)

$^{13}$C-NMR spectrum of 2b (DMSO-$d_6$, 150 MHz)
$^1$H-NMR spectrum of 2c (DMSO-$d_6$, 600 MHz)
$^{13}$C-NMR spectrum of 2c (DMSO-$d_6$, 150 MHz)

$^{19}$F-NMR spectrum of 2c (DMSO-$d_6$, 565 MHz)
$^{1}$H-NMR spectrum of 2d (DMSO-$d_6$, 600 MHz)

$^{13}$C-NMR spectrum of 2d (DMSO-$d_6$, 150 MHz)
$^1$H-NMR spectrum of 2e (DMSO-$d_6$, 600 MHz)
$^{13}$C-NMR spectrum of 2e (DMSO-$d_6$, 150 MHz)
1H-NMR spectrum of 2f (DMSO-\textit{d}_6, 600 MHz)

13C-NMR spectrum of 2f (DMSO-\textit{d}_6, 150 MHz)
$^{19}$F-NMR spectrum of 2f (DMSO-$d_6$, 565 MHz)
\textsuperscript{1}H-NMR spectrum of $2g$ (DMSO-$d_6$, 600 MHz)
\textsuperscript{13}C-NMR spectrum of $2g$ (DMSO-$d_6$, 150 MHz)
$^1$H-NMR spectrum of 2h (DMSO-$d_6$, 400 MHz)
$^{13}$C-NMR spectrum of 2h (DMSO-$d_6$, 100 MHz)
$^1$H-NMR spectrum of 2i (DMSO-$d_6$, 400 MHz)

$^{13}$C-NMR spectrum of 2i (DMSO-$d_6$, 100 MHz)
$^1$H-NMR spectrum of 2j (DMSO-$d_6$, 600 MHz)
$^{13}$C-NMR spectrum of 2j (DMSO-$d_6$, 150 MHz)

$^{19}$F-NMR spectrum of 2j (DMSO-$d_6$, 565 MHz)
$^1$H-NMR spectrum of 2k (DMSO-$d_6$, 400 MHz)

$^{13}$C-NMR spectrum of 2k (DMSO-$d_6$, 100 MHz)
$^1$H-NMR spectrum of 2l (DMSO-$d_6$, 400 MHz)
$^{13}$C-NMR spectrum of 2l (DMSO-$d_6$, 100 MHz)
$^1$H-NMR spectrum of 2m (DMSO-$d_6$, 400 MHz)

$^{13}$C-NMR spectrum of 2m (DMSO-$d_6$, 100 MHz)
$^1$H-NMR spectrum of 2n (DMSO-$d_6$, 600 MHz)
$^{13}$C-NMR spectrum of 2n (DMSO-$d_6$, 150 MHz)
$^1$H-NMR spectrum of 2o (DMSO-$d_6$, 400 MHz)

$^{13}$C-NMR spectrum of 2o (DMSO-$d_6$, 100 MHz)
$^1$H-NMR spectrum of 2p (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 2p (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 2q (DMSO-$d_6$, 400 MHz)

$^{13}$C-NMR spectrum of 2q (DMSO-$d_6$, 100 MHz)
$^1$H-NMR spectrum of 2r (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of 2r (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 2s (DMSO-$d_6$, 400 MHz)

$^{13}$C-NMR spectrum of 2s (DMSO-$d_6$, 100 MHz)
$^1$H-NMR spectrum of 2t (CDCl$_3$, 400 MHz)
$^{13}$C-NMR spectrum of 2t (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 2u (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 2u (CDCl$_3$, 100 MHz)
S107

**H-NMR spectrum of 2v (CDCl₃, 600 MHz)**
$^{13}$C-NMR spectrum of 2v (CDCl$_3$, 150 MHz)
$^{1}$H-NMR spectrum of 2w (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 2w (CDCl$_3$, 100 MHz)
\[ ^1H\text{-NMR spectrum of } 2x \text{ (CDCl}_3, \text{ 400 MHz)} \]
$^{13}$C-NMR spectrum of 2x (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 2y (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 2y (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 2z (CDCl$_3$, 400 MHz)
$^{13}$C-NMR spectrum of 2z (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 3 (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 3 (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 4 (CD$_3$OD, 400 MHz)
$^{13}$C-NMR spectrum of 4 (CD$_3$OD, 100 MHz)
$^1$H-NMR spectrum of 5 (DMSO-$d_6$, 600 MHz)

$^{13}$C-NMR spectrum of 5 (DMSO-$d_6$, 150 MHz)
$^1$H-NMR spectrum of 6 (CDCl$_3$, 400 MHz)
$^{13}$C-NMR spectrum of 6 (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 7 (CDCl$_3$, 400 MHz)

$^{13}$C-NMR spectrum of 7 (CDCl$_3$, 100 MHz)
$^1$H-NMR spectrum of 8 (CDCl$_3$, 400 MHz)
$^{13}$C-NMR spectrum of 8 (acetone-$d_6$, 150 MHz)
$^1$H-NMR spectrum of 9 (CDCl$_3$, 600 MHz)
$^{13}$C-NMR spectrum of 9 (CDCl$_3$, 150 MHz)
$^1$H-NMR spectrum of 10 (CDCl$_3$, 400 MHz)
\(^{13}\text{C-NMR spectrum of 10 (CDCl}_3, \text{ 100 MHz)}\)