Supporting Information

**Metal-free C(sp$^3$)–H functionalization: Oxidative carbo-oxygenation of α-diazo carbonyls via radical dediazotization**

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General Information

$^1$H NMR ($^{13}$C NMR) spectra were measured on a Bruker DPX 400 MHz spectrometer in CDCl$_3$ (DMSO-$d_6$) with chemical shift ($\delta$) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (ESI) was determined by using microTOF-QII HRMS/MS instrument (BRUKER). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

Figure 1 The ORTEP Drawing of 4a (Thermal ellipsoids are set at 30% probability level)

Scheme 1. Control experiments
Competing Kinetic Isotope Effect (KIE) Experiment:

KIE experimental procedure:
A mixture of \(N, N\)-dimethyl aniline (1a, 0.5 mmol, 1.0 equiv.), \([D_6] \cdot N, N\)-dimethyl aniline ([D\(_6\)]-1a, 0.5 mmol, 1.0 equiv.), \(N\)-hydroxyphthalimide (3, 0.50 mmol, 1.0 equiv.), 2-diazo-1-(p-tolyl)ethan-1-one (2a, 1.0 mmol, 2.0 equiv.), and phenyliodine diacetate (PIDA, 1.0 mmol, 2.0 equiv.) in dry 1,2-dichloroethane (DCE, 2.0 mL) was stirred at room temperature for about 12 hour. After the reaction finished, the mixture was evaporated under vacuum and purified by column chromatography to afford a mixture of products 4a and \([D_5]\)-4a. The KIE value was determined by \(^1\)H NMR spectra of the mixture of 4a and \([D_5]\)-4a, which has been described in details as follows.

\[^1\text{H}\text{ NMR spectra of products 4a and [D}_5\text{]-4a}\]

Note: The value of \(k_H/k_D\) was calculated from the \(^1\)H NMR spectra above. \(k_H/k_D = 2.13\)

\(k_H/k_D = 1/(1.47-1) = 2.13\)
**General procedure for the synthesis of 4**

Example for the synthesis of **4a**

*N,N*-Dimethyl aniline (**1a**, 1.0 mmol, 2.0 equiv.), *N*-hydroxyphthalimide (**3**, 0.50 mmol, 1.0 equiv.) and 2-diazoo-1-(p-tolyl)ethan-1-one (**2a**, 1.0 mmol, 2.0 equiv.) were introduced in a 10-mL Schlenk tube, dry 1,2-dichloroethane (DCE, 2.0 mL) and phenyliodine diacetate (PIDA, 1.0 mmol, 2.0 equiv.) were then successively added and the mixture stirred at room temperature for about 12 hours (monitored by TLC). After the reaction finished, the mixture was evaporated under vacuum and purified by column chromatography (petroleum ether/ethyl acetate) to afford the desired product **4a**.

2-(1-(Methyl(phenyl)amino)-3-oxo-3-(p-tolyl)propoxy)isoindoline-1,3-dione (**4a**)

Yellow solid, mp 129-130 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.07–7.62 (m, 6H), 7.29–7.12 (m, 4H), 6.77 (d, *J* = 8.4 Hz, 3H), 5.84 (s, 1H), 4.06–4.02 (m, 2H), 3.01 (s, 3H), 2.40 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 195.0, 163.2, 148.2, 145.1, 134.6, 132.9, 129.5, 129.3, 129.1, 128.7, 123.7, 117.3, 112.7, 84.9, 53.9, 39.7, 21.8; IR (KBr, ν, cm⁻¹) 3067, 2910, 1791, 1739, 1660, 1505, 1376, 1182, 1082, 973, 836, 699; HRMS (APCI) m/z Calcd. For C₂₅H₂₂N₂O₄Na, 437.1477 [M+Na]+, found 437.1488.

2-((1-(4-Methoxyphenyl)-3-(methyl(phenyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4b**)

Yellow solid, mp 119-120 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.07-7.99 (m, 2H), 7.83-7.71 (m, 4H), 7.28-7.24 (m, 2H), 6.95-6.90 (m, 2H), 6.94-6.90 (m, 2H), 5.85 (s, 1H), 4.08-4.04 (m, 2H), 3.88 (s, 3H), 3.02 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 193.7, 164.2, 163.2, 146.3, 134.6, 134.6, 131.4, 129.8, 128.8, 128.4, 126.5, 123.7, 113.9, 113.1, 84.8, 55.5, 54.2, 39.8, 20.3; IR (KBr, ν, cm⁻¹) 3054, 2931, 1792, 1732, 1677, 1597, 1348, 1254, 1171, 973, 873, 700; HRMS (APCI) m/z Calcd. For C₂₅H₂₂N₂O₄Na, 453.1426 [M+Na]+, found 453.1428.

2-(3-(Methyl(phenyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (**4c**)

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S4
Yellow solid, mp 113-114 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.06-7.98 (m, 2H), 7.77-7.75 (m, 4H), 7.60-7.59 (m, 1H), 7.46 (m, 2H), 7.31-7.20 (m, 2H), 6.83-6.72 (m, 3H), 5.87-5.85 (m, 1H), 4.08-4.04 (m, 2H), 3.02 (s, 3H), 3.02 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 195.6, 163.2, 148.2, 135.3, 134.9, 134.7, 134.0, 129.4, 129.3, 129.0, 128.9, 128.8, 128.7, 128.7, 123.9, 123.7, 117.4, 112.7, 85.0, 53.9, 39.7; IR (KBr, ν, cm⁻¹) 3065, 2911, 1785, 1727, 1690, 1597, 1507, 1375, 1185, 977, 880, 750, 690; HRMS (APCI) m/z Calcd. For C₂₄H₂₀N₂O₄Na, 423.1321 [M+Na]⁺, found 423.1302.

2-(((1-(4-Fluorophenyl)-3-(methyl(phenyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4d)

Yellow solid, mp 113-114 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.02-7.93 (m, 2H), 7.72-7.63 (m, 4H), 7.15-6.99 (m, 4H), 6.68-6.66 (m, 3H), 5.66 (t, J = 6.0 Hz 1H), 3.99-3.95 (m, 2H), 2.90 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 194.0, 166.2 (J = 255.2 Hz), 163.2, 148.1, 134.7, 134.3, 131.9 (J = 9.5 Hz), 131.7 (J = 3.0 Hz), 129.4, 128.7, 123.8, 123.6, 117.6, 115.9 (J = 21.8), 112.8, 85.2, 53.9, 39.8; IR (KBr, ν, cm⁻¹) 3055, 2924, 1774, 1687, 1596, 1508, 1352, 1230, 1081, 975, 701; HRMS (APCI) m/z Calcd. For C₂₄H₁₉FN₂O₄Na, 441.1227 [M+Na]⁺, found 441.1206.

2-(((1-(4-Chlorophenyl)-3-(methyl(phenyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4e)

Yellow solid, mp 112-113 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.03-7.95 (m, 2H), 7.90-7.89 (m, 1H), 7.83-7.74 (m, 5H), 7.44-7.42 (m, 1H), 7.26-7.23 (m, 2H), 6.76 (d, J = 8.0 Hz, 2H), 5.76-5.72 (m, 1H), 4.09-4.05 (m, 2H), 3.01 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 194.4, 167.8, 163.2, 140.6, 134.8, 134.4, 133.6, 132.6, 130.5, 129.4, 129.1, 128.7, 123.8, 123.6, 117.7, 112.9, 85.3, 53.9, 39.9; IR (KBr, ν, cm⁻¹) 3199, 2920, 1737, 1604, 1500, 1373, 1185, 969, 875, 700; HRMS (APCI) m/z Calcd. For C₂₄H₁₉ClN₂O₄Na, 457.0931 [M+Na]⁺, found 457.0924.
2-((1-(4-Bromophenyl)-3-(methyl(phenyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4f)

Yellow solid, mp 152-153 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 7.94-7.88 (m, 2H), 7.83-7.73 (m, 4H), 7.63-7.54 (m, 2H), 7.28-7.22 (m, 2H), 6.79-6.75 (m, 3H), 5.72 (d, $J$ = 6.0 Hz, 1H), 4.09-4.05 (m, 2H), 3.00 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 194.7, 163.2, 148.1, 134.8, 134.3, 134.0, 132.0, 130.5, 129.4, 128.6, 123.8, 123.6, 117.5, 112.7, 85.4, 53.8, 39.8; IR (KBr, ν, cm$^{-1}$) 3054, 1793, 1774, 1686, 1507, 1350, 1257, 1061, 972, 873, 700; HRMS (APCI) m/z Calcd. For C$_{24}$H$_{19}$N$_2$O$_4$BrNa, 501.0426 [M+Na]$^+$, found 501.0420.

Ethyl 2-((1,3-dioxoisindolin-2-yl)oxy)-3-(methyl(phenyl)amino)propanoate (4g)

Yellow solid, mp 99-100 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 7.82-7.72 (m, 4H), 7.29-7.25 (m, 2H), 6.84-6.67 (m, 3H), 4.98-4.95 (m, 1H), 4.22 (q, $J$ = 7.2 Hz, 2H), 3.99-3.95 (m, 2H), 3.12 (s, 3H), 1.27 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 168.6, 162.9, 148.4, 134.7, 129.3, 128.8, 123.7, 117.2, 112.6, 84.0, 62.0, 53.2, 39.4, 14.0; IR (KBr, ν, cm$^{-1}$) 2996, 1792, 1730, 1599, 1508, 1374, 1264, 1121, 1025, 971, 878, 701; HRMS (APCI) m/z Calcd. For C$_{20}$H$_{20}$N$_2$O$_5$Na, 391.1270 [M+Na]$^+$, found 391.1274.

2-((3-(Methyl(m-tolyl)amino)-1-oxo-1-(p-tolyl)propan-2-yl)oxy)isoindoline-1,3-dione (4h)

Yellow solid; mp 99-100 °C; $^1$H NMR (400 MHz, CDCl$_3$; δ, ppm) 7.94 (d, $J$ = 8.4 Hz, 2H), 7.83-7.72 (m, 4H), 7.26 (d, $J$ = 8.0 Hz, 2H), 7.14 (m, 1H), 6.60 (d, $J$ = 7.6 Hz, 3H), 5.87 (t, $J$ = 5.6 Hz, 1H), 4.05-4.03 (m, 2H), 3.01 (s, 3H), 2.42 (s, 3H), 2.28 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$; δ, ppm) 194.9, 167.9, 163.2, 148.3, 145.1, 139.0, 134.6, 134.3, 132.8, 132.6, 129.5, 129.2, 129.1, 128.7, 123.7, 123.6, 118.2, 113.5, 110.0, 85.0, 53.9, 39.7, 29.7, 21.9, 21.8; IR (KBr, ν, cm$^{-1}$) 3199,
1791, 1737, 1655, 1604, 1500, 1185, 1053, 969, 875, 700; HRMS (APCI) m/z Calcd. For C_{26}H_{24}N_{2}O_{4}Na, 451.1634 \text{[M+Na]^+}, found 451.1633.

2-((3-(Methyl(p-tolyl)amino)-1-oxo-1-(p-tolyl)propan-2-yl)oxy)isoindoline-1,3-dione (4i)

Yellow solid; mp 138-139 °C; \text{^1}H NMR (400 MHz, CDCl$_3$; δ, ppm) 7.93 (d, J = 8.0 Hz, 2H), 7.80-7.78 (m, 4H), 7.26 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.4 Hz, 2H), 5.85 (t, J = 6.0 Hz, 1H), 4.03-4.01 (m, 2H), 2.99 (s, 3H), 2.42 (s, 3H), 2.27 (s, 1H); \text{^13}C NMR (100 MHz, CDCl$_3$; δ, ppm) 195.0, 163.2, 146.3, 145.0, 134.6, 132.9, 129.5, 129.1, 128.7, 126.6, 123.7, 113.1, 85.0, 54.2, 39.8, 21.8, 20.3; IR (KBr, \text{v}, \text{cm}^{-1}) 2910, 1736, 1664, 1522, 1372, 1261, 1187, 1121, 970, 810, 702; HRMS (APCI) m/z Calcd. For C_{26}H_{24}N_{2}O_{4}Na, 451.1634 \text{[M+Na]^+}, found 451.1631.

2-((1-(4-Methoxyphenyl)-3-(methyl(p-tolyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4j)

Yellow solid, mp 126-127 °C; \text{^1}H NMR (400 MHz, CDCl$_3$; δ, ppm) 8.02 (d, J = 8.8 Hz, 2H), 7.83-7.70 (m, 4H), 7.05 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 6.70 (d, J = 7.2 Hz, 2H), 5.83 (s, 1H), 4.03-4.01 (m, 2H), 3.88 (s, 3H), 2.98 (s, 3H), 2.27 (s, 3H); \text{^13}C NMR (100 MHz, CDCl$_3$; δ, ppm) 193.7, 164.2, 163.2, 148.3, 134.6, 131.4, 129.3, 128.7, 128.4, 123.7, 117.2, 114.0, 112.6, 84.7, 55.5, 53.7, 39.6; IR (KBr, \text{v}, \text{cm}^{-1}) 2912, 1735, 1600, 1522, 1256, 1174, 970, 842, 702; HRMS (APCI) m/z Calcd. For C_{26}H_{24}N_{2}O_{5}Na, 467.1583 \text{[M+Na]^+}, found 467.1555.

2-((3-(Methyl(p-tolyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (4k)
Yellow solid; mp 138-139 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.06-7.99 (m, 2H), 7.81-7.72 (m, 4H), 7.60 (s, 1H), 7.48-7.44 (m, 2H), 7.04 (d, \(J = 8.4\) Hz, 2H), 6.69 (d, \(J = 8.4\) Hz, 2H), 5.87 (t, \(J = 6.0\) Hz, 1H), 4.04-4.02 (m, 2H), 2.98 (s, 3H), 2.26 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 195.6, 167.9, 163.2, 146.2, 135.3, 134.6, 134.3, 133.9, 132.6, 129.8, 129.0, 128.7, 126.7, 123.7, 123.6, 113.2, 85.1, 54.2, 39.8, 20.3; IR (KBr, v, cm\(^{-1}\)) 2911, 1774, 1736, 1667, 1523, 1377, 1257, 970, 877, 701, 634; HRMS (APCI) m/z Calcd. for C\(_{25}\)H\(_{22}\)N\(_2\)O\(_4\)Na, 437.1477 [M+Na]\(^+\), found 437.1476.

2-((1-(4-Fluorophenyl)-3-(methyl(p-tolyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4l)

Yellow solid; mp 141-142 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.10-8.07 (m, 2H), 7.85-7.75 (m, 4H), 7.19-6.98 (m, 4H), 6.68 (d, \(J = 7.9\) Hz, 2H), 5.77 (t, \(J = 6.0\) Hz, 1H), 4.05-4.02 (m, 2H), 2.97 (s, 3H), 2.26 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 194.0, 166.2 (\(J_{CF} = 255.0\) Hz), 163.2, 146.1, 134.7, 134.3, 131.9 (\(J_{CF} = 9.5\) Hz), 131.7 (\(J_{CF} = 2.9\) Hz), 129.9, 128.7, 123.7, 115.9 (\(J_{CF} = 21.8\) Hz), 113.2, 85.3, 54.2, 39.9, 20.3; IR (KBr, v, cm\(^{-1}\)) 3199, 2909, 1774, 1736, 1660, 1596, 1522, 1307, 1186, 1053, 971, 804, 714; HRMS (APCI): m/z Calcd. for C\(_{25}\)H\(_{21}\)FN\(_2\)O\(_4\)Na, 455.1383 [M+Na]\(^+\), found 455.1377.

2-((1-(4-Bromophenyl)-3-(methyl(p-tolyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4m)

Yellow solid; mp 160-161 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 7.92-7.89 (m, 2H), 7.82-7.74 (m, 4H), 7.60 (d, \(J = 8.4\) Hz, 2H), 7.04 (d, \(J = 8.4\) Hz, 2H), 6.68 (d, \(J = 7.6\) Hz, 2H), 5.73 (t, \(J = 6.0\) Hz, 1H), 4.04-4.02 (m, 2H), 2.97 (s, 3H), 2.26 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 194.7, 167.9, 163.2, 134.7, 134.3, 134.0, 132.6, 132.0, 130.5, 129.9, 129.3, 128.7, 123.8, 123.6, 113.2, 85.4, 54.2, 40.0, 20.3; IR (KBr, v, cm\(^{-1}\)) 3067, 2911, 1791, 1735, 1660, 1596, 1520, 1375, 1186, 1053, 971, 714; HRMS (APCI): m/z Calcd. for C\(_{25}\)H\(_{21}\)BrN\(_2\)O\(_4\), 515.0582 [M+Na]\(^+\), found 515.0580.

2-((3-((4-Fluorophenyl)(methyl)amino)-1-oxo-1-(p-tolyl)propan-2-yl)oxy)isoindoline-1,3-dione (4n)
Yellow solid; mp 146-147 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 7.91 (d, \(J = 8.4\) Hz, 2H), 7.85-7.65 (m, 4H), 7.28 (d, \(J = 6.8\) Hz, 2H), 6.99-6.87 (m, 2H), 6.77-6.66 (m, 2H), 5.83 (t, \(J = 6.0\) Hz, 1H), 4.02-4.00 (m, 2H), 2.99 (s, 3H), 2.42 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 194.8, 163.2, 156.0 (\(J_{CF} = 236.4\) Hz), 145.2, 144.9 (\(J_{CF} = 1.0\) Hz), 134.6, 132.8, 129.5, 129.0, 128.7, 123.7, 115.7 (\(J_{CF} = 21.9\) Hz), 114.3 (\(J_{CF} = 6.3\) Hz), 84.9, 54.7, 40.1, 21.8; IR (KBr, \(v\), cm\(^{-1}\)) 2913, 1791, 1738, 1663, 1510, 1226, 1124, 971, 817, 689; HRMS (APCI) m/z Calcd. For C\(_{25}\)H\(_{21}\)N\(_2\)O\(_4\) Na, 455.1383 [M+Na]\(^+\), found 455.1382.

2-((3-((4-Fluorophenyl)(methyl)amino)-1-(4-methoxyphenyl)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4o)

Yellow solid, mp 135-136 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.05-7.92 (m, 2H), 7.781-7.73 (m, 4H), 7.10-6.80 (m, 4H), 6.78-6.63 (m, 2H), 5.80 (t, \(J = 6.0\) Hz, 1H), 4.02-4.00 (m, 2H), 3.88 (s, 3H), 2.98 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 193.5, 164.3, 163.2, 156.0 (\(J_{CF} = 235.0\) Hz), 145.0 (\(J_{CF} = 5.9\) Hz), 134.7, 131.4, 128.7, 128.3, 123.7, 115.7 (\(J_{CF} = 22.0\) Hz), 114.2 (\(J_{CF} = 5.6\) Hz), 114.0, 84.7, 55.6, 54.7, 40.1; IR (KBr, \(v\), cm\(^{-1}\)) 2912, 1790, 1738, 1599, 1511, 1255, 1023, 971, 816, 701; HRMS (APCI) m/z Calcd. For C\(_{25}\)H\(_{21}\)N\(_2\)O\(_5\)FNa, 471.1332 [M+Na]\(^+\), found 471.1335.

2-((3-((4-Fluorophenyl)(methyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (4p)

Yellow solid, mp 114-115 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.02-8.00 (m, 2H), 7.86-7.71 (m, 4H), 7.65-7.56 (m, 1H), 7.49-7.48 (m, 2H), 6.96-6.92 (m, 2H), 6.75-6.71 (m, 2H), 5.86 (t, \(J = 6.0\) Hz, 1H), 4.04-4.01 (m, 2H), 3.00 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 195.4, 163.2, 156.0 (\(J_{CF} = 235.6\) Hz), 144.9 (\(J_{CF} = 0.9\) Hz), 135.3, 134.7, 134.0, 128.9, 128.8, 128.7, 123.7, 115.9 (\(J_{CF} =
21.8 Hz), 114.4 (JCF = 7.2 Hz), 85.0, 54.6, 40.1; IR (KBr, ν, cm⁻¹) 3067, 2912, 1791, 1738, 1599, 1511, 1255, 1228, 1173, 971, 816, 701; HRMS (APCI) m/z Calcd. For C₂₄H₁₉N₂O₄FNa, 441.1227 [M+Na]⁺, found 441.1219.

2-((1-(4-Fluorophenyl)-3-((4-fluorophenyl)(methyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4q)

Yellow solid, mp 123-124 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.10-8.06 (m, 2H), 7.87-7.72 (m, 4H), 7.14 (m, 2H), 6.96-6.91 (m, 2H), 6.76-6.63 (m, 2H), 5.72 (t, J = 6.0 Hz, 1H), 4.03-4.01 (m, 2H), 2.97 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 193.9, 166.2 (JCF = 255.3 Hz), 163.2, 156.0 (JCF = 235.2 Hz), 145.0 (JCF = 1.6 Hz), 134.8, 131.8 (JCF = 9.5 Hz), 131.7 (JCF = 3.0 Hz), 128.6, 123.8, 115.9 (JCF = 22.3 Hz), 115.7 (JCF = 22.5 Hz), 114.3 (JCF = 7.4 Hz), 85.4, 54.6, 40.2; IR (KBr, ν, cm⁻¹) 2911, 1790, 1737, 1664, 1595, 1512, 1230, 969, 817, 700; HRMS (APCI) m/z Calcd. For C₂₄H₁₈N₂O₄F₂Na, 459.1132 [M+Na]⁺, found 459.1146.

2-((3-((4-Bromophenyl)(methyl)amino)-1-oxo-1-(p-tolyl)propan-2-yl)oxy)isoindoline-1,3-dione (4r)

Yellow solid, mp 159-160 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 7.96-7.71 (m, 6H), 7.35-7.29 (m, 2H), 7.27 (d, J = 8.0 Hz, 2H), 6.73-6.56 (m, 2H), 5.81-5.78 (m, 1H), 4.04-4.00 (m, 2H), 3.00 (s, 3H), 2.43 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 194.8, 163.2, 147.2, 145.3, 134.7, 132.7, 132.0, 129.5, 129.0, 128.7, 123.7, 114.3, 109.4, 84.8, 53.8, 39.8, 21.8; IR (KBr, ν, cm⁻¹) 2912, 1735, 1659, 1591, 1498, 1257, 1121, 970, 810, 701; HRMS (APCI) m/z Calcd. For C₂₅H₂₁N₂O₄BrNa, 515.0582 [M+Na]⁺, found 515.0585.

2-((3-((4-Bromophenyl)(methyl)amino)-1-((4-methoxyphenyl)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4s)
2-((3-(4-Bromophenyl)(methyl)amino)-1-oxo-1-phenylpropan-2-yl)oxyisoindoline-1,3-dione (4t)

Yellow solid; mp 146-147 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.04-7.99 (m, 2H), 7.83-7.72 (m, 4H), 7.36-7.30 (m, 2H), 6.97-6.91 (m, 2H), 6.71 (d, \(J = 8.8\) Hz, 2H), 5.83 (t, \(J = 6.0\) Hz, 1H), 4.05-4.01 (m, 2H), 3.88 (s, 3H), 3.02 (s, 3H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 193.5, 164.3, 163.2, 147.2, 134.7, 132.0, 131.4, 128.7, 123.7, 114.2, 114.0, 100.0, 84.6, 55.6, 53.8, 39.7; IR (KBr, \(\nu\), cm\(^{-1}\)) 2932, 1735, 1598, 1499, 1373, 1255, 1174, 1027, 968, 810, 701; HRMS (APCI) m/z Calcd. For C\(_{25}\)H\(_{21}\)N\(_2\)O\(_5\)BrNa, 508.0634 [M+Na]+, found 503.0635.

2-((3-(4-Bromophenyl)(methyl)amino)-1-oxo-1-phenylpropan-2-yl)oxyisoindoline-1,3-dione (4u)

Yellow solid, mp 147-148 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.10-7.97 (m, 2H), 7.94-7.68 (m, 4H), 7.66-7.51 (m, 1H), 7.51-7.40 (m, 2H), 7.33-7.29 (m, 2H), 6.76-6.50 (m, 2H), 5.82 (t, \(J = 6.0\) Hz, 1H), 4.06-4.02 (m, 2H), 3.00 (s, 3H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 195.3, 163.2, 147.2, 135.2, 134.7, 134.1, 132.0, 128.9, 128.8, 128.7, 123.8, 114.4, 109.5, 84.9, 53.8, 39.7; IR (KBr, \(\nu\), cm\(^{-1}\)) 3068, 2914, 1789, 1735, 1666, 1499, 1256, 1016, 968, 812, 700; HRMS (APCI) m/z Calcd. For C\(_{24}\)H\(_{19}\)N\(_2\)O\(_4\)BrNa, 501.0426 [M+Na]+, found 501.0401.

2-((3-(4-Bromophenyl)(methyl)amino)-1-(4-fluorophenyl)-1-oxopropan-2-yl)oxyisoindoline-1,3-dione (4u)

Yellow solid; mp 166-167 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 8.13-7.99 (m, 2H), 7.93-7.69 (m, 4H), 7.42-7.30 (m, 2H), 7.17-7.13 (m, 2H), 6.68 (d, \(J = 9.2\) Hz, 2H), 5.74 (t, \(J = 6.0\) Hz, 1H), 4.18-3.88 (m, 2H), 3.01 (s, 3H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 193.8, 166.3 \((J_{CF} = 255.8\) Hz), 163.2, 147.2, 135.0, 134.8, 134.2, 131.6 \((J_{CF} = 3.1\) Hz), 132.0, 130.1 \((J_{CF} = 8.9\) Hz), 128.6, 123.8, 116.0 \((J_{CF} = 21.8\) Hz), 114.3, 85.3, 53.7, 39.8; IR (KBr, \(\nu\), cm\(^{-1}\)) 2913, 1788, 1735, 1664,
1592, 1498, 969, 810, 709; HRMS (APCI) m/z Calcd. For C_{24}H_{18}N_{2}O_{4}BrFNa, 519.0332 [M+Na]⁺, found 519.0340.

2-((3-((4-Bromophenyl)(methyl)amino)-1-(4-chlorophenyl)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4v)

Yellow solid, mp 164-165 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.06-7.96 (m, 2H), 7.91-7.66 (m, 4H), 7.53-7.40 (m, 2H), 7.38-7.29 (m, 2H), 6.66 (d, J = 9.2 Hz, 2H), 5.69 (t, J = 6.0 Hz, 1H), 4.06-4.03 (m, 2H), 3.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 194.2, 163.2, 147.0, 140.7, 134.8, 133.5, 132.1, 130.5, 129.1, 128.6, 123.8, 114.5, 85.4, 53.8, 39.9; IR (KBr, ν, cm⁻¹) 2911, 1735, 1666, 1587, 1497, 1258, 969, 875, 700; HRMS (APCI) m/z Calcd. For C_{24}H_{18}N_{2}O_{4}BrClNa, 535.0036 [M+Na]⁺, found 535.0040.

2-((1-(4-Bromophenyl)-3-((4-bromophenyl)(methyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4w)

Yellow solid; mp 147-148 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 7.95-7.88 (m, 2H), 7.85-7.73 (m, 4H), 7.66-7.59 (m, 2H), 7.35-7.26 (m, 3H), 6.66 (d, J = 9.0 Hz, 2H), 5.68 (t, J = 6.0 Hz, 1H), 4.06-4.02 (s, 2H), 3.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 194.5, 163.2, 147.0, 134.8, 133.9, 132.1, 132.1, 130.5, 129.6, 128.6, 123.8, 114.4, 109.7, 85.4, 53.8, 39.9; IR (KBr, ν, cm⁻¹) 2911, 1735, 1666, 1587, 1497, 1258, 969, 875, 700; HRMS (APCI) m/z Calcd. For C_{24}H_{18}N_{2}O_{4}BrClNa, 578.9531 [M+Na]⁺, found 578.9533.

2-((3-(Ethyl(phenyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (4x) (major)
Yellow solid; mp 99-100 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 7.94–7.71 (m, 7H), 7.27-7.22 (m, 3H), 6.79-6.73 (m, 3H), 5.88-5.85 (m, 1H), 4.09-3.94 (m, 2H), 3.46-3.33 (m, 2H), 2.41 (s, 3H), 1.10 (t, \(J = 6.8\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\); \(\delta\), ppm) 195.1, 163.2, 147.0, 145.1, 134.6, 133.0, 129.4, 129.1, 128.7, 123.7, 123.6, 117.1, 113.0, 84.1, 51.6, 46.0, 21.8, 11.7. IR (KBr, \(\nu\), cm\(^{-1}\) ): 3060, 2965, 1791, 1736, 1661, 1604, 1506, 1353, 1187, 1080, 971, 876, 702; HRMS (APCI): m/z Calcd. For: C\(_{26}\)H\(_{24}\)N\(_2\)O\(_4\), 451.1634 [M+Na], found: 451.1635.

**Scheme 2.** Further synthetic transformations

To a solution of 4a (53 mg, 0.2 mmol) in a mixed solvent of MeOH and CHCl\(_3\) (2.0 mL V/V = 9:1), hydrazine monohydrate (80% in water, 0.03 mL, 0.6 mmol) was added. The reaction mixture was stirred at room temperature for about 16 hours. After the reaction finished, the mixture was evaporated under vacuum and purified by column chromatography to afford a product 5 as a colorless oil (64%).

\(^1\)H NMR (400 MHz, CDCl\(_3\); \(\delta\), ppm) 7.93 (d, \(J = 8.0\) Hz, 2H), 7.42-7.18 (m, 5H), 6.82 (s, 2H), 5.65 (s, 1H), 4.06–3.73 (m, 2H), 3.00 (s, 3H), 2.43 (s, 3H), 1.84 (s, 2H), 1.80 (s, 2H). IR (KBr, \(\nu\), cm\(^{-1}\)) 3350, 3320, 3257, 3107, 1601, 1523, 1432, 1080, 965, 821; HRMS (APCI) m/z Calcd. for C\(_{17}\)H\(_{21}\)N\(_4\)O, 297.1715 [M-H]^-, found 297.1721.
Copies of $^1$H NMR and $^{13}$C NMR of compounds

$^1$H NMR Spectrum of Compound 4a

$^{13}$C NMR Spectrum of Compound 4a
$\text{\textsuperscript{1}H NMR Spectrum of Compound 4b}$

$\text{\textsuperscript{13}C NMR Spectrum of Compound 4b}$
$^1$H NMR Spectrum of Compound 4c

$^{13}$C NMR Spectrum of Compound 4c
$^1$H NMR Spectrum of Compound 4d

$^{13}$C NMR Spectrum of Compound 4d
**1H NMR Spectrum of Compound 4f**

**13C NMR Spectrum of Compound 4f**
$^1$H NMR Spectrum of Compound 4g

$^{13}$C NMR Spectrum of Compound 4g
$^1$H NMR Spectrum of Compound 4h

$^{13}$C NMR Spectrum of Compound 4h
$^1$H NMR Spectrum of Compound 4j

$^{13}$C NMR Spectrum of Compound 4j
\(^1\)H NMR Spectrum of Compound 4k

\(^{13}\)C NMR Spectrum of Compound 4k
$^1$H NMR Spectrum of Compound 4l

$^{13}$C NMR Spectrum of Compound 4l
**1H NMR Spectrum of Compound 4m**

**13C NMR Spectrum of Compound 4m**

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S26
$\text{S27}$

$\text{1H NMR Spectrum of Compound 4n}$

$\text{13C NMR Spectrum of Compound 4n}$

S27
$^1$H NMR Spectrum of Compound 4o

$^{13}$C NMR Spectrum of Compound 4o
$^1$H NMR Spectrum of Compound 4p

$^{13}$C NMR Spectrum of Compound 4p
$^1$H NMR Spectrum of Compound 4s

$^{13}$C NMR Spectrum of Compound 4s
$^1$H NMR Spectrum of Compound 4t

$^{13}$C NMR Spectrum of Compound 4t
$^1$H NMR Spectrum of Compound 4u

$^{13}$C NMR Spectrum of Compound 4u
$^1$H NMR Spectrum of Compound 4v

$^{13}$C NMR Spectrum of Compound 4v

S35
$^{1}H$ NMR Spectrum of Compound 4w

$^{13}C$ NMR Spectrum of Compound 4w
1H NMR Spectrum of Compound 4x

13C NMR Spectrum of Compound 4x
$^1$H NMR Spectrum of Compound 5