Facile synthesis of 2-(2-aminobenzoyl)benzoic acid via a base-promoted aerobic cascade reaction

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1. General information:

Unless otherwise stated, all commercial materials and solvents were used directly without further purification. \(^1\)H NMR spectra were recorded on 400 MHz spectrometers, and \(^{13}\)C NMR spectra were recorded on a 100 MHz spectrometer. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in DMSO-d\(_6\) as an internal standard at room temperature. \(^{13}\)C NMR spectra were obtained by using the same NMR spectrometers and were calibrated with DMSO-d\(_6\) (δ = 40.00 ppm). High-resolution mass spectra (HRMS) were equipped with an ESI source and a TOF detector. Column chromatography was performed on silica gel (70-230 mesh ASTM) using the reported eluents. Thin-layer chromatography (TLC) was carried out on 4×15 cm plates with a layer thickness of 0.2 mm (silica gel 60 F254).

2. Materials preparation:

Substrates 1 were prepared as follow:

Amine (10 mmol) and aldehyde (10 mmol) dissolved in anhydrous 15 mL of DCM, and Mg\(_2\)SO\(_4\) (2 g) was added. The mixture was stirred at rt for 2 h, and then filtered, and concentrated in vacuo. The residue was dissolved in anhydrous 15 mL of MeOH, and cooled to 0\(°\)C, NaBH\(_4\) (10 mmol) was added, the mixture was stirred at rt for 2 h. Water was then added and the mixture was extracted with EtOAc. The combined organic layers was washed with H\(_2\)O and brine, dried over anhydrous Na\(_2\)SO\(_4\), filtered, and concentrated in vacuo. At last, the residue was dissolved in 15 mL of DMF. Then benzoic acid (12 mmol), EDCI (12 mmol), HOBt (12 mmol) and DIPEA (20 mmol) were added, and the mixture was stirred at rt for 24 h. Water was then added and the mixture was extracted with EtOAc. The combined organic layers was washed with H\(_2\)O and brine, dried over anhydrous Na\(_2\)SO\(_4\), filtered, and concentrated in vacuo. The residue was purified by silica gel flash chromatography (EtOAc/PE: 1/10) to give substrates 1.

3. General procedure for synthesis of 2-(2-Aminobenzoyl)benzoic acids 2:

A mixture of amides 1 (0.25 mmol), KOtBu (0.75 mmol, 3 equiv) and H\(_2\)O (2.5 mmol, 10 equiv) in DMSO (1 mL) was stirred in 100 °C oil bath under air for 4 h (monitored by TLC). 1 M HCl (1 mL) and ethyl acetate(10 mL) was added to get a biphasic system which was extracted with DCM (3 x 15 mL). The combined organic phase was washed with H\(_2\)O (20 mL), brine (20 mL), dried over Na\(_2\)SO\(_4\) and concentrated. The residue was purified by chromatography on silica (EtOAc/PE: 1/4) to afford 2-(2-Aminobenzoyl)benzoic acids 2.
For **2p** (gram-scale): A mixture of *N*-benzyl-2-fluoro-*N*-(2-fluorobenzyl)benzamide **1p** (5 mmol), KOrBu (15 mmol, 3 equiv), and H₂O (50 mmol, 10 equiv) in DMSO (25 mL) was stirred in 100 °C oil bath under air for 4 h (monitored by TLC). 1 M HCl (10 mL) and ethyl acetate (20 mL) was added to get a biphasic system which was extracted with DCM (3 x 30 mL). The combined organic phase was washed with H₂O (50 mL), brine (50 mL), dried over Na₂SO₄ and concentrated. The residue was purified by chromatography on silica (EtOAc/PE: 1/4) to afford 1.21 g of 2-(2-aminobenzoyl)benzoic acid **2p** in 69% yield.

4. **Labeling Experiment**

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          Ph
N-O
       O
H         O
N-O
       O
H         Ph

6p
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HRMS (ESI) m/z calcd for C_{21}H_{18}NO_{2}^{18}O (MH+ 334.1324, found 3334.1327.
5. Characterization data for products:

2-(2-(Butylamino)benzoyl)benzoic acid 2a
62 mg, 83% yield (X = F). Yellow solid. $^1$H NMR (400 MHz, DMSO) $\delta$ 13.03 (s, 1H), 8.73 (t, $J = 5.1$ Hz, 1H), 8.03 – 7.91 (m, 1H), 7.63 (ddt, $J = 32.4$, 7.5, 1.1 Hz, 2H), 7.38 – 7.31 (m, 2H), 6.97 (dd, $J = 8.0$, 1.5 Hz, 1H), 6.82 (d, $J = 8.5$ Hz, 1H), 6.43 (t, $J = 7.4$ Hz, 1H), 3.27 (dd, $J = 12.2$, 6.8 Hz, 2H), 1.73 – 1.59 (m, 2H), 1.50 – 1.40 (m, 2H), 0.96 (t, $J = 7.3$ Hz, 3H); $^{13}$C NMR (100 MHz, DMSO) $\delta$ 199.5, 167.3, 151.6, 142.9, 135.5, 134.8, 132.6, 130.3, 129.8, 129.5, 127.8, 117.6, 114.1, 112.0, 42.1, 31.2, 20.3, 14.2; HRMS (ESI) m/z calcd for C$_{18}$H$_{20}$NO$_3$ (MH+) 298.1438, found 298.1439.
2-(2-(Butylamino)benzoyl)-4-methylbenzoic acid 2b
61 mg, 78% yield. Yellow solid. \(^{1}H\) NMR (400 MHz, DMSO) \(\delta\) 12.84 (s, 1H), 8.71 (t, \(J = 4.8\) Hz, 1H), 7.86 (d, \(J = 8.0\) Hz, 1H), 7.36 (dd, \(J = 17.5, 8.2\) Hz, 2H), 7.13 (s, 1H), 6.96 (d, \(J = 7.9\) Hz, 1H), 6.81 (d, \(J = 8.5\) Hz, 1H), 6.42 (t, \(J = 7.5\) Hz, 1H), 3.26 (dd, \(J = 12.4, 6.7\) Hz, 2H), 2.38 (s, 3H), 1.73 – 1.55 (m, 2H), 1.45 (dq, \(J = 14.5, 7.3\) Hz, 2H), 0.96 (t, \(J = 7.3\) Hz, 3H); \(^{13}C\) NMR (100 MHz, DMSO) \(\delta\) 199.7, 167.1, 151.5, 143.1, 143.0, 135.4, 134.8, 130.4, 129.9, 128.2, 126.8, 117.7, 114.1, 111.9, 42.1, 31.2, 21.4, 20.2, 14.2; HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{22}\)NO\(_3\) (MH\(^+\)) 312.1594, found 312.1592.

2-(2-(Butylamino)benzoyl)-5-methylbenzoic acid 2c
64 mg, 82% yield. Yellow solid. \(^{1}H\) NMR (400 MHz, DMSO) \(\delta\) 12.93 (s, 1H), 8.70 (t, \(J = 5.0\) Hz, 1H), 7.76 (s, 1H), 7.47 (d, \(J = 7.6\) Hz, 1H), 7.40 – 7.29 (m, 1H), 7.21 (d, \(J = 7.7\) Hz, 1H), 6.97 (dd, \(J = 8.0, 1.2\) Hz, 1H), 6.81 (d, \(J = 8.5\) Hz, 1H), 6.42 (t, \(J = 7.4\) Hz, 1H), 3.26 (dd, \(J = 12.3, 6.8\) Hz, 2H), 2.42 (s, 3H), 1.74 – 1.56 (m, 2H), 1.44 (dq, \(J = 14.8, 7.5\) Hz, 2H), 0.96 (t, \(J = 7.3\) Hz, 3H); \(^{13}C\) NMR (100 MHz, DMSO) \(\delta\) 199.7, 167.5, 151.5, 140.2, 139.1, 135.4, 134.8, 132.9, 130.6, 130.0, 127.9, 117.8, 114.0, 111.9, 42.1, 31.2, 21.1, 20.2, 14.2; HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{22}\)NO\(_3\) (MH\(^+\)) 312.1594, found 312.1591.

2-(2-(Butylamino)benzoyl)-4-fluorobenzoic acid 2d
48 mg, 61% yield. Yellow solid. \(^{1}H\) NMR (400 MHz, DMSO) \(\delta\) 13.08 (s, 1H), 8.68 (d, \(J = 5.3\) Hz, 1H), 8.04 (dt, \(J = 8.7, 5.1\) Hz, 1H), 7.46 – 7.34 (m, 2H), 7.28 (dd, \(J = 8.8, 2.5\) Hz, 1H), 7.00 – 6.93 (m, 1H), 6.83 (d, \(J = 8.6\) Hz, 1H), 6.45 (t, \(J = 7.3\) Hz, 1H), 3.27 (dd, \(J = 12.2, 6.8\) Hz, 2H), 1.70 – 1.60 (m, 2H), 1.45 (dq, \(J = 14.4, 7.3\) Hz, 2H), 0.96 (t, \(J = 7.3\) Hz, 3H); \(^{13}C\) NMR (100 MHz, DMSO) \(\delta\) 197.5, 166.3, 164.4 (d, \(J = 252.8\) Hz), 151.6, 145.7 (d, \(J = 7.5\) Hz), 135.7, 134.7, 133.5 (d, \(J = 9.5\) Hz), 126.1 (d, \(J = 3.0\) Hz), 117.2, 116.4 (d, \(J = 21.7\) Hz), 115.1 (d, \(J = 23.5\) Hz), 114.2, 112.0, 42.1, 31.1, 20.2, 14.2; HRMS (ESI) m/z calcd for C\(_{22}\)H\(_{20}\)NO\(_2\) (MH\(^+\)) 316.1343, found 316.1344.
4-Bromo-2-(2-(butylamino)benzoyl)benzoic acid 2e
56 mg, 60% yield. Yellow solid. \( ^1H \) NMR (400 MHz, DMSO) \( \delta \) 13.21 (s, 1H), 8.66 (s, 1H), 7.89 (d, \( J = 8.4 \) Hz, 1H), 7.80 (d, \( J = 8.3 \) Hz, 1H), 7.58 (s, 1H), 7.37 (t, \( J = 7.6 \) Hz, 1H), 6.98 (t, \( J = 12.8 \) Hz, 1H), 6.83 (d, \( J = 8.5 \) Hz, 1H), 6.45 (t, \( J = 7.5 \) Hz, 1H), 3.27 (dd, \( J = 12.4, 6.5 \) Hz, 2H), 1.72 – 1.53 (m, 2H), 1.44 (dq, \( J = 14.5, 7.4 \) Hz, 2H), 0.96 (t, \( J = 7.3 \) Hz, 3H); \(^{13}C\) NMR (100 MHz, DMSO) \( \delta \) 197.4, 166.6, 151.6, 144.6, 135.7, 134.8, 132.5, 130.4, 129.1, 126.4, 117.3, 114.2, 112.0, 42.1, 31.1, 20.2, 14.2; HRMS (ESI) m/z calcd for C\(_{18}\)H\(_{19}\)BrNO\(_3\) (MH\(^+\)) 376.0543, found 376.0542.

2-(2-(Butylamino)benzoyl)nicotinic acid 2f
37 mg, 47% yield. Yellow solid. \( ^1H \) NMR (400 MHz, DMSO) \( \delta \) 13.46 (s, 1H), 8.77 (dd, \( J = 4.8, 1.6 \) Hz, 1H), 8.63 (t, \( J = 5.1 \) Hz, 1H), 8.36 (dd, \( J = 8.0, 1.6 \) Hz, 1H), 7.64 (dd, \( J = 8.0, 4.8 \) Hz, 1H), 7.44 – 7.32 (m, 1H), 7.01 – 6.76 (m, 2H), 6.44 (dd, \( J = 11.1, 3.9 \) Hz, 1H), 3.29 (dd, \( J = 12.3, 6.8 \) Hz, 2H), 1.77 – 1.56 (m, 2H), 1.44 (dq, \( J = 14.6, 7.4 \) Hz, 2H), 0.96 (t, \( J = 7.3 \) Hz, 3H); \(^{13}C\) NMR (100 MHz, DMSO) \( \delta \) 196.7, 166.4, 159.1, 152.2, 151.9, 138.9, 135.8, 135.1, 125.6, 124.5, 116.4, 114.2, 112.0, 42.1, 31.2, 20.2, 14.5; HRMS (ESI) m/z calcd for C\(_{17}\)H\(_{19}\)N\(_2\)O\(_3\) (MH\(^+\)) 299.1390, found 299.1388.

2-(2-(Butylamino)-4-methylbenzoyl)benzoic acid 2g
67 mg, 86% yield. Yellow solid. \( ^1H \) NMR (400 MHz, DMSO) \( \delta \) 12.96 (s, 1H), 8.72 (t, \( J = 5.0 \) Hz, 1H), 7.95 (d, \( J = 7.5 \) Hz, 1H), 7.71 – 7.52 (m, 2H), 7.30 (d, \( J = 7.3 \) Hz, 1H), 6.85 (d, \( J = 8.2 \) Hz, 1H), 6.63 (s, 1H), 6.26 (d, \( J = 8.1 \) Hz, 1H), 3.25 (dd, \( J = 12.2, 6.8 \) Hz, 2H), 2.25 (s, 3H), 1.77 – 1.57 (m, 2H), 1.52 – 1.39 (m, 2H), 0.96 (t, \( J = 7.3 \) Hz, 3H); \(^{13}C\) NMR (100 MHz, DMSO) \( \delta \) 198.8, 167.4, 151.7, 146.1, 143.0, 134.9, 132.5, 130.3, 129.9, 129.3, 127.8, 115.6, 115.6, 111.9, 42.1, 31.2, 22.2, 20.3, 14.2; HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{22}\)NO\(_3\) (MH\(^+\)) 312.1594, found 312.1599.

2-(2-(Butylamino)-5-methylbenzoyl)benzoic acid 2h
65 mg, 83% yield. Yellow solid. \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 13.00 (s, 1H), 8.57 (t, \(J = 4.8\) Hz, 1H), 7.96 (d, \(J = 7.6\) Hz, 1H), 7.66 (dt, \(J = 7.5, 3.7\) Hz, 1H), 7.59 (dt, \(J = 7.5, 3.8\) Hz, 1H), 7.30 (d, \(J = 7.1\) Hz, 1H), 7.21 (dd, \(J = 8.6, 1.5\) Hz, 1H), 6.89 – 6.66 (m, 2H), 3.24 (dd, \(J = 12.2, 6.7\) Hz, 2H), 2.01 (s, 3H), 1.72 – 1.54 (m, 2H), 1.50 – 1.37 (m, 2H), 0.95 (t, \(J = 7.3\) Hz, 3H); \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) 199.3, 167.4, 149.8, 142.9, 136.7, 134.2, 132.4, 130.3, 130.1, 129.4, 127.8, 122.2, 117.4, 112.2, 42.2, 31.2, 20.3, 20.2, 14.2; HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{22}\)NO\(_3\) (MH\(^+\)) 312.1594, found 312.1591.

\[
\begin{align*}
\text{HO} & \quad \text{O} \\
\text{H} & \quad \text{nBu}
\end{align*}
\]

2-(2-(Butylamino)-6-methylbenzoyl)benzoic acid \(2i\)

57 mg, 73% yield. Yellow solid. \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 13.35 (s, 1H), 7.84 – 7.75 (m, 1H), 7.62 – 7.45 (m, 2H), 7.25 – 7.18 (m, 1H), 7.15 (d, \(J = 7.4\) Hz, 1H), 6.61 (d, \(J = 8.4\) Hz, 1H), 6.46 (d, \(J = 7.3\) Hz, 2H), 3.04 (t, \(J = 6.7\) Hz, 2H), 1.97 (s, 3H), 1.48 – 1.34 (m, 2H), 1.19 (td, \(J = 14.9, 7.5\) Hz, 2H), 0.81 (t, \(J = 7.3\) Hz, 3H); \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) 199.7, 169.8, 149.1, 143.8, 138.6, 133.0, 132.8, 131.6, 131.0, 129.9, 127.5, 121.8, 118.5, 109.7, 42.7, 30.9, 21.7, 20.0, 14.1; HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{22}\)NO\(_3\) (MH\(^+\)) 312.1598, found 312.1598.

\[
\begin{align*}
\text{HO} & \quad \text{O} \\
\text{H} & \quad \text{nBu}
\end{align*}
\]

2-(2-(Butylamino)-4-chlorobenzoyl)benzoic acid \(2j\)

46 mg, 55% yield. Yellow solid. \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 13.07 (s, 1H), 8.81 (t, \(J = 5.2\) Hz, 1H), 7.97 (dd, \(J = 7.7, 0.8\) Hz, 1H), 7.64 (dtd, \(J = 32.8, 7.5, 1.2\) Hz, 2H), 7.39 – 7.31 (m, 1H), 6.95 (d, \(J = 8.6\) Hz, 1H), 6.86 (d, \(J = 1.9\) Hz, 1H), 6.47 (dd, \(J = 8.6, 2.0\) Hz, 1H), 3.28 (dd, \(J = 12.4, 6.9\) Hz, 2H), 1.72 – 1.57 (m, 2H), 1.49 – 1.38 (m, 2H), 0.96 (t, \(J = 7.3\) Hz, 3H); \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) 198.9, 167.2, 152.2, 142.4, 140.5, 136.5, 132.7, 130.4, 129.7, 129.7, 127.8, 116.6, 114.2, 111.2, 42.1, 30.9, 20.2, 14.1; HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{19}\)ClNO\(_3\) (MH\(^+\)) 332.1048, found 332.1051.

\[
\begin{align*}
\text{HO} & \quad \text{O} \\
\text{H} & \quad \text{nBu}
\end{align*}
\]

2-(2-(Butylamino)-5-chlorobenzoyl)benzoic acid \(2k\)

47 mg, 57% yield. Yellow solid. \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 13.13 (s, 1H), 8.71 (t, \(J = 5.2\) Hz, 1H), 7.99 (d, \(J = 7.7\) Hz, 1H), 7.67 (ddt, \(J = 31.5, 7.5, 1.1\) Hz, 2H), 7.42 – 7.35 (m, 2H), 6.87 (dd, \(J = 16.0, 5.9\) Hz, 2H), 3.30 – 3.26 (m, 2H), 1.68 – 1.59 (m, 2H), 1.43 (dq, \(J = 14.4, 7.3\) Hz, 2H), 0.95 (t, \(J = 7.3\) Hz, 3H); \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) 198.6, 167.2, 150.2, 142.0, 135.1, 132.9, 132.8, 130.5, 129.9, 129.8, 127.8, 118.4, 117.1, 114.4, 42.2, 31.0, 20.6, 14.2; HRMS (ESI) m/z calcd for C\(_{19}\)H\(_{19}\)ClNO\(_3\) (MH\(^+\)) 332.1048, found 332.1052.
2-(3-(Butylamino)isonicotinoyl)benzoic acid 2l

61 mg, 82% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) δ 12.81 (s, 1H), 8.50 (s, 1H), 7.87 (d, $J$ = 7.4 Hz, 1H), 7.70 (s, 1H), 7.62 (t, $J$ = 7.2 Hz, 1H), 7.52 (t, $J$ = 7.4 Hz, 1H), 7.37 – 7.25 (m, 3H), 3.29 (d, $J$ = 5.8 Hz, 2H), 1.63 (dd, $J$ = 14.0, 6.9 Hz, 2H), 1.44 (dd, $J$ = 14.5, 7.2 Hz, 2H), 0.96 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO) δ 200.4, 167.7, 147.7, 143.6, 135.8, 134.2, 132.1, 130.8, 129.2, 129.0, 128.8, 127.9, 120.0, 41.7, 31.1, 20.2, 14.2; HRMS (ESI) m/z calcd for C$_{17}$H$_{19}$N$_2$O$_3$ (MH$^+$) 299.1390, found 299.1395.

2-(2-(Methylamino)benzoyl)benzoic acid 2m

57 mg, 90% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) δ 13.01 (s, 1H), 8.63 (d, $J$ = 4.9 Hz, 1H), 7.97 (d, $J$ = 7.7 Hz, 1H), 7.63 (ddt, $J$ = 33.1, 7.5, 1.3 Hz, 2H), 7.39 (dddt, $J$ = 8.5, 7.2, 1.5 Hz, 1H), 7.32 (dd, $J$ = 7.5, 0.8 Hz, 1H), 6.96 (dd, $J$ = 8.0, 1.3 Hz, 1H), 6.78 (d, $J$ = 8.4 Hz, 1H), 6.53 – 6.36 (m, 1H), 2.93 (d, $J$ = 4.9 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO) δ 199.3, 167.3, 152.2, 142.9, 135.5, 134.7, 132.6, 130.3, 129.8, 129.4, 127.8, 117.8, 114.1, 111.6, 29.6; HRMS (ESI) m/z calcd for C$_{15}$H$_{14}$NO$_3$ (MH$^+$) 256.0968, found 256.0964.

2-(2-(Isopropylamino)benzoyl)benzoic acid 2n

63 mg, 88% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) δ 13.00 (s, 1H), 8.67 (d, $J$ = 7.4 Hz, 1H), 7.96 (dd, $J$ = 7.7, 0.8 Hz, 1H), 7.62 (dddt, $J$ = 31.9, 7.5, 1.2 Hz, 2H), 7.39 – 7.30 (m, 2H), 6.96 (dd, $J$ = 8.0, 1.4 Hz, 1H), 6.84 (d, $J$ = 8.6 Hz, 1H), 6.41 (t, $J$ = 7.2 Hz, 1H), 3.83 (dq, $J$ = 12.9, 6.4 Hz, 1H), 1.26 (d, $J$ = 6.3 Hz, 6H); $^{13}$C NMR (100 MHz, DMSO) δ 199.5, 167.3, 150.6, 142.9, 135.4, 135.0, 132.5, 130.3, 129.9, 129.4, 127.8, 117.5, 113.9, 112.4, 43.1, 23.1.; HRMS (ESI) m/z calcd for C$_{17}$H$_{18}$NO$_3$ (MH$^+$) 284.1281, found 284.1278.

2-(2-(Phenethylamino)benzoyl)benzoic acid 2o
47 mg 55% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) $\delta$ 13.02 (s, 1H), 8.77 (s, 1H), 7.97 (d, $J = 7.6$ Hz, 1H), 7.67 (t, $J = 7.1$ Hz, 1H), 7.59 (t, $J = 7.2$ Hz, 1H), 7.35 (ddt, $J = 22.3$, 15.2, 7.4 Hz, 6H), 7.23 (t, $J = 6.8$ Hz, 1H), 6.97 (d, $J = 7.9$ Hz, 1H), 6.90 (d, $J = 8.5$ Hz, 1H), 6.45 (t, $J = 7.5$ Hz, 1H), 3.52 (dd, $J = 12.8$, 6.9 Hz, 2H), 2.96 (t, $J = 7.2$ Hz, 2H); $^{13}$C NMR (100 MHz, DMSO) $\delta$ 199.4, 167.3, 151.2, 142.8, 139.7, 135.5, 134.9, 132.6, 130.3, 129.8, 129.5, 129.3, 128.9, 127.8, 126.7, 117.8, 114.3, 112.0, 44.1, 35.2; HRMS (ESI) m/z calcd for C$_{22}$H$_{20}$NO$_3$ (MH$^+$) 346.1438, found 346.1438.

2-(2-(Benzylamino)benzoyl)benzoic acid 2p
72 mg, 87% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) $\delta$ 13.07 (s, 1H), 9.12 (d, $J = 5.7$ Hz, 1H), 8.03 – 7.95 (m, 1H), 7.68 (t, $J = 7.4$ Hz, 1H), 7.60 (td, $J = 7.6$, 1.0 Hz, 1H), 7.48 – 7.33 (m, 5H), 7.48 – 7.26 (m, 2H), 7.04 – 6.96 (m, 1H), 6.81 – 6.73 (m, 1H), 6.45 (t, $J = 7.2$ Hz, 1H), 4.56 (d, $J = 5.6$ Hz, 2H); $^{13}$C NMR (100 MHz, DMSO) $\delta$ 199.7, 167.3, 151.2, 142.8, 139.5, 135.3, 134.7, 132.6, 130.3, 129.9, 129.5, 127.8, 127.5, 118.2, 114.6, 112.4, 46.2; HRMS (ESI) m/z calcd for C$_{21}$H$_{18}$NO$_3$ (MH$^+$) 332.1281, found 332.1283.

2-(2-((2-Fluorobenzyl)amino)benzoyl)benzoic acid 2q
73 mg, 84% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) $\delta$ 13.08 (s, 1H), 9.09 (d, $J = 5.6$ Hz, 1H), 7.98 (d, $J = 7.7$ Hz, 1H), 7.64 (dt, $J = 33.9$, 7.5 Hz, 2H), 7.44 (t, $J = 7.4$ Hz, 1H), 7.40 – 7.29 (m, 3H), 7.22 (dt, $J = 14.9$, 8.8 Hz, 2H), 7.00 (d, $J = 8.0$ Hz, 1H), 6.79 (d, $J = 8.5$ Hz, 1H), 6.47 (t, $J = 7.5$ Hz, 1H), 4.63 (d, $J = 5.8$ Hz, 2H); $^{13}$C NMR (100 MHz, DMSO) $\delta$ 199.7, 167.3, 160.9 (d, $J = 244.2$ Hz), 150.9, 142.8, 135.4, 134.8, 132.6, 130.3, 129.9, 129.7 (d, $J = 4.4$ Hz), 129.6, 129.6, 127.8, 126.2 (d, $J = 14.6$ Hz), 125.0 (d, $J = 3.4$ Hz), 118.4, 115.8 (d, $J = 21.1$ Hz), 114.8, 112.1, 40.1; HRMS (ESI) m/z calcd for C$_{21}$H$_{16}$FNO$_3$ (MH$^+$) 350.1187, found 350.1184.

2-(2-((2-Methylbenzyl)amino)benzoyl)benzoic acid 2r
75 mg, 87% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) $\delta$ 13.08 (s, 1H), 9.01 (s, 1H), 7.98 (d, $J = 7.7$ Hz, 1H), 7.64 (dt, $J = 34.4$, 7.5, 1.1 Hz, 2H), 7.34 (ddd, $J = 15.4$, 7.9, 1.1 Hz, 3H), 7.25 – 7.15 (m, 3H), 7.00 (d, $J = 8.0$ Hz, 1H), 6.79 (d, $J = 8.6$ Hz, 1H), 6.46 (t, $J = 7.4$ Hz, 1H), 4.51 (d, $J = 5.5$ Hz, 2H), 2.37 (s, 3H); $^{13}$C NMR (100 MHz, DMSO) $\delta$ 199.7, 167.4, 151.3, 142.8, 137.0, 136.4, 135.4,
2-(2-(3-Methylbenzyl)amino)benzoyl)benzoic acid 2s
76 mg, 88% yield. Yellow solid. \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 13.06 (s, 1H), 9.09 (d, \(J = 5.2\) Hz, 1H), 7.98 (d, \(J = 7.7\) Hz, 1H), 7.65 (ddd, \(J = 34.0, 10.8, 4.2\) Hz, 2H), 7.39 – 7.17 (m, 5H), 7.09 (d, \(J = 7.3\) Hz, 1H), 6.99 (d, \(J = 8.0\) Hz, 1H), 6.77 (d, \(J = 8.5\) Hz, 1H), 6.45 (t, \(J = 7.5\) Hz, 1H), 4.51 (d, \(J = 5.6\) Hz, 2H), 2.31 (s, 3H); \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) 199.6, 167.3, 151.2, 142.8, 139.4, 138.2, 135.3, 134.7, 132.6, 130.4, 129.8, 129.5, 129.0, 128.2, 128.2, 127.8, 124.7, 118.1, 114.6, 112.4, 46.3, 21.6; HRMS (ESI) m/z calcd for C\(_{22}\)H\(_{20}\)NO\(_3\) (MH\(^+\)) 346.1438, found 346.1435.

2-(2-((4-Methylbenzyl)amino)benzoyl)benzoic acid 2t
78 mg, 90% yield. Yellow solid. \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 13.04 (s, 1H), 9.07 (t, \(J = 5.2\) Hz, 1H), 7.97 (d, \(J = 7.6\) Hz, 1H), 7.64 (dt, \(J = 34.5, 7.2\) Hz, 2H), 7.51 – 7.23 (m, 4H), 7.18 (d, \(J = 7.8\) Hz, 2H), 6.98 (d, \(J = 7.9\) Hz, 1H), 6.76 (d, \(J = 8.5\) Hz, 1H), 6.44 (t, \(J = 7.5\) Hz, 1H), 4.50 (d, \(J = 5.5\) Hz, 2H), 2.29 (s, 3H); \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) 199.6, 167.3, 151.1, 142.8, 136.6, 136.3, 135.3, 134.7, 132.6, 130.3, 129.8, 129.6, 129.5, 129.0, 128.2, 127.8, 124.7, 118.1, 114.5, 112.4, 46.0, 21.2; HRMS (ESI) m/z calcd for C\(_{22}\)H\(_{20}\)NO\(_3\) (MH\(^+\)) 346.1438, found 346.1435.

2-(2-((4-Methoxybenzyl)amino)benzoyl)benzoic acid 2u
65 mg, 72% yield. Yellow solid. \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 13.05 (s, 1H), 9.03 (s, 1H), 8.00 – 7.94 (m, 1H), 7.68 (td, \(J = 7.5, 1.2\) Hz, 1H), 7.59 (td, \(J = 7.6, 1.2\) Hz, 1H), 7.32 (dt, \(J = 8.6, 4.0\) Hz, 4H), 7.00 – 6.91 (m, 3H), 6.79 (d, \(J = 8.5\) Hz, 1H), 6.45 (t, \(J = 7.2\) Hz, 1H), 4.47 (d, \(J = 5.6\) Hz, 2H), 3.75 (s, 3H); \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) 199.6, 167.3, 158.9, 151.1, 142.8, 135.3, 134.7, 132.6, 131.2, 130.3, 129.9, 129.5, 128.9, 127.8, 118.1, 114.5, 112.4, 55.5, 45.7; HRMS (ESI) m/z calcd for C\(_{22}\)H\(_{20}\)NO\(_4\) (MH\(^+\)) 362.1387, found 362.1386.
2-(2-((4-Chlorobenzyl)amino)benzoyl)benzoic acid 2v
48 mg, 53% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) δ 13.06 (s, 1H), 9.13 (t, $J = 5.9$ Hz, 1H), 7.98 (d, $J = 7.7$ Hz, 1H), 7.65 (ddt, $J = 34.8, 7.5, 1.1$ Hz, 2H), 7.42 (s, 4H), 7.37 (d, $J = 7.3$ Hz, 1H), 7.32 – 7.27 (m, 1H), 6.98 (d, $J = 7.0$ Hz, 1H), 6.71 (d, $J = 8.5$ Hz, 1H), 6.46 (t, $J = 7.4$ Hz, 1H), 4.57 (d, $J = 6.0$ Hz, 2H); $^{13}$C NMR (100 MHz, DMSO) δ 199.7, 167.3, 150.9, 142.8, 138.8, 135.3, 134.7, 132.6, 131.9, 130.3, 129.9, 129.6, 129.3, 129.0, 127.8, 118.4, 114.7, 112.4, 45.4; HRMS (ESI) m/z calcd for C$_{21}$H$_{17}$ClNO$_3$ (MH+) 366.0891, found 366.0893.

2-(2-(Butylamino)-4-methylbenzoyl)-5-methylbenzoic acid 2w
63 mg, 77% yield. Yellow solid. $^1$H NMR (400 MHz, DMSO) δ 12.83 (s, 1H), 8.56 (t, $J = 5.1$ Hz, 1H), 7.86 (d, $J = 8.0$ Hz, 1H), 7.38 (d, $J = 8.0$ Hz, 1H), 7.20 (dd, $J = 8.7, 1.8$ Hz, 1H), 7.11 (s, 1H), 6.75 (d, $J = 8.5$ Hz, 2H), 3.24 (dd, $J = 12.2, 6.8$ Hz, 2H), 2.39 (s, 3H), 2.01 (s, 3H), 1.67 – 1.59 (m, 2H), 1.48 – 1.39 (m, 2H), 0.95 (t, $J = 7.3$ Hz, 3H); $^{13}$C NMR (100 MHz, DMSO) δ 199.5, 167.1, 149.8, 143.2, 143.0, 136.6, 134.2, 130.4, 129.9, 128.2, 126.8, 122.2, 117.5, 112.1, 42.2, 31.2, 21.4, 20.3, 20.2, 14.2; HRMS (ESI) m/z calcd for C$_{20}$H$_{24}$NO$_3$ (MH+) 326.1751, found 326.1753.

5-Benzyl-5H-dibenzo[b,e]azepine-6,11-dione 6p
54 mg, 69% yield. White solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.16 (d, $J = 7.3$ Hz, 1H), 7.62 (ddd, $J = 21.1, 15.2, 6.8$ Hz, 4H), 7.39 – 7.19 (m, 8H), 5.33 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 195.2, 166.6, 140.2, 139.7, 137.0, 136.9, 132.4, 132.4, 132.3, 132.0, 131.2, 128.7, 128.2, 127.2, 126.6, 126.1, 125.8, 122.5, 54.9; HRMS (ESI) m/z calcd for C$_{21}$H$_{16}$NO$_2$ (MH+) 314.1176, found 314.1178.
6. $^1$H NMR, $^{13}$C NMR spectra of products: