

# Supporting Information

## Palladium-Catalyzed post-Ugi Arylative Dearomatization/Michael Addition Cascade towards Plicamine Analogues

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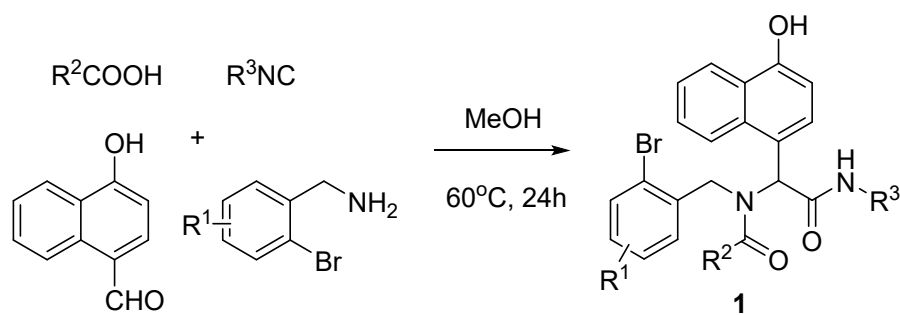
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## 1. General information

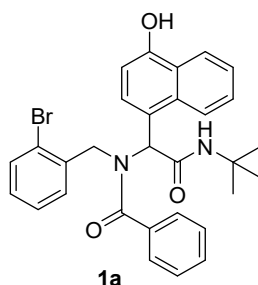
Commercially available reagents were used without additional purification. Column chromatography was performed with silica gel (70-230 mesh).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AM (300 or 400 or 600 MHz) spectrometer at ambient temperature using  $\text{CDCl}_3$  or  $\text{DMSO}-d_6$  as solvent. HRMS (ESI) spectrometry data were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer [Synapt G2 high definition mass spectrometer (HDMS), Waters, Milford, MA]. Samples were infused at  $3 \mu\text{L min}^{-1}$ , and spectra were obtained in the positive ionization mode with a resolution of 15000 [full width at half maximum (FWHM)] with leucine enkephalin as lock mass. Melting points were recorded on a Reichert Thermovar apparatus and were uncorrected. All the palladium catalysts are known compounds and commercially available.

## 2. General procedure for the synthesis of Ugi adducts



To a solution of aldehyde (2.0 mmol, 1.0 equiv.) in methanol 2 mL were added successively amine (2.2 mmol, 1.1 equiv.), acid (2.2 mmol, 1.1 equiv) and isocyanide (2.2 mmol, 1.1 equiv.) in a screw capped vial equipped with a magnetic stir bar. The reaction mixture was stirred in an oil bath at  $60^\circ\text{C}$  for 24 h in a closed vial. After completion of the reaction, the mixture was evaporated under reduced pressure to obtain residue which was purified by a silica gel column chromatography (eluent: *n*-heptane/ethyl acetate = 4:1~2:1 v/v) to afford the desired Ugi products **1**.

## 3. Characterization of Ugi adducts



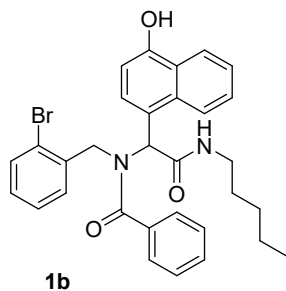
**1a** was obtained as a yellow solid, Yield 81% (884 mg), Melting point  $178 - 180^\circ\text{C}$ .

$^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  10.14 (s, 1H), 8.18 – 8.01 (m, 1H), 7.97 – 7.93 (m, 1H), [7.71 (s), 7.60 (s), 3H], 7.57 – 7.52 (m, 1H), 7.51 – 7.44 (m, 1H), 7.40 – 7.33 (m, 1H), 7.31 – 7.24 (m, 2H), 7.18 (dd, *J*

= 20.7, 7.8 Hz, 1H), [7.05 – 6.99 (m), 6.82 – 6.77 (m), 1H], 6.74 – 6.65 (m, 3H), 6.55 – 6.50 (m, 1H), 5.88 (s, 1H), 4.73 (dd,  $J = 45.8, 16.6$  Hz, 1H), 4.55 – 4.44 (m, 1H), 3.36 (s, 9H). Mixture of rotamers (~3:2).

$^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  172.3, 170.6, 154.2, 137.3, 136.8, 136.5, 134.1, 133.4, 131.9, 131.6, 130.5, 129.9, 129.8, 129.4, 129.2, 128.8, 128.5, 128.3, 128.2, 127.8, 127.2, 127.2, 126.9, 126.8, 126.5, 126.4, 125.1, 124.9, 124.3, 123.8, 123.1, 122.9, 122.6, 121.6, 121.2, 107.7, 62.4, 51.1, 48.9, 29.0, 28.9. Mixture of rotamers.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{30}\text{H}_{29}\text{BrN}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 545.1434, found 545.1450.

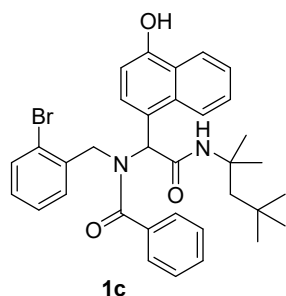


**1b** was obtained as a gray solid, Yield 87% (974 mg), Melting point 108 - 111 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  10.16 (s, 1H), [8.23 (s), 8.15 – 8.09 (m), 1H], 8.08 – 7.91 (m, 2H), [7.69 – 7.64 (m), 7.59 (s), 3H], 7.51 (s, 1H), 7.47 – 7.36 (m, 1H), 7.32 – 7.24 (m, 2H), 7.23 – 7.15 (m, 1H), 7.07 – 6.97 (m, 1H), 6.83 – 6.68 (m, 2H), 6.65 (d,  $J = 7.9$  Hz, 1H), 6.58 – 6.48 (m, 1H), 5.91 (s, 1H), 4.86 – 4.65 (m, 1H), 4.57 – 4.43 (m, 1H), 3.17 (s, 1H), 3.11 – 2.98 (m, 1H), 1.46 – 1.36 (m, 2H), 1.31 – 1.24 (m, 2H), 1.23 – 1.16 (m, 2H), 0.90 – 0.82 (m, 3H). Mixture of rotamers (~1:1).

$^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  173.2, 172.3, 169.7, 156.2, 155.9, 154.6, 137.0, 136.4, 134.0, 133.3, 132.8, 131.9, 130.7, 130.0, 129.6, 128.9, 128.5, 128.3, 127.9, 127.6, 127.3, 126.7, 126.6, 125.3, 124.1, 123.5, 123.3, 121.8, 121.6, 121.3, 114.6, 107.8, 63.1, 58.2, 55.9, 55.6, 51.1, 48.7, 31.9, 22.8. Mixture of rotamers.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{31}\text{H}_{31}\text{BrN}_2\text{O}_3$  ( $[\text{M}+\text{Na}]^+$ ): 581.1410, found 581.1390.



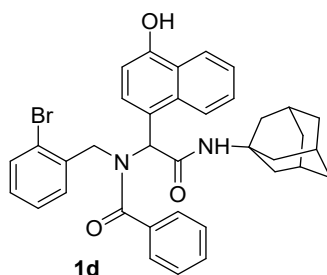
**1c** was obtained as a brown solid, Yield 82% (986 mg), Melting point 105 - 107 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  10.11 (s, 1H), [8.33 – 8.31 (m), 8.20 (d,  $J = 6.7$  Hz), 1H], 8.09 – 7.93 (m, 1H), [7.84 (s), 7.65 – 7.58 (m), 3H], 7.56 – 7.49 (m, 1H), 7.49 – 7.43 (m, 1H), 7.42 – 7.32 (m, 1H), 7.31 – 7.25 (m, 1H), 7.25 – 7.15 (m, 2H), [7.08 (s), 7.03 (d,  $J = 7.7$  Hz), 1H], 6.78 – 6.60 (m, 3H), 6.55 – 6.43 (m, 1H), 5.96 (s, 1H), 4.87 – 4.69 (m, 1H), 4.51 (d,  $J = 17.2$  Hz, 1H), [3.36 (s), 2.17 (d,  $J =$

13.9 Hz), 2H)], [1.75 – 1.59 (m), 1.46 – 1.32 (m), 6H], [0.97 (s), 0.89 (s), 9H]. Mixture of rotamers (~1:1).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 172.8, 172.3, 170.5, 170.2, 154.2, 137.5, 137.3, 137.0, 136.6, 134.2, 133.5, 131.3, 131.8, 130.6, 129.8, 129.5, 128.9, 128.6, 128.4, 128.2, 127.9, 127.2, 127.1, 126.9, 126.5, 125.2, 125.0, 124.5, 123.9, 122.7, 122.4, 121.7, 121.2, 107.6, 107.5, 79.9, 62.6, 57.2, 55.5, 55.0, 52.5, 51.1, 49.0, 32.0, 31.7, 30.2, 29.3, 29.0, 28.5. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C<sub>34</sub>H<sub>37</sub>BrN<sub>2</sub>O<sub>3</sub> ([M+H]<sup>+</sup>): 601.2060, found 601.2055.

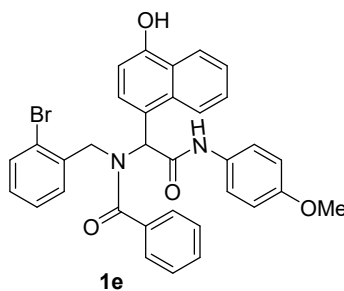


**1d** was obtained as a gray solid, Yield 95% (1185 mg), Melting point 157 - 159 °C.

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ 8.19 – 8.00 (m, 1H), 7.98 – 7.87 (m, 1H), 7.80 (d, *J* = 16.3 Hz, 1H), 7.61 (s, 4H), 7.56 – 7.41 (m, 2H), 7.39 – 7.34 (m, 1H), 7.30 – 7.26 (m, 1H), 7.25 – 7.20 (m, 1H), 7.16 (d, *J* = 7.7 Hz, 1H), 7.05 – 6.97 (m, 1H), 6.81 – 6.71 (m, 1H), 6.70 – 6.66 (m, 1H), 6.53 (t, *J* = 7.2 Hz, 1H), 5.86 (s, 1H), [4.75 (d, *J* = 16.7 Hz), 4.65 (d, *J* = 17.8 Hz), 1H], 4.54 – 4.42 (m, 1H), 3.17 (s, 1H), 2.03 (s, 3H), 1.96 (s, 5H), 1.64 (s, 6H). Mixture of rotamers (~3:2).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 172.3, 170.5, 154.3, 137.3, 136.6, 133.4, 131.6, 130.6, 129.8, 129.4, 128.8, 128.5, 128.3, 128.2, 127.7, 126.8, 126.4, 125.1, 124.9, 123.8, 123.1, 122.5, 121.6, 107.7, 62.5, 51.8, 49.2, 48.9, 41.5, 41.3, 36.7, 35.9, 29.4, 29.1. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C<sub>36</sub>H<sub>35</sub>BrN<sub>2</sub>O<sub>3</sub> ([M+H]<sup>+</sup>): 623.1904, found 623.1907.



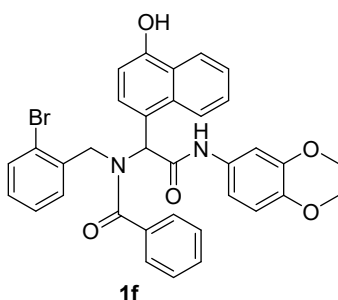
**1e** was obtained as a gray solid, Yield 89% (855 mg), Melting point 210 - 212 °C.

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ [10.22 (d, *J* = 6.4 Hz), 9.89 (s), 2H], 8.19 – 8.04 (m, 1H), [8.02 – 7.94 (m), 7.74 – 7.67 (m), 1H], 7.63 – 7.39 (m, 6H), 7.37 – 6.99 (m, 6H), 6.93 – 6.88 (m, 2H), 6.80 – 6.65 (m, 2H), 6.62 – 6.49 (m, 1H), 6.10 (s, 1H), 4.92 – 4.65 (m, 1H), 4.62 – 4.36 (m, 1H), 3.73 (s, 3H). Mixture of rotamers (~3:2).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 177.2, 176.3, 173.7, 160.2, 159.9, 158.6, 141.1, 141.0, 140.4, 138.0, 137.3, 136.8, 136.3, 135.9, 135.8, 134.7, 134.0, 133.6, 132.9, 132.6, 132.5, 132.5, 132.3,

132.3, 131.9, 131.6, 131.3, 130.7, 130.6, 129.3, 127.5, 127.3, 125.8, 125.6, 125.3, 118.6, 111.8, 67.1, 62.2, 59.9, 59.6, 55.1, 52.7. Mixture of rotamers.

HRMS (ESI,  $m/z$ ) calcd for  $C_{33}H_{27}BrN_2O_4$  ( $[M+Na]^+$ ): 617.1046, found 617.1028.

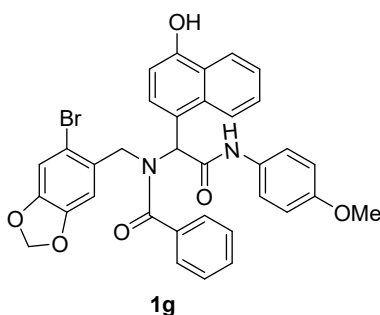


**1f** was obtained as a gray solid, Yield 89% (1110 mg), Melting point 128 - 130 °C.

$^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  10.24 (s, 1H), [10.19 (s), 9.86 (s), 1H], 8.18 – 8.12 (m, 1H), 8.07 – 7.96 (m, 1H), [7.96 – 7.92 (m), 7.73 – 7.68 (m), 1H], 7.60 (s, 2H), 7.51 – 7.46 (m, 1H), 7.45 – 7.37 (m, 1H), 7.30 (s, 2H), 7.27 – 7.22 (m, 1H), 7.19 (d,  $J$  = 12.3 Hz, 1H), [7.12 (s), 7.05 – 6.98 (m), 1H], 6.91 – 6.84 (m, 1H), 6.80 (s, 1H), 6.78 (s, 1H), 6.76 – 6.71 (m, 1H), 6.69 – 6.65 (m, 1H), 6.60 – 6.50 (m, 1H), 6.06 (s, 1H), [4.85 (d,  $J$  = 16.7 Hz), 4.71 (d,  $J$  = 18.0 Hz), 1H], 4.55 – 4.45 (m, 1H), 4.23 (d,  $J$  = 4.9 Hz, 2H), 4.20 (d,  $J$  = 4.8 Hz, 2H). Mixture of rotamers (~1:1).

$^{13}C$  NMR (101 MHz,  $DMSO-d_6$ )  $\delta$  173.2, 172.3, 169.7, 154.6, 143.6, 140.3, 140.0, 137.12, 137.0, 136.4, 134.0, 133.4, 133.3, 133.1, 132.8, 131.9, 131.8, 130.7, 130.0, 129.9, 129.7, 129.6, 129.2, 128.9, 128.6, 128.4, 128.3, 127.9, 127.5, 127.3, 126.7, 126.6, 125.3, 124.0, 123.5, 123.3, 123.3, 121.6, 121.5, 121.4, 121.2, 117.5, 113.3, 113.0, 109.3, 108.9, 107.8, 64.9, 64.6, 60.4. Mixture of rotamers.

HRMS (ESI,  $m/z$ ) calcd for  $C_{34}H_{27}BrN_2O_5$  ( $[M+Na]^+$ ): 645.0996, found 645.0994.



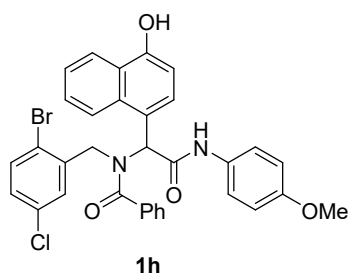
**1g** was obtained as a black solid, Yield 82% (1110 mg), Melting point 234 - 236 °C.

$^1H$  NMR (300 MHz,  $DMSO-d_6$ )  $\delta$  10.25 (s, 1H), [10.23 – 10.19 (m), 9.89 (s), 1H], 8.16 – 8.06 (m, 1H), [8.03 (d,  $J$  = 4.3 Hz), 7.95 (d,  $J$  = 7.6 Hz), 1H], 7.74 – 7.64 (m, 1H), 7.59 (s, 2H), 7.55 – 7.45 (m, 3H), 7.44 – 7.30 (m, 3H), 7.28 – 7.20 (m, 1H), [7.13 (s), 7.07 (s), 1H], 6.90 (d,  $J$  = 8.9 Hz, 2H), 6.73 – 6.66 (m, 1H), [6.62 – 6.56 (m), 6.39 (s), 1H], [6.26 (s), 6.01 (s), 1H], 5.84 (s, 1H), 5.61 (s, 1H), [4.80 (d,  $J$  = 16.4 Hz), 4.58 (d,  $J$  = 17.0 Hz), 1H], 4.42 (t,  $J$  = 15.2 Hz, 1H), [3.73 (s), 3.46 (s), 3H]. Mixture of rotamers (~1:1).

$^{13}C$  NMR (101 MHz,  $DMSO-d_6$ )  $\delta$  173.2, 169.7, 157.9, 156.3, 156.0, 154.6, 146.7, 146.6, 137.1, 134.0, 133.8, 133.5, 133.2, 132.9, 132.3, 130.8, 130.1, 129.9, 129.8, 129.6, 129.4, 129.2, 129.1, 128.7, 128.5,

128.3, 126.7, 123.2, 121.8, 121.3, 114.6, 111.9, 111.7, 111.6, 111.5, 108.5, 108.3, 107.9, 102.0, 101.8, 63.1, 58.4, 55.9, 50.9. Mixture of rotamers.

HRMS (ESI, m/z) calcd for  $C_{34}H_{27}BrN_2O_6$  ( $[M+Na]^+$ ): 661.0945, found 661.0918.



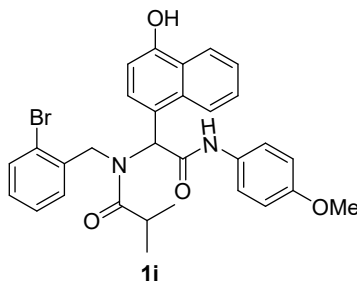
**1h** was obtained as a brown solid, Yield 85% (1071 mg), Melting point 125 - 127 °C.

$^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  10.27 (s, 1H), 9.94 (s, 1H), 8.20 – 8.08 (m, 1H), 8.05 – 7.96 (m, 1H), 7.80 – 7.72 (m, 1H), 7.60 – 7.41 (m, 5H), 7.37 – 7.29 (m, 3H), 7.28 – 7.19 (m, 1H), 7.19 – 7.03 (m, 1H), 6.92 (d,  $J$  = 9.0 Hz, 2H), 6.80 – 6.63 (m, 3H), 6.09 (s, 1H), [4.92 (d,  $J$  = 16.9 Hz), 4.75 (d,  $J$  = 18.1 Hz), 1H], 4.63 – 4.49 (m, 1H), 3.74 (s, 3H). Mixture of rotamers (~1:1).

$^{13}C$  NMR (101 MHz,  $DMSO-d_6$ )  $\delta$  173.2, 172.4, 169.6, 156.3, 156.0, 154.7, 138.7, 138.6, 136.8, 133.9, 133.5, 133.2, 132.8, 132.3, 132.1, 130.9, 129.7, 129.2, 128.5, 128.0, 127.5, 126.7, 125.6, 125.2, 125.1, 123.5, 123.0, 121.8, 121.8, 121.4, 121.3, 119.9, 119.4, 114.8, 114.5, 107.9, 107.6, 62.9, 58.1, 56.0, 55.7.

Mixture of rotamers.

HRMS (ESI, m/z) calcd for  $C_{33}H_{26}BrClN_2O_4$  ( $[M+Na]^+$ ): 651.0657, found 651.0653.

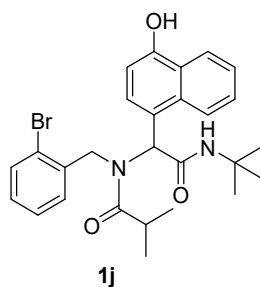


**1i** was obtained as a brown solid, Yield 80% (898 mg), Melting point 210 - 212 °C.

$^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  10.24 – 10.06 (m, 2H), 8.04 (d,  $J$  = 8.2 Hz, 1H), 7.97 – 7.86 (m, 1H), 7.66 – 7.59 (m, 1H), 7.56 – 7.49 (m, 2H), 7.48 – 7.40 (m, 1H), 7.33 – 7.21 (m, 2H), 7.18 – 7.09 (m, 1H), 6.90 – 6.85 (m, 2H), 6.84 – 6.74 (m, 1H), 6.69 (d,  $J$  = 7.9 Hz, 1H), 6.65 – 6.58 (m, 1H), 6.58 – 6.49 (m, 1H), 4.77 – 4.56 (m, 2H), [3.71 (d,  $J$  = 6.7 Hz), 3.60 (d,  $J$  = 12.4 Hz), 3H], 2.45 – 2.32 (m, 1H), 1.11 – 0.89 (m, 6H). Mixture of rotamers (~7:3).

$^{13}C$  NMR (101 MHz,  $DMSO-d_6$ )  $\delta$  178.6, 169.8, 155.9, 154.3, 137.0, 133.8, 132.8, 132.4, 128.7, 128.3, 127.6, 127.3, 126.9, 125.3, 125.3, 124.0, 123.2, 122.2, 121.4, 121.2, 115.6, 115.1, 114.5, 107.7, 57.4, 55.9, 55.8, 49.3, 31.7, 20.4, 20.1. Mixture of rotamers.

HRMS (ESI, m/z) calcd for  $C_{30}H_{29}BrN_2O_4$  ( $[M+Na]^+$ ): 583.1203, found 583.1192.

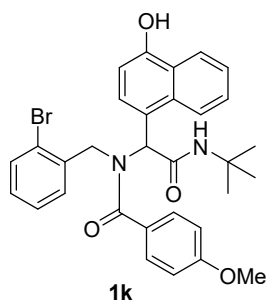


**1j** was obtained as a brown solid, Yield 78% (798 mg), Melting point 119 - 121 °C.

$^1\text{H NMR}$  (300 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.18 (d,  $J = 8.2$  Hz, 1H), 8.00 (d,  $J = 8.5$  Hz, 2H), 7.56 (t,  $J = 7.2$  Hz, 1H), 7.47 – 7.41 (m, 2H), 7.15 (d,  $J = 7.8$  Hz, 1H), 6.93 (s, 1H), 6.81 (d,  $J = 7.9$  Hz, 1H), 6.73 – 6.64 (m, 1H), 6.53 (d,  $J = 4.3$  Hz, 2H), 5.50 (s, 1H), 4.72 (s, 2H), 2.59 – 2.44 (m, 1H), 1.32 (s, 9H), 1.21 (d,  $J = 6.6$  Hz, 3H), 1.10 (d,  $J = 6.4$  Hz, 3H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  178.2, 170.5, 153.9, 137.4, 133.9, 132.4, 128.6, 127.7, 126.9, 125.3, 125.0, 124.2, 123.6, 123.1, 121.4, 107.6, 56.8, 51.0, 49.4, 31.6, 29.0, 20.1. Major rotamer.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{27}\text{H}_{31}\text{BrN}_2\text{O}_3$  ( $[\text{M}+\text{Na}]^+$ ): 533.1410, found 533.1397.

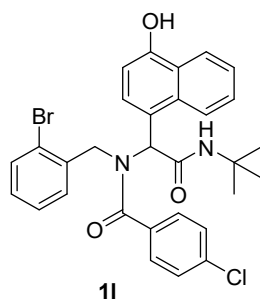


**1k** was obtained as a red solid, Yield 82% (944 mg), Melting point 128 - 130 °C.

$^1\text{H NMR}$  (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  10.12 (s, 1H), 8.14 – 7.95 (m, 1H), 7.92 – 7.73 (m, 1H), 7.62 – 7.36 (m, 4H), 7.30 – 7.07 (m, 4H), 6.98 – 6.62 (m, 4H), 6.57 – 6.49 (m, 1H), 5.97 (s, 1H), 4.59 (dd,  $J = 84.1, 15.5$  Hz, 2H), 3.78 (d,  $J = 66.1$  Hz, 3H), 1.30 (s, 9H).

$^{13}\text{C NMR}$  (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  172.1, 170.7, 161.0, 154.1, 136.8, 131.6, 129.4, 128.9, 128.4, 128.0, 127.7, 126.9, 126.4, 125.1, 124.9, 123.7, 123.1, 122.9, 121.6, 114.7, 107.6, 62.5, 56.0, 51.1, 49.0, 28.9. Major rotamer.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{31}\text{H}_{31}\text{BrN}_2\text{O}_4$  ( $[\text{M}+\text{H}]^+$ ): 575.1540, found 575.1520.

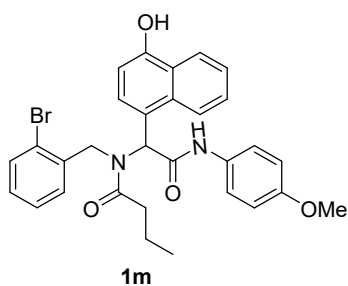


**1l** was obtained as a red solid, Yield 40% (464 mg), Melting point 141 -143 °C.

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 10.17 (s, 1H), 8.16 – 7.91 (m, 2H), 7.76 – 7.59 (m, 4H), 7.52 (d, *J* = 2.6 Hz, 1H), 7.41 – 7.32 (m, 1H), 7.30 – 7.17 (m, 2H), 7.16 – 6.97 (m, 1H), 6.80 – 6.66 (m, 3H), 6.54 (t, *J* = 7.4 Hz, 1H), 5.81 (d, *J* = 32.9 Hz, 1H), 4.85 – 4.43 (m, 2H), 1.29 (s, 9H).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 171.4, 170.5, 154.3, 136.3, 136.1, 135.2, 133.4, 131.7, 129.6, 129.0, 128.8, 128.5, 128.3, 127.9, 126.9, 126.5, 125.1, 123.7, 123.2, 122.3, 121.6, 107.7, 62.3, 51.1, 48.9, 28.8.

HRMS (ESI, *m/z*) calcd for C<sub>30</sub>H<sub>28</sub>BrClN<sub>2</sub>O<sub>3</sub> ([*M*+*H*]<sup>+</sup>): 579.1045, found 579.1050.

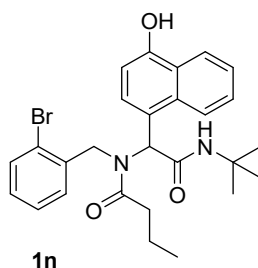


**1m** was obtained as a gray solid, Yield 75% (842 mg), Melting point 176 - 178 °C

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 10.31 – 10.07 (m, 2H), 8.18 – 7.94 (m, 2H), 7.71 – 7.59 (m, 1H), 7.56 – 7.42 (m, 3H), 7.38 – 6.99 (m, 4H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.81 – 6.64 (m, 2H), 6.54 (s, 1H), 4.81 – 4.26 (m, 2H), 3.72 (s, 3H), 2.40 – 2.27 (m, 1H), 2.10 – 1.96 (m, 1H), 1.70 – 1.50 (m, 2H), 1.02 – 0.74 (m, 3H).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 174.5, 169.9, 155.9, 154.3, 136.7, 133.9, 132.9, 132.3, 128.6, 128.2, 127.8, 127.4, 126.9, 125.3, 124.0, 123.3, 122.2, 121.5, 121.2, 114.5, 107.7, 57.4, 55.8, 49.5, 35.4, 18.9, 14.3.

HRMS (ESI, *m/z*) calcd for C<sub>30</sub>H<sub>29</sub>BrN<sub>2</sub>O<sub>4</sub> ([*M*+*Na*]<sup>+</sup>): 583.1203, found 583.1189.



**1n** was obtained as a brown solid, Yield 43% (440 mg), Melting point 114 - 116 °C.

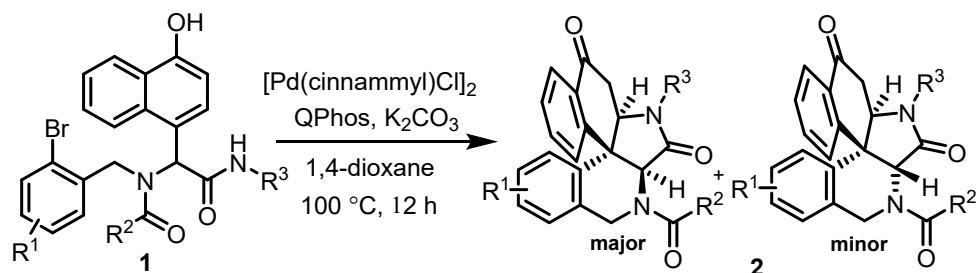
<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.16 – 8.02 (m, 2H), 7.64 – 7.55 (m, 1H), 7.51 – 7.39 (m, 2H), 7.16 (d, *J* = 7.9 Hz, 1H), 6.97 (s, 1H), 6.72 – 6.63 (m, 2H), 6.44 (d, *J* = 4.3 Hz, 2H), 6.28 (s, 1H), 5.41 (s, 1H), 4.80 – 4.63 (m, 2H), 2.46 – 2.31 (m, 1H), 2.18 – 2.03 (m, 1H), 1.80 – 1.66 (m, 2H), 1.34 (s, 9H), 0.89 (t, *J* = 7.3 Hz, 3H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 174.0, 170.7, 153.9, 136.9, 133.9, 132.3, 128.5, 127.7, 127.6, 126.9, 126.7, 125.2, 125.0, 124.3, 123.4, 123.1, 121.5, 107.6, 56.6, 51.0, 49.6, 35.4, 29.0, 18.9, 14.2. Major rotamer.

HRMS (ESI, *m/z*) calcd for C<sub>27</sub>H<sub>31</sub>BrN<sub>2</sub>O<sub>3</sub> ([*M*+*H*]<sup>+</sup>): 511.1591, found 511.1580.

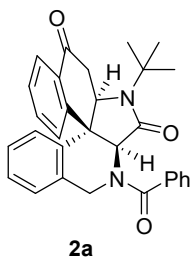


## 4. Palladium-catalyzed cascade reaction



Ugi product **1** (0.1 mmol, 1.0 equiv), palladium( $\pi$ -cinnamyl) chloride dimer (0.005 mmol, 0.05 equiv), Q-phos (0.0075 mmol, 0.075 equiv) and potassium carbonate (0.15 mmol, 1.5 equiv) were placed to the screw cap vial followed by addition of 1,4-dioxane (1.0 ml). The resulting mixture was flushed with argon, sealed and stirred in an oil bath at  $100\text{ }^\circ\text{C}$  for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure to obtain residue which was purified by a silica gel column chromatography (eluent: *n*-heptane/ethyl acetate = 2:1~1:1 v/v) to afford the desired products **2**.

## 5. Characterization of products

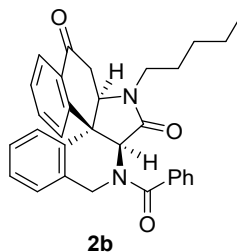


**2a** was obtained as a yellow solid, Yield 52% (24 mg, d. r.  $\approx$  1.8:1), Melting point  $205 - 207\text{ }^\circ\text{C}$ .

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 – 7.97 (m, 1H), 7.56 – 7.51 (m, 1H), 7.50 – 7.46 (m, 1H), 7.46 – 7.40 (m, 1H), 7.39 – 7.31 (m, 1H), 7.29 (d,  $J = 4.0$  Hz, 1H), 7.25 – 7.21 (m, 1H), 7.21 – 7.18 (m, 1H), 7.17 – 7.08 (m, 2H), 7.01 (d,  $J = 7.3$  Hz, 1H), 6.98 – 6.93 (m, 1H), [6.92 (d,  $J = 8.3$  Hz), 6.84 – 6.80 (m), 1H], [6.10 (s), 5.67 (d,  $J = 17.8$  Hz), 1H], 4.88 – 4.82 (m, 1H), [4.75 – 4.68 (m), 4.62 – 4.58 (m), 1H], 4.57 – 4.52 (m, 1H), [3.30 (dd,  $J = 15.7, 5.4$  Hz), 3.17 (dd,  $J = 11.6, 4.5$  Hz), 1H], [3.14 – 3.08 (m), 2.58 – 2.50 (m), 1H], [1.25 (s), 1.19 (s), 9H].

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.2, 194.6, 172.7, 171.5, 168.8, 168.3, 144.8, 144.3, 138.6, 137.5, 135.4, 134.8, 134.7, 134.7, 134.1, 133.5, 131.0, 130.8, 130.3, 130.2, 130.0, 128.8, 128.6, 128.5, 128.2, 128.0, 127.9, 127.9, 127.9, 127.7, 127.3, 127.1, 126.9, 126.7, 125.9, 65.1, 62.6, 61.7, 59.3, 55.5, 47.6, 47.1, 47.0, 44.9, 44.5, 41.8, 27.9.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 465.2173, found 465.2166.

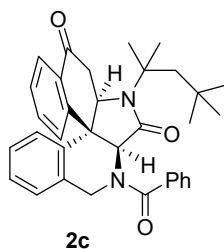


**2b** was obtained as a brown solid, Yield 31% (15 mg, d. r.  $\approx$  1.5:1), Melting point 112 - 114 °C.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 (dd,  $J = 17.6, 7.2$  Hz, 1H), 7.70 – 7.33 (m, 4H), 7.31 – 7.23 (m, 3H), 7.19 – 7.12 (m, 3H), 7.00 – 6.85 (m, 2H), [6.17 (s), 5.76 (d,  $J = 17.6$  Hz), 1H], 4.98 – 4.77 (m, 1H), 4.74 – 4.50 (m, 1H), 4.35 (dd,  $J = 11.9, 5.2$  Hz, 1H), 3.74 – 3.58 (m, 1H), 3.33 – 3.10 (m, 1H), 3.02 – 2.73 (m, 1H), 2.49 – 2.30 (m, 1H), 1.18 – 0.71 (m, 6H), 0.65 (t,  $J = 7.2$  Hz, 3H).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.3, 194.6, 172.7, 171.4, 169.5, 168.2, 144.2, 137.8, 134.9, 134.6, 133.6, 133.2, 130.8, 130.2, 130.5, 130.2, 130.1, 129.1, 128.8, 128.7, 128.4, 128.3, 128.0, 128.0, 127.7, 127.4, 127.3, 127.2, 126.8, 126.7, 126.6, 125.9, 64.3, 62.6, 61.7, 58.5, 47.0, 46.6, 46.3, 41.8, 41.7, 41.4, 40.7, 29.8, 28.1, 26.5, 26.4, 22.2, 13.9.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{31}\text{H}_{30}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 479.2329, found 479.2331.

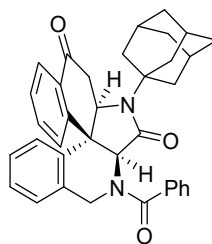


**2c** was obtained as a black solid, Yield 38% (20 mg, d. r.  $\approx$  1.5:1), Melting point 98 - 100 °C

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  [8.03 (dd,  $J = 7.8, 1.3$  Hz), 7.98 (dd,  $J = 7.8, 1.2$  Hz), 1H], 7.57 – 7.52 (m, 1H), 7.51 – 7.40 (m, 2H), 7.40 – 7.33 (m, 1H), 7.31 – 7.25 (m, 2H), 7.25 – 7.16 (m, 2H), 7.13 (t,  $J = 7.8$  Hz, 1H), 7.02 (d,  $J = 7.3$  Hz, 1H), 6.99 – 6.93 (m, 1H), [6.93 – 6.90 (m), 6.84 – 6.80 (m), 1H], [6.10 (s), 5.68 (d,  $J = 17.9$  Hz), 1H], 4.86 (d,  $J = 16.6$  Hz, 1H), [4.73 (d,  $J = 16.8$  Hz), 4.58 (d,  $J = 6.1$  Hz), 1H], 4.65 – 4.60 (m, 1H), [3.36 (dd,  $J = 15.5, 5.3$  Hz), 3.22 (dd,  $J = 10.9, 5.0$  Hz), 1H], [3.17 (dd,  $J = 10.5, 7.3$  Hz), 2.57 (dd,  $J = 15.9, 12.2$  Hz), 1H], 1.92 (dd,  $J = 30.4, 14.7$  Hz, 1H), [1.62 (d,  $J = 14.7$  Hz), 1.49 (d,  $J = 14.7$  Hz), 1H], [1.40 (s), 1.33 (s), 3H], [1.19 (s), 1.18 (s), 3H], [0.80 (s), 0.77 (s), 9H]

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.4, 194.8, 172.7, 171.5, 169.0, 168.4, 144.9, 144.4, 138.6, 137.5, 135.4, 134.8, 134.7, 134.7, 134.0, 133.5, 131.0, 130.7, 130.4, 130.2, 130.2, 130.0, 128.8, 128.6, 128.2, 128.0, 128.0, 127.8, 127.7, 127.3, 127.1, 126.8, 126.8, 126.6, 126.0, 65.1, 62.6, 61.7, 60.3, 59.2, 51.0, 50.9, 47.3, 47.1, 46.8, 45.1, 44.8, 41.9, 31.4, 28.5, 26.8.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{34}\text{H}_{36}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 521.2799, found 521.2800.



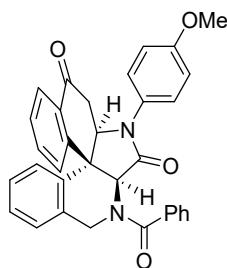
**2d**

**2d** was obtained as a brown solid, Yield 38% (21 mg, d. r.  $\approx$  1.9:1), Melting point 135 - 137 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.11 – 8.01 (m, 1H), [8.00 – 7.97 (m), 7.63 – 7.57 (m), 1H], 7.56 – 7.47 (m, 2H), 7.47 – 7.40 (m, 1H), 7.40 – 7.32 (m, 1H), 7.31 – 7.28 (m, 1H), 7.25 – 7.15 (m, 2H), 7.12 (t,  $J$  = 7.7 Hz, 1H), 7.01 (d,  $J$  = 8.1 Hz, 1H), 6.98 – 6.92 (m, 1H), [6.91 (d,  $J$  = 4.8 Hz), 6.82 (d,  $J$  = 7.6 Hz), 1H], [6.10 (s), 5.67 (d,  $J$  = 17.8 Hz), 1H], 4.87 – 4.81 (m, 1H), 4.73 – 4.60 (m, 1H), 4.60 – 4.54 (m, 1H), [3.36 – 3.28 (m), 3.21 – 3.15 (m), 1H], [3.15 – 3.11 (m), 2.62 – 2.47 (m), 1H], 2.05 – 1.95 (m, 4H), 1.94 – 1.83 (m, 3H), 1.62 – 1.56 (m, 2H), 1.62 – 1.57 (m, 6H).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.4, 194.9, 172.8, 171.5, 168.7, 168.2, 144.8, 144.4, 138.6, 137.5, 135.4, 134.8, 134.7, 134.6, 134.0, 133.7, 133.5, 131.0, 130.9, 130.3, 130.3, 130.2, 130.0, 128.8, 128.6, 128.6, 128.2, 128.0, 127.9, 127.9, 127.8, 127.7, 127.2, 127.1, 126.9, 126.7, 125.9, 65.4, 61.5, 60.7, 59.5, 56.7, 47.5, 47.0, 47.0, 45.5, 45.1, 41.8, 39.8, 36.2, 36.1, 29.6, 29.5.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{36}\text{H}_{34}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 543.2642, found 543.2643.



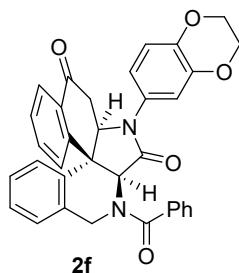
**2e**

**2e** was obtained as a black solid, Yield 52% (28 mg, d. r.  $\approx$  1.5:1), Melting point 142 - 144 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 – 7.96 (m, 1H), 7.59 – 7.39 (m, 4H), 7.36 – 7.28 (m, 2H), 7.24 – 7.18 (m, 2H), 7.18 – 7.16 (m, 1H), 7.15 – 7.09 (m, 3H), 7.08 – 7.01 (m, 1H), 7.00 – 6.94 (m, 1H), 6.92 – 6.81 (m, 2H), [6.35 (s), 5.77 (d,  $J$  = 17.8 Hz), 1H], [5.09 (s), 4.80 (d,  $J$  = 13.9 Hz), 1H], 4.94 – 4.84 (m, 1H), 4.70 – 4.53 (m, 1H), 3.76 (s, 3H), 3.33 – 3.15 (m, 1H), [3.13 – 3.04 (m), 2.64 – 2.52 (m), 1H].

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  194.9, 194.3, 172.7, 171.5, 167.7, 167.3, 158.3, 144.5, 144.0, 138.5, 137.3, 135.3, 134.9, 134.5, 133.6, 133.1, 132.8, 132.6, 131.2, 130.8, 130.5, 130.2, 129.4, 128.9, 128.7, 128.4, 128.2, 127.9, 127.4, 127.3, 127.1, 127.0, 126.9, 126.7, 126.5, 126.2, 124.5, 114.8, 88.3, 65.0, 64.7, 55.6, 47.0, 46.3, 41.8, 41.7, 27.0.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{33}\text{H}_{26}\text{N}_2\text{O}_4$  ( $[\text{M}+\text{H}]^+$ ): 515.1965, found 515.1956.

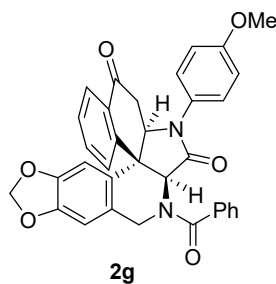


**2f** was obtained as a brown solid, Yield 48% (26 mg, d. r.  $\approx$  1.2:1), Melting point 140 - 142 °C.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 – 7.95 (m, 1H), 7.62 – 7.28 (m, 6H), 7.23 – 7.15 (m, 2H), 7.15 – 6.88 (m, 4H), 6.85 – 6.66 (m, 3H), [6.33 (s), 5.76 (d,  $J = 17.5$  Hz), 1H], [5.07 (s), 4.61 (d,  $J = 17.9$  Hz), 1H], 4.96 – 4.73 (m, 2H), 4.23 (d,  $J = 13.1$  Hz, 4H), 3.37 – 3.16 (m, 1H), [3.13 – 2.97 (m), 2.62 – 2.50 (m), 1H].

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  194.8, 194.2, 172.6, 171.5, 167.6, 167.2, 144.5, 143.9, 142.4, 138.4, 137.2, 134.9, 134.5, 133.5, 133.1, 131.2, 130.8, 130.7, 130.5, 130.2, 130.1, 128.9, 128.7, 128.5, 128.3, 128.2, 127.9, 127.3, 127.1, 127.0, 126.9, 126.7, 126.2, 117.8, 116.3, 116.1, 112.4, 112.3, 65.6, 64.9, 64.7, 64.4, 64.4, 58.9, 47.0, 46.2, 45.7, 41.8, 41.6, 29.8.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{34}\text{H}_{26}\text{N}_2\text{O}_5$  ( $[\text{M}+\text{H}]^+$ ): 543.1914, found 543.1920.

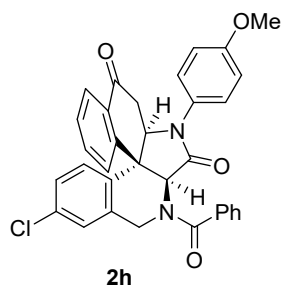


**2g** was obtained as a black solid, Yield 46% (27 mg, d. r.  $\approx$  1.8:1), Melting point 163 - 165 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  7.94 (t,  $J = 8.9$  Hz, 1H), 7.72 – 7.25 (m, 7H), 7.15 (t,  $J = 7.6$  Hz, 1H), 7.02 – 6.83 (m, 5H), [6.71 (s), 6.24 (s), 1H], 6.05 – 5.87 (m, 2H), [5.48 – 5.26 (m), 5.11 (s), 2H], 4.73 – 4.52 (m, 1H), 4.30 (d,  $J = 17.7$  Hz, 1H), 3.73 (d,  $J = 6.5$  Hz, 3H), [3.64 – 3.47 (m), 3.16 – 3.04 (m), 1H], 3.03 – 2.84 (m, 1H).

$^{13}\text{C}$  NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  194.8, 194.5, 172.0, 170.9, 168.0, 167.6, 157.5, 147.7, 145.0, 144.3, 135.8, 135.0, 134.9, 134.9, 131.7, 131.2, 130.9, 130.8, 130.8, 130.6, 129.5, 129.0, 128.4, 128.0, 127.5, 127.4, 127.0, 126.7, 126.3, 123.4, 123.4, 115.0, 108.8, 108.3, 101.9, 64.9, 63.3, 62.9, 59.2, 55.9, 46.9, 46.4, 45.8, 42.4, 41.3, 41.0.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{34}\text{H}_{26}\text{N}_2\text{O}_6$  ( $[\text{M}+\text{H}]^+$ ): 559.1864, found 559.1867.

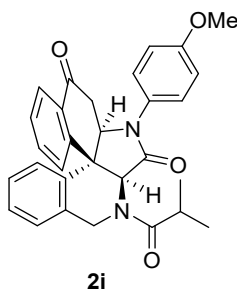


**2h** was obtained as a brown solid, Yield 31% (18 mg, d. r.  $\approx$  1.5:1), Melting point 295 – 297 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 – 7.94 (m, 1H), 7.63 – 7.37 (m, 4H), 7.31 (d,  $J$  = 12.6 Hz, 1H), 7.26 – 6.66 (m, 10H), [6.33 (s), 5.09 (s), 1H], [5.75 (d,  $J$  = 18.0 Hz), 4.58 (d,  $J$  = 18.0 Hz), 1H], 4.90 – 4.74 (m, 2H), 3.78 (s, 3H), 3.36 – 3.14 (m, 1H), [3.13 – 3.03 (m), 2.65 – 2.49 (m), 1H].

$^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  193.8, 192.1, 172.5, 166.9, 158.3, 143.3, 135.9, 135.4, 134.9, 134.0, 130.6, 130.2, 129.6, 129.1, 128.8, 128.6, 128.3, 127.2, 127.0, 127.0, 126.7, 124.4, 124.4, 114.7, 65.5, 64.8, 64.5, 58.7, 55.5, 46.6, 45.9, 41.5, 41.4

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{33}\text{H}_{25}\text{ClN}_2\text{O}_4$  ( $[\text{M}+\text{H}]^+$ ): 549.1576, found 549.1559.

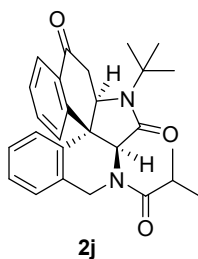


**2i** was obtained as a brown solid, Yield 59% (28.4 mg, d. r.  $\approx$  1.5:1). Melting point 219 - 221 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 – 7.97 (m, 1H), 7.47 – 7.27 (m, 3H), 7.25 – 7.16 (m, 2H), 7.15 – 7.09 (m, 2H), 7.03 – 6.95 (m, 1H), 6.89 – 6.83 (m, 2H), 6.83 – 6.77 (m, 1H), [6.28 (s), 5.68 (d,  $J$  = 17.8 Hz), 1H], [5.19 (s), 5.02 (d,  $J$  = 16.6 Hz), 1H], 4.94 – 4.89 (m, 1H), [4.89 – 4.85 (m), 4.41 – 4.36 (m), 1H], [3.77 (s), 3.76 (s), 3H], 3.37 – 3.20 (m, 1H), [3.17 – 3.08 (m), 2.51 – 2.41 (m), 1H], 3.07 – 2.91 (m, 1H), [1.27 (d,  $J$  = 6.7 Hz), 0.84 (d,  $J$  = 6.6 Hz), 3H], [1.23 (d,  $J$  = 6.8 Hz, 2H), 1.17 (d,  $J$  = 6.8 Hz, 1H), 3H].

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.0, 194.5, 177.5, 177.3, 168.0, 167.3, 158.4, 158.1, 144.4, 144.3, 138.7, 137.4, 134.9, 134.7, 134.2, 133.1, 131.1, 130.9, 130.6, 130.1, 129.5, 129.4, 128.8, 128.5, 128.2, 128.1, 128.0, 127.9, 127.0, 126.9, 126.6, 126.4, 124.7, 124.6, 114.8, 114.7, 65.6, 65.3, 63.1, 58.3, 55.6, 46.2, 45.6, 44.7, 41.8, 41.5, 31.0, 30.1, 20.1, 19.9, 19.2, 19.1.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_4$  ( $[\text{M}+\text{H}]^+$ ): 481.2122, found 481.2111 .

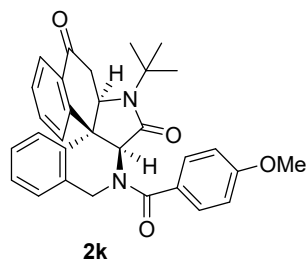


**2j** was obtained as a brown solid, Yield 43% (18.5 mg, d. r.  $\approx$  1.2:1), Melting point 205 - 207 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 – 7.97 (m, 1H), 7.42 – 7.34 (m, 1H), 7.33 – 7.24 (m, 2H), 7.23 – 7.13 (m, 2H), 6.98 – 6.89 (m, 1H), [6.80 – 6.76 (m), 6.72 – 6.65 (m), 1H], [6.04 (s), 5.60 (d,  $J$  = 17.8 Hz), 1H], 4.96 (t,  $J$  = 8.3 Hz, 1H), [4.86 (d,  $J$  = 16.5 Hz), 4.60 (dd,  $J$  = 12.2, 5.6 Hz), 1H], [4.56 – 4.50 (m), 4.37 – 4.31 (m), 1H], 3.36 – 3.22 (m, 1H), 3.10 – 3.02 (m, 1H), [2.97 – 2.87 (m), 2.40 – 2.30 (m), 1H], 1.26 – 1.11 (m, 14H), 0.75 (d,  $J$  = 6.6 Hz, 1H).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.4, 194.9, 177.6, 177.3, 169.1, 168.3, 144.7, 144.6, 138.7, 137.5, 134.8, 134.6, 134.5, 133.5, 130.7, 130.7, 130.3, 130.1, 128.5, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 126.9, 126.6, 126.6, 126.0, 63.5, 62.3, 62.0, 58.6, 55.6, 55.3, 47.4, 47.0, 44.7, 44.1, 41.4, 31.0, 30.0, 27.8, 20.1, 19.9, 19.2, 19.1.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{27}\text{H}_{30}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 431.2329, found 431.2318 .

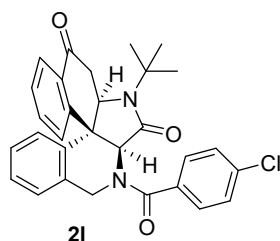


**2k** was obtained as a gray solid, Yield 37% (18.4 mg, d. r.  $\approx$  1.8:1), Melting point 216 - 218 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 – 7.97 (m, 1H), 7.55 – 7.32 (m, 3H), 7.28 (d,  $J$  = 4.0 Hz, 1H), 7.23 – 7.04 (m, 2H), 7.00 (d,  $J$  = 8.4 Hz, 1H), 6.98 – 6.92 (m, 2H), 6.91 – 6.78 (m, 1H), 6.62 (d,  $J$  = 8.8 Hz, 1H), [6.08 (s), 5.63 (d,  $J$  = 17.8 Hz), 1H], 4.98 – 4.78 (m, 1H), 4.60 – 4.51 (m, 2H), [3.87 (s), 3.72 (s), 3H], [3.29 (dd,  $J$  = 15.7, 5.3 Hz), 3.18 (dd,  $J$  = 16.1, 5.6 Hz), 1H], [3.12 – 3.06 (m), 2.64 – 2.55 (m), 1H], [1.25 (s), 1.20 (s), 9H].

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.3, 194.8, 172.7, 171.3, 168.9, 168.4, 161.3, 160.9, 144.8, 144.4, 138.7, 137.5, 134.8, 134.7, 134.2, 133.7, 131.0, 130.8, 130.3, 130.3, 129.4, 129.1, 128.6, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4, 126.9, 126.7, 126.7, 126.6, 125.9, 65.3, 62.5, 61.8, 59.4, 55.6, 55.5, 55.4, 55.3, 47.5, 47.2, 47.1, 44.8, 44.6, 42.0, 27.8.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{31}\text{H}_{30}\text{N}_2\text{O}_4$  ( $[\text{M}+\text{H}]^+$ ): 495.2278, found 495.2272 .

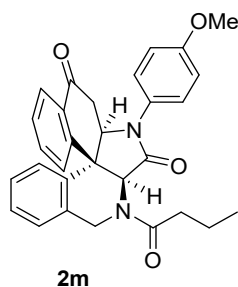


**2l** was obtained as a yellow solid, Yield 43% (21.5 mg, d. r.  $\approx$  1.9:1), Melting point 223 - 225 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 – 7.99 (m, 1H), [7.75 – 7.71 (m, 1H), 7.64 – 7.57 (m), 1H], 7.54 – 7.46 (m, 2H), 7.45 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 7.23 – 7.17 (m, 1H), 7.11 (d,  $J$  = 8.4 Hz, 1H), 7.02 – 6.92 (m, 2H), [6.90 (d,  $J$  = 7.8 Hz), 6.78 (d,  $J$  = 7.7 Hz), 1H], [6.08 – 5.98 (m), 5.71 – 5.56 (m), 1H], 4.89 – 4.78 (m, 1H) 4.69 – 4.52 (m, 2H), [3.35 – 3.27 (m), 3.24 – 3.16 (m), 1H], [3.15 – 3.06 (m), 2.64 – 2.53 (m), 1H], [1.24 (s), 1.20 (s), 9H].

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.1, 194.5, 171.7, 170.5, 168.6, 168.1, 144.6, 144.2, 138.4, 137.3, 136.6, 136.2, 134.8, 134.7, 133.7, 133.6, 133.2, 133.0, 130.8, 130.3, 130.1, 129.1, 129.0, 128.8, 128.7, 128.6, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.0, 126.8, 126.7, 125.9, 65.3, 62.6, 61.9, 59.4, 55.6, 55.5, 47.5, 47.1, 44.8, 44.6, 41.1, 27.9, 27.8.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{30}\text{H}_{27}\text{ClN}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 499.1783, found 499.1772.

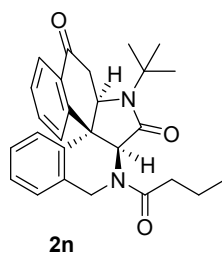


**2m** was obtained as a brown solid, Yield 47% (23 mg, d. r.  $\approx$  1.3:1), Melting point 217 - 219 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 – 7.98 (m, 1H), 7.49 – 7.40 (m, 1H), 7.39 – 7.28 (m, 2H), 7.25 – 7.17 (m, 2H), 7.14 – 7.09 (m, 2H), 7.03 – 6.95 (m, 1H), 6.91 – 6.78 (m, 3H), [6.27 (s), 5.13 (s), 1H], [5.68 (d,  $J$  = 17.7 Hz), 4.39 (d,  $J$  = 17.8 Hz), 1H], 4.99 – 4.83 (m, 2H), [3.77 (s), 3.76 (s), 3H], 3.35 – 3.21 (m, 1H), 3.07 – 2.88 (m, 1H), 2.64 – 2.58 (m, 3H), [2.32 – 2.22 (m), 1.95 – 1.87 (m), 1H], [1.81 – 1.72 (m), 1.57 – 1.52 (m), 2H], [1.03 (t,  $J$  = 7.4 Hz), 0.82 (t,  $J$  = 7.4 Hz, 1H), 3H].

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.0, 194.5, 173.4, 173.2, 168.0, 167.3, 158.4, 158.2, 144.4, 138.6, 137.4, 135.1, 134.9, 134.1, 133.0, 131.1, 130.4, 130.1, 129.5, 128.8, 128.5, 128.2, 128.2, 128.1, 128.0, 127.9, 127.0, 126.9, 126.6, 126.4, 124.8, 124.6, 114.8, 114.7, 65.6, 65.4, 63.3, 58.3, 55.6, 46.2, 45.6, 44.9, 41.8, 41.3, 35.8, 34.8, 29.8, 18.7, 18.4, 14.0.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_4$  ( $[\text{M}+\text{H}]^+$ ): 481.2122, found 481.2114.



**2n** was obtained as a brown solid, Yield 49% (21 mg, d. r.  $\approx$  1.2:1), Melting point 224 - 226 °C.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 – 7.98 (m, 1H), 7.44 – 7.37 (m, 1H), 7.37 – 7.32 (m, 1H), 7.31 – 7.27 (m, 1H), 7.25 – 7.20 (m, 1H), 7.19 – 7.12 (m, 1H), 6.97 – 6.88 (m, 1H), [6.81 – 6.78 (m), 6.72 – 6.68 (m), 1H], [6.02 (s), 5.59 (d,  $J = 17.8$  Hz), 1H], 4.89 (t,  $J = 8.2$  Hz, 1H), [4.83 (d,  $J = 16.5$  Hz), 4.38 – 4.32 (m), 1H], 4.62 – 4.51 (m, 1H), 3.36 – 3.22 (m, 1H), [3.06 (dd,  $J = 15.6, 12.3$  Hz), 2.93 (dd,  $J = 16.0, 12.3$  Hz), 1H], 2.59 – 2.53 (m, 1H), [2.22 – 2.14 (m), 1.85 – 1.77 (m), 1H], 1.76 – 1.68 (m, 1H), 1.55 – 1.43 (m, 1H), [1.23 (s), 1.21 (s), 1H], [1.01 (t,  $J = 7.4$  Hz), 0.78 (t,  $J = 7.4$  Hz), 3H].

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.4, 194.9, 173.4, 173.3, 169.0, 168.3, 144.7, 144.6, 138.6, 137.5, 135.0, 134.7, 134.4, 133.4, 130.7, 130.5, 130.1, 128.5, 128.2, 128.0, 127.9, 127.8, 127.7, 127.7, 126.8, 126.6, 126.1, 63.7, 62.4, 62.0, 58.7, 55.6, 55.3, 47.3, 46.9, 44.9, 44.7, 41.3, 35.8, 34.7, 27.9, 18.7, 18.4, 14.0, 13.9.

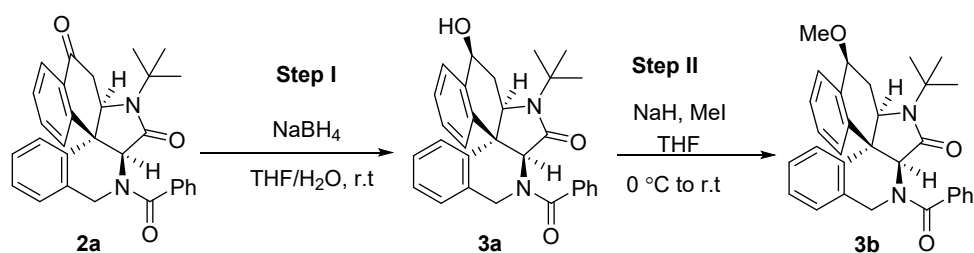
HRMS (ESI,  $m/z$ ) calcd for for  $\text{C}_{27}\text{H}_{30}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 431.2329, found 431.2313.

## Scale-up reaction for the synthesis of **2a**.

Ugi adduct **1a** (1 mmol, 1.0 equiv), palladium( $\pi$ -cinnamyl) chloride dimer (0.05 mmol, 0.05 equiv), Qphos (0.075 mmol, 0.075 equiv) and potassium carbonate (1.5 mmol, 1.5 equiv) were placed to the screw cap vial followed by addition of 1,4-dioxane (10.0 ml). The resulting mixture was flushed with argon, sealed and stirred in an oil bath at 100 °C for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure to obtain residue which was purified by a silica gel column chromatography (eluent: n-heptane/ethyl acetate = 2:1~1:1 v/v) to afford 190 mg **2a** in 41% yield.

## 6. Transformations of compound **2a**

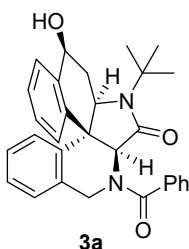
### 1) Synthesis of compound **3a** and **3b**





**Step I:** To a glass vial of **2a** (37.2 mg, 0.08 mmol) in THF/H<sub>2</sub>O (0.7 ml/0.07 mL) was slowly added NaBH<sub>4</sub> (3.9 mg, 0.16 mmol) at room temperature and the resulting mixture was stirred for 1 h at room temperature. After completion, the mixture was diluted with H<sub>2</sub>O and extracted with DCM. The organic layer was dried with sodium sulfate and concentrated. The residue was purified by column chromatography on silica gel (eluent: *n*-heptane/ethyl acetate = 1:1~1:2 v/v) to afford the desired products **3a**.

**Step II:** To a glass vial of **3a** (10 mg, 0.022 mmol) in THF (0.2 ml) was slowly added NaH (1.6 mg, 0.066 mmol), MeI (9.4 mg, 0.066 mmol) at 0 °C and the resulting mixture was stirred for 12 h at room temperature. After the solvent was concentrated under reduced pressure, the residue was purified by flash column chromatography on silica gel (eluent: *n*-heptane/ethyl acetate = 1:1~1:2 v/v) to afford the desired products **3b**.

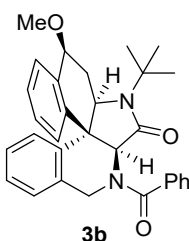


**3a** was obtained as a white solid, Yield 82% (38.4 mg, d. r.  $\approx$  2.3:1), Melting point 112 – 114 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  [7.79 – 7.75 (m), 7.68 – 7.67 (m), 1H], 7.66 – 7.64 (m, 1H), 7.60 – 7.54 (m, 1H), 7.39 – 7.36 (m, 1H), 7.36 – 7.34 (m, 1H), 7.34 – 7.32 (m, 1H), 7.31 – 7.28 (m, 1H), 7.28 – 7.18 (m, 4H), 7.06 – 6.98 (m, 1H), 6.98 – 6.89 (m, 1H), [6.05 (s, 1H), 5.76 (d,  $J$  = 17.6 Hz), 1H], 5.19 – 5.06 (m, 1H), 4.89 (d,  $J$  = 1.1 Hz, 1H), 4.88 – 4.74 (m, 1H), 4.58 (d,  $J$  = 17.6 Hz, 1H), 4.38 – 4.31 (m, 1H), [2.89 – 2.83 (m), 2.68 – 2.61 (m), 1H], [2.25 – 2.14 (m), 1.78 – 1.67 (m), 1H], [1.39 (s), 1.34 (s), 9H].

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  172.7, 171.4, 168.7, 168.2, 139.5, 138.7, 138.5, 138.4, 137.8, 135.5, 134.9, 133.3, 132.9, 130.1, 129.8, 129.6, 129.2, 128.7, 128.6, 128.3, 128.2, 128.1, 127.9, 127.6, 127.3, 127.3, 127.2, 127.2, 127.1, 127.0, 126.3, 125.5, 125.0, 124.9, 67.5, 67.3, 66.1, 62.7, 62.1, 60.4, 55.2, 55.1, 47.7, 47.2, 46.8, 41.5, 39.4, 39.1, 27.8.

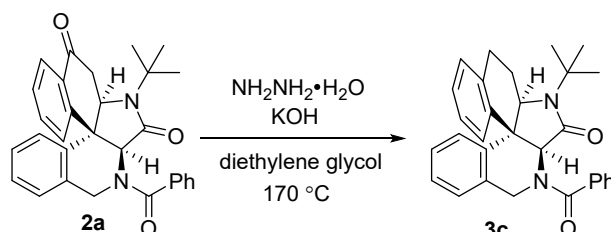
HRMS (ESI,  $m/z$ ) calcd for C<sub>30</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub> ([M+H]<sup>+</sup>): 467.2329, found 467.2335.



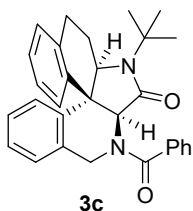
**3b** was obtained as a white solid, Yield 70% (33.6 mg, d. r.  $\approx$  3.5:1), Melting point 84 - 86°C.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  [7.62 – 7.51 (m), 7.47 – 7.39 (m), 2H], 7.28 – 7.22 (m, 3H), 7.21 – 7.13 (m, 3H), 7.12 – 7.04 (m, 3H), 6.92 (d,  $J = 7.4$  Hz, 1H), 6.81 (d,  $J = 7.6$  Hz, 1H), [5.67 (s), 5.61 (s), 1H], [4.81 (s), 4.68 (d,  $J = 8.4$  Hz), 1H], 4.54 – 4.47 (m, 1H), 4.42 (d,  $J = 17.6$  Hz, 1H), 4.26 – 4.18 (m, 1H), [3.57 (s), 3.16 (s), 3H], 2.51 – 2.40 (m, 1H), 1.89 – 1.75 (m, 1H), [1.30 (s, 1H), 1.27 (s, 3H), 9H].  
 $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  172.8, 168.7, 139.7, 138.9, 135.4, 135.2, 133.9, 130.1, 129.6, 128.6, 128.4, 127.7, 127.3, 127.3, 127.1, 126.7, 126.4, 76.5, 66.8, 62.6, 56.0, 55.3, 47.8, 41.4, 34.6, 28.1.  
 HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{31}\text{H}_{32}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}]^+$ ): 481.2486, found 549.1559.

## 2) Synthesis of compound **3c**



To the glass vial were added **2a** (32.5 mg, 0.07 mmol), KOH (19.6 mg, 0.35 mmol), diethylene glycol (0.7 mL) and hydrazine hydrate (17.5 mg, 0.35 mmol). The resulting mixture was flushed with argon, sealed and stirred in an oil bath at  $170\text{ }^\circ\text{C}$  for 12 h. After completion, the mixture was quenched with  $\text{H}_2\text{O}$  and extracted with DCM. The organic layer was dried with sodium sulfate and concentrated. The residue was purified by flash column chromatography on silica gel with (eluent: *n*-heptane/ethyl acetate = 1:1~1:2 v/v) to afford the desired products **3c**.



**3c** was obtained as a white solid, Yield 25% (11.3 mg, d. r.  $\approx$  2.3:1), Melting point  $201 - 203\text{ }^\circ\text{C}$ .

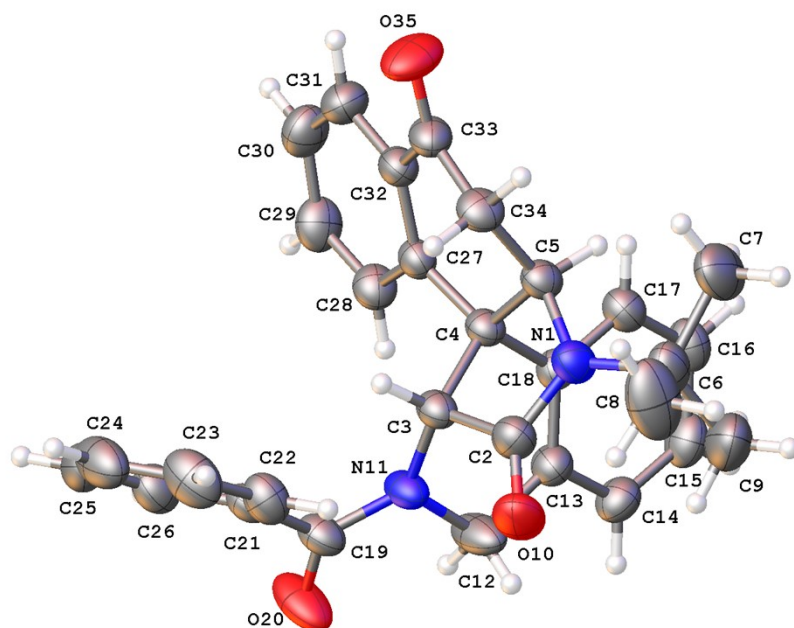
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  [7.57 – 7.54 (m), 7.47 – 7.45 (m), 1H], 7.25 – 7.19 (m, 2H), 7.18 – 7.06 (m, 7H), 7.06 – 6.91 (m, 2H), 6.87 – 6.79 (m, 1H), [5.89 (s), 5.64 (d,  $J = 17.7$  Hz), 1H], 4.76 – 4.62 (m, 1H), 4.49 (d,  $J = 17.7$  Hz, 1H), 4.17 – 4.09 (m, 1H), 3.12 – 2.95 (m, 1H), 2.85 – 2.75 (m, 1H), 2.46 – 2.26 (m, 1H), 2.26 – 2.03 (m, 1H), [1.28 (s), 1.23 (s), 9H].

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  172.8, 168.5, 139.8, 139.0, 135.2, 134.4, 133.6, 130.3, 129.6, 128.5, 128.4, 127.6, 127.4, 127.2, 126.9, 126.4, 66.2, 64.1, 55.1, 47.8, 41.7, 29.9, 28.5, 28.0.

HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{30}\text{H}_{30}\text{N}_2\text{O}_2$  ( $[\text{M}+\text{H}]^+$ ): 451.2380, found 451.2372.

## 7. Single crystal X-ray diffraction

A single crystal of **2a** was obtained by slow diffusion from a solution of the compound in CHCl<sub>3</sub> layered with heptane at room temperature for several days. X-ray intensity data were collected at 293(2) K on an Agilent SuperNova diffractometer with Eos CCD detector using MoK $\alpha$  radiation. The images were processed (unit cell determination, intensity data integration, correction for Lorentz and polarization effects, and empirical absorption correction) using CrysAlisPRO<sup>1</sup>. Using Olex2<sup>2</sup>, the structure was solved with the ShelXT<sup>3</sup> structure solution program using Intrinsic Phasing and refined with the ShelXL<sup>4</sup> refinement package using full-matrix least-squares minimization on F<sup>2</sup>. The asymmetric unit contains one molecule **2a**. All H atoms were placed in idealized positions and refined in the riding mode. Non-hydrogen atoms were refined anisotropically and hydrogen atoms in the riding mode with isotropic temperature factors fixed at 1.2 times U<sub>eq</sub> of the parent atoms (1.5 for methyl groups). Crystal data, data collection and structure refinement details are summarized in Table S1. Crystallographic data for **2a** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC- 2088708.



**Figure S1.** Molecular structure of **2a** showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown as small circles of arbitrary radii.

**Table S1.** Crystal data, data collection and structure refinement details of compound **2a**

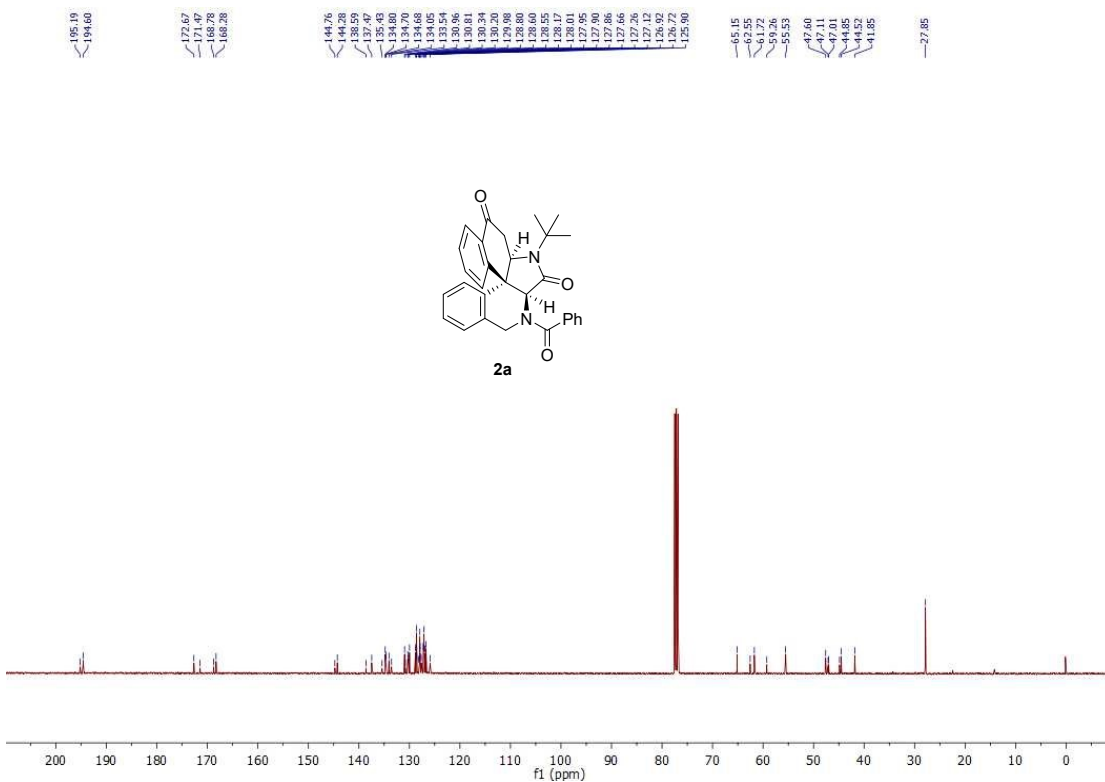
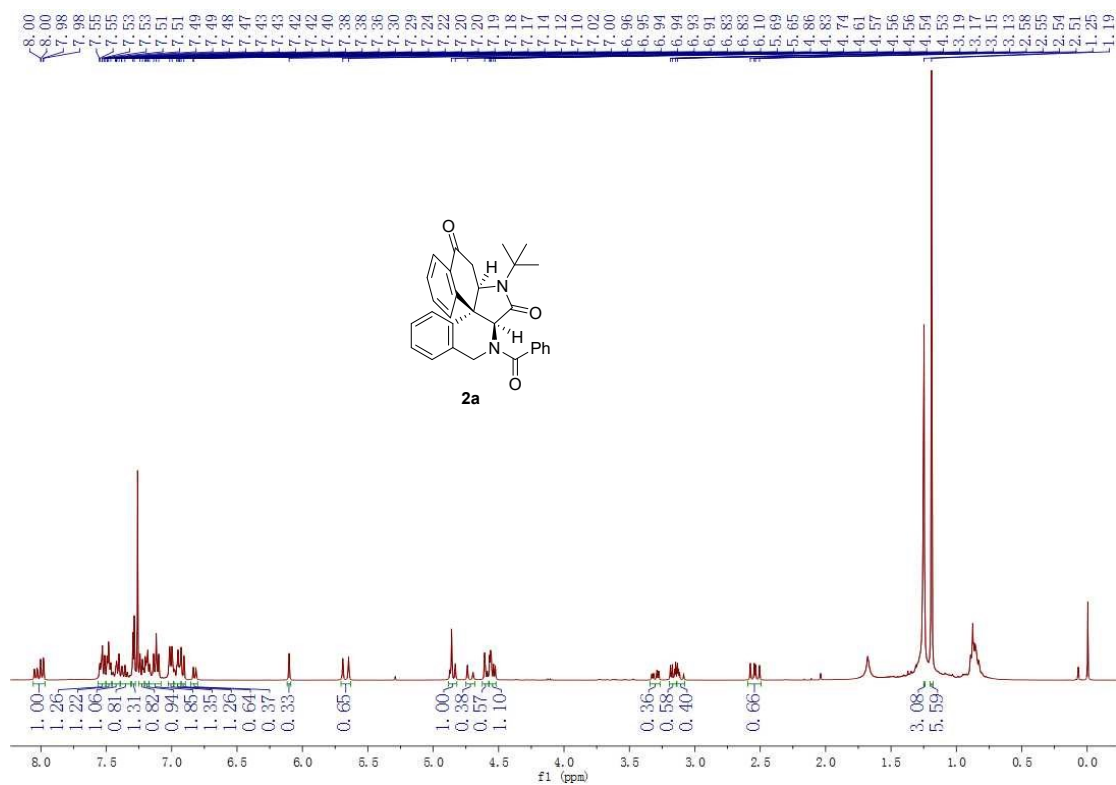
Empirical formula	C <sub>30</sub> H <sub>28</sub> N <sub>2</sub> O <sub>3</sub>
Formula weight	464.54
Temperature/K	293(2)

Crystal system	triclinic
Space group	<i>P</i> -1
<i>a</i> /Å	9.1811(2)
<i>b</i> /Å	9.9659(2)
<i>c</i> /Å	14.9148(4)
$\alpha$ /°	85.493(2)
$\beta$ /°	80.059(2)
$\gamma$ /°	63.776(3)
Volume/Å <sup>3</sup>	1205.83(6)
<i>Z</i>	2
$\rho_{\text{calc}}$ g/cm <sup>3</sup>	1.279
$\mu$ /mm <sup>-1</sup>	0.083
F(000)	492.0
Crystal size/mm <sup>3</sup>	0.35 × 0.35 × 0.3
Radiation	MoK $\alpha$ ( $\lambda$ = 0.71073 Å)
2 $\Theta$ range for data collection/°	5.006 to 52.742
Index ranges	-11 ≤ <i>h</i> ≤ 11, -12 ≤ <i>k</i> ≤ 12, -18 ≤ <i>l</i> ≤ 18
Reflections collected	49581
Independent reflections	4945 [ <i>R</i> <sub>int</sub> = 0.0355, <i>R</i> <sub>sigma</sub> = 0.0178]
Data/restraints/parameters	4945/0/319
Goodness-of-fit on F <sup>2</sup>	1.075
Final <i>R</i> indexes [ <i>I</i> ≥ 2 $\sigma$ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0470, <i>wR</i> <sub>2</sub> = 0.1133
Final <i>R</i> indexes [all data]	<i>R</i> <sub>1</sub> = 0.0583, <i>wR</i> <sub>2</sub> = 0.1204
Largest diff. peak/hole / e Å <sup>-3</sup>	0.24/-0.19

## 8. References

- [1] CrysAlis PRO (2012). Agilent Technologies UK Ltd, Yarnton, Oxfordshire, England.
- [2] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339-341.
- [3] G.M. Sheldrick, *Acta. Cryst.*, 2015, **A71**, 3-8.
- [4] G.M. Sheldrick, *Acta. Cryst.*, 2015, **C71**, 3-8

## 9. Copies of $^1\text{H}$ NMR and $^{13}\text{C}$ NMR spectra for the products



# NOESY NMR spectra of compound **2a**

