Supporting Information

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

Chao Liu, a Ruiqi Zhao, a Liangliang Song, * b Zhenghua Li, a Guilong Tian, a Yi He, a Luc Van Meervelt, c Vsevolod A. Peshkov d e and Erik V. Van der Eycken* a f

a Laboratory for Organic & Microwave-Assisted Chemistry (LOMAC), Department of Chemistry, KU Leuven Celestijnenlaan 200F, 3001, Leuven, Belgium.
b Jiangsu Provincial Key Lab for the Chemistry and Utilization of Agro-Forest Biomass, Jiangsu Co-Innovation Center of Efficient Processing and Utilization of Forest Resources, Jiangsu Key Lab of Biomass-Based Green Fuels and Chemicals, International Innovation Center for Forest Chemicals and Materials, College of Chemical Engineering, Nanjing Forestry University, Nanjing 210037, Jiangsu, China.
c Biomolecular Architecture, Department of Chemistry, KU Leuven Celestijnenlaan 200F, 3001, Leuven, Belgium.
d College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Dushu Lake Campus, Suzhou 215123, P. R. China.
e Department of Chemistry, School of Sciences and Humanities, Nazarbayev University, 53 Kabanbay Batyr Ave, Nur-Sultan 010000, Republic of Kazakhstan.
f Peoples’ Friendship University of Russia (RUDN University), Miklukho-Maklaya street 6, Moscow, 117198, Russia.

Table of Content

1. General information ............................................................................................. S2
2. General procedure for the synthesis of Ugi adducts ............................................ S2
3. Characterization of Ugi adducts ........................................................................... S2
4. Palladium-catalyzed cascade reaction .................................................................. S9
5. Characterization of products ................................................................................ S9
6. Transformations of compound 2a ....................................................................... S16
7. Single crystal X-ray diffraction .......................................................................... S18
8. References .......................................................................................................... S20
9. Copies of 1H NMR and 13C NMR spectra for the products ............................... S21
1. General information

Commercially available reagents were used without additional purification. Column chromatography was performed with silica gel (70-230 mesh). \(^1\)H and \(^{13}\)C NMR spectra were recorded on a Bruker AM (300 or 400 or 600 MHz) spectrometer at ambient temperature using CDCl\(_3\) or 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 \(\mu\)L \text{min}^{-1}, and spectra were obtained in the positive ionization mode with a resolution of 15000 [full width at half maximum (FWHM)] with leucine encephalin 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

\[
\begin{align*}
\text{R}^2\text{COOH} \quad \text{R}^3\text{NC} & \quad \text{MeOH} \\
\text{CHO} & \quad 60^\circ\text{C}, 24\text{h}
\end{align*}
\]

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 isonitrile (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 °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 °C.

\(^1\)H NMR (400 MHz, 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, \text{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).

$^{13}$C NMR (101 MHz, 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 C$_{30}$H$_{29}$BrN$_2$O$_3$ ([M+H]+): 545.1434, found 545.1450.

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

$^1$H NMR (400 MHz, 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).

$^{13}$C NMR (101 MHz, 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 C$_{31}$H$_{31}$BrN$_2$O$_3$ ([M+Na]+): 581.1410, found 581.1390.

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

$^1$H NMR (400 MHz, 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 =
\[
\begin{align*}
13.9 \text{ Hz}), & [1.75 – 1.59 (m), 1.46 – 1.32 (m), 6H], [0.97 (s), 0.89 (s), 9H]. \text{Mixture of rotamers (~1:1).} \\
^{13}\text{C NMR (101 MHz, DMSO-d}_6\text{)} & \delta 172.8, 172.3, 170.5, 170.2, 154.2, 137.5, 137.3, 137.0, 136.6, 134.2, 133.5, 131.3, 131.8, 130.6, 129.8, 129.5, 128.9, 128.6, 128.4, 128.2, 127.9, 127.2, 127.1, 126.9, 126.5, 125.2, 125.0, 124.5, 123.9, 122.7, 122.4, 121.7, 121.2, 107.6, 107.5, 79.9, 62.6, 57.2, 55.5, 55.0, 52.5, 51.1, 49.0, 32.0, 31.7, 30.2, 29.3, 29.0, 28.5. \text{Mixture of rotamers.} \\
\text{HRMS (ESI, m/z) calcd for C}_{34}\text{H}_{37}\text{BrN}_2\text{O}_3 ([M+H]^+): 601.2060, found 601.2055.}
\end{align*}
\]

\[1\text{d}\] was obtained as a gray solid, Yield 95% (1185 mg), Melting point 157 - 159 °C.

\[^1\text{H NMR (400 MHz, DMSO-d}_6\text{)}: \delta 8.19 – 8.00 (m, 1H), 7.98 – 7.87 (m, 1H), 7.80 (d, \text{ } J = 16.3 \text{ Hz}, 1H), 7.61 (s, 4H), 7.56 – 7.41 (m, 2H), 7.39 – 7.34 (m, 1H), 7.30 – 7.26 (m, 1H), 7.25 – 7.20 (m, 1H), 7.16 (d, \text{ } J = 7.7 \text{ Hz}, 1H), 7.05 – 6.97 (m, 1H), 6.81 – 6.71 (m, 1H), 6.70 – 6.66 (m, 1H), 6.53 (t, \text{ } J = 7.2 \text{ Hz}, 1H), 5.86 (s, 1H), [4.75 (d, \text{ } J = 16.7 \text{ Hz}), 4.65 (d, \text{ } J = 17.8 \text{ Hz}), 1H], 4.54 – 4.42 (m, 1H), 3.17 (s, 1H), 2.03 (s, 3H), 1.96 (s, 5H), 1.64 (s, 6H). \text{Mixture of rotamers (~3:2).} \\
^{13}\text{C NMR (101 MHz, DMSO-d}_6\text{)} & \delta 172.3, 170.5, 154.3, 137.3, 136.6, 133.4, 131.6, 130.6, 129.8, 129.4, 128.8, 128.5, 128.3, 128.2, 127.7, 126.8, 126.4, 125.1, 124.9, 123.8, 123.1, 122.5, 121.6, 107.7, 62.5, 51.8, 49.2, 48.9, 41.5, 41.3, 36.7, 35.9, 29.4, 29.1. \text{Mixture of rotamers.} \\
\text{HRMS (ESI, m/z) calcd for C}_{36}\text{H}_{35}\text{BrN}_2\text{O}_3 ([M+H]^+): 623.1904, found 623.1907.}
\]

\[1\text{e}\] was obtained as a gray solid, Yield 89% (855 mg), Melting point 210 - 212 °C.

\[^1\text{H NMR (400 MHz, DMSO-d}_6\text{)}: \delta [10.22 (d, \text{ } J = 6.4 \text{ 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). \text{Mixture of rotamers (~3:2).} \\
^{13}\text{C NMR (101 MHz, DMSO-d}_6\text{)} & \delta 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, 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$_2$O$_4$ ([M+Na]$^+$): 617.1046, found 617.1028.

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

$^1$H 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, 121.6, 121.5, 121.4, 121.2, 117.5, 113.3, 113.0, 109.3, 107.6, 107.8, 64.9, 64.6, 60.4. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{34}$H$_{27}$BrN$_2$O$_5$ ([M+Na]$^+$): 645.0996, found 645.0994.

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

$^1$H 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\textsubscript{34}H\textsubscript{27}BrN\textsubscript{2}O\textsubscript{6} ([M+Na\textsuperscript{+}]): 661.0945, found 661.0918.

![Chemical structure of 1h](image)

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

\(^1\)H NMR (400 MHz, DMSO-\textit{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-\textit{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, 121.4, 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\textsubscript{33}H\textsubscript{26}BrClN\textsubscript{2}O\textsubscript{4} ([M+Na\textsuperscript{+}]): 651.0657, found 651.0653.

![Chemical structure of 1i](image)

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

\(^1\)H NMR (400 MHz, DMSO-\textit{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-\textit{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\textsubscript{30}H\textsubscript{29}BrN\textsubscript{2}O\textsubscript{4} ([M+Na\textsuperscript{+}]): 583.1203, found 583.1192.
**1j** was obtained as a brown solid, Yield 78% (798 mg), Melting point 119 - 121 °C.

$^1$H NMR (300 MHz, 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).

$^{13}$C NMR (101 MHz, 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 C$_{27}$H$_{31}$BrN$_2$O$_3$ ([M+Na]$^+$): 533.1410, found 533.1397.

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

$^1$H NMR (400 MHz, 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).

$^{13}$C NMR (101 MHz, 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 C$_{31}$H$_{31}$BrN$_2$O$_4$ ([M+H]$^+$): 575.1540, found 575.1520.
**1m** was obtained as a red solid, Yield 40% (464 mg), Melting point 141 -143 °C.

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 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).

$^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 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$_{30}$H$_{28}$BrClN$_2$O$_3$ ([M+H]$^+$): 579.1045, found 579.1050.

![Image](image1)

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

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 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).

$^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 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$_{30}$H$_{29}$BrN$_2$O$_4$ ([M+Na]$^+$): 583.1203, found 583.1189.

![Image](image2)

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

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 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).

$^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 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$_{30}$H$_{28}$BrClN$_2$O$_3$ ([M+H]$^+$): 579.1045, found 579.1050.

![Image](image1)

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

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 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).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 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$_{27}$H$_{31}$BrN$_2$O$_3$ ([M+H]$^+$): 511.1591, found 511.1580.

![Image](image2)
4. Palladium-catalyzed cascade reaction

Ugi product 1 (0.1 mmol, 1.0 equiv), palladium(π-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 °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. ≈ 1.8:1), Melting point 205 - 207 °C.

\[ ^{1}H \text{ NMR (400 MHz, 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 \text{ 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 \text{ Hz, 1H}), 6.98 – 6.93 (m, 1H), [6.92 (d, } J = 8.3 \text{ Hz), 6.84 – 6.80 (m, 1H), [6.10 (s), 5.67 (d, } J = 17.8 \text{ Hz), 1H}, 4.88 – 4.82 (m, 1H), [4.75 – 4.68 (m, 1H), 4.62 – 4.58 (m, 1H), 4.57 – 4.52 (m, 1H), [3.30 (dd, } J = 15.7, 5.4 \text{ Hz), 3.17 (dd, } J = 11.6, 4.5 \text{ Hz), 1H}, [3.14 – 3.08 (m, 2.58 – 2.50 (m, 1H), [1.25 (s), 1.19 (s), 9H).

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

HRMS (ESI, m/z) calcd for C_{30}H_{28}N_{2}O_{3} ([M+H]^+): 465.2173, found 465.2166.
2b was obtained as a brown solid, Yield 31% (15 mg, d. r. = 1.5:1), Melting point 112 - 114 °C.

\[ \text{H NMR (300 MHz, CDCl}_3 \] \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).

\[ \text{C NMR (101 MHz, CDCl}_3 \] \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, 127.8, 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 C31H30N2O3 ([M+H]+): 479.2329, found 479.2331.

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

\[ \text{H NMR (400 MHz, CDCl}_3 \] \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), 1H \], \[ 1.49 (d, \( J = 14.7 \) Hz), 1H \], \[ 1.40 (s), 1.33 (s), 3H \], \[ 1.19 (s), 1.18 (s), 3H \], \[ 0.80 (s), 0.77 (s), 9H \]

\[ \text{C NMR (101 MHz, CDCl}_3 \] \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, 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 C34H36N2O3 ([M+H]+): 521.2799, found 521.2800.
2d was obtained as a brown solid, Yield 38% (21 mg, d. r. ≈ 1.9:1), Melting point 135 - 137 °C.

1H NMR (400 MHz, CDCl₃) δ 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).

13C NMR (101 MHz, CDCl₃) δ 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, 45.0, 45.5, 45.1, 41.8, 39.8, 36.2, 36.1, 29.6, 29.5.

HRMS (ESI, m/z) calcd for C₃₆H₃₄N₂O₃ ([M+H]+): 543.2642, found 543.2643.

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

1H NMR (400 MHz, CDCl₃) δ 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].

13C NMR (101 MHz, CDCl₃) δ 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.

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

$^1$H NMR (300 MHz, CDCl$_3$) δ 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].

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 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 C$_{34}$H$_{26}$N$_2$O$_5$ ([M+H]$^+$): 543.1914, found 543.1920.

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

$^1$H NMR (400 MHz, DMSO-$_d_6$) δ 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).

$^{13}$C NMR (151 MHz, DMSO-$_d_6$) δ 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, 130.6, 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 C$_{34}$H$_{30}$N$_2$O$_6$ ([M+H]$^+$): 559.1864, found 559.1867.
**2h** was obtained as a brown solid, Yield 31% (18 mg, d. r. ≈ 1.5:1), Melting point 295 – 297 °C.

$^1$H NMR (400 MHz, CDCl$_3$) δ 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].

$^{13}$C NMR (151 MHz, CDCl$_3$) δ 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, 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 C$_{33}$H$_{25}$ClN$_2$O$_4$ ([M+H]$^+$): 549.1576, found 549.1559.

---

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

$^1$H NMR (400 MHz, CDCl$_3$) δ 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].

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 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 C$_{30}$H$_{28}$N$_2$O$_4$ ([M+H]$:)$: 481.2122, found 481.2111.
2j was obtained as a brown solid, Yield 43% (18.5 mg, d. r. ≈ 1.2:1), Melting point 205 - 207 °C.

$^1$H NMR (400 MHz, CDCl$_3$) δ 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).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 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, 130.3, 130.1, 128.5, 128.0, 127.9, 127.8, 127.7, 126.9, 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 C$_{27}$H$_{30}$N$_2$O$_3$ ([M+H]$^+$): 431.2329, found 431.2318.

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

$^1$H NMR (400 MHz, CDCl$_3$) δ 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].

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 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, 130.2, 129.4, 129.1, 128.6, 128.1, 127.8, 127.9, 127.8, 127.6, 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 C$_{31}$H$_{30}$N$_2$O$_4$ ([M+H]$^+$): 495.2278, found 495.2272.
2l was obtained as a yellow solid, Yield 43% (21.5 mg, d. r. ≈ 1.9:1), Melting point 223 - 225 °C.

\[ ^1 \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 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].

\[ ^{13} \text{C NMR (101 MHz, CDCl}_3 \] \( \delta \) 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, 128.0, 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 C\(_{30}\)H\(_{27}\)ClN\(_2\)O\(_3\) ([M+H]\(^+\)): 499.1783, found 499.1772.

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

\[ ^1 \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 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].

\[ ^{13} \text{C NMR (101 MHz, CDCl}_3 \] \( \delta \) 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 C\(_{30}\)H\(_{28}\)N\(_2\)O\(_4\) ([M+H]\(^+\)): 481.2122, found 481.2114.
2n was obtained as a brown solid, Yield 49% (21 mg, d. r. ≈ 1.2:1), Melting point 224 - 226 °C. 

1H NMR (400 MHz, CDCl$_3$) δ 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].

13C NMR (101 MHz, CDCl$_3$) δ 195.4, 194.9, 173.4, 167.3, 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, 126.8, 126.8, 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 C$_{27}$H$_{30}$N$_2$O$_3$ ([M+H]$^+$): 431.2329, found 431.2313.

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

Ugi adduct 1a (1 mmol, 1.0 equiv), palladium(π-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: NaBH₄ → HO → Step II: NaH, Mel → MeO](image)
**Step I**: To a glass vial of 2a (37.2 mg, 0.08 mmol) in THF/H$_2$O (0.7 ml/0.07 mL) was slowly added NaBH$_4$ (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$_2$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. = 2.3:1), Melting point 112 – 114 °C.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ [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].

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 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, 127.1, 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$_{30}$H$_{30}$N$_2$O$_3$ ([M+H]$^+$): 467.2329, found 467.2335.

3b was obtained as a white solid, Yield 70% (33.6 mg, d. r. = 3.5:1), Melting point 84 - 86°C.
$\text{^1H NMR (300 MHz, CDCl}_3\text{) } \delta [7.62 – 7.51 \text{ (m), 7.47 – 7.39 \text{ (m), 2H}, 7.28 – 7.22 \text{ (m, 3H), 7.21 – 7.13 \text{ (m, 3H), 7.12 – 7.04 \text{ (m, 3H), 6.92 (d, } J = 7.4 \text{ Hz, 1H), 6.81 (d, } J = 7.6 \text{ Hz, 1H}, [5.67 \text{ (s), 5.61 \text{ (s), 1H}], [4.81 \text{ (s), 4.68 (d, } J = 8.4 \text{ Hz}, 1H), 4.54 – 4.47 \text{ (m, 1H), 4.42 (d, } J = 17.6 \text{ Hz, 1H), 4.26 – 4.18 \text{ (m, 1H), [3.57 \text{ (s), 3.16 \text{ (s), 3H}], 2.51 – 2.40 \text{ (m, 1H), 1.89 – 1.75 \text{ (m, 1H), [1.30 \text{ (s, 1H), 1.27 \text{ (s, 3H), 9H}.}}]]$

$\text{^{13}C NMR (101 MHz, CDCl}_3\text{) } \delta 172.8, 168.7, 139.7, 138.9, 135.4, 135.2, 133.9, 130.1, 129.6, 128.6, 128.4, 127.7, 127.3, 127.1, 126.7, 126.4, 76.5, 66.8, 62.6, 56.0, 55.3, 47.8, 41.4, 34.6, 28.1.$

HRMS (ESI, m/z) calcd for C$_{31}$H$_{32}$N$_2$O$_3$ ([M+H]$^+$): 481.2486, found 549.1559.

2) Synthesis of compound 3c

![Chemical reaction diagram]

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 °C for 12 h. After completion, the mixture was quenched with H$_2$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. = 2.3:1), Melting point 201 – 203 °C.

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

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

HRMS (ESI, m/z) calcd for C$_{30}$H$_{30}$N$_2$O$_2$ ([M+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 CHCl₃ 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 MoKα radiation. The images were processed (unit cell determination, intensity data integration, correction for Lorentz and polarization effects, and empirical absorption correction) using CrysAlisPRO. Using Olex2, the structure was solved with the ShelXT structure solution program using Intrinsic Phasing and refined with the ShelXL refinement package using full-matrix least-squares minimization on F². 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 Ueq 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

<table>
<thead>
<tr>
<th>Empirical formula</th>
<th>C₃₀H₂₈N₂O₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula weight</td>
<td>464.54</td>
</tr>
<tr>
<td>Temperature/K</td>
<td>293(2)</td>
</tr>
<tr>
<td>Property</td>
<td>Value</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>Crystal system</td>
<td>triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P-1</td>
</tr>
<tr>
<td>a/Å</td>
<td>9.1811(2)</td>
</tr>
<tr>
<td>b/Å</td>
<td>9.9659(2)</td>
</tr>
<tr>
<td>c/Å</td>
<td>14.9148(4)</td>
</tr>
<tr>
<td>α/°</td>
<td>85.493(2)</td>
</tr>
<tr>
<td>β/°</td>
<td>80.059(2)</td>
</tr>
<tr>
<td>γ/°</td>
<td>63.776(3)</td>
</tr>
<tr>
<td>Volume/Å³</td>
<td>1205.83(6)</td>
</tr>
<tr>
<td>Z</td>
<td>2</td>
</tr>
<tr>
<td>ρcalc g/cm³</td>
<td>1.279</td>
</tr>
<tr>
<td>μ/mm⁻¹</td>
<td>0.083</td>
</tr>
<tr>
<td>F(000)</td>
<td>492.0</td>
</tr>
<tr>
<td>Crystal size/mm³</td>
<td>0.35 × 0.35 × 0.3</td>
</tr>
<tr>
<td>Radiation</td>
<td>MoKα (λ = 0.71073 Å)</td>
</tr>
<tr>
<td>2Θ range for data collection/°</td>
<td>5.006 to 52.742</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-11 ≤ h ≤ 11, -12 ≤ k ≤ 12, -18 ≤ l ≤ 18</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>49581</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>4945 [Rint = 0.0355, Rsigma = 0.0178]</td>
</tr>
<tr>
<td>Data/restraints/parameters</td>
<td>4945/0/319</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.075</td>
</tr>
<tr>
<td>Final R indexes [I&gt;=2σ (I)]</td>
<td>R₁ = 0.0470, wR₂ = 0.1133</td>
</tr>
<tr>
<td>Final R indexes [all data]</td>
<td>R₁ = 0.0583, wR₂ = 0.1204</td>
</tr>
<tr>
<td>Largest diff. peak/hole / e Å⁻³</td>
<td>0.24/-0.19</td>
</tr>
</tbody>
</table>

8. References

9. Copies of $^1$H NMR and $^{13}$C NMR spectra for the products
NOESY NMR spectra of compound 2a