Supporting Information

Transition Metal-Free Selective C-S Bond Cleavage of Ugi-Adducts for Rapid Preparation of Peptidomimetics

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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). Substrates 1a-b, 1g-i, 1k-p and 1r-u were synthesized according to literature, 1w was commercially available. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker AM (300 or 400 MHz) spectrometer at ambient temperature using CDCl$_3$ or DMSO-$d_6$ or MeOH-$d_4$ 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 μL 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 are uncorrected.

2. General procedure for the synthesis of Ugi adducts
To a solution of aldehyde (1.0 mmol, 1.0 equiv) in TFE (1.0 mL) were added successively ammonia solution (7 N in methanol, 2.0 equiv), acid (1.2 mmol, 1.2 equiv) and isonitrile (1.2 mmol, 1.2 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 12 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 = 1:4 v/v) to afford the desired Ugi products 1c-f, 1j, 1q and 1v.

3. Characterization of Ugi adducts

1c was obtained as a white solid (68%). Melting point 233 – 235 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.37 – 9.21 (m, 1H), 8.66 (d, $J = 8.1$ Hz, 1H), 7.97 – 7.81 (m, 2H), 7.60 – 7.37 (m, 5H), 7.37 – 7.28 (m, 2H), 7.21 (d, $J = 8.0$ Hz, 2H), 6.98 – 6.86 (m, 2H), 5.66 (d, $J = 8.0$ Hz, 1H), 4.85 – 4.73 (m, 1H), 4.70 – 4.57 (m, 1H), 3.78 (s, 3H), 2.28 (s, 3H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.1, 166.6, 159.6, 144.9, 135.0, 134.4, 132.1, 130.2, 130.1, 129.8, 129.1, 128.8, 128.4, 114.2, 60.8, 56.6, 55.8, 21.7.

HRMS (ESI) calculated for C$_{24}$H$_{23}$N$_2$O$_5$SNa$^+$ ([M+Na]$^+$): 475.1298, found 475.1303.
**1d** was obtained as a yellow solid (58%). Melting point 267 – 269 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 9.43 – 9.36 (m, 1H), 8.78 (d, $J = 8.1$ Hz, 1H), 7.90 – 7.86 (m, 2H), 7.57 – 7.43 (m, 9H), 7.22 – 7.18 (m, 2H), 5.76 – 5.71 (m, 1H), 4.86 – 4.79 (m, 1H), 4.67 – 4.59 (m, 1H), 2.29 (s, 3H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 170.4, 166.8, 145.0, 137.1, 134.9, 134.2, 133.2, 132.1, 130.3, 130.1, 129.0, 128.8, 128.4, 128.4, 60.6, 56.5, 21.7.

HRMS (ESI) calculated for C$_{23}$H$_{21}$ClN$_2$O$_4$SNa$^+$ ([M+Na]$^+$): 479.0803, found 479.0820.

**1e** was obtained as a white solid, Yield 85% (380 mg), Melting point 240 – 242 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) δ [9.51 (t, $J = 6.6$ Hz), 9.39 (t, $J = 6.6$ Hz), 1H], [8.82 (d, $J = 8.1$ Hz), 8.03 – 7.99 (m), 1H], [7.91 – 7.86 (m), 7.74 – 7.67 (m), 2H], 7.61 – 7.37 (m, 9H), 7.22 – 7.17 (m, 2H), [6.09 (s), 5.73 (d, $J = 8.0$ Hz), 1H], 4.88 – 4.77 (m, 1H), 4.68 – 4.58 (m, 1H), 4.29 (d, $J = 24.5$ Hz, 1H), [2.31 (s), 2.29 (s), 3H]. Mixture of rotamers (~4:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 170.4, 168.3, 166.8, 165.3, 145.0, 138.7, 136.1, 134.9, 134.8, 134.5, 134.2, 132.8, 132.1, 131.8, 131.7, 131.1, 130.2, 130.1, 129.5, 129.3, 129.3, 129.0, 128.8, 128.4, 122.6, 122.4, 84.0, 83.7, 82.0, 81.6, 75.1, 60.7, 56.8, 21.7. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{25}$H$_{22}$N$_2$O$_4$S ([M+Na]$^+$): 469.1192, found 469.1176.
**1f** was obtained as a white solid, Yield 56% (231 mg), Melting point 212 – 214 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.37 – 9.20 (m, 1H), 8.74 (d, $J = 8.2$ Hz, 1H), 7.98 – 7.87 (m, 2H), 7.68 – 7.52 (m, 5H), 7.50 – 7.43 (m, 2H), 7.27 (d, $J = 8.1$ Hz, 2H), 6.56 (d, $J = 1.8$ Hz, 1H), 5.77 – 5.58 (m, 1H), 4.89 – 4.73 (m, 1H), 4.72 – 4.57 (m, 1H), 2.29 (s, 3H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 170.8, 166.9, 145.0, 143.8, 141.4, 135.1, 134.3, 132.1, 130.2, 129.1, 128.8, 128.4, 122.4, 111.1, 60.8, 49.8, 21.7.

HRMS (ESI, m/z) calcd for C$_{21}$H$_{20}$N$_2$O$_5$S ([M+Na]$^+$): 435.0985, found 435.0970.

**1j** was obtained as a yellow solid, Yield 60% (202 mg), Melting point 180 – 182 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.09 – 8.93 (m, 1H), 8.63 – 8.47 (m, 1H), [7.87 – 7.83 (m, 7.63 – 7.56 (m), 1H], 7.76 – 7.66 (m, 2H), 7.43 – 7.34 (m, 2H), [7.16 – 7.11 (m, 6.78 – 6.70 (m, 1H), [6.78 – 6.70 (m, 1H), 6.65 – 6.60 (m, 1H), 4.66 (d, $J = 6.3$ Hz, 2H), 3.79 (d, $J = 6.0$ Hz, 2H), 2.37 (s, 3H). Mixture of rotamers (~3:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.8, 162.1, 158.6, 148.2, 145.8, 145.1, 144.0, 135.3, 130.4, 129.1, 114.4, 113.3, 112.5, 111.6, 60.9, 42.2, 21.8. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{15}$H$_{16}$N$_2$O$_5$S ([M+Na]$^+$): 359.0672, found 359.0681.
1q was obtained as a yellow solid, Yield 75% (288 mg), Melting point 150 – 152 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 9.19 (s, 1H), 7.88 – 7.68 (m, 2H), 7.57 – 7.38 (m, 6H), 7.36 – 7.19 (m, 1H), 4.74 (d, $J = 6.5$ Hz, 2H), 4.06 (d, $J = 24.5$ Hz, 2H), 3.88 (d, $J = 43.3$ Hz, 2H), [3.44 (s), 3.33 (s), 1H], [2.40 (s), 2.38 (s), 3H]. Mixture of rotamers (~1.1:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 171.2, 171.0, 168.4, 145.4, 135.6, 135.3, 135.0, 130.8, 130.7, 130.4, 129.3, 129.2, 127.4, 127.3, 79.3, 76.5, 75.9, 60.7, 50.5, 47.0, 35.0, 21.8.

HRMS (ESI, m/z) calcd for C$_{20}$H$_{20}$N$_2$O$_4$S ([M+Na]$^+$): 407.1036, found 407.1038.

1v was obtained as a white solid, Yield 80% (413 mg, dr 1:1), Melting point 88 – 90°C.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.00 (s, 1H), 7.87 – 7.67 (m, 2H), 7.65 – 7.41 (m, 2H), 7.40 – 7.27 (m, 4H), 7.25 – 7.20 (m, 1H), 7.15 – 7.03 (m, 1H), [5.78 – 5.29 (m), 4.91 – 4.70 (m), 1H], 4.69 – 4.55 (m, 1H), 4.52 – 3.96 (m, 2H), 3.74 – 3.19 (m, 2H), [2.41 (s), 2.34 (s), 3H], [2.40 – 2.34 (m), 2.31 – 1.89 (m), 4H], [1.88 – 1.76 (m), 1.60 – 1.08 (m), 9H].

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 174.6, 172.6, 170.0, 165.0, 160.8, 145.6, 145.0, 133.7, 130.4, 130.0, 129.8, 128.9, 128.7, 127.4, 80.8, 63.2, 60.4, 58.9, 57.3, 47.3, 47.1, 28.5, 28.3, 24.7, 24.4, 21.8, 21.7, 20.8, 14.3.


4. General procedure for the synthesis of products
(0.1 mmol, 1.0 equiv), CsOAc (0.2 mmol, 2.0 equiv) (Note: Ugi adducts 1 are stable in this work) were placed to the screw cap vial followed by addition of alcohol (1.0 mL). The resulting mixture was sealed and stirred at 120 °C for 1 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 = 1:4 v/v) to afford the desired products 2.

5. Characterization of products

2-1 was obtained as a white solid, Yield 94% (22.2 mg), Melting point 143 – 145 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.94 – 7.83 (m, 2H), 7.60 – 7.51 (m, 1H), 7.50 – 7.41 (m, 2H), 4.68 (s, 2H), 4.06 (s, 2H), 3.60 – 3.47 (m, 2H), 1.16 (t, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 172.6, 170.5, 135.0, 132.9, 129.5, 128.5, 70.7, 64.7, 44.1, 15.4.

HRMS (ESI, m/z) calcld for C_{12}H_{16}N_{2}O_{3} ([M+Na$^+$]): 259.1053, found 259.1054.

2-2 was obtained as a white solid, Yield 97% (30.3 mg), Melting point 116 – 118 °C.
$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.88 – 7.85 (m, 2H), 7.57 – 7.50 (m, 3H), 7.48 – 7.46 (m, 1H), 7.45 – 7.43 (m, 1H), 7.41 – 7.31 (m, 3H), 5.65 (s, 1H), 4.72 (d, $J = 10.4$ Hz, 1H), 4.61 (d, $J = 10.4$ Hz, 1H), 3.46 – 3.40 (m, 2H), 1.08 (t, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 173.4, 169.8, 138.6, 135.1, 132.9, 129.8, 129.5, 129.0, 128.6, 70.8, 64.6, 59.5, 15.3.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{20}$N$_2$O$_3$ ([M+ Na]$^+$): 335.1366, found 335.1368.

2-3 was obtained as a white solid, Yield 94% (33.2 mg), Melting point 155 – 157 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.93 – 8.85 (m, 1H), 8.75 (d, $J = 7.7$ Hz, 1H), 7.93 – 7.88 (m, 2H), 7.57 – 7.50 (m, 1H), 7.49 – 7.41 (m, 4H), 6.92 (d, $J = 8.3$ Hz, 2H), 5.58 (d, $J = 7.6$ Hz, 1H), 4.59 – 4.47 (m, 2H), 3.74 (s, 3H), 3.39 – 3.32 (m, 2H), 1.03 (t, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.70, 166.73, 159.49, 134.52, 132.01, 130.64, 129.66, 128.77, 128.34, 114.32, 69.63, 63.16, 57.36, 55.77, 15.58.

HRMS (ESI, m/z) calcd for C$_{19}$H$_{22}$N$_2$O$_4$ ([M+ Na]$^+$): 365.1472, found 365.1464.

2-4 was obtained as a white solid, Yield 83% (29 mg), Melting point 163 – 165 °C.

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.03 – 8.97 (m, 1H), 8.89 (d, $J = 7.7$ Hz, 1H), 7.94 – 7.89 (m, 2H), 7.53 (d,
$J = 7.9 \text{ Hz, 3H}$, $7.49 - 7.42$ (m, 4H), $5.66$ (d, $J = 7.6 \text{ Hz, 1H}$), $4.60 - 4.47$ (m, 2H), $3.40 - 3.33$ (m, 2H), $1.03$ (t, $J = 7.0 \text{ Hz, 3H}$).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 171.04, 166.88, 137.70, 134.35, 133.07, 132.12, 130.32, 128.90, 128.80, 128.38, 69.68, 63.24, 57.25, 15.57.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{19}$ClN$_2$O$_3$ ([M+ Na]$^+$): 369.0976, found 369.0967.

2-5 was obtained as a white solid, Yield 96% (32.3 mg), Melting point 115 – 117 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.88 – 7.85 (m, 2H), 7.67 – 7.65 (m, 1H), 7.56 – 7.51 (m, 2H), 7.48 – 7.45 (m, 1H), 7.45 – 7.43 (m, 2H), 7.39 – 7.35 (m, 1H), 5.65 (s, 1H), 4.73 (d, $J = 10.4 \text{ Hz, 1H}$), 4.61 (d, $J = 10.4 \text{ Hz, 1H}$), 3.53 (s, 1H), 3.46 – 3.41 (m, 2H), 1.09 (t, $J = 7.1 \text{ Hz, 3H}$).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 172.9, 169.8, 139.2, 135.0, 133.0, 132.9, 132.5, 130.0, 129.5, 129.4, 128.6, 124.3, 83.9, 79.3, 70.9, 64.7, 59.0, 15.3.

HRMS (ESI, m/z) calcd for C$_{20}$H$_{20}$N$_2$O$_3$ ([M+ Na]$^+$): 359.1366, found 359.1365.

2-6 was obtained as a white solid, Yield 94% (28.4 mg), Melting point 148 – 150 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.89 – 7.85 (m, 2H), 7.65 – 7.64 (m, 1H), 7.57 – 7.50 (m, 2H), 7.48 – 7.43 (m, 2H), 6.57 – 6.56 (m, 1H), 5.63 (s, 1H), 4.74 (d, $J = 10.4 \text{ Hz, 1H}$), 4.64 (d, $J = 10.4 \text{ Hz, 1H}$), 3.52 – 3.47
(m, 2H), 1.14 (t, J = 7.0 Hz, 3H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 173.3, 170.0, 144.8, 142.5, 135.1, 132.9, 129.5, 128.6, 122.9, 110.7, 70.9, 64.7, 51.6, 15.3.

HRMS (ESI, m/z) calcd for C$_{16}$H$_{18}$N$_2$O$_4$ ([M+ Na]$^+$): 325.1159, found 325.1154.

2-7 was obtained as a white solid, Yield 68% (27.2 mg), Melting point 74 – 76 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 8.05 (d, J = 8.6 Hz, 2H), 7.91 (d, J = 8.5 Hz, 2H), 4.68 (s, 2H), 4.08 (s, 2H), 3.56 – 3.51 (m, 2H), 3.17 – 3.08 (m, 4H), 1.60 – 1.56 (m, 2H), 1.54 (d, J = 7.5 Hz, 2H), 1.17 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 7.4 Hz, 6H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 172.3, 168.9, 144.3, 138.8, 129.4, 128.3, 70.7, 64.8, 64.7, 51.2, 44.1, 23.1, 15.4, 11.4.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{29}$N$_3$O$_5$S ([M+ Na]$^+$): 422.1720, found 422.1719.

2-8 was obtained as a white solid, Yield 45% (19.4 mg), Melting point 164 – 166 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.71 (t, J = 6.6 Hz, 1H), 8.41 (t, J = 5.9 Hz, 1H), 8.24 (d, J = 2.3 Hz, 1H), 8.20 – 8.15 (m, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.56 – 4.53 (m, 2H), 4.00 (d, J = 6.5 Hz, 2H), 3.88 – 3.86 (m, 2H), 3.45 – 3.40 (m, 2H), 2.63 (s, 3H), 2.15 – 2.04 (m, 1H), 1.09 (t, J = 7.0 Hz, 3H), 1.02 (d, J = 6.7 Hz, 6H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 170.1, 164.5, 162.5, 161.8, 155.7, 133.5, 131.9, 127.0, 126.1, 116.1,
114.6, 102.2, 75.7, 69.5, 63.2, 43.3, 28.2, 19.3, 17.7, 15.6.

HRMS (ESI, m/z) calcd for C_{21}H_{26}N_{4}O_{4}S ([M+ Na]^+): 453.1567, found 453.1563.

2-9 was obtained as a white solid, Yield 89% (23.4 mg), Melting point 85 – 87 °C.

$^1$H NMR (400 MHz, MeOH-\(d_4\)) $\delta$ 7.63 – 7.44 (m, 2H), 7.42 – 7.21 (m, 3H), 5.89 (s, 1H), 5.77 (s, 1H), 4.67 (s, 2H), 3.96 (s, 2H), 3.58 – 3.45 (m, 2H), 1.16 (t, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (101 MHz, MeOH-\(d_4\)) $\delta$ 172.1, 171.7, 146.6, 137.9, 129.5, 129.3, 128.7, 120.3, 70.7, 64.7, 43.8, 15.4.

HRMS (ESI, m/z) calcd for C_{14}H_{18}N_{2}O_{3} ([M+ Na]^+): 285.1210, found 285.1227.

2-10 was obtained as a yellow solid, Yield 50% (11.3 mg), Melting point 98 – 100 °C.

$^1$H NMR (400 MHz, MeOH-\(d_4\)) $\delta$ 7.75 – 7.62 (m, 1H), 7.22 – 7.07 (m, 1H), 6.68 – 6.52 (m, 1H), 4.67 (s, 2H), 4.02 (s, 2H), 3.61 – 3.45 (m, 2H), 1.16 (t, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.6, 158.9, 147.3, 144.7, 115.1, 112.4, 70.1, 64.3, 43.1, 15.2.

HRMS (ESI, m/z) calcd for C_{13}H_{14}N_{2}O_{4} ([M+ Na]^+): 249.0846, found 249.0862.
2-11 was obtained as a white solid, Yield 84% (27.4 mg), Melting point 82 – 84 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.56 – 7.52 (m, 1H), 7.48 – 7.43 (m, 4H), 7.38 – 7.33 (m, 3H), 7.33 – 7.27 (m, 1H), 7.21 (d, $J = 7.5$ Hz, 1H), 4.78 (s, 1H), 4.68 (s, 1H), 4.60 (d, $J = 5.7$ Hz, 2H), 4.10 (s, 1H), 3.85 (s, 1H), 3.56 – 3.40 (m, 2H), 1.16 (t, $J = 6.8$ Hz, 3H). Mixture of rotamers (~1:1).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 174.9, 171.2, 137.7, 137.5, 137.0, 136.7, 131.3, 131.1, 130.0, 129.9, 129.8, 129.7, 129.4, 128.9, 128.8, 128.3, 127.9, 127.7, 70.7, 64.7, 55.3, 51.9, 50.5, 15.4. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{19}$H$_{22}$N$_2$O$_3$ ([M+ Na]$^+$): 349.1523, found 349.1526.

![2-12](image)

2-12 was obtained as a yellow oil, Yield 95% (34 mg).

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.57 – 7.39 (m, 5H), 7.28 (d, $J = 8.2$ Hz, 1H), 7.11 (d, $J = 8.2$ Hz, 1H), 6.95 – 6.84 (m, 2H), [4.71 (s), 4.67 (s), 2H], [4.59 (s), 4.52 (s), 2H], [4.07 (s), 3.82 (s), 2H], [3.78 (s), 3.77 (s), 3H], 3.56 – 3.38 (m, 2H), 1.19 – 1.12 (m, 3H). Mixture of rotamers (~1:1).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 174.8, 174.7, 171.3, 171.2, 160.9, 137.1, 136.8, 131.2, 131.1, 130.9, 129.8, 129., 129.5, 129.1, 127.9, 127.7, 115.3, 115.2, 70.6, 64.7, 55.7, 54.8, 51.7, 49.9, 15.4. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{20}$H$_{24}$N$_2$O$_4$ ([M+ Na]$^+$): 379.1628, found 379.1628.

![2-13](image)

2-13 was obtained as a yellow oil, Yield 95% (25.2 mg).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.43 – 7.39 (m, 6H), 4.73 (d, $J = 6.7$ Hz, 2H), 4.14 (s, 2H), 3.53 (d, $J = 7.0$ Hz,
2H), 3.43 – 3.37 (m, 2H), 1.19 (t, J = 7.1 Hz, 6H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.9, 170.2, 135.5, 130.1, 128.7, 126.7, 69.9, 64.1, 50.1, 45.9, 15.2, 14.0.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{20}$N$_2$O$_3$ ([M+ Na]$^+$): 287.1366, found 287.1371.

2-14 was obtained as a yellow oil, Yield 98% (30 mg).

$^1$H NMR (400 MHz, MeOH-d$_4$) δ 7.49 – 7.38 (m, 5H), [4.71 (s), 4.61 (s), 2H], [4.18 (s), 3.96 (s), 2H], 3.61 – 3.50 (m, 2H), 3.48 – 3.32 (m, 2H), 1.70 – 1.52 (m, 1H), 1.50 – 1.34 (m, 2H), 1.20 – 1.12 (m, 3H), [0.98 (d, J = 6.5 Hz), 0.73 (d, J = 6.5 Hz), 6H]. Mixture of rotamers (~3:2).

$^{13}$C NMR (101 MHz, MeOH-d$_4$) δ 174.6, 171.7, 171.5, 137.5, 137.2, 130.9, 129.6, 127.7, 127.6, 70.7, 53.0, 50.6, 46.7, 38.3, 36.8, 27.4, 26.9, 22.9, 22.6, 15.4. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{17}$H$_{26}$N$_2$O$_3$ ([M+Na]$^+$): 329.1836, found 329.1835.

2-15 was obtained as a yellow oil, Yield 90% (34 mg).

$^1$H NMR (400 MHz, MeOH-d$_4$) δ 7.49 – 7.39 (m, 5H), 4.71 (s, 1H), 4.61 (s, 1H), 4.18 (s, 1H), 3.96 (s, 1H), 3.60 – 3.51 (m, 2H), 3.48 – 3.31 (m, 2H), 1.75 – 1.59 (m, 3H), 1.58 – 1.43 (m, 9H), 1.42 – 1.29 (m, 4H), 1.20 – 1.13 (m, 4H). Mixture of rotamers (~3:2).

$^{13}$C NMR (101 MHz, MeOH-d$_4$) δ 174.6, 171.7, 171.5, 137.5, 137.2, 130.9, 129.6, 127.7, 127.6, 70.7, 64.7, 52.9, 50.6, 46.6, 37.5, 36.5, 36.2, 36.0, 33.6, 33.0, 28.3, 27.5, 27.2, 26.6, 26.3, 15.4. Mixture of rotamers.
HRMS (ESI, m/z) calcd for C_{22}H_{34}N_{2}O_{3} ([M + Na]^{+}): 397.2462, found 397.2453.

2-16 was obtained as a green oil, Yield 86% (25 mg).

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.56 – 7.34 (m, 5H), [4.74 (s), 4.61 (s), 2H], [4.34 (s), 4.09 (s), 2H], [3.62 – 3.38 (m), 3.21 (d, $J = 6.6$ Hz), 4H], 1.21 – 0.91 (m, 4H), 0.63 – 0.46 (m, 2H), [0.30 (d, $J = 4.1$ Hz), 0.06 (d, $J = 4.0$ Hz), 2H]. Mixture of rotamers (~3:2).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 174.8, 174.5, 171.7, 137.4, 137.1, 130.9, 129.6, 127.9, 127.6, 70.7, 64.8, 56.4, 52.7, 51.9, 15.4, 10.6, 9.8, 4.1. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C_{16}H_{22}N_{2}O_{3} ([M + Na]^{+}): 313.1523, found 313.1521.

2-17 was obtained as a white solid, Yield 94% (26 mg), Melting point 73 – 75 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.69 – 7.23 (m, 5H), [4.70 (s), 4.63 (s), 2H], [4.42 (s), 4.30 (s), 2H], [4.15 (s), 4.12 (s), 2H], 3.60 – 3.42 (m, 2H), [2.89 (s), 2.77 (s), 1H], 1.20 – 1.14 (m, 3H). Mixture of rotamers (~3:2).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 174.2, 174.0, 171.1, 136.5, 135.9, 131.7, 131.4, 129.7, 128.1, 127.8, 79.0, 75.2, 74.5, 70.7, 64.8, 51.8, 41.7, 36.5, 15.4. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C_{15}H_{18}N_{2}O_{3} ([M + Na]^{+}): 297.1210, found 297.1202.
2-18 was obtained as a yellow oil, Yield 96% (28 mg).

$^1$H NMR (400 MHz, MeOH-d$_4$) $\delta$ 7.49 – 7.36 (m, 5H), [5.94 – 5.82 (m), 5.68 – 5.53 (m), 1H], 5.19 – 4.95 (m, 2H), [4.71 (s), 4.61 (s), 2H], [4.20 (s), 3.98 (s), 2H], 3.63 – 3.51 (m, 2H), 3.46 – 3.35 (m, 2H), [2.48 – 2.39 (m), 2.34 – 2.25 (m), 2H], 1.21 – 1.11 (m, 3H). Mixture of rotamers (~1:1).

$^{13}$C NMR (101 MHz, MeOH-d$_4$) $\delta$ 174.8, 171.6, 171.5, 137.4, 136.6, 135.6, 130.9, 129.6, 127.8, 127.6, 117.8, 117.3, 70.7, 64.7, 53.3, 51.5, 47.6, 33.9, 32.6, 15.4. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{16}$H$_{22}$N$_2$O$_3$ ([M+ Na]$^+$): 313.1523, found 313.1518.

2-19 was obtained as a yellow solid, Yield 90% (28.5 mg), Melting point 86 – 88 °C.

$^1$H NMR (400 MHz, MeOH-d$_4$) $\delta$ 7.63 – 7.58 (m, 1H), 7.53 – 7.39 (m, 5H), [6.42 – 6.37 (m), 6.33 – 6.28 (m), 2H], [4.77 (s), 4.68 (s), 2H], [4.60 (s), 4.52 (s), 2H], [4.13 (s), 3.92 (s), 2H], [3.59 – 3.50 (m), 3.47 – 3.40 (m), 2H], 1.21 – 1.13 (m, 3H). Mixture of rotamers (~7:3).

$^{13}$C NMR (101 MHz, MeOH-d$_4$) $\delta$ 174.6, 171.2, 151.2, 150.8, 144.5, 144.1, 136.5, 131.3, 129.7, 128.3, 127.7, 111.5, 110.5, 70.7, 64.7, 52.0, 43.4, 15.4. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{17}$H$_{20}$N$_2$O$_4$ ([M+ Na]$^+$): 339.1315, found 339.1312.

2-20 was obtained as a yellow oil, Yield 78% (26 mg).

$^1$H NMR (400 MHz, MeOH-d$_4$) $\delta$ 7.60 – 7.54 (m, 1H), 7.50 – 7.41 (m, 4H), 7.39 – 7.37 (m, 1H), [7.13 – 7.05 (m), 7.00 – 6.96 (m), 2H], [4.92 (s), 4.74 (s), 2H], [4.69 (s), 4.62 (s), 2H], [4.14 (s), 3.89 (s), 2H], 3.57 – 3.43 (m, 2H), 1.20 – 1.15 (m, 3H). Mixture of rotamers (~1:1).
$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 174.4, 171.2, 140.1, 139.9, 136.7, 136.5, 131.3, 129.8, 128.9, 128.2, 128.1, 128.0, 127.7, 127.4, 127.0, 70.7, 64.8, 51.7, 50.4, 45.5, 15.4. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{17}$H$_{20}$N$_2$O$_3$ $([M+Na]^+)$: 355.1087, found 355.1083.

2-21 was obtained as a white solid, Yield 75% (30 mg), Melting point 126 – 128 °C

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.38 – 7.34 (m, 5H), 4.58 (s, 2H), 3.99 (s, 2H), 3.47 – 3.41 (m, 2H), 2.19 (s, 3H), 2.03 – 1.92 (m, 4H), 1.47 – 1.41 (m, 2H), 1.36 – 1.31 (m, 2H), 1.20 – 1.18 (m, 2H), 1.14 (t, $J$ = 7.0 Hz, 3H), 0.88 (s, 6H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 176.0, 173.0, 140.5, 130.2, 129.6, 126.9, 70.6, 64.7, 62.5, 51.6, 50.8, 46.3, 43.7, 38.8, 33.9, 32.2, 31.0, 15.4.

HRMS (ESI, m/z) calcd for C$_{24}$H$_{34}$N$_2$O$_3$ $([M+Na]^+)$: 421.2462, found 421.2454.

2-22 was obtained as a white solid, Yield 92% (20.5 mg), Melting point 137 – 139 °C.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.86 – 7.81 (m, 2H), 7.55 – 7.50 (m, 1H), 7.48 – 7.41 (m, 3H), 7.37 – 7.32 (m, 1H), 4.71 (d, $J$ = 6.7 Hz, 2H), 4.21 (d, $J$ = 5.2 Hz, 2H), 3.33 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.3, 168.1, 133.4, 132.2, 128.8, 127.3, 71.6, 56.2, 44.0.

HRMS (ESI, m/z) calcd for C$_{11}$H$_{14}$N$_2$O$_3$ $([M+Na]^+)$: 245.0897, found 245.0909.
2-23 was obtained as a white solid, Yield 90% (24 mg), Melting point 128 – 130 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.91 – 7.86 (m, 2H), 7.58 – 7.52 (m, 1H), 7.50 – 7.44 (m, 2H), 4.67 (s, 2H), 4.06 (s, 2H), 3.48 (t, $J = 6.5$ Hz, 2H), 1.57 – 1.48 (m, 2H), 1.43 – 1.31 (m, 2H), 0.92 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 172.6, 170.5, 135.0, 132.9, 129.5, 128.5, 70.9, 69.1, 44.1, 32.8, 20.3, 14.2.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{20}$N$_2$O$_3$ ([M+Na]$^+$): 287.1366, found 287.1368.

2-24 was obtained as a white solid, Yield 93% (23.3 mg), Melting point 120 – 122 °C.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 – 7.81 (m, 2H), 7.54 – 7.49 (m, 1H), 7.46 – 7.40 (m, 2H), 7.38 – 7.27 (m, 2H), 4.77 (d, $J = 6.6$ Hz, 2H), 4.19 (d, $J = 5.1$ Hz, 2H), 3.77 (p, $J = 6.1$ Hz, 1H), 1.16 (d, $J = 6.1$ Hz, 6H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.8, 168.0, 133.5, 132.1, 128.8, 127.3, 69.7, 68.1, 44.0, 22.4.

HRMS (ESI, m/z) calcd for C$_{13}$H$_{18}$N$_2$O$_3$ ([M+Na]$^+$): 273.1210, found 273.1223.

2-25 was obtained as a white solid, Yield 70% (18.5 mg), Melting point 101 – 103 °C.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.84 – 7.81 (m, 2H), 7.54 – 7.49 (m, 1H), 7.46 – 7.41 (m, 2H), 7.22 – 7.18 (m, 1H), 7.00 – 6.94 (m, 1H), 4.79 (d, $J = 6.4$ Hz, 2H), 4.15 (d, $J = 5.0$ Hz, 2H), 1.24 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.1, 167.9, 133.6, 132.0, 128.8, 127.3, 74.3, 64.5, 44.0, 28.1.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{20}$N$_2$O$_3$ ([M+Na]$^+$): 287.1366, found 287.1387.
2-26 was obtained as a green solid, Yield 58% (16.3mg), Melting point 96 – 98 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.90 – 7.86 (m, 2H), 7.58 – 7.52 (m, 1H), 7.50 – 7.44 (m, 2H), 4.70 (s, 2H), 4.04 (s, 2H), 1.58 – 1.50 (m, 2H), 1.19 (s, 6H), 0.89 (t, $J = 7.5$ Hz, 3H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 171.9, 170.4, 135.1, 132.9, 129.5, 128.5, 128.2, 77.2, 64.7, 44.1, 34.2, 25.8, 8.6.

HRMS (ESI, m/z) calcd for $C_{15}H_{22}N_2O_3$ ([M+Na$^+$]): 301.1523, found 301.1525.

2-27 was obtained as a white solid, Yield 45% (15.3 mg), Melting point 111 – 113 °C.

$^1$H NMR (300 MHz, MeOH-$d_4$) $\delta$ 7.90 – 7.86 (m, 2H), 7.59 – 7.53 (m, 1H), 7.47 (t, $J = 7.4$ Hz, 2H), 7.34 – 7.26 (m, 1H), 7.25 – 7.20 (m, 3H), 7.19 – 7.14 (m, 1H), [4.80 (s), 4.55 (s), 2H], [4.07 (s), 4.04 (s), 2H], 2.80 (s, 2H), 1.19 (s, 6H). Mixture of rotamers (~4:1).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 171.9, 170.5, 139.4, 135.1, 132.9, 131.7, 129.6, 129.3, 128.9, 128.8, 128.5, 128.5, 127.2, 77.5, 71.2, 70.5, 65.0, 48.3, 44.2, 26.0. Mixture of rotamers.

HRMS (ESI, m/z) calcd for $C_{20}H_{24}N_2O_3$ ([M+Na$^+$]): 363.1679, found 363.1668.

2-28 was obtained as a yellow solid, Yield 84% (21 mg), Melting point 133 – 135 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.90 – 7.87 (m, 2H), 7.58 – 7.53 (m, 1H), 7.50 – 7.44 (m, 2H), 4.76 (s, 2H), 4.17 (d, $J = 2.4$ Hz, 2H), 4.06 (s, 2H), 2.82 (t, $J = 2.4$ Hz, 1H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 172.8, 170.5, 135.0, 132.9, 129.5, 128.5, 128.0, 80.5, 75.6, 69.8, 56.1, 44.1.

HRMS (ESI, m/z) calcd for $C_{13}H_{14}N_2O_3$ ([M+Na$^+$]): 269.0897, found 269.0908.
2-29 was obtained as a yellow solid, Yield 82% (21.4 mg), Melting point 144 – 146 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.91 – 7.86 (m, 2H), 7.58 – 7.52 (m, 1H), 7.50 – 7.44 (m, 2H), 4.71 (s, 2H), 4.06 (s, 2H), 3.60 (t, $J = 6.9$ Hz, 2H), 2.44 – 2.39 (m, 2H), 2.24 (t, $J = 2.7$ Hz, 1H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 172.5, 170.3, 134.8, 132.7, 129.3, 128.3, 81.7, 70.6, 70.2, 67.5, 43.9, 20.2.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{16}$N$_2$O$_3$ ([M+Na]$^+$): 283.1053, found 283.1058.

2-30 was obtained as a white solid, Yield 80% (21 mg), Melting point 118 – 120 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.91 – 7.86 (m, 2H), 7.58 – 7.53 (m, 1H), 7.50 – 7.44 (m, 2H), 5.89 – 5.68 (m, 1H), [5.28 – 5.10 (m), 5.10 – 4.97 (m), 2H], [4.69 (s), 4.68 (s), 2H], [4.06 (s), 4.05 (s), 2H], 3.53 (t, $J = 6.7$ Hz, 2H), 2.35 – 2.22 (m, 2H). Mixture of rotamers (~4:1).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 172.7, 170.5, 141.1, 136.4, 135.0, 135.0, 132.9, 129.6, 129.6, 128.5, 116.7, 116.5, 75.6, 70.8, 68.8, 68.7, 44.1, 35.1, 21.6. Mixture of rotamers.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{18}$N$_2$O$_3$ ([M+Na]$^+$): 285.1210, found 285.1214.

2-31 was obtained as a white solid, Yield 78% (25 mg), Melting point 103 – 105 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.91 – 7.87 (m, 2H), 7.57 – 7.52 (m, 1H), 7.50 – 7.44 (m, 2H), 4.67 (s, 2H), 4.06 (s, 2H), 3.51 (t, $J = 6.6$ Hz, 2H), 1.74 – 1.69 (m, 2H), 1.68 – 1.61 (m, 2H), 1.46 – 1.40 (m, 2H), 1.39 –
1.31 (m, 1H), 1.30 – 1.04 (m, 4H), 0.97 – 0.85 (m, 2H).

$^1$H NMR (101 MHz, MeOH-$d_4$) $\delta$ 7.90 – 7.86 (m, 2H), 7.57 – 7.52 (m, 1H), 7.49 – 7.44 (m, 2H), 7.26 – 7.22 (m, 1H), 7.22 – 7.19 (m, 3H), 7.18 – 7.13 (m, 1H), 4.68 (s, 2H), 4.04 (s, 2H), 3.69 (t, $J$ = 7.0 Hz, 2H), 2.83 (t, $J$ = 7.1 Hz, 2H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 172.7, 170.5, 140.2, 135.0, 132.9, 129.9, 129.5, 129.3, 128.5, 127.1, 70.8, 70.3, 44.1, 37.1.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{20}$N$_2$O$_3$ ([M+Na]$^+$): 335.1366, found 335.1359.

2-33 was obtained as a white solid, Yield 74% (23 mg), Melting point 117 – 119 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.91 – 7.87 (m, 2H), 7.57 – 7.53 (m, 1H), 7.50 – 7.44 (m, 2H), 4.67 (s, 2H), 4.05 (s, 2H), 3.62 – 3.56 (m, 2H), 0.93 – 0.88 (m, 2H), 0.01 (s, 9H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 172.6, 170.4, 135.0, 132.9, 129.5, 128.5, 70.3, 66.6, 44.1, 18.8, -1.3.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{20}$N$_2$O$_3$Si ([M+Na]$^+$): 331.1448, found 331.1448.
**2-34** was obtained as a white solid, Yield 46% (15 mg), Melting point 111 – 113 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.91 – 7.86 (m, 2H), 7.59 – 7.52 (m, 1H), 7.51 – 7.44 (m, 2H), 7.28 – 7.21 (m, 2H), 6.94 – 6.88 (m, 3H), 4.78 (s, 2H), 4.11 – 4.06 (m, 4H), 3.86 – 3.83 (m, 2H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 172.79, 170.53, 160.24, 135.01, 132.93, 130.44, 129.56, 128.50, 121.86, 115.61, 71.21, 68.34, 68.11, 44.16.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{20}$N$_2$O$_4$ ([M+Na]$^+$): 351.1315, found 351.1306.

![2-35](image)

**2-35** was obtained as a white solid, Yield 56% (22 mg), Melting point 95 – 97 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ 7.90 – 7.86 (m, 2H), 7.58 – 7.44 (m, 4H), 7.34 – 7.30 (m, 1H), 7.26 – 7.21 (m, 1H), 7.12 – 7.06 (m, 1H), 4.70 (s, 2H), 4.05 (s, 2H), 3.71 (t, $J = 7.1$ Hz, 2H), 3.00 (t, $J = 7.1$ Hz, 2H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) $\delta$ 172.7, 170.5, 139.3, 135.0, 133.7, 132.9, 132.4, 129.5, 129.2, 128.6, 128.5, 125.4, 70.9, 68.5, 44.1, 37.2.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{19}$BrN$_2$O$_3$ ([M+Na]$^+$): 413.0471, found 413.0458.

![2-36](image)

**2-36** was obtained as a yellow solid, Yield 93% (23.5 mg), Melting point 115 – 117 °C.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 – 7.82 (m, 2H), 7.55 – 7.50 (m, 1H), 7.47 – 7.41 (m, 2H), 7.38 – 7.33 (m, 1H), 7.24 (d, $J = 7.0$ Hz, 1H), 4.42 (d, $J = 6.2$ Hz, 2H), 4.20 (d, $J = 5.1$ Hz, 2H), 2.64 – 2.58 (m, 2H), 1.26 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.2, 168.1, 133.4, 132.2, 128.8, 127.3, 44.1, 40.9, 25.3, 14.9.

HRMS (ESI, m/z) calcd for C$_{12}$H$_{16}$N$_2$O$_2$S ([M+Na]$^+$): 275.0825, found 275.0832.
2-37 was obtained as a white solid, Yield 96% (26.6 mg), Melting point 98 – 100 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.90 – 7.86 (m, 2H), 7.58 – 7.52 (m, 1H), 7.50 – 7.44 (m, 2H), 4.38 (s, 2H), 4.03 (s, 2H), 3.10 – 3.02 (m, 1H), 1.27 (d, $J = 6.7$ Hz, 6H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 171.5, 170.4, 135.0, 132.9, 129.5, 128.5, 44.1, 40.7, 35.2, 23.9.

HRMS (ESI, m/z) calcd for C$_{13}$H$_{18}$N$_2$O$_2$S ([M+Na]$^+$): 289.0981, found 289.0976.

2-38 was obtained as a white solid, Yield 93% (27.2 mg), Melting point 108 – 110 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.92 – 7.85 (m, 2H), 7.58 – 7.52 (m, 1H), 7.51 – 7.42 (m, 2H), 4.37 (s, 2H), 4.04 (s, 2H), 3.28 – 3.19 (m, 1H), 2.10 – 1.99 (m, 2H), 1.77 – 1.65 (m, 2H), 1.65 – 1.41 (m, 4H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 171.5, 170.4, 135.0, 132.9, 129.5, 128.5, 44.2, 44.1, 41.9, 35.0, 25.7.

HRMS (ESI, m/z) calcd for C$_{15}$H$_{20}$N$_2$O$_2$S ([M+Na]$^+$): 315.1138, found 315.1129.

2-39 was obtained as a yellow solid, Yield 75% (25 mg), Melting point 104 – 106 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) δ 7.90 – 7.85 (m, 2H), 7.57 – 7.52 (m, 1H), 7.49 – 7.43 (m, 2H), 7.29 – 7.11 (m, 5H), 4.38 (s, 2H), 4.04 (s, 2H), 2.94 – 2.87 (m, 2H), 2.86 – 2.81 (m, 2H).

$^{13}$C NMR (101 MHz, MeOH-$d_4$) δ 171.7, 170.5, 142.0, 135.0, 132.9, 129.7, 129.5, 129.4, 128.5, 127.2, 44.2, 41.5, 37.4, 33.3.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{20}$N$_2$O$_2$S ([M+Na]$^+$): 351.1138, found 351.1131.

S22
2-40 was obtained as a white solid, Yield 72% (34.2 mg), Melting point 85 – 87 °C.

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 8.81 – 8.75 (m, 2H), 8.61 – 8.55 (m, 2H), 7.90 – 7.87 (m, 4H), 7.57 – 7.51 (m, 2H), 7.50 – 7.45 (m, 4H), 4.29 (d, \(J = 6.3\) Hz, 4H), 3.87 (d, \(J = 5.9\) Hz, 4H), 2.97 – 2.94 (m, 2H), 2.88 – 2.86 (m, 2H).

\(^{13}\)C NMR (101 MHz, DMSO-\(d_6\)) \(\delta\) 169.8, 167.1, 134.6, 132.0, 128.9, 128.0, 43.4, 38.5, 30.4.

HRMS (ESI, m/z) calcd for C\(_{22}\)H\(_{26}\)N\(_4\)O\(_4\)S\(_2\) ([M+Na\(^+\)]: 497.1288, found 497.1288.

2-41 was obtained as a white oil, Yield 35% (14.3 mg, dr 1.3:1).

\(^1\)H NMR (400 MHz, MeOH-\(d_4\)) \(\delta\) 7.49 – 7.42 (m, 2H), 7.40 – 7.29 (m, 3H), 5.64 – 5.22 (m, 1H), 4.74 – 4.64 (m, 1H), 4.62 – 4.51 (m, 1H), 4.34 – 4.16 (m, 1H), 3.55 – 3.46 (m, 1H), 3.44 – 3.34 (m, 3H), 2.49 – 2.11 (m, 1H), 2.05 – 1.80 (m, 3H), [1.46 (s), 1.27 (s), 9H], 1.06 (t, \(J = 7.0\) Hz, 3H).

\(^{13}\)C NMR (101 MHz, MeOH-\(d_4\)) \(\delta\) 175.2, 173.2, 156.1, 138.8, 130.0, 129.9, 129.7, 129.5, 129.1, 81.5, 70.9, 64.7, 61.4, 58.9, 48.1, 32.5, 31.2, 28.9, 28.7, 25.5, 24.8, 15.5.

HRMS (ESI, m/z) calcd for C\(_{21}\)H\(_{31}\)N\(_3\)O\(_5\) ([M+Na\(^+\)]: 428.2156, found 428.2156.

2-42 was obtained as a white oil, Yield 64% (11.3 mg).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.27 (s, 1H), 4.61 (d, \(J = 7.2\) Hz, 2H), 3.53 (q, \(J = 7.0\) Hz, 2H), 1.45 (s, 9H), 1.20 (t, \(J = 7.0\) Hz, 3H).
13C NMR (101 MHz, CDCl3) δ 155.8, 80.1, 71.9, 63.6, 28.4, 15.3.

HRMS (ESI, m/z) calcd for C8H17NO3 ([M+Na]+): 198.1101, found 198.1102.

**Synthesis of compound 2-43**

\[
\begin{align*}
&\text{1a} + \text{CsOAc} \rightarrow \text{toluene} \rightarrow \text{2-43} \\
&\text{1a} (0.2 \text{ mmol}, 1.0 \text{ equiv}), \text{CsOAc} (0.4 \text{ mmol}, 2.0 \text{ equiv}) \text{ were placed to the screw cap vial followed by addition of Boc-Ser-OMe (1.0 mmol, 5.0 equiv) and toluene (2.0 mL). The resulting mixture was sealed and stirred at 120 °C for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure to obtain residue which was purified by a silica gel column chromatography (eluent: n-heptane/ethyl acetate = 1:4 v/v) to afford the desired product 2-43.}
\end{align*}
\]

2-43 was obtained as a white oil, Yield 20% (16.4 mg).

1H NMR (400 MHz, CDCl3) δ 7.84 (d, J = 7.7 Hz, 2H), 7.60 – 7.50 (m, 1H), 7.49 – 7.39 (m, 2H), 7.23 – 7.04 (m, 2H), 5.41 (d, J = 8.8 Hz, 1H), 4.76 (d, J = 6.7 Hz, 2H), 4.47 – 4.36 (m, 1H), 4.18 (d, J = 5.1 Hz, 2H), 3.96 – 3.89 (m, 1H), 3.81 – 3.73 (m, 1H), 3.72 (s, 3H), 1.43 (s, 9H).

13C NMR (101 MHz, CDCl3) δ 171.3, 170.2, 168.0, 155.7, 133.4, 132.2, 128.8, 127.3, 80.3, 70.6, 69.0, 54.0, 52.7, 44.0, 28.4.

HRMS (ESI, m/z) calcd for C19H27N3O7 ([M+Na]+): 432.1741, found 432.1739.

**Synthesis of compound 2-44**

\[
\begin{align*}
&\text{1a} + \text{CsOAc} \rightarrow \text{CH3CN} \rightarrow \text{2-44} \\
&\text{1a} (0.2 \text{ mmol}, 1.0 \text{ equiv}), \text{CsOAc} (0.4 \text{ mmol}, 2.0 \text{ equiv}) \text{ were placed to the screw cap vial followed by addition of Boc-Ser-OMe (1.0 mmol, 5.0 equiv) and CH3CN (2.0 mL). The resulting mixture was sealed and stirred at 120 °C for 12 h. After completion of the reaction, the mixture was evaporated under reduced pressure to obtain residue which was purified by a silica gel column chromatography (eluent: n-heptane/ethyl acetate = 1:4 v/v) to afford the desired product 2-44.}
\end{align*}
\]
1a (0.2 mmol, 1.0 equiv), CsOAc (0.4 mmol, 2.0 equiv) were placed to the screw cap vial followed by
addition of N-Boc-L-cysteine methyl ester (1.0 mmol, 5.0 equiv) and CH$_3$CN (2.0 mL). The resulting mixture
was sealed and stirred at 120 °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 = 1:4 v/v) to afford the desired product 2-44.

2-44 was obtained as a white oil, Yield 18% (15.4 mg).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 – 7.76 (m, 2H), 7.59 – 7.38 (m, 3H), 7.37 – 7.19 (m, 2H), 5.57 – 5.34 (m,
1H), 4.54 – 4.47 (m, 1H), 4.44 (d, $J$ = 4.3 Hz, 2H), 4.19 (d, $J$ = 4.9 Hz, 2H), 3.73 (s, 3H), 3.16 – 2.99 (m,
1H), 2.97 – 2.79 (m, 1H), 1.44 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.6, 169.3, 167.9, 155.8, 133.6, 132.1, 128.8, 127.4, 80.8, 54.1, 52.9, 43.9,
42.5, 35.1, 28.5.

HRMS (ESI, m/z) calcd for C$_{19}$H$_{27}$N$_3$O$_6$S ([M+Na]$^+$): 448.1513, found 448.1505.

Synthesis of compound 2-45

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 – 7.76 (m, 2H), 7.59 – 7.38 (m, 3H), 7.37 – 7.19 (m, 2H), 5.57 – 5.34 (m,
1H), 4.54 – 4.47 (m, 1H), 4.44 (d, $J$ = 4.3 Hz, 2H), 4.19 (d, $J$ = 4.9 Hz, 2H), 3.73 (s, 3H), 3.16 – 2.99 (m,
1H), 2.97 – 2.79 (m, 1H), 1.44 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.6, 169.3, 167.9, 155.8, 133.6, 132.1, 128.8, 127.4, 80.8, 54.1, 52.9, 43.9,
42.5, 35.1, 28.5.

HRMS (ESI, m/z) calcd for C$_{19}$H$_{27}$N$_3$O$_6$S ([M+Na]$^+$): 448.1513, found 448.1505.

Synthesis of compound 2-45

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 – 7.76 (m, 2H), 7.59 – 7.38 (m, 3H), 7.37 – 7.19 (m, 2H), 5.57 – 5.34 (m,
1H), 4.54 – 4.47 (m, 1H), 4.44 (d, $J$ = 4.3 Hz, 2H), 4.19 (d, $J$ = 4.9 Hz, 2H), 3.73 (s, 3H), 3.16 – 2.99 (m,
1H), 2.97 – 2.79 (m, 1H), 1.44 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.6, 169.3, 167.9, 155.8, 133.6, 132.1, 128.8, 127.4, 80.8, 54.1, 52.9, 43.9,
42.5, 35.1, 28.5.

HRMS (ESI, m/z) calcd for C$_{19}$H$_{27}$N$_3$O$_6$S ([M+Na]$^+$): 448.1513, found 448.1505.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (d, $J = 7.6$ Hz, 2H), 7.61 – 7.40 (m, 3H), 7.04 – 6.85 (m, 2H), 5.75 (d, $J = 3.7$ Hz, 1H), 5.05 – 4.82 (m, 2H), 4.75 – 4.63 (m, 1H), 4.44 – 4.32 (m, 1H), 4.30 – 3.84 (m, 6H), 1.58 (s, 3H), 1.48 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.0, 167.8, 133.4, 132.2, 128.9, 127.2, 113.1, 110.0, 104.1, 78.6, 78.4, 75.0, 70.3, 65.3, 43.9, 27.0, 26.4, 24.9.

HRMS (ESI, m/z) calcd for C$_{22}$H$_{30}$N$_2$O$_8$ ([M+Na]$^+$): 473.1894, found 473.1890.

6. References

7. Copies of $^1$H NMR and $^{13}$C NMR spectra for the Ugi adducts

$^1$H NMR spectra of compound 1c (400 MHz, DMSO-$d_6$)

$^{13}$C NMR spectra of compound 1c (101 MHz, DMSO-$d_6$)
$^1$H NMR spectra of compound 1d (400 MHz, DMSO-$d_6$)

$^{13}$C NMR spectra of compound 1d (101 MHz, DMSO-$d_6$)
$^1$H NMR spectra of compound 1e (400 MHz, DMSO-$d_6$)

Mixture of rotamers (~4:1)

$^{13}$C NMR spectra of compound 1e (101 MHz, DMSO-$d_6$)

Mixture of rotamers
$^{1}$H NMR spectra of compound 1f (400 MHz, DMSO-$d_6$)

13C NMR spectra of compound 1f (101 MHz, DMSO-$d_6$)
$^1$H NMR spectra of compound 1j (400 MHz, DMSO-$d_6$)

Mixture of rotamers (~3:1)

$^{13}$C NMR spectra of compound 1j (101 MHz, DMSO-$d_6$)

Mixture of rotamers
\(^1\)H NMR spectra of compound \(1q\) (400 MHz, DMSO-\(d_6\))

\(1^3C\) NMR spectra of compound \(1q\) (101 MHz, DMSO-\(d_6\))

Mixture of rotamers (~1.1:1)
$^1$H NMR spectra of compound 1v (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 1v (101 MHz, CDCl$_3$)
8. Copies of $^1$H NMR and $^{13}$C NMR spectra for the products

$^1$H NMR spectra of compound 2-1 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-1 (101 MHz, MeOH-$d_4$)
\[\text{1H NMR spectra of compound 2-2 (400 MHz, MeOH-}d_4)\]

\[\text{13C NMR spectra of compound 2-2 (101 MHz, MeOH-}d_4)\]
$^1$H NMR spectra of compound 2-3 (400 MHz, DMSO-$d_6$)

$^{13}$C NMR spectra of compound 2-3 (101 MHz, DMSO-$d_6$)
$^1$H NMR spectra of compound 2-4 (300 MHz, DMSO-$d_6$)

$^{13}$C NMR spectra of compound 2-4 (101 MHz, DMSO-$d_6$)
$^1$H NMR spectra of compound 2-5 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-5 (101 MHz, MeOH-$d_4$)
$^1$H NMR spectra of compound 2-6 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-6 (101 MHz, MeOH-$d_4$)
\textsuperscript{1}H NMR spectra of compound 2-7 (400 MHz, MeOH-\textit{d}_4)

\textsuperscript{13}C NMR spectra of compound 2-7 (101 MHz, MeOH-\textit{d}_4)
$^1$H NMR spectra of compound 2-8 (400 MHz, DMSO-$d_6$)

$^{13}$C NMR spectra of compound 2-8 (101 MHz, DMSO-$d_6$)
$^1$H NMR spectra of compound 2-9 (400 MHz, MeOH-$d_4$)

13C NMR spectra of compound 2-9 (101 MHz, MeOH-$d_4$)
$^1$H NMR spectra of compound 2-10 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-10 (101 MHz, CDCl$_3$)
$^1$H NMR spectra of compound 2-11 (400 MHz, MeOH-$d_4$)

Mixture of rotamers (~1:1)

$^{13}$C NMR spectra of compound 2-11 (101 MHz, MeOH-$d_4$)

Mixture of rotamers
$^1$H NMR spectra of compound 2-12 (400 MHz, MeOH-$d_4$)

Mixture of rotamers (~1:1)

$^{13}$C NMR spectra of compound 2-12 (101 MHz, MeOH-$d_4$)

Mixture of rotamers
$^1$H NMR spectra of compound 2-13 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-13 (101 MHz, CDCl$_3$)
$^1$H NMR spectra of compound 2-14 (400 MHz, MeOH-$d_4$)

Mixture of rotamers (~3:2)

$^{13}$C NMR spectra of compound 2-14 (101 MHz, MeOH-$d_4$)

Mixture of rotamers
$^1$H NMR spectra of compound 2-15 (400 MHz, MeOH-$d_4$)

Mixture of rotamers (~3:2)

$^{13}$C NMR spectra of compound 2-15 (101 MHz, MeOH-$d_4$)

Mixture of rotamers
$^1$H NMR spectra of compound 2-16 (400 MHz, MeOH-$d_4$)

Mixture of rotamers (~3:2)

$^{13}$C NMR spectra of compound 2-16 (101 MHz, MeOH-$d_4$)

Mixture of rotamers
\(^1\)H NMR spectra of compound 2-17 (400 MHz, MeOH-\(d_4\))

\[^13\]C NMR spectra of compound 2-17 (101 MHz, MeOH-\(d_4\))
$^1$H NMR spectra of compound 2-18 (400 MHz, MeOH-$d_4$)

Mixture of rotamers (~1:1)

$^{13}$C NMR spectra of compound 2-18 (101 MHz, MeOH-$d_4$)

Mixture of rotamers
\[ ^1\text{H NMR spectra of compound 2-19 (400 MHz, MeOH-}d_4) \]

\[ ^{13}\text{C NMR spectra of compound 2-19 (101 MHz, MeOH-}d_4) \]
\(^1\)H NMR spectra of compound 2-20 (400 MHz, MeOH-\(d_4\))

![H NMR spectra](image)

Mixture of rotamers (~1:1)

13\(^C\) NMR spectra of compound 2-20 (101 MHz, MeOH-\(d_4\))

![C NMR spectra](image)

Mixture of rotamers
$^1$H NMR spectra of compound 2-21 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-21 (101 MHz, MeOH-$d_4$)
$^1$H NMR spectra of compound 2-22 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-22 (101 MHz, CDCl$_3$)
\(^1\)H NMR spectra of compound 2-23 (400 MHz, MeOH-\(d_4\))

\(^{13}\)C NMR spectra of compound 2-23 (101 MHz, MeOH-\(d_4\))
$^1$H NMR spectra of compound 2-24 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-24 (101 MHz, CDCl$_3$)
$^1$H NMR spectra of compound 2-25 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-25 (101 MHz, CDCl$_3$)
$^1$H NMR spectra of compound 2-26 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-26 (101 MHz MeOH-$d_4$)
$^{1}$H NMR spectra of compound 2-27 (300 MHz, MeOH-$d_4$)

Mixture of rotamers (~4:1)

$^{13}$C NMR spectra of compound 2-27 (101 MHz MeOH-$d_4$)

Mixture of rotamers
$^1$H NMR spectra of compound 2-28 (400 MHz, MeOH-d$_4$)

$^{13}$C NMR spectra of compound 2-28 (101 MHz MeOH-d$_4$)
$^1$H NMR spectra of compound 2-29 (400 MHz, MeOH-$_d^4$)

$^{13}$C NMR spectra of compound 2-29 (101 MHz MeOH-$_d^4$)
$^1\text{H}$ NMR spectra of compound 2-30 (400 MHz, MeOH-$d_4$)

Mixture of rotamers (~4:1)

$^{13}\text{C}$ NMR spectra of compound 2-30 (101 MHz MeOH-$d_4$)

Mixture of rotamers
\(^1\)H NMR spectra of compound 2-31 (400 MHz, MeOH-\(d_4\))

\(^{13}\)C NMR spectra of compound 2-31 (101 MHz MeOH-\(d_4\))
$^1$H NMR spectra of compound 2-32 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-32 (101 MHz MeOH-$d_4$)
$^1$H NMR spectra of compound 2-33 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-33 (101 MHz MeOH-$d_4$)
$^1$H NMR spectra of compound 2-34 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-34 (101 MHz MeOH-$d_4$)
$^1$H NMR spectra of compound 2-35 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-35 (101 MHz, MeOH-$d_4$)
$^1$H NMR spectra of compound 2-36 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-36 (101 MHz, CDCl$_3$)
$^1$H NMR spectra of compound 2-37 (400 MHz, MeOH-$d_4$)

![H NMR spectrum image]

$^{13}$C NMR spectra of compound 2-37 (101 MHz, MeOH-$d_4$)

![C NMR spectrum image]
$^1$H NMR spectra of compound 2-38 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-38 (101 MHz, MeOH-$d_4$)
$^1$H NMR spectra of compound 2-39 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-39 (101 MHz, MeOH-$d_4$)
$^1$H NMR spectra of compound 2-40 (400 MHz, DMSO-$d_6$)

$^{13}$C NMR spectra of compound 2-40 (101 MHz, DMSO-$d_6$)
$^1$H NMR spectra of compound 2-41 (400 MHz, MeOH-$d_4$)

$^{13}$C NMR spectra of compound 2-41 (101 MHz, MeOH-$d_4$)
$^1$H NMR spectra of compound 2-42 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-42 (101 MHz, CDCl$_3$)

2-42
$^1$H NMR spectra of compound 2-43 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-43 (101 MHz, CDCl$_3$)
$^1$H NMR spectra of compound 2-44 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-44 (101 MHz, CDCl$_3$)
$^1$H NMR spectra of compound 2-45 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectra of compound 2-45 (101 MHz, CDCl$_3$)