Supporting Information

Combinatorial Aid for Underprivileged Scaffolds: Solution and Solid-phase Strategies for a Rapid and Efficient Access To Novel Aza-diketopiperazines (Aza-DKP)

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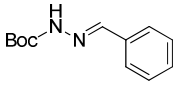
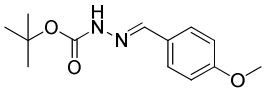
General methods. Reagents were obtained from commercial sources and used without any further purification. Fmoc-protected amino acid loaded on Wang resin were purchased from Aldrich and the overall yields for the solid-phase syntheses of aza-DKPs were calculated based on the initial loadings provided by the supplier. Solid-phase reactions conducted at room temperature were performed in polypropylene tubes equipped with polyethylene frits and polypropylene caps using an orbital agitator shaking device. Solid-phase reactions at 70°C were conducted in sealed glassware tubes using the Chemflex rotating oven from Robbins Scientific as the shaking device. Thin-layer chromatography was performed on silica gel $60F_{254}$ plates. Flash chromatography was performed on silica gel (40 µm, Grace) or RP18 (25-40 µm, Merck) pre-packed columns on a SpotII ultima from Armen. ^{1}H NMR spectra were recorded at 200, 300 et 500 MHz on a Bruker Advance spectrometer. Chemical shifts are reported in parts per million (ppm), coupling constants (*J*) are reported in hertz (Hz). LC/MS spectra were obtained on a ZQ (Z quadripole) Waters/Micromass spectrometer equipped with an X-Terra C18 column (4.6 x 50 mm, 3.5 µm) using electrospray ionisation mode (ESI). Analytical HPLC analyses were performed on a Chromolith SpeedROD column (50 x 4.6 mm, C_{18}) from Merck using the following conditions: flow rate 7 $mL.min^{-1}$. Buffer A: 0.1% aqueous TFA. Buffer B: 0.1% TFA in CH_3CN. Gradient: 0% B in 1 min than 0-100% B over 5 min. Detection at 220/254 nm. Retention times (t_R) from analytical RP-HPLC are reported in minutes.

N'-Benzylidene-*tert*-butyl carbazate **5a**.



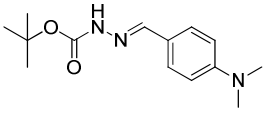
White crystalline solid. mp 185 – 186 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (br s, 1H), 7.84 (br s, 1H), 7.69 – 7.66 (m, 2H), 7.37 – 7.35 (m, 3H), 1.54 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 143.8, 134.1, 129.9, 128.6, 127.3, 81.5, 28.4. MS (ESI) *m*/*z* 221.1 [M + H^+].

N'-(4-Methoxy-benzylidene)-*tert*-butyl carbazate **5b**.



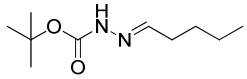
White crystalline solid. mp 133 – 134 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 and 7.78 (2 x br s, 2H), 7.62 (d, 2H, *J* = 8.8 Hz), 6.89 (d, 2H, *J* = 8.8 Hz), 3.82 (s, 3H), 1.53 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 152.9, 143.8, 128.8, 126.9, 114.1, 81.3, 55.4, 28.4. MS (ESI) *m*/*z* 251.1 [M + H^+].

N'-(4-Dimethylamino-benzylidene)-*tert*-butyl carbazate **5c**.



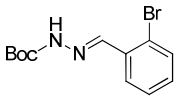
White crystalline solid. mp 156 – 157 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.65 (s, 1H), 7.55 (d, 2H, J = 8.8 Hz), 6.67 (d, 2H, J = 8.8 Hz), 3.00 (s, 6H), 1.53 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4, 151.6, 144.7, 128.7, 121.9, 111.9, 81.0, 40.3, 28.5. MS (ESI) *m*/*z* 264.2 [M + H^+].

N'-Pentylidene-*tert*-butyl carbazate **5d**.



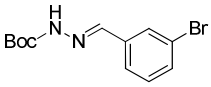
Product did not crystallize from toluene, the solvent was removed *in vacuo* and the residue triturated with hexane to give the product as a fine white crystalline solid. mp 54 – 56 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (br s, 1H), 7.14 (t, 1H, *J* = 5.7 Hz), 2.29 (dt, 2H, *J* = 7.9, 5.7 Hz), 1.50 (s, 9H), 1.53 – 1.44 (m, 2H), 1.41 – 1.29 (m, 2H), 0.91 (t, 3H, *J* = 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 147.7, 80.9, 32.0, 28.9, 28.4, 22.5, 13.9. MS (ESI) *m*/*z* 201.1 [M + H^+].

N'-(2-Bromo-benzylidene)-*tert*-butyl carbazate **5e**.



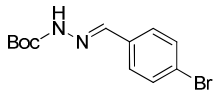
White crystalline solid. mp 179 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (br s, 1H), 8.22 (br s, 1H), 8.07 (d, 1H, *J* = 7.8 Hz), 7.52 (d, 1H, *J* = 7.8 Hz), 7.31 – 7.26 (m, 1H), 7.21 – 7.16 (m, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 142.4, 133.0, 131.0, 129.2, 128.1, 127.7, 123.8, 81.8, 28.4. MS (ESI) *m*/*z* 623.0, 621.0, 619.0 [2M + Na^+] (1:2:1 ratio).

N'-(3-Bromo-benzylidene)-*tert*-butyl carbazate **5f**.



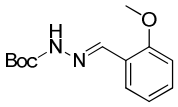
White crystalline solid. mp 131 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (br s, 1H), 7.85 (br s, 1H), 7.80 (br s, 1H), 7.57 (d, 1H, *J* = 8.0 Hz), 7.47 (ddd, 1H, *J* = 8.0, 2.0, 1.0 Hz), 7.36 – 7.22 (m, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 142.2, 136.2, 132.8, 130.2, 129.9, 125.9, 123.0, 81.9, 28.4. MS (ESI) *m*/*z* 623.0, 621.0, 619.0 [2M + Na^+] (1:2:1 ratio).

N'-(4-Bromo-benzylidene)-*tert*-butyl carbazate **5g**.



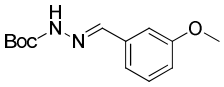
White crystalline solid. mp 155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (br s, 1H), 7.81 (br s, 1H), 7.54 (d, 2H, *J* = 8.5 Hz), 7.49 (d, 2H, *J* = 8.5 Hz), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 142.5, 133.1, 132.0, 128.7, 124.1, 81.8, 28.4. MS (ESI *m*/*z* 623.0, 621.0, 619.0 [2M + Na^+] (1:2:1 ratio).

N'-(2-Methoxy-benzylidene)-*tert*-butyl carbazate **5h**.



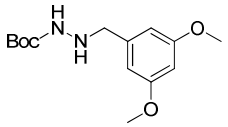
White crystalline solid. mp 135 – 136 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (br s, 1H), 8.00 (dd, 1H, *J* = 7.7, 1.6 Hz), 7.90 (br s, 1H), 7.31 (ddd, 1H, *J* = 8.4, 7.3, 1.6 Hz), 6.98 – 6.93 (m, 1H), 6.87 (dd, 1H, *J* = 8.4, 0.7 Hz), 3.83 (s, 3H), 1.53 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 139.6, 135.5, 131.1, 126.8, 122.6, 121.0, 111.0, 81.3, 55.6, 28.4. MS (ESI) *m*/*z* 251.1 [M + H^+].

N'-(3-Methoxy-benzylidene)-*tert*-butyl carbazate **5i**.



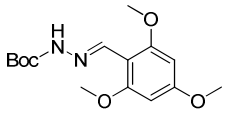
White crystalline solid. mp 121 – 122 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (br s, 1H), 7.81 (br s, 1H), 7.31 – 7.29 (m, 1H), 7.28 – 7.24 (m, 1H), 7.18 – 7.15 (m, 1H), 6.91 (ddd, 1H, *J* = 8.2, 2.7, 1.1 Hz), 3.83 (s, 3H), 1.54 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 152.8, 143.9, 135.5, 129.5, 120.6, 116.7, 110.7, 81.4, 55.3, 28.3. MS (ESI) *m*/*z* 273.1 [M + Na^+].

N'-(3,5-Dimethoxy-benzylidene)-*tert*-butyl carbazate **5j**.



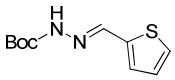
White crystalline solid. mp 161 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (br s, 1H), 7.76 (br s, 1H), 6.83 – 6.82 (m, 2H), 6.47 – 6.45 (m, 1H), 3.80 (s, 6H), 1.54 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 152.8, 143.9, 136.1, 105.0, 102.8, 81.4, 55.5, 28.4. MS (ESI) *m/z* 305.2 [M + Na^+].

N'-(2,4,6-Trimethoxy-benzylidene)-*tert*-butyl carbazate **5k**.



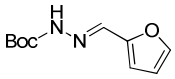
White crystalline solid. mp 172 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (br s, 1H), 7.69 (br s, 1H), 6.11 (s, 2H), 3.85 (s, 9H), 1.53 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 160.4, 152.6, 139.7, 104.5, 90.7, 80.6, 56.0, 55.3, 28.3. MS (ESI) *m/z* 311.2 [M + H^+].

N'-Thiophen-2-ylmethylene-*tert*-butyl carbazate **5l**.



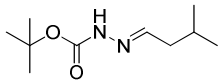
White crystalline solid. mp 194 – 195 °C. H NMR (300 MHz, $CDCl_3$) δ 8.17 (br s, 1H), 7.77 (br s, 1H), 7.35 – 7.33 (m, 1H); 7.20 (dd, 1H, *J* = 3.7, 0.9 Hz), 7.02 (dd, 1H, *J* = 5.1, 3.7 Hz), 1.53 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 139.1, 129.0, 127.9, 127.2, 81.5, 28.3. MS (ESI) *m/z* 453.2 [2M + H^+].

N'-Furan-2-ylmethylene-*tert*-butyl carbazate **5m**.



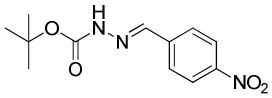
White crystalline solid. mp 161 – 162 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (br s, 1H), 7.90 (br s, 1H), 7.46 (dd, 1H, *J* = 1.8, 0.7 Hz), 6.71 (dd, 1H, *J* = 3.3 Hz), 6.45 (dd, 1H, *J* = 3.3, 1.8 Hz), 1.53 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.5, 149.6, 143.9, 134.3, 111.7, 81.5, 28.3. MS (ESI) *m*/*z* 438.2 [2M + NH_4^+].

N'-(3-methylbutylidene)-*tert*-butyl carbazate **5n**.



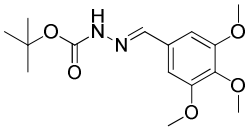
White solid. mp 97-98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (sl, 1H), 7.16 (t, 1H, *J* = 5.6 Hz), 2.15 (t, 2H, *J* = 6.8 Hz), 1.46 (s, 9H), 0.91 (d, 6H, *J* = 6.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 146.9, 80.8, 40.9, 28.3, 26.9, 22.4. MS (ESI) *m*/*z* 201.2 [M + H^+].

N'-(4-Nitro-benzylidene)-*tert*-butyl carbazate **5o**.



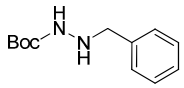
Yellow crystalline solid. mp 165 – 166 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (d, 2H, *J* = 8.8 Hz), 8.10 (br s, 1H), 7.96 (br s, 1H), 7.83 (d, 2H, *J* = 8.8 Hz), 1.55 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 148.3, 140.8, 140.3, 127.7, 124.1, 82.4, 28.3. MS (ESI) *m*/*z* 288.1 [M + Na^+].

N'-(3,4,5-Trimethoxy-benzylidene)-*tert*-butyl carbazate **5p**.



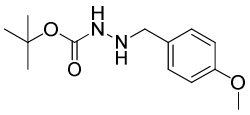
White crystalline solid. mp 167 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 and 7.77 (2 x br s, 2H), 6.91 (s, 2H), 3.88 (s, 9H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 143.7, 139.6, 129.6, 129.1, 104.3, 81.5, 60.9, 56.2, 28.4. MS (ES^+) *m*/*z* 311.2 [M + H^+].

N'-Benzyl-*tert*-butyl carbazate **6a**.



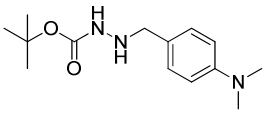
Clear oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 5H), 6.10 (br s, 1H), 4.20 (br s, 1H), 4.01 (s, 2H), 1.47 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 137.7, 129.1, 128.6, 127.6, 80.7, 55.9, 28.5. MS (ESI) *m/z* 223.1 [M + H^+].

N'-(4-Methoxybenzyl)-*tert*-butyl carbazate **6b**.



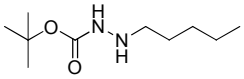
Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, 2H, *J* = 8.8 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 6.04 (br s, 1H), 3.91 (s, 2H), 3.80 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 156.8, 130.4, 129.6, 114.1, 80.8, 55.3, 55.3, 28.5. MS (ESI) *m/z* 275.1 [M + Na^+].

N'-(4-Dimethylaminobenzyl)-*tert*-butyl carbazate **6c**.



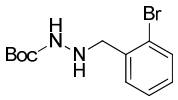
Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (d, 2H, *J* = 8.8 Hz), 6.71 (d, 2H, *J* = 8.8 Hz), 3.88 (s, 2H), 2.94 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 150.3, 130.1, 125.0, 112.8, 80.7, 55.5, 40.7, 28.5. MS (ESI) *m/z* 288.2 [M + Na^+].

N'-Pentyl-*tert*-butyl carbazate **6d**.



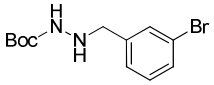
Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.02 (br s, 1H), 2.82 (t, 2H, *J* = 7.1 Hz), 1.49 (s, 9H), 1.33 – 1.30 (m, 4H), 0.92 – 0.87 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.1, 80.7, 52.4, 29.4, 28.5, 27.6, 22.7, 14.1. MS (ESI) *m/z* 203.2 [M+H^+].

N'-(2-Bromobenzyl)-*tert*-butyl carbazate **6e**.



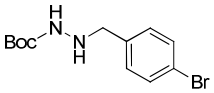
White crystalline solid. mp 70 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (dd, 1H, *J* = 7.7, 1.3 Hz), 7.40 (dd, 1H, *J* = 7.7, 1.8 Hz), 7.28 (td, 1H, *J* = 7.7, 1.3 Hz), 7.14 (td, 1H, *J* = 7.7, 1.8 Hz), 6.04 (br s, 1H), 4.33 (br s, 1H), 4.10 (s, 2H), 1.45 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 137.1, 133.0, 131.1, 129.2, 127.5, 124.8, 80.7, 55.9, 28.5. MS (ESI): *m*/*z* 303.0, 301.0 [M + H^+] (1:1 ratio).

N'-(3-Bromobenzyl-*tert*-butyl carbazate **6f**.



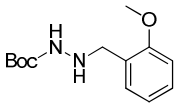
White crystalline solid. mp 68 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (br s, 1H), 7.42 – 7.38 (m, 1H), 7.27 – 7.25 (m, 1H), 7.20 (t, 1H, *J* = 7.7 Hz), 6.14 (br s, 1H), 4.23 (br s, 1H), 3.99 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 140.3, 132.0, 130.7, 130.1, 127.6, 122.6, 80.8, 55.2, 28.5. MS (ESI): *m*/*z* 325.0, 323.0 [M + Na^+] (1:1 ratio).

N'-(4-Bromobenzyl)-*tert*-butyl carbazate **6g**.



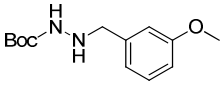
White crystalline solid. mp 74 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, 2H, *J* = 7.4 Hz), 7.24 (d, 1H, *J* = 7.4 Hz), 7.21 (d, 1H, *J* = 7.4 Hz), 6.02 (br s, 1H), 4.20 (br s, 1H), 3.94 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 136.9, 131.7, 130.8, 121.5, 80.8, 55.3, 28.5. MS (ESI) *m*/*z*, 303.0, 301.0 [M+H^+] (1:1 ratio).

N'-(2-Methoxybenzyl)-*tert*-butyl carbazate **6h**.



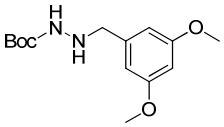
White crystalline solid. mp 60-61 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 – 7.24 (m, 2H), 6.95 – 6.86 (m, 2H), 5.93 (br s, 1H), 4.01 (s, 2H), 3.85 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 156.6, 130.8, 129.0, 125.9, 120.5, 110.5, 80.3, 55.5, 51.5, 28.5. MS (ESI) *m*/*z* 253.1 [M + H^+].

N'-(3-Methoxybenzyl)-*tert*-butyl carbazate **6i**.



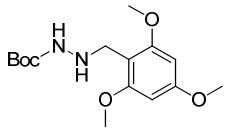
Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 1H), 6.94 – 6.91 (m, 2H), 6.84 – 6.80 (m, 1H), 6.06 (br s, 1H), 4.20 (br s, 1H), 3.97 (s, 2H), 3.80 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 156.8, 139.4, 129.5, 121.3, 114.3, 113.2, 80.5, 55.8, 55.3, 28.4. MS (ESI) *m*/*z* 505.3 [2M + H^+].

N'-(3,5-Dimethoxybenzyl)-*tert*-butyl carbazate **6j**.



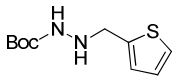
White crystalline solid. mp 45-46 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.52 – 6.51 (d, 2H, *J* = 2.2 Hz), 6.38 (t, 2H, *J* = 2.2 Hz), 6.01 (br s, 1H), 4.20 (br s, 1H), 3.94 (s, 2H), 3.79 (s, 6H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 156.7, 140.2, 106.7, 99.7, 80.5, 55.9, 55.4, 28.4. MS (ESI) *m*/*z* 565.3 [2M + H^+].

N'-(2,4,6-Trimethoxybenzyl)-*tert*-butyl carbazate **6k**.



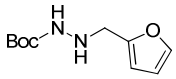
Clear colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (s, 2H), 5.91 (br s, 1H), 4.01 (s, 2H), 3.81 (s, 9H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 159.9, 156.5, 106.5, 90.5, 79.8, 55.8, 55.3, 43.9, 28.4. MS (ESI) *m/z* 625.3 [2M + H^+].

N'-Thiophen-2-ylmethyl-*tert*-butyl carbazate **6l**.



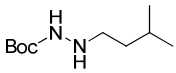
White crystalline solid. mp 31 – 32 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 1H), 7.0 – 6.95 (m, 2H), 6.22 (br s, 1H), 4.28 (br s, 1H), 4.19 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 140.8, 126.9, 126.4, 125.3, 80.8, 50.4, 28.5. MS (ESI) *m/z* 229.1 [M + H^+].

N'-Furan-2-ylmethyl-*tert*-butyl carbazate **6m**.



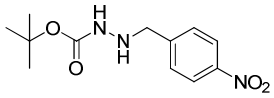
White crystalline solid. mp 44 – 45 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 1H), 6.32 – 6.31 (m, 1H), 6.24 – 6.23 (m, 2H), 4.22 (br s, 1H), 3.99 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 151.7, 142.4, 110.3, 108.5, 80.7, 48.5, 28.4. MS (ESI) *m/z* 235.2 [M + Na^+].

N'-isopentyl-*tert*-butyl carbazate **6n**.



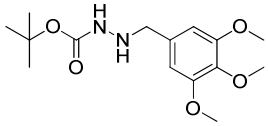
Colourless oil. ^{1}H RMN (400 MHz, $CDCl_3$) δ 2.88 (t, 2H, *J* = 7.6 Hz), 1.68-1.60 (m, 1H), 1.47 (s, 9H), 1.40-1.34 (m, 2H), 0.90 (d, 6H, *J* = 6.8 Hz). ^{13}C RMN (100 MHz, $CDCl_3$) δ 156.7, 80.8, 50.5, 36.6, 28.5, 26.1, 22.8. (ES^+) *m/z* 147.2. MS (ESI) *m/z* 203.1 [$M+H^+$].

N'-(4-Nitrobenzyl)-*tert*-butyl carbazate **6o**.



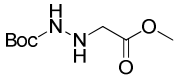
Yellow crystalline solid. mp 89 – 90 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, 2H, *J* = 9.0 Hz), 7.53 (d, 2H, *J* = 9.0 Hz), 6.00 (br s, 1H), 4.32 (br s, 1H), 4.11 (d, 2H, *J* = 3.8 Hz), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.5, 145.7, 136.6, 129.6, 123.8, 81.1, 55.1, 28.4. MS (ESI) *m/z* 535.2 [$2M + H^+$].

N'-(3,4,5-Trimethoxybenzyl)-*tert*-butyl carbazate **6p**.



White crystalline solid. mp 62 – 64 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.59 (s, 2H), 6.04 (br s, 1H), 3.94 (s, 2H), 3.86 (s, 9H), 1.47 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 153.5, 137.7, 131.4, 106.3, 82.1, 60.9, 56.3, 56.2, 28.2, 20.8. MS (ESI) *m/z* 313.2 [$M+H^+$]

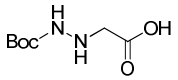
Boc-Aza-β^3-glycine methyl ester **7**.



The title compound was prepared according to a published procedure (Huang, N. *et al*, *J. Med. Chem.* **2010**, 53, 5229-5239). Colourless oil (78% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.50 (br s, 1H), 4.23 (q, 2H, *J* = 7.2 Hz), 4.07 (br s, 1H), 3.68 (s, 2H), 1.46 (s, 9H), 1.29 (t,

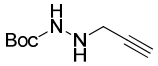
3H, J = 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 156.1, 81.0, 61.1, 52.8, 28.2, 14.2. MS (ESI) *m/z* 204.1 [M + Na^+].

Boc-Aza-β^3-glycine **8**.



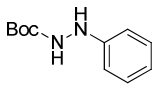
Lithium hydroxide (227 mg, 9.5 mmol) was added to a solution of **7** (206.6 mg, 0.95 mmol) in dioxane/water : 2/1 (9.4 mL). The mixture was heated at 40°C for 1 hour and cooled to room temperature. The pH of the solution was adjusted to pH 4 by adding solid citric acid and the mixture was extracted with DCM. The combined organic extracts were washed with brine, dried over sodium sulfate, and the solvent was removed *in vacuo* to afford **8** (132.5 mg, 79% yield) as an off-white solid. mp 144.4°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 2H), 3.06 (br s, 1H), 3.68 (s, 2H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 156.1, 81.2, 67.0, 52.5, 28.2. MS (ESI) *m/z* 189.1 [M-H^+].

N'-Prop-2-ynyl-*tert*-butyl carbazate **9**.



The title compound was prepared according to a published procedure (Bare, T.M. *et al*, *J. Med. Chem.* **2007**, 50, 3113-3131). White solid (48% yield). mp 62.5 °C. ^{1}H RMN (400 MHz, $CDCl_3$) δ 4.51 (s, 1H), 3.85 (s, 2H), 1.69 (s, 9H). ^{13}C RMN (100 MHz, $CDCl_3$) δ 156.3, δ 80.2, 80.0, 72.2, 40.8, 28.1. MS (ESI) *m/z* 171.0 [M+H^+].

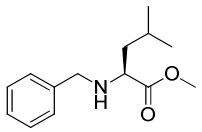
N'-Phenyl-*tert*-butyl carbazate **10**.



A solution of di-*tert*-butyl dicarbonate (2.02 g, 2.25 mmol) in dichloromethane (10 mL) was added to a stirred ice-cold solution of phenyl hydrazine (1.00 g, 9.25 mmol) in dichloromethane (10mL). The reaction was heated to reflux for 2.5h and the solvent was then removed *in vacuo*. The crude product was purified by column chromatography (50% ethyl acetate/hexane) to give the title compound as a crystalline white solid (1.39 g, 72%). mp 86 – 87 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 2H), 6.90 – 6.81 (m, 3H), 6.34 (br s, 1H), 5.71 (br s, 1H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 146.8, 129.3, 121.0, 113.2, 81.4, 28.4. MS (ESI) *m*/*z* 439.1 [2M + Na^+].

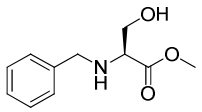
General procedure for the synthesis of *N*-alkyl-amino acid methyl esters 2a-2f. A solution of the amino acid methyl ester hydrochloride (5 mmol, 1 equiv), triethylamine (5 mmol, 1 equiv) and dried magnesium sulfate (1.00 g) in MeOH (10 mL) was stirred for approximately 10 minutes at room temperature. The aldehyde (5 mmol, 1 equiv) was added and the reaction mixture stirred at room temperature overnight. The reaction mixture was then filtered to remove the $MgSO_4$. Sodium borohydride (10 mmol, 2 equiv) was added portion-wise and the reaction mixture was stirred for a further 1 h. NaOH $_{(aq.)}$ (1 N, 20 mL) was added to the reaction mixture, and the aqueous layer was extracted with diethyl ether (3 x 30 mL). The combined organic extrcts were washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (10 - 50% ethyl acetate/hexane) to give the pure title compound.

N-Benzyl-(S)-leucine methyl ester **2a**.



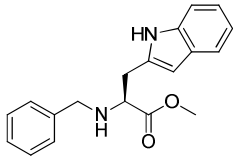
Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 5H), 3.80 (d, 1H, *J* = 12.8 Hz), 3.71 (s, 3H), 3.60 (d, 1H, *J* = 12.8 Hz), 3.30 (t, 1H, *J* = 7.3 Hz), 1.85 – 1.71 (m, 2H), 1.50 – 1.43 (m, 2H), 0.91 (d, 3H, *J* = 6.6 Hz), 0.84 (d, 3H, *J* = 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 140.1, 128.4, 128.3, 127.1, 59.4, 52.3, 51.7, 43.0, 25.0, 22.9, 22.3. MS (ESI) *m/z* 236.1 [M + H^+].

N-Benzyl-(*S*)-serine methyl ester **2b**.



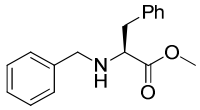
Colourless oil. $[\alpha]_D$ – 44.9 (*c* 0.5, $CHCl_3$, 26 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H), 3.88 (d, 1H, *J* = 12.8 Hz), 3.80 – 3.76 (m, 2H), 3.74 (s, 3H), 3.61 (dd, 1H, *J* = 10.7, 6.0 Hz), 3.43 (dd, 1H, *J* = 6.0, 4.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 139.4, 128.7, 128.4, 127.5, 62.6, 62.0, 52.30, 52.25. MS (ESI) *m/z* 210.1 [M + H^+].

N-Benzyl-(*S*)-tryptophan methyl ester **2c**.



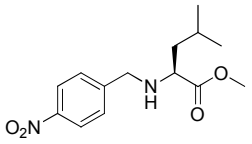
Colourless oil. $[\alpha]_D$ – 7.8 (*c* 0.5, $CHCl_3$, 26 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.57 (d, 1H, *J* = 8.1 Hz), 7.37 – 7.00 (m, 9H), 3.82 (d, 1H, *J* = 13.2 Hz), 3.71 – 3.64 (m, 2H, m), 3.62 (s, 3H), 3.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 139.9, 136.3, 128.5, 128.3, 128.1, 127.5, 122.7, 122.1, 119.4, 118.8, 111.4, 111.1, 61.3, 52.1, 51.7, 29.3. MS (ESI) *m/z* 309.2 [M + H^+].

N-Benzyl-(*S)*-phenylalanine methyl ester **2d**.



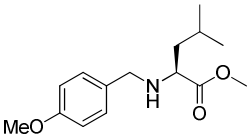
Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 – 7.15 (m, 10H), 3.83 – 3.64 (m, 2H), 3.65 (s, 3H), 3.54 (t, 1H, *J* = 6.8 Hz), 2.96 (d, 2H, *J* = 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.6, 140.2, 137.9, 129.8, 128.9, 128.8, 128.7, 127.6, 127.2, 62.6, 52.6, 52.2, 40.3. MS (ESI) *m/z* 270.1 [M+H^+].

N-(4-Nitrobenzyl)-(*S*)-leucine methyl ester **2e**.



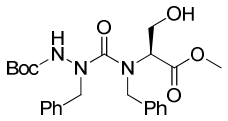
Crystalline white solid. mp 167 °C. $[\alpha]_D$ – 1.54 (*c* 0.7, MeOH, 26 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (d, 2H, *J* = 8.4 Hz), 7.90 (d, 2H, *J* = 8.4 Hz), 4.33 (d, 1H, *J* = 13.9 Hz), 4.27 (d, 1H, *J* = 13.9 Hz), 3.80 (s, 3H), 3.60 (t, 1H, *J* = 6.8 Hz), 1.99 – 1.79 (m, 3H), 0.89 (d, 3H, *J* = 6.6 Hz), 0.88 (d, 3H, *J* = 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 147.8, 130.5, 128.7, 123.6, 59.3, 51.7, 51.3, 42.8, 24.9, 22.8, 22.0. MS (ESI) *m/z* 281.1 [M + H$^+$].

N-(4-Methoxybenzyl)-(*S*)-leucine methyl ester **2f**.



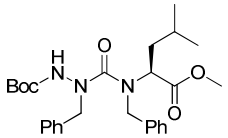
Colourless oil. $[\alpha]_D$ – 31.17 (*c* 1.5, $CDCl_3$, 27 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, 2H, *J* = 8.6 Hz), 6.85 (d, 2H, d, *J* = 8.6 Hz), 3.79 (s, 3H), 3.78 (d, 1H, 11.7 Hz), 3.72 (s, 3H), 3.55 (d, 1H, *J* = 11.7 Hz), 3.29 (t, 1H, *J* = 7.3 Hz), 1.76 (spet, 1H, *J* = 7.0 Hz), 1.46 (t, 2H, *J* = 7.3 Hz), 0.91 (d, 3H, *J* = 6.6 Hz, C<u>H</u>$_3$), 0.85 (d, 3H, *J* = 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.7, 158.8, 132.2, 129.6, 113.9, 59.3, 55.4, 51.7, 51.6, 42.9, 25.0, 22.9, 22.3. MS (ESI) *m/z* 266.2 [M + H$^+$].

Boc-Aza-phenylalaninyl-*N*-benzyl-serine methyl ester **3a**.



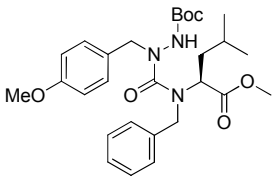
Colourless oil. $[\alpha]_D$ -16.6 (*c* 1.0, $CHCl_3$, 27 °C). ^{1}H NMR (400 MHz, $CDCl_3$, rotamers) δ 7.28 – 7.18 (m, 10H), 4.82 (d, 1H, *J* = 14.6 Hz), 4.55 (s, 2H), 4.33 (dd, 1H, *J* = 9.5, 9.0 Hz), 4.27 (dd, 1H, *J* = 9.0, 5.0 Hz), 4.17 (dd, 1H, *J* = 14.6 Hz), 4.03 (dd, 1H, *J* = 9.5, 5.0 Hz), 3.70 and 3.67 (2 x s, 3H), 1.36 and 1.24 (2 x s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, rotamers) δ 171.2 and 170.0, 157.7, 137.3, 135.2 (x 2), 129.3, 128.9, 128.8, 128.6, 128.4, 127.0, 127.4, 127.0, 82.4, 64.4, 56.0, 52.9, 52.4 and 53.3, 47.5, 28.2. MS (ESI) *m*/*z* 458.2 [M + H^+].

Boc-Aza-benzylglycinyl-*N*-benzyl-leucine methyl ester **3c**.



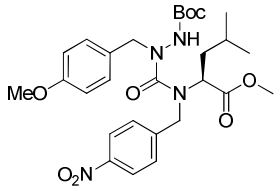
Colourless oil. $[\alpha]_D$ -24.0 (*c* 0.5, $CHCl_3$, 24 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.71 (m, 2H), 7.36 – 7.10 (m, 8H), 3.73 (d, 1H, *J* = 12.8 Hz), 3.64 (s, 3H), 3.54 (d, 1H, *J* = 12.8 Hz), 3.23 (m, 1H), 1.81 – 1.64 (m, 1H), 1.56 (s, 9H), 1.43 – 1.38 (m, 2H), 0.85 (d, 3H, *J* = 6.6 Hz), 0.77 (d, 3H, *J* = 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 153.4, 140.1, 136.5, 129.2, 128.5, 128.4, 127.1, 126.6, 125.5, 118.0, 88.2, 59.4, 52.3, 51.7, 43.0, 27.9, 25.0, 22.9, 22.3. MS (ESI) *m*/*z* 484.3 [M+H^+].

Boc-Aza-4-methoxyphenylalaninyl-*N*-benzyl-leucine methyl ester **3d**.



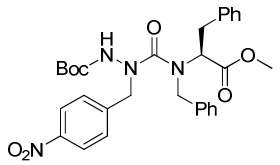
Colourless oil. $[\alpha]_D$ + 1.3 (*c* 0.5, MeOH, 26 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (br s, 1H), 7.56 (d, 2H, *J* = 6.5 Hz), 7.38 – 7.05 (m, 5H), 6.96 – 6.58 (m, 2H), 4.69 – 4.58 (m, 2H), 4.12 (s, 2H), 3.79 – 3.63 (m, 6H), 3.56 – 3.46 (m, 1H), 2.03 – 1.49 (m, 3H), 1.44 – 1.15 (m, 9H), 0.88 – 0.60 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rotamers) δ 173.0, 168.7, 162.0, 159.1, 153.6, 138.1, 130.9, 130.4, 129.6, 129.0, 128.3, 127.4, 127.0, 114.1, 113.9, 82.2, 58.9, 56.5, 55.2, 52.8, 51.9, 49.5, 38.5, 34.4, 28.0, 24.7, 22.6, 21.4. MS (ESI) *m*/*z* 514.2 [M + H$^+$].

Boc-Aza-4-methoxyphenylalaninyl-*N*-(4-nitrobenzyl)-leucine methyl ester **3e**.



Colourless oil. $[\alpha]_D$ – 11.7 (*c* 0.5, $CHCl_3$, 27 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, 2H, *J* = 8.8 Hz), 7.58 (d, 2H, *J* = 8.8 Hz), 7.02 (d, 2H, *J* = 8.8 Hz), 6.79 (d, 2H, *J* = 8.8 Hz), 5.85 (br s, 1H), 4.59 (s, 2H), 4.39 – 4.33 (m, 3H), 3.79 (s, 3H), 3.71 (s, 3H), 1.84 – 1.61 (m, 3H), 1.39 (s, 9H), 0.92 (d, 3H, *J*= 6.6 Hz), 0.87 (d, 3H, *J* = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 163.4, 159.8, 154.6, 147.4, 146.9, 143.0, 131.0, 128.8, 123.8, 114.5, 82.0, 59.8, 55.7, 52.8, 52.5, 50.0, 39.9, 28.5, 25.6, 23.2, 22.3. MS (ESI) *m*/*z* 559.2 [M + H$^+$].

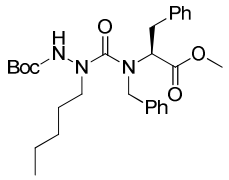
Boc-Aza-4-nitrophenylalaninyl-*N*-benzyl-phenylalanine methyl ester **3f**.



Colourless oil. $[\alpha]_D$ – 32.8 (*c* 0.5, $CHCl_3$, 25 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 – 8.07 (m, 2H), 7.44 – 7.41 (m, 2H), 7.28 – 7.07 (m, 10H), 4.79 (s, 2H), 3.86 (d, 1H, *J* = 13.5 Hz), 3.77 (d, 1H, *J* = 13.5 Hz), 3.61 – 3.57 (m, 1H), 3.54 (s, 3H), 3.12 (dd, 1H, *J* = 13.5, 6.2 Hz),

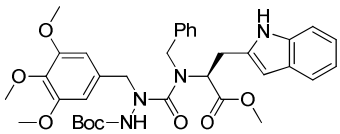
3.03 (dd, 1H, J = 13.5, 7.7 Hz), 1.44 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, rotamers) δ 172.5 and 171.6, 153.5 and 151.6, 147.9 and 147.6, 144.0, 142.3, 137.0, 136.2 and 135.9, 129.8, 129.5, 129.3, 126.2, 128.9, 128.7, 128.6, 128.5, 128.1, 127.1, 126.8, 124.1, 124.0, 123.7, 88.1, 61.3 and 60.5, 52.3 and 52.1, 51.4, 48.5, 38.4, 28.1. MS (ESI) m/z 563.2 [M + H$^+$].

Boc-Aza-pentylglycinyl-*N*-benzyl-phenylalanine methyl ester **3g**.



Colourless oil. $[\alpha]_D$ -38.3 (c 0.8, $CHCl_3$, 27 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 – 7.01 (m, 10H), 6.24 (br s, 1H), 4.42 (d, 1H, J = 16.9 Hz), 4.29 (d, 1H, J = 16.9 Hz), 4.00 (br s, 1H), 3.69 (s, 3H), 3.40 (dd, 1H, J = 14.1, 6.5 Hz), 3.38 – 3.27 (m, 3H), 1.55 – 1.51 (m, 2H), 1.31 (s, 9H), 1.30 – 1.16 (m, 4H), 0.87 (t, 3H, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, rotamers) δ 171.9, 154.6, 151.6, 138.6, 137.3, 129.7, 129.3, 128.6, 128.5, 128.4, 128.3, 127.3, 127.1, 126.8, 126.7, 80.7, 62.6 and 62.2, 53.3, 52.2 and 52.1, 51.7, 36.0, 29.0, 28.2, 26.4, 22.6, 14.1. MS (ESI) m/z 498.3 [M + H$^+$].

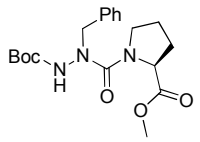
Boc-Aza-3,4,5-trimethoxyphenylalaninyl-*N*-benzyl-tryptophan methyl ester **3h**.



Colourless oil. $[\alpha]_D$ - 10.5 (c 1.3, $CHCl_3$, 27 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (br s, 1H), 8.24 (br s, 1H), 7.56 (d, 1H, J = 7.5 Hz), 7.33 – 6.99 (m, 9H), 6.85 (br s, 1H), 6.60 (br s, 1H), 4.43 (m, 1H), 3.85 – 3.80 (m, 2H), 3.80 (s, 9H), 3.70 – 3.67 (m, 2H), 3.61 (s, 3H), 3.20 (dd, 1H, J = 14.6, 5.8 Hz), 3.14 (dd, 1H, J = 14.6, 7.0 Hz), 1.19 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 171.5, 161.6, 153.4, 152.7, 139.0, 137.0, 136.6, 135.5, 130.8, 127.6, 126.4,

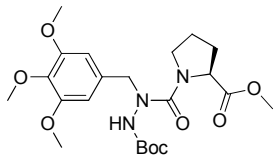
122.3, 121.3, 118.6, 118.1, 117.7, 110.5, 106.1, 80.5, 60.6, 60.2, 55.5, 52.1, 51.4, 28.7, 27.3. MS (ESI) *m/z* 647.3 [M + H^+].

Boc-Aza-phenylalaninyl-proline methyl ester **3i**.



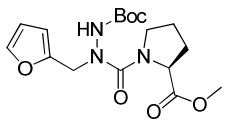
Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 5H), 6.3 (br s, 1H), 4.55 – 4.36 (m, 3H), 3.61 (s, 3H), 3.53 – 3.49 (m, 2H), 2.15 – 1.72 (m, 4H), 1.35 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 159.1, 154.4, 136.1, 129.2, 128.4, 127.5, 81.3, 60.6, 52.8, 51.8, 48.4, 29.7, 28.0, 24.4. MS (ESI) *m/z* 778.4 and 777.4 [2M + Na^+] (0.42: 1 ratio).

Boc-Aza-3,4,5-phenylalaninyl-proline methyl ester **3j**.



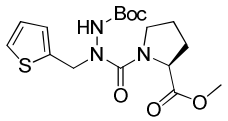
White foam. $[\alpha]_D$ – 16.5 (*c* 0.89, $CHCl_3$, 27 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.56 (s, 2H), 6.16 (br s, 1H), 4.46 (m, 1H), 3.85 (br s, 11H), 3.71 (s, 3H), 3.59 – 3.58 (m, 2H), 2.21 – 2.17 (m, 1H), 1.95 – 1.88 (m, 3H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 159.3, 154.6, 153.4, 137.6, 131.7, 106.3, 81.5, 60.8, 56.2, 53.2, 52.1, 48.7, 29.9, 28.2, 24.8. MS (ESI) *m/z* 957.4 [2M + Na^+].

Boc-Aza-furan-2-ylmethylglycinyl-proline methyl ester **3k**.



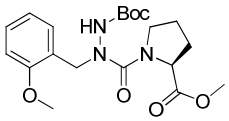
Colourless oil. $[\alpha]_D$ – 26.1 (*c* 0.7, $CDCl_3$, 26 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 1H), 6.35 – 6.31 (m, 1H), 6.29 (d, 1H, *J* = 2.9 Hz), 4.60 (br s, 2H), 4.43 (m, 1H), 3.71 (s, 3H), 3.59 (t, 2H, *J* = 6.4 Hz), 2.26 – 2.07 (m, 1H), 2.01 – 1.79 (m, 3H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 158.8, 154.4, 150.1, 142.5, 110.4, 109.7, 80.6, 60.7, 52.0, 48.5, 45.8, 29.9, 28.1, 24.4. MS (ESI) *m*/*z* 390.1 [M + Na^+].

Boc-Aza-thiophen-2-ylmethylglycinyl-proline methyl ester **3l**.



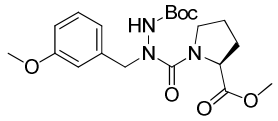
Colourless oil. $[\alpha]_D$ – 26.9 (*c* 0.3, $CDCl_3$, 24 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, 1H, *J* = 5.0 Hz), 6.80 – 6.93 (m, 2H), 6.26 (br s, 1H), 4.75 (br s, 2H), 4.36 – 4.35 (m, 1H), 3.62 (s, 3H), 3.50 (t, 2H, *J* = 6.5 Hz), 2.16 – 1.96 (m, 1H), 1.92 – 1.70 (m, 3H), 1.38 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 157.8, 153.4, 137.0, 127.2, 125.7, 125.3, 80.7, 59.7, 51.1, 47.5, 46.4, 29.2, 27.2, 22.5. MS (ESI) *m*/*z* 384.1 [M + H^+].

Boc-Aza-2-methoxyphenylalaninyl-proline methyl ester **3m**.



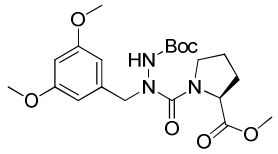
Colourless oil. $[\alpha]_D$ – 20.4 (*c* 1.0, $CDCl_3$, 24 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.15 (m, 2H), 6.82 – 6.77 (m, 2H), 6.32 (br s, 1H), 4.57 (br s, 2H), 4.35 (m, 1H), 3.71 (s, 3H), 3.59 (s, 3H), 3.49 (m, 2H), 2.13 – 1.95 (m, 1H), 1.92 – 1.61 (m, 3H), 1.34 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 159.2, 157.9, 154.8, 131.3, 128.8, 124.2, 120.5, 110.3, 81.2, 60.5, 55.2, 51.8, 48.4, 48.1, 29.9, 28.0, 24.3. MS (ESI) *m*/*z* 430.2 [M + Na^+].

Boc-Aza-3-methoxyphenylalaninyl-proline methyl ester **3n**.



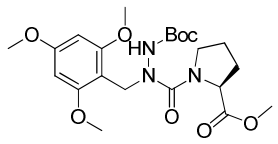
Colourless oil. $[\alpha]_D$ – 23.6 (*c* 0.7, MeOH, 23 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, 1H, *J* = 8.0 Hz), 6.91 – 6.79 (m, 3H), 6.24 (br s, 1H), 4.64 (br s, 2H), 4.46 (m, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 3.60 (t, 2H, *J* = 6.3 Hz), 2.22 – 2.13 (m, 1H), 2.02 – 1.80 (m, 3H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 159.7, 159.1, 154.4, 137.6, 129.4, 121.3, 114.3, 113.4, 81.4, 60.6, 55.1, 52.8, 51.9, 48.5, 29.8, 28.0, 24.4. MS (ESI) *m/z* 408.2 [M + H$^+$].

Boc-Aza-3,5-dimethoxyphenylalaninyl-proline methyl ester **3o**.



Colourless oil. $[\alpha]_D$ – 28.7 (*c* 0.9, MeOH, 23 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (br s, 2H), 6.36 (t, 1H, *J* = 2.0 Hz), 6.21 (br s, 1H), 4.66 (br s, 2H), 4.45 (m, 1H), 3.76 (s, 6H), 3.69 (s, 3H), 3.59 (t, 2H, *J* = 6.0 Hz), 2.26 – 2.08 (m, 1H), 1.95 – 1.75 (m, 3H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 160.9, 159.2, 154.4, 138.4, 106.8, 99.7, 81.4, 60.7, 55.3, 52.8, 52.0, 48.6, 29.8, 28.1, 24.6. MS (ESI) *m/z* 438.2 [M + H$^+$].

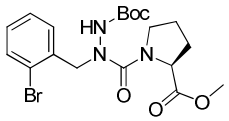
Boc-Aza-2,4,6-trimethoxyphenylalaninyl-proline methyl ester **3p**.



Colourless oil. $[\alpha]_D$ – 18.5 (*c* 1.7, MeOH, 23 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.11 (s, 2H), 5.68 (br s, 1H), 4.84 – 4.13 (m, 3H), 3.78 (s, 9H), 3.74 – 3.42 (m, 5H), 2.26 – 2.07 (m, 1H), 2.01 – 1.66 (m, 3H), 1.49 – 1.20 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, rotamers) δ 173.8,

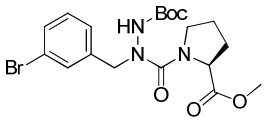
161.1, 160.1, 159.8, 155.2, 154.9, 103.8, 90.3, 90.2, 80.8, 80.0, 60.1, 60.9, 55.6, 55.4, 55.1, 51.6, 48.8, 47.7, 41.5, 40.9, 29.9, 27.8, 24.3, 23.7. MS (ESI) *m/z* 468.2 [M + H^+].

Boc-Aza-2-bromophenylalaninyl-proline methyl ester **3q**.



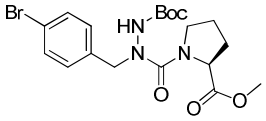
Colourless oil. $[\alpha]_D$ – 20.3 (*c* 0.5, $CDCl_3$, 26 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (dd, 1H, *J* = 7.7, 1.0 Hz), 7.31 – 7.26 (m, 2H), 7.14 (ddd, 1H, *J* = 7.7, 7.7, 1.0 Hz), 6.25 (br s, 1H), 4.80 (s, 2H), 4.46 (t, 1H, *J* = 6.2 Hz), 3.75 (s, 3H), 3.59 (t, 2H, *J* = 6.2 Hz), 2.19 – 1.85 (m, 4H), 1.44 (br s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.7, 173.2, 154.8, 136.2, 133.3, 131.9, 129.6, 128.1, 108.1, 81.0, 77.6, 68.4, 52.5, 49.0, 30.3, 28.6, 26.0. MS (ESI) *m/z* 480.1, 478.1 [M + Na^+] (1:1 ratio).

Boc-Aza-3-bromophenylalaninyl-proline methyl ester **3r**.



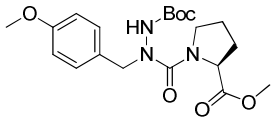
Colourless oil. $[\alpha]_D$ – 12.0 (*c* 0.5, $CDCl_3$, 24 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 2H), 7.28 – 7.18 (m, 2H), 6.25 (br s, 1H), 4.48 (br s, 2H), 4.46 – 4.45 (m, 1H), 3.73 (s, 3H), 3.59 (t, 2H, *J* = 6.2 Hz), 2.19 – 1.86 (m, 4H), 1.45 (br s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 158.0, 153.3, 137.7, 131.2, 129.8, 129.2, 126.9, 121.6, 80.7, 59.8, 51.2, 51.1, 47.6, 28.9, 27.2, 23.6. MS (ESI) *m/z* 458.1, 456.1 [M + H^+] (1:1 ratio).

Boc-Aza-4-bromophenylalaninyl-proline methyl ester **3s**.



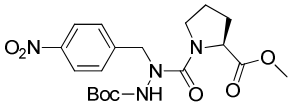
Yellow oil. $[\alpha]_D$ – 10.0 (*c* 0.5, $CDCl_3$, 25 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, 2H, *J* = 8.2 Hz), 7.23 (d, 2H, *J* = 8.2 Hz), 6.25 (br s, 1H), 4.44 (br s, 2H), 4.45 (t, 1H, *J* = 6.2 Hz), 3.65 (s, 3H), 3.60 (t, 2H, *J* = 6.2 Hz), 2.04 – 1.65 (m, 4H), 1.45 (br s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 170.1, 153.4, 134.3, 130.7, 130.1, 120.7, 80.2, 59.7, 59.4, 51.2, 47.6, 28.9, 27.0, 23.6. MS (ESI) *m*/*z* 937.2, 935.2, 933.2 [2M + Na^+] (1:2:1 ratio).

Boc-Aza-4-methoxyphenylalaninyl-proline methyl ester **3t**.



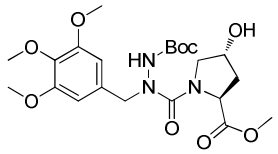
White foam. $[\alpha]_D$ – 4.7 (*c* 0.5, $CDCl_3$, 24 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, 2H, *J* = 8.4 Hz), 6.86 (d, 2H, *J* = 8.4 Hz), 6.06 (br s, 1H), 4.60 (br s, 2H), 4.46 (t, 1H, *J* = 7.7 Hz), 3.79 (s, 3H), 3.71 (s, 3H), 3.59 (t, 2H, *J* = 5.5 Hz), 2.17 – 1.82 (m, 4H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 159.3, 154.5, 145.7, 130.7, 128.0, 114.0, 81.5, 60.7, 55.3, 52.1, 48.6, 38.5, 29.9, 28.2, 24.5. MS (ESI) *m*/*z* 837.4 [2M + Na^+].

Boc-Aza-4-nitrophenylalaninyl-proline methyl ester **3u**.



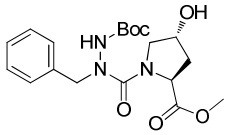
Yellow oil. $[\alpha]_D$ – 46.5 (*c* 0.5, $CDCl_3$, 24 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, 2H, *J* = 8.6 Hz), 7.54 (d, 2H, *J* = 8.6 Hz), 6.37 (br s, 1H), 4.69 (br s, 2H), 4.46 (dd, 1H, *J* = 7.7, 5.1 Hz), 3.72 (s, 3H), 3.59 (t, 2H, *J* = 6.2 Hz), 2.21 – 1.81 (m, 4H), 1.45 (br s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 159.0, 154.2, 147.5, 144.1, 129.7, 123.7, 80.3, 60.7, 53.7, 52.1, 48.5, 29.8, 28.1, 24.7. MS (ESI) *m*/*z* 445.2 [M + Na^+].

Boc-Aza-3,4,5-trimethoxyphenylalaninyl-*trans*-4-hydroxyproline methyl ester **3v**.



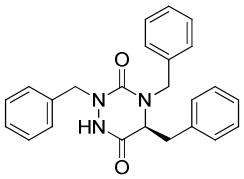
Colourless oil. $[\alpha]_D$ 10.5 (*c* 0.7, MeOH, 25 °C). ^{1}H NMR (400 MHz, MeOD) δ 6.54 (s, 2H), 4.50 (t, 1H, *J* = 8.3 Hz), 4.30 (m, 1H), 3.74 (s, 6H), 3.64 – 3.62 (m, 7H), 3.43 – 3.30 (m, 1H), 3.22 – 3.19 (m, 2H), 2.20 – 1.98 (m, 1H), 1.91 – 1.74 (m, 1H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.4, 154.8, 153.1, 136.8, 133.0, 105.9, 80.1, 69.2, 60.4, 56.2, 53.6, 52.1, 51.1, 37.3, 28.5. MS (ESI) *m*/*z* 989.4 [2M + Na^+].

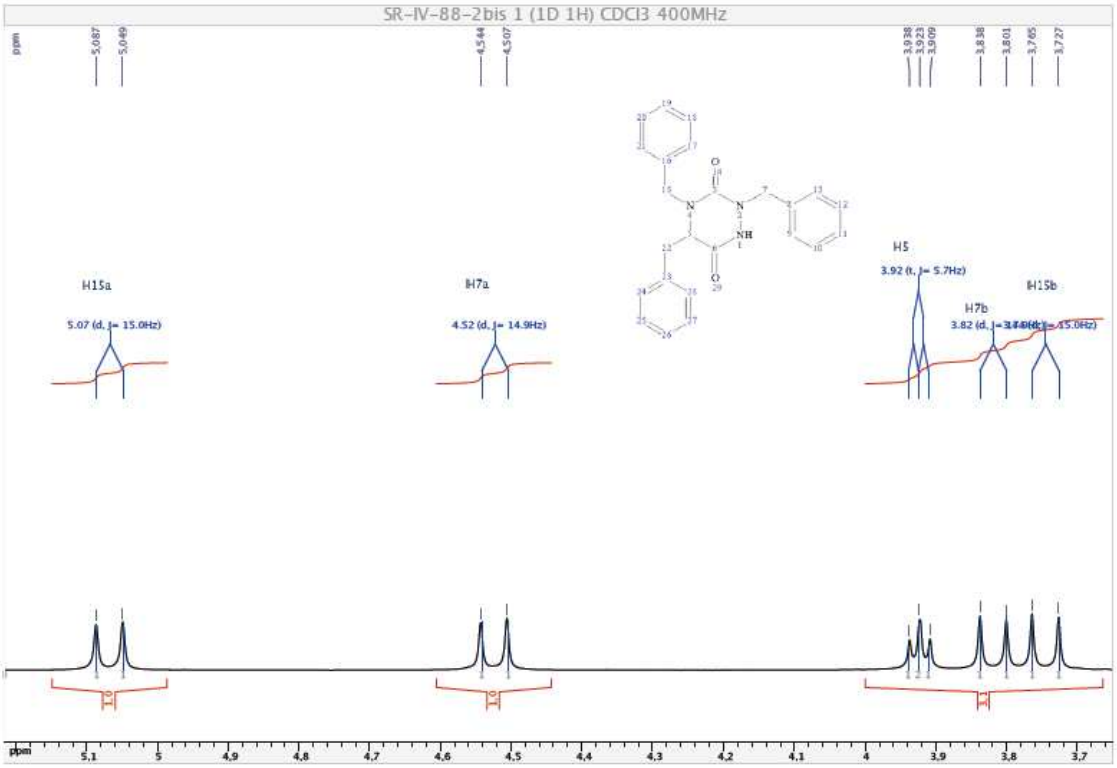
Boc-Aza-phenylalaninyl-*trans*-4-hydroxyproline methyl ester **3w**.



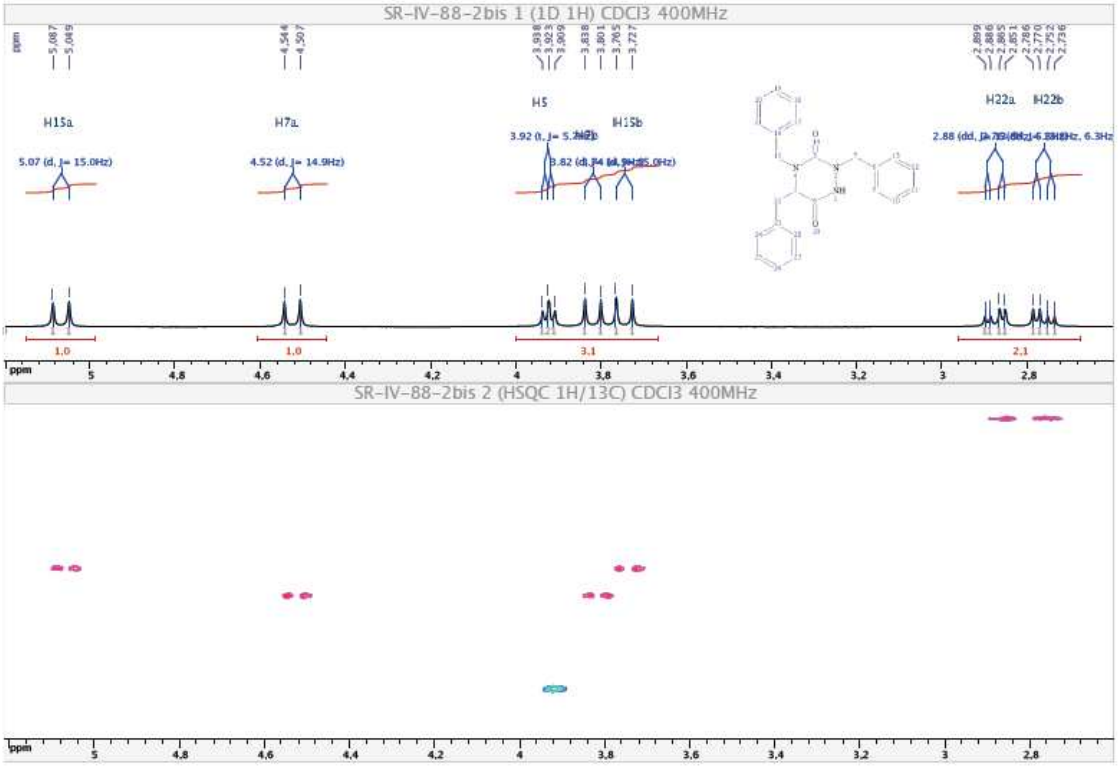
Colourless oil. $[\alpha]_D$ + 1.6 (*c* 0.7, $CDCl_3$, 25 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.08 (m, 5H), 6.78 (br s, 1H), 4.73 – 4.41 (m, 2H), 4.37 – 4.19 (m, 1H), 3.71 – 3.52 (m, 5H), 3.50 – 3.31 (m, 1H), 2.24 – 1.97 (m, 1H), 1.91 – 1.65 (m, 1H), 1.34 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 159.7, 154.4, 136.0, 129.1, 128.4, 127.5, 81.3, 69.9, 59.2, 56.9, 53.1, 52.1, 37.2, 28.1. MS (ESI) *m*/*z* 495.3 [M + NEt_3 + H^+].

^{1}H, ^{13}C and 2D NMR (HSQC, HMBC and NOESY experiments) for compound **16a**

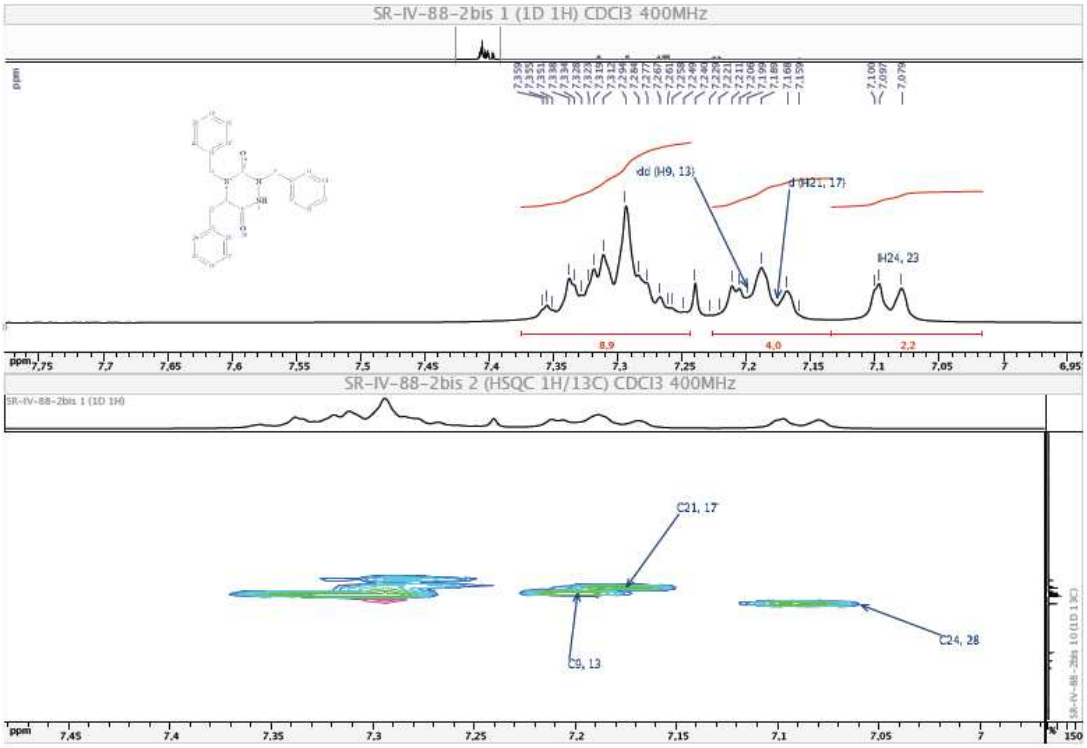




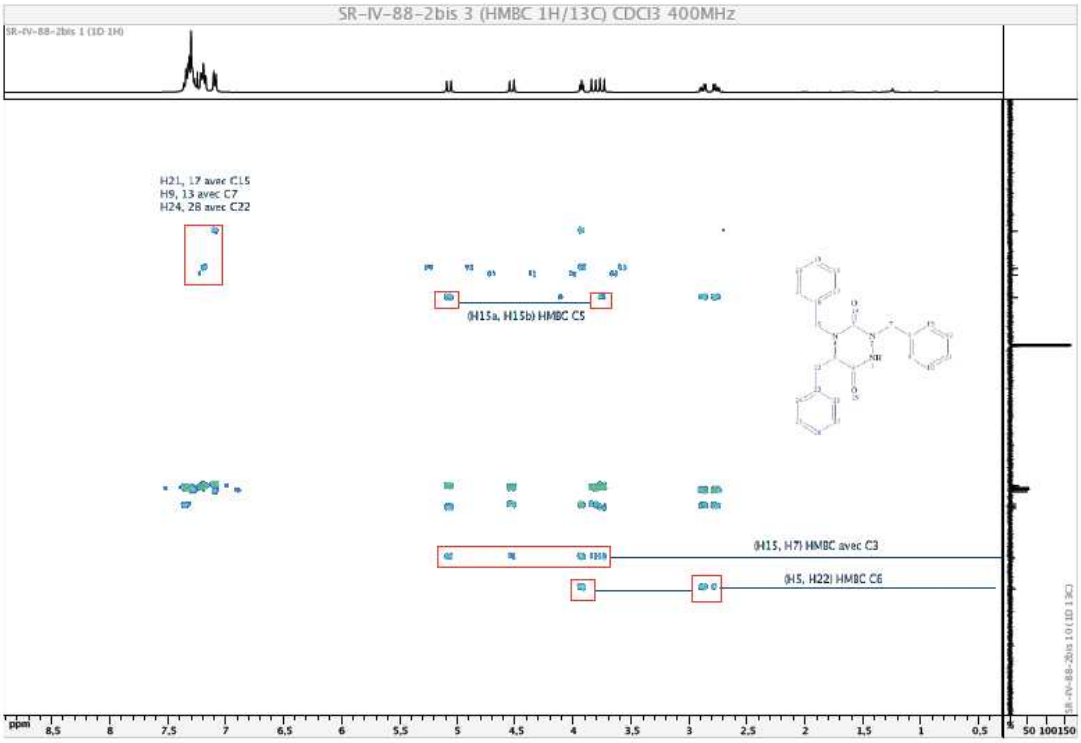
^{1}H NMR (400 MHz), $CDCl_3$



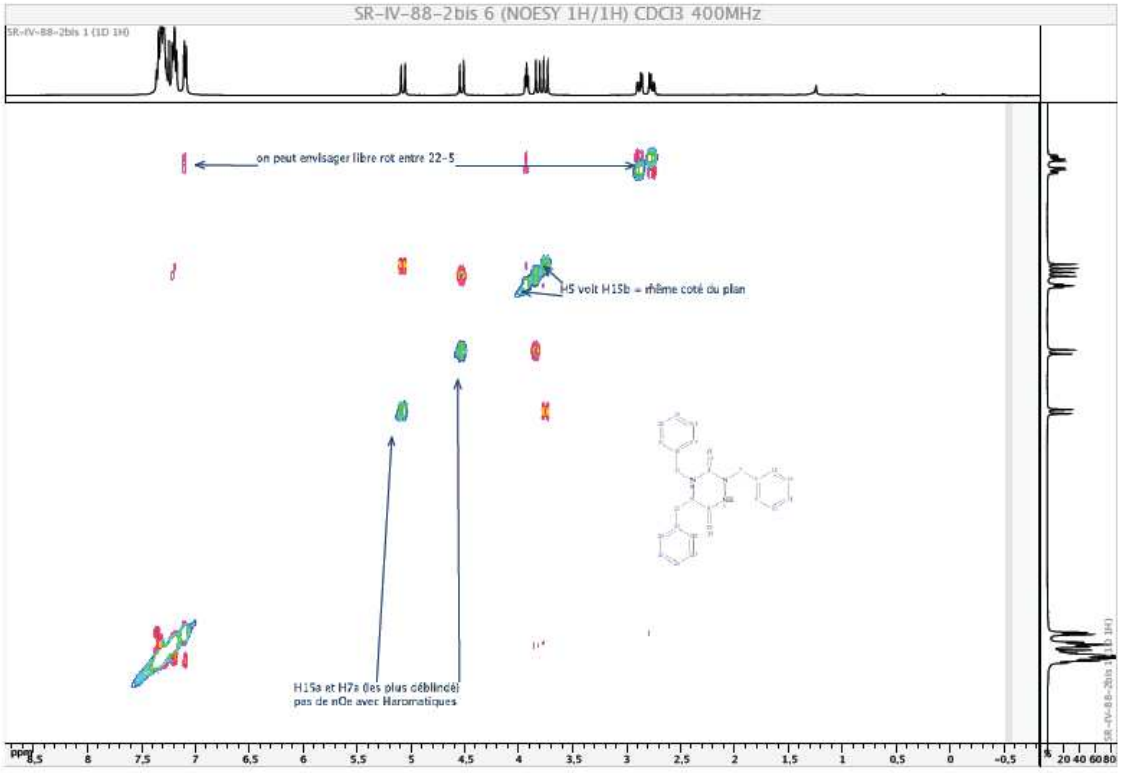
^{1}H-^{1}H COSY NMR (400 MHz), $CDCl_3$



^{1}H-^{13}C HSQC NMR (400 MHz), $CDCl_3$

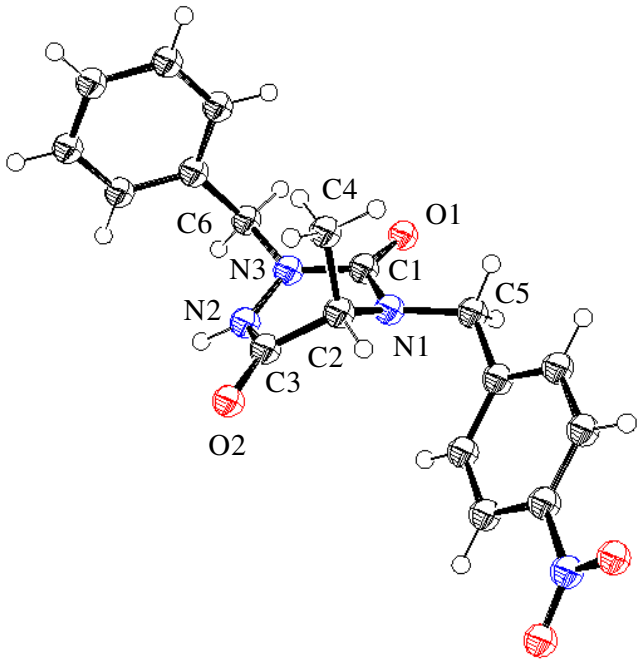


^{1}H-^{13}C HSQC NMR (400 MHz), $CDCl_3$



^{1}H-^{1}H NOESY NMR (400 MHz), $CDCl_3$

X ray crystallographic data of compound **16o**



ORTEP diagram of compounds **16o** (mhep101118)

Table 1. Crystal data and structure refinement for mhep101118.

Identification code	mhep101118
Empirical formula	C18 H18 N4 O4
Formula weight	354.36
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P 21
Unit cell dimensions	a = 10.2851(7) A alpha = 90 deg. b = 7.8759(3) A beta = 111.425(2) deg. c = 11.0783(8) A gamma = 90 deg.
Volume	835.38(9) A^3
Z, Calculated density	2, 1.409 Mg/m^3
Absorption coefficient	0.102 mm^-1
F(000)	372
Crystal size	0.45 x 0.15 x 0.05 mm
Theta range for data collection	1.97 to 27.45 deg.
Limiting indices	-13<=h<=10, -10<=k<=10, -14<=l<=12
Reflections collected / unique	5909 / 2053 [R(int) = 0.0575]
Completeness to theta = 27.45	99.8 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2053 / 1 / 241
Goodness-of-fit on F^2	1.178
Final R indices [I>2sigma(I)]	R1 = 0.0503, wR2 = 0.1105
R indices (all data)	R1 = 0.0669, wR2 = 0.1399
Absolute structure parameter	-10(10)
Extinction coefficient	0.21(2)
Largest diff. peak and hole	0.504 and -0.386 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for mhep101118. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	412(3)	2392(4)	1806(3)	24(1)
C(2)	-212(3)	4560(4)	3043(3)	24(1)
C(3)	-240(3)	3215(4)	4015(3)	24(1)
C(4)	-1671(4)	4977(4)	2058(3)	34(1)
C(5)	1540(4)	5133(4)	1979(3)	30(1)
C(6)	2236(3)	6488(4)	2974(3)	26(1)
C(7)	2188(3)	8162(4)	2580(3)	27(1)
C(8)	2764(3)	9444(4)	3475(3)	30(1)
C(9)	3384(3)	9011(4)	4761(3)	29(1)
C(10)	3486(3)	7353(4)	5190(3)	31(1)
C(11)	2911(3)	6086(4)	4289(3)	31(1)
C(12)	-1078(3)	-188(4)	1695(3)	25(1)
C(13)	-2613(3)	6(4)	1464(3)	25(1)
C(14)	-3144(4)	-704(4)	2330(3)	28(1)
C(15)	-4543(3)	-494(5)	2148(3)	31(1)
C(16)	-5405(3)	451(5)	1116(3)	35(1)
C(17)	-4890(4)	1155(5)	247(4)	40(1)
C(18)	-3500(4)	934(5)	414(3)	33(1)
N(1)	760(3)	3908(3)	2458(2)	24(1)
N(2)	-291(3)	1639(3)	3579(2)	24(1)
N(3)	-279(3)	1320(3)	2338(2)	24(1)
N(4)	3911(3)	10377(4)	5721(3)	42(1)
O(1)	689(2)	2002(3)	850(2)	33(1)
O(2)	-178(3)	3537(3)	5128(2)	33(1)
O(3)	3609(4)	11844(4)	5356(3)	59(1)
O(4)	4625(3)	9987(4)	6842(3)	56(1)

Table 3. Bond lengths [A] and angles [deg] for mhep101118.

C(1)-O(1)	1.232(4)
C(1)-N(3)	1.367(4)
C(1)-N(1)	1.373(4)
C(2)-N(1)	1.469(4)
C(2)-C(3)	1.518(4)
C(2)-C(4)	1.535(5)
C(2)-H(2)	1.0000
C(3)-O(2)	1.237(4)
C(3)-N(2)	1.326(4)
C(4)-H(4A)	0.9800
C(4)-H(4B)	0.9800
C(4)-H(4C)	0.9800
C(5)-N(1)	1.472(4)
C(5)-C(6)	1.513(4)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-C(7)	1.383(5)
C(6)-C(11)	1.403(4)
C(7)-C(8)	1.387(5)
C(7)-H(7)	0.9500
C(8)-C(9)	1.374(5)
C(8)-H(8)	0.9500
C(9)-C(10)	1.380(5)
C(9)-N(4)	1.470(4)
C(10)-C(11)	1.382(5)
C(10)-H(10)	0.9500
C(11)-H(11)	0.9500
C(12)-N(3)	1.472(4)
C(12)-C(13)	1.512(4)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.384(4)
C(13)-C(18)	1.394(5)
C(14)-C(15)	1.388(5)
C(14)-H(14)	0.9500
C(15)-C(16)	1.381(5)
C(15)-H(15)	0.9500
C(16)-C(17)	1.374(5)
C(16)-H(16)	0.9500
C(17)-C(18)	1.384(5)
C(17)-H(17)	0.9500
C(18)-H(18)	0.9500
N(2)-N(3)	1.403(3)
N(2)-H(2N)	0.98(5)
N(4)-O(3)	1.226(5)
N(4)-O(4)	1.229(4)

O(1)-C(1)-N(3)	122.4(3)
O(1)-C(1)-N(1)	124.8(3)
N(3)-C(1)-N(1)	112.8(3)
N(1)-C(2)-C(3)	105.1(2)
N(1)-C(2)-C(4)	114.0(3)
C(3)-C(2)-C(4)	112.8(3)
N(1)-C(2)-H(2)	108.2
C(3)-C(2)-H(2)	108.2
C(4)-C(2)-H(2)	108.2
O(2)-C(3)-N(2)	122.4(3)
O(2)-C(3)-C(2)	123.8(3)
N(2)-C(3)-C(2)	113.8(3)
C(2)-C(4)-H(4A)	109.5
C(2)-C(4)-H(4B)	109.5
H(4A)-C(4)-H(4B)	109.5
C(2)-C(4)-H(4C)	109.5
H(4A)-C(4)-H(4C)	109.5
H(4B)-C(4)-H(4C)	109.5
N(1)-C(5)-C(6)	112.0(2)
N(1)-C(5)-H(5A)	109.2
C(6)-C(5)-H(5A)	109.2
N(1)-C(5)-H(5B)	109.2
C(6)-C(5)-H(5B)	109.2
H(5A)-C(5)-H(5B)	107.9
C(7)-C(6)-C(11)	119.3(3)
C(7)-C(6)-C(5)	119.3(3)
C(11)-C(6)-C(5)	121.3(3)
C(6)-C(7)-C(8)	120.8(3)
C(6)-C(7)-H(7)	119.6
C(8)-C(7)-H(7)	119.6
C(9)-C(8)-C(7)	118.4(3)
C(9)-C(8)-H(8)	120.8
C(7)-C(8)-H(8)	120.8
C(8)-C(9)-C(10)	122.7(3)
C(8)-C(9)-N(4)	118.5(3)
C(10)-C(9)-N(4)	118.8(3)
C(9)-C(10)-C(11)	118.4(3)
C(9)-C(10)-H(10)	120.8
C(11)-C(10)-H(10)	120.8
C(10)-C(11)-C(6)	120.3(3)
C(10)-C(11)-H(11)	119.8
C(6)-C(11)-H(11)	119.8
N(3)-C(12)-C(13)	111.4(2)
N(3)-C(12)-H(12A)	109.3
C(13)-C(12)-H(12A)	109.3
N(3)-C(12)-H(12B)	109.3
C(13)-C(12)-H(12B)	109.3
H(12A)-C(12)-H(12B)	108.0
C(14)-C(13)-C(18)	119.2(3)

C(14)-C(13)-C(12)	119.6(3)
C(18)-C(13)-C(12)	121.2(3)
C(13)-C(14)-C(15)	120.1(3)
C(13)-C(14)-H(14)	120.0
C(15)-C(14)-H(14)	120.0
C(16)-C(15)-C(14)	120.2(3)
C(16)-C(15)-H(15)	119.9
C(14)-C(15)-H(15)	119.9
C(17)-C(16)-C(15)	120.1(3)
C(17)-C(16)-H(16)	119.9
C(15)-C(16)-H(16)	119.9
C(16)-C(17)-C(18)	120.0(3)
C(16)-C(17)-H(17)	120.0
C(18)-C(17)-H(17)	120.0
C(17)-C(18)-C(13)	120.4(3)
C(17)-C(18)-H(18)	119.8
C(13)-C(18)-H(18)	119.8
C(1)-N(1)-C(2)	116.6(3)
C(1)-N(1)-C(5)	116.9(2)
C(2)-N(1)-C(5)	118.6(2)
C(3)-N(2)-N(3)	120.8(3)
C(3)-N(2)-H(2N)	123(3)
N(3)-N(2)-H(2N)	116(3)
C(1)-N(3)-N(2)	120.3(2)
C(1)-N(3)-C(12)	125.2(2)
N(2)-N(3)-C(12)	114.5(2)
O(3)-N(4)-O(4)	123.7(3)
O(3)-N(4)-C(9)	118.0(3)
O(4)-N(4)-C(9)	118.3(3)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for mhep101118.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	25(2)	28(2)	20(1)	0(1)	8(1)	-2(1)
C(2)	29(2)	22(2)	24(2)	-2(1)	12(1)	-2(1)
C(3)	22(2)	27(2)	23(2)	-2(1)	9(1)	-3(1)
C(4)	37(2)	29(2)	35(2)	0(2)	10(2)	3(1)
C(5)	38(2)	30(2)	24(2)	1(1)	13(1)	-8(1)
C(6)	24(2)	29(2)	25(2)	1(1)	10(1)	-3(1)
C(7)	28(2)	29(2)	25(2)	6(1)	10(1)	1(1)
C(8)	27(2)	25(2)	43(2)	5(2)	16(2)	1(1)
C(9)	26(2)	30(2)	34(2)	-5(1)	13(1)	-5(1)
C(10)	31(2)	33(2)	27(2)	2(1)	6(1)	-1(1)
C(11)	33(2)	29(2)	27(2)	4(1)	7(1)	-4(1)
C(12)	31(2)	23(2)	19(1)	-3(1)	8(1)	-3(1)
C(13)	29(2)	25(2)	20(1)	-4(1)	6(1)	-3(1)
C(14)	31(2)	26(2)	22(2)	1(1)	5(1)	1(1)
C(15)	31(2)	35(2)	31(2)	-2(2)	14(1)	-3(1)
C(16)	26(2)	35(2)	39(2)	-1(2)	8(1)	-1(1)
C(17)	33(2)	43(2)	34(2)	9(2)	3(2)	0(2)
C(18)	34(2)	37(2)	25(2)	5(1)	7(1)	-6(1)
N(1)	28(1)	23(1)	24(1)	-3(1)	13(1)	-4(1)
N(2)	34(1)	24(1)	15(1)	-2(1)	10(1)	-1(1)
N(3)	31(1)	25(1)	17(1)	-5(1)	9(1)	-4(1)
N(4)	41(2)	40(2)	47(2)	-12(2)	19(2)	-12(1)
O(1)	42(1)	36(1)	25(1)	-7(1)	18(1)	-7(1)
O(2)	45(1)	34(1)	22(1)	-7(1)	16(1)	-7(1)
O(3)	73(2)	31(2)	71(2)	-11(2)	23(2)	-1(1)
O(4)	67(2)	58(2)	38(2)	-12(1)	11(1)	-20(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for mhep101118.

	x	y	z	U(eq)
H(2)	195	5621	3531	29
H(4A)	-2107	3940	1599	52
H(4B)	-1591	5812	1433	52
H(4C)	-2248	5447	2513	52
H(5A)	892	5679	1181	36
H(5B)	2261	4521	1753	36
H(7)	1755	8436	1687	33
H(8)	2731	10593	3206	37
H(10)	3941	7090	6083	38
H(11)	2973	4935	4563	37
H(12A)	-706	-1200	2242	30
H(12B)	-963	-366	855	30
H(14)	-2550	-1337	3051	33
H(15)	-4908	-1002	2735	38
H(16)	-6357	615	1006	42
H(17)	-5488	1793	-468	47
H(18)	-3147	1418	-190	40
H(2N)	-290(50)	640(70)	4110(40)	53(13)

Table 6. Torsion angles [deg] for mhep101118.

N(1)-C(2)-C(3)-O(2)	135.4(3)
C(4)-C(2)-C(3)-O(2)	-99.8(4)
N(1)-C(2)-C(3)-N(2)	-42.6(3)
C(4)-C(2)-C(3)-N(2)	82.3(3)
N(1)-C(5)-C(6)-C(7)	-137.2(3)
N(1)-C(5)-C(6)-C(11)	41.8(4)
C(11)-C(6)-C(7)-C(8)	-1.8(5)
C(5)-C(6)-C(7)-C(8)	177.3(3)
C(6)-C(7)-C(8)-C(9)	0.0(5)
C(7)-C(8)-C(9)-C(10)	1.7(5)
C(7)-C(8)-C(9)-N(4)	-175.9(3)
C(8)-C(9)-C(10)-C(11)	-1.5(5)
N(4)-C(9)-C(10)-C(11)	176.0(3)
C(9)-C(10)-C(11)-C(6)	-0.3(5)
C(7)-C(6)-C(11)-C(10)	1.9(5)
C(5)-C(6)-C(11)-C(10)	-177.1(3)
N(3)-C(12)-C(13)-C(14)	-97.3(3)
N(3)-C(12)-C(13)-C(18)	80.6(4)
C(18)-C(13)-C(14)-C(15)	0.2(5)
C(12)-C(13)-C(14)-C(15)	178.2(3)
C(13)-C(14)-C(15)-C(16)	-1.2(5)
C(14)-C(15)-C(16)-C(17)	1.5(5)
C(15)-C(16)-C(17)-C(18)	-0.8(6)
C(16)-C(17)-C(18)-C(13)	-0.3(6)
C(14)-C(13)-C(18)-C(17)	0.5(5)
C(12)-C(13)-C(18)-C(17)	-177.4(3)
O(1)-C(1)-N(1)-C(2)	147.6(3)
N(3)-C(1)-N(1)-C(2)	-33.0(4)
O(1)-C(1)-N(1)-C(5)	-1.0(5)
N(3)-C(1)-N(1)-C(5)	178.5(3)
C(3)-C(2)-N(1)-C(1)	60.9(3)
C(4)-C(2)-N(1)-C(1)	-63.1(3)
C(3)-C(2)-N(1)-C(5)	-151.1(3)
C(4)-C(2)-N(1)-C(5)	84.9(3)
C(6)-C(5)-N(1)-C(1)	-162.8(3)
C(6)-C(5)-N(1)-C(2)	49.3(4)
O(2)-C(3)-N(2)-N(3)	-176.2(3)
C(2)-C(3)-N(2)-N(3)	1.7(4)
O(1)-C(1)-N(3)-N(2)	165.3(3)
N(1)-C(1)-N(3)-N(2)	-14.2(4)
O(1)-C(1)-N(3)-C(12)	-16.3(5)
N(1)-C(1)-N(3)-C(12)	164.2(3)
C(3)-N(2)-N(3)-C(1)	30.9(4)
C(3)-N(2)-N(3)-C(12)	-147.6(3)
C(13)-C(12)-N(3)-C(1)	-115.6(3)
C(13)-C(12)-N(3)-N(2)	62.9(3)

C(8)-C(9)-N(4)-O(3)	9.6(5)
C(10)-C(9)-N(4)-O(3)	-168.1(3)
C(8)-C(9)-N(4)-O(4)	-170.6(3)
C(10)-C(9)-N(4)-O(4)	11.7(5)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for mhep101118 [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2N)...O(2)#1	0.98(5)	1.84(5)	2.784(4)	160(4)

Symmetry transformations used to generate equivalent atoms:
#1 -x,y-1/2,-z+1