

## Macrocyclic Scaffolds Derived from *para*-Aminobenzoic acid

### Electronic Supplementary material

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### General Details

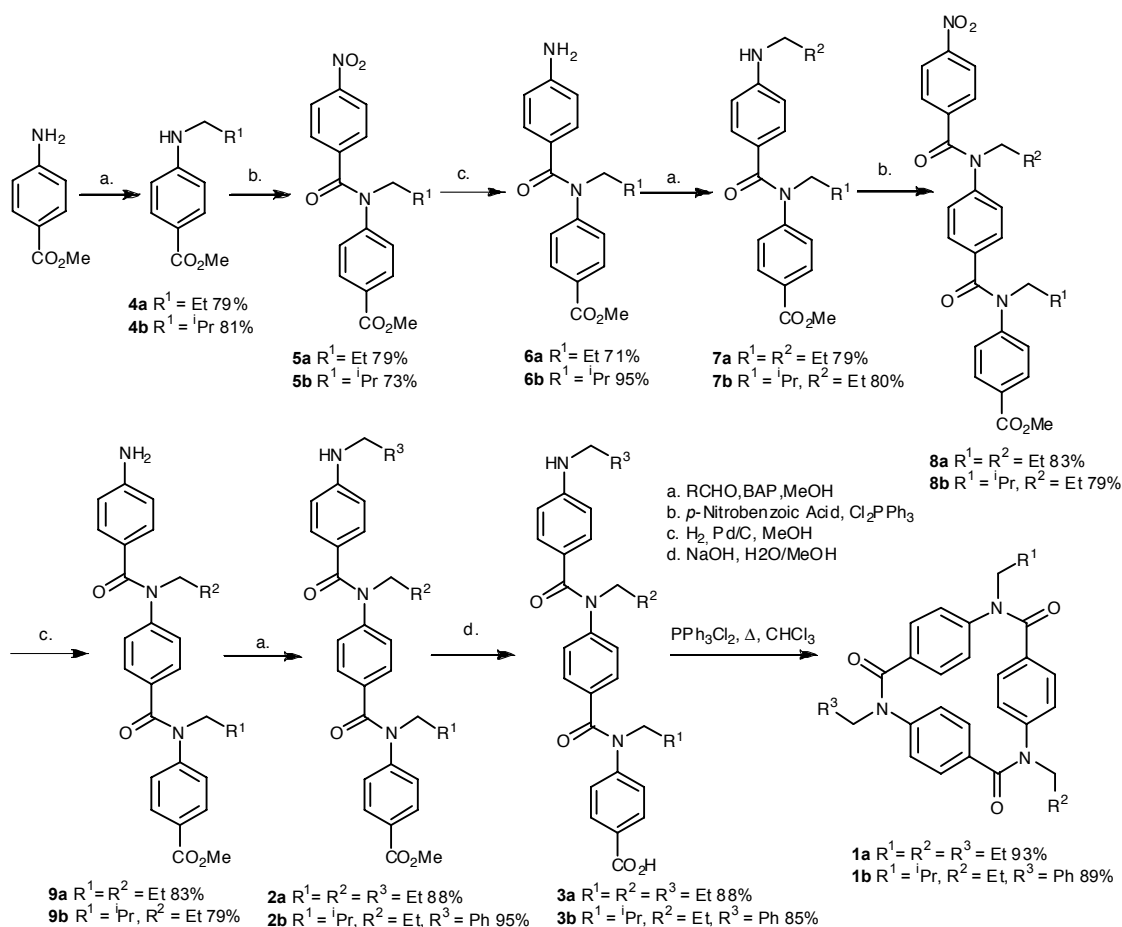
All chemicals were purchased from Sigma-Aldrich and were used without further purification. All solvents used were HPLC grade. Chloroform-d ( $\text{CDCl}_3$ , >99.9%) and methanol-d<sub>4</sub> (MeOD, >99.7%) were purchased from *Euriso-top* and stored at 4°C.

The recorded  $R_f$  values were determined by Thin Layer Chromatography (TLC) using 0.2 mm silica gel 60 F<sub>254</sub> pre-coated aluminium sheets, commercially available from Merck. Visualisation was determined by UV at 254nm or, in the case of amine intermediates, by staining with a ninhydrin solution. Column chromatography was carried out using silica gel 60, 35 to 70 micron particles, commercially available from FluoroChem. Solvent ratios are described where appropriate.

<sup>1</sup>H NMR spectra were recorded using a Bruker DPX 300 or Bruker DRX 500 instrument. <sup>13</sup>C Nuclear Magnetic Resonance were recorded at 75 MHz or 125 MHz using a Bruker DPX 300 instrument or Bruker DRX 500 instrument. <sup>1</sup>H spectra are referenced to tetramethylsilane and chemical shifts given in parts per million downfield from TMS. Coupling constants are reported to the nearest 0.1 Hz. <sup>1</sup>H NOESY Spectroscopy was carried out using the standard Bruker *noesygtp-X* program with the following parameters: sample concentration 60 mM, 2048 (F2).1024(F1) data points in TPPI mode with Z gradients, relaxation delay 1.77s, 40 scans per increment, sweep width 4529 Hz in both directions and 1.2s mixing time.

Melting points were determined using a Griffin D5 variable temperature apparatus and are uncorrected. Microanalyses were obtained on a Carlo Erba Elemental Analyser MOD 1106 instrument, found composition is reported to the nearest 0.05%. Infrared spectra were recorded on a Perkin-Elmer FTIR spectrometer and samples analysed as solids. Mass spectra were obtained using a micrOTOF spectrometer using time-of-flight electro-spray analysis. Positive or negative ion detection is specified.

## Synthesis of Cyclic Trimers



*Scheme S1. Full synthesis of cyclic trimers 1a and 1b*

### Reductive amination

To a stirred solution of primary amine (1 eq.) and aldehyde ( $\geq 1$  eq.) in methanol, under an atmosphere of nitrogen, was added borane-pyridine (small excess). The reaction mixture was stirred at 35 °C for 12-36 h, until TLC indicated reaction completion. Concentration and direct purification by column chromatography gave target material which was dried under vacuum and fully characterised.

(Note: borane-picoline – a white solid with greater stability and reactivity than borane-pyridine can be also be used for this reaction)

### Amide coupling

To a stirred solution of secondary amine (1 eq.) and acid (1 eq.) in chloroform, under an atmosphere of nitrogen, was added dichlorotriphenylphosphorane (2.4 eq.). The reaction mixture was heated at reflux (65°C) for 24-36 h, until TLC indicated no further reaction. Concentration and direct purification by column chromatography isolated target material which was dried under vacuum and fully characterised.

## Hydrogenation

To a stirred solution of nitro compound (1 eq.) in anhydrous methanol, under an atmosphere of nitrogen, was added palladium on charcoal catalyst (10% w/w). The nitrogen atmosphere was flushed out under vacuum and hydrogen gas introduced *via* a balloon (2L, excess). The mixture was stirred at room temperature for 6-24 h, until TLC indicated no further reaction. The mixture was passed through a pad of celite, concentrated and the isolated product dried under vacuum. Purification of the target amine was achieved by recrystallisation or chromatography where appropriate.

### Methyl -4-propylaminobenzoate: 4a

Methyl-4-aminobenzoate (4.00 g, 26.60 mmol), propionaldehyde (3 mL, 2.42 g, 41.58 mmol) and borane.pyridine (4 mL, 3.68 g, 39.60 mmol) in methanol (25 mL), were stirred at room temperature for 24 hours. The crude mixture was concentrated and recrystallisation from the minimum amount of hexane yielding pure target material as a colourless crystalline solid. Yield: 4.02 g, 79%; m.p. 111–12°C;  $R_F$ : 0.25 (2% EtOAc in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.03 (t, 3H,  $J$  = 7.4 Hz,  $\text{CH}_3\text{CH}_2\text{CH}_2$ ), 1.69 (m, 2H,  $\text{CH}_3\text{CH}_2\text{CH}_2$ ), 3.16 (t, 2H,  $J$  = 7.2 Hz,  $\text{CH}_3\text{CH}_2\text{CH}_2$ ), 3.88 (s, 3H,  $\text{CO}_2\text{Me}$ ), 4.33 (broad s, 1H, NH), 6.58 (d, 2H,  $J$  = 8.8 Hz, ArH), 7.89 (d, 2H,  $J$  = 8.8 Hz, ArH);  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 11.97, 22.89, 45.64, 51.93, 111.84, 118.52, 131.96, 152.39, 167.77; IR (solid state):  $\nu_{\text{max}}/\text{cm}^{-1}$  = 3407, 3229, ~1600 (CO); TOF-MS ESI:  $m/z$  = 194  $[\text{M}+\text{H}]^+$ ; CHN Anal.: (Found: C, 68.40, H, 7.80; N, 7.05;  $\text{C}_{11}\text{H}_{15}\text{NO}_2$  requires: C, 68.37; H, 7.82; N, 7.25%).

### Methyl-4-isobutylamino-benzoate: 4b

Methyl-4-aminobenzoate (2.00 g, 13.25 mmol), isobutylaldehyde (2 mL, 21.91 mmol) and BAP (3 mL, 29.7 mmol) in methanol (12 mL), were stirred at room temperature for 36 hours. Purification by column chromatography (*Stationary Phase*: Silica, 75g; *Mobile Phase*: 2% EtOAc in  $\text{CH}_2\text{Cl}_2$ ) isolated both target material and pyridine salt. Partition of the reaction mixture between EtOAc (30mL) and 1N HCl (3 x 20mL), followed by drying ( $\text{MgSO}_4$ ), concentration and final drying under vacuum, isolated pure target material as a cream crystalline solid. Yield: 2.23g, 81%; m.p. 53–58°C;  $R_F$ : 0.35 (5 % EtOAc in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.98 (d, 6H,  $J$  = 6.7 Hz,  $\text{CH}_3$ ), 1.90 (sept, 1H,  $J$  = 6.7 Hz, CH), 2.98 (apparent t, 2H,  $J$  = 6.0 Hz,  $\text{CH}_2$ ), 3.84 (s, 3H,  $\text{CO}_2\text{Me}$ ), 4.18 (broad s, 1H, NH), 6.54 (d, 2H,  $J$  = 8.8 Hz, ArH), 7.84 (d, 2H,  $J$  = 8.9 Hz, ArH);  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ ): 20.77, 28.47, 51.52, 51.86, 111.72, 118.36, 131.95, 152.66, 167.74; IR (solid state):  $\nu_{\text{max}}/\text{cm}^{-1}$  = 3333 (NH), 2951, 2871 (alkyl CH), 1683 (CO); HRMS-ESI: Found:  $m/z$  = 206.1186  $[\text{M}-\text{H}]^-$ ;  $\text{C}_{12}\text{H}_{16}\text{N}_1\text{O}_2$  requires: 206.1187.

**Methyl-4-[N-(4-nitrobenzoyl)-N'-propylamido]-benzoate: 5a**

Methyl-4-propylaminobenzoate (2.39 g, 12.38 mmol), *p*-nitrobenzoic acid (2.08 g, 12.46 mmol) and dichlorotriphenylphosphorane (9.94 g, 29.83 mmol) in chloroform (25 mL), were stirred at reflux for 26h. Column chromatography (*Stationary Phase*: Silica, 100g; *Mobile Phase*: 2% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>) isolated title product as a yellow viscous oil. Yield: 3.32 g, 79%; R<sub>F</sub>: 0.08 (5% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 0.88 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.60 (m, 2H, *J* = ~7.5 Hz, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.82 (s, 3H, CO<sub>2</sub>Me), 3.87 (t, 2H, *J* = 7.5 Hz, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 7.01 (d, 2H, *J* = 8.5 Hz, ArH), 7.36 (d, 2H, *J* = 8.8 Hz, ArH), 7.85 (d, 2H, *J* = 8.5 Hz, ArH), 7.96 (d, 2H, *J* = 8.8 Hz, ArH); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): δ = 11.66, 21.32, 52.27, 52.69, 123.60, 127.84, 129.23, 129.90, 131.23, 142.46, 146.96, 148.46, 166.26, 168.45; IR (solid state): ν<sub>max</sub>/cm<sup>-1</sup> = 2966 (Aromatic CH), 1655 (Amide CO), 1348 (NO<sub>2</sub>); TOF-MS ESI: *m/z* = 343 [M+H]<sup>+</sup>;

**Methyl-4-[N-(4-nitrobenzoyl)-N'-isobutylamido]-benzoate 5b**

Methyl-4-isobutylamino-benzoate (1.50 g, 7.25 mmol), *p*-nitrobenzoic acid (1.22 g, 7.31 mmol) and dichlorotriphenylphosphorane (5.82 g, 17.47 mmol) in chloroform (15 mL), were heated at reflux for 20 hours. Column chromatography (*Stationary Phase*: Silica, 150 g; *Mobile Phase*: 3% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>) isolated title product as a yellow viscous oil. Yield: 1.89 g, 73%; R<sub>F</sub>: 0.25 (CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 0.97 (d, 6H, *J* = 6.7 Hz, CH<sub>3</sub>), 1.90 (sept, 1H, *J* = 6.9 Hz, CH), 3.86 (d, 2H, *J* = 7.5 Hz, CH<sub>2</sub>), 3.89 (s, 3H, CO<sub>2</sub>Me), 7.09 (d, 2H, *J* = 8.5 Hz, ArH), 7.43 (d, 2H, *J* = 8.8 Hz, ArH), 7.91 (d, 2H, *J* = 8.6 Hz, ArH), 8.03 (d, 2H, *J* = 8.8 Hz, ArH); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): 20.56, 27.49, 52.79, 57.23, 123.68, 127.72, 129.15, 129.85, 131.26, 142.63, 147.12, 148.44, 166.29, 168.80; IR (solid state): ν<sub>max</sub>/cm<sup>-1</sup> = 3076, 2960, 2882 (alkyl CH), 1720 (CO), 1657, 1602, 1528; HRMS-ESI *m/z* = Found: 357.1450 [M+H]<sup>+</sup>; C<sub>19</sub>H<sub>21</sub>N<sub>2</sub>O<sub>5</sub> requires: 357.1445.

**Methyl-4-[N-(4-aminobenzoyl)-N'-propylamido]-benzoate 6a**

Methyl-4-[N-(4-nitrobenzoyl)-N'-propylamido]-benzoate (3.41 g, 9.97 mmol) was hydrogenated for 24 hours. Target amine was isolated as a pale cream crystalline solid. Yield: 2.21 g, 71%; m.p. 127–129°C; R<sub>F</sub>: 0.15 (10% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 0.95 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.67 (m, 2H, *J* = 7.6 Hz, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.91 (m, 5H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub> and CO<sub>2</sub>Me), 6.44 (d, 2H, *J* = 8.6 Hz, ArH), 7.11 (d, 2H, *J* = 8.7 Hz, ArH), 7.14 (d, 2H, *J* = 8.7 Hz, ArH), 7.92 (d, 2H, *J* = 8.6 Hz, ArH); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): δ = 10.37, 20.13, 51.03, 51.13, 112.57, 123.91, 125.84, 126.17, 129.43, 130.07, 147.43, 147.92, 165.40, 169.32; IR (solid state): ν<sub>max</sub>/cm<sup>-1</sup> = 3431, 3356, 3251 (NH), 1706 (Ester CO); HRMS-ESI *m/z* = Found: 313.1541 [M+H]<sup>+</sup>; C<sub>18</sub>H<sub>21</sub>N<sub>2</sub>O<sub>5</sub> requires: 313.1547.

**Methyl-4-[N-(4-amino-benzoyl)-N'-isobutylamido]-benzoate: 6b**

Methyl-4-[N-(4-nitrobenzoyl)-N'-isobutylamido]-benzoate (1.73g, 4.86mmol) was hydrogenated for 14 hours. Target amine was isolated as a pale cream crystalline solid. Yield: 1.81g, 95%; m.p.: 136–137°C;  $R_F$ : 0.13 (10% EtOAc in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.93 (d, 6H,  $J$  = 6.7 Hz,  $\text{CH}_3$ ), 1.95 (sept, 1H,  $J$  = 6.9 Hz, CH), 3.80 (d, 2H,  $J$  = 7.5 Hz,  $\text{CH}_2$ ), 3.88 (s, 3H,  $\text{CO}_2\text{Me}$ ), 6.39 (d, 2H,  $J$  = 8.6 Hz, ArH), 7.08 (d, 2H,  $J$  = 8.6 Hz, ArH), 7.10 (d, 2H,  $J$  = 8.6 Hz, ArH), 7.88 (d, 2H,  $J$  = 8.6 Hz, ArH);  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ ): 20.68, 27.64, 52.58, 57.38, 114.04, 125.49, 127.11, 127.40, 130.80, 131.45, 148.78, 149.53, 166.85, 171.10; IR (solid state):  $\nu_{\text{max}}/\text{cm}^{-1}$  = 3412, 3336, 3236 (NH), 1717 (CO); HRMS-ESI  $m/z$  = Found: 349.1523 [ $\text{M}+\text{Na}^+$ ];  $\text{C}_{19}\text{H}_{22}\text{N}_2\text{NaO}_3$  requires: 349.1523.

**Methyl-4-[N-(4-N-propylamino)benzoyl)-N'-propylamido]-benzoate 7a**

Methyl-4-[N-(4-aminobenzoyl)-N'-propylamido]-benzoate (1.03 g, 3.28 mmol), propionaldehyde (240  $\mu\text{L}$ , 193 mg, 3.32 mmol) and Pic-BH<sub>3</sub> (370 mg, 3.46 mmol) in methanol (8 mL), were stirred at room temperature for 20 hours. Purification by column chromatography (*Stationary Phase*: Silica, 50g; *Mobile Phase*: 10% EtOAc in  $\text{CH}_2\text{Cl}_2$ ) isolated target material as a glassy crystalline solid. Yield: 916 mg, 79%; m.p. 85–86°C;  $R_F$ : 0.20 (10% EtOAc in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.98 (2 x t, 6H,  $J$  = ~7.5 Hz,  $\underline{\text{CH}_3\text{CH}_2\text{CH}_2}$ ), 1.62 (m, 4H,  $J$  = ~7.5 Hz,  $\text{CH}_3\underline{\text{CH}_2\text{CH}_2}$ ), 3.03 (t, 2H,  $J$  = 7.1 Hz,  $\text{CH}_3\underline{\text{CH}_2\text{CH}_2}$ ), 3.92 (m, 5H,  $\text{CO}_2\text{Me}$  +  $\text{CH}_3\underline{\text{CH}_2\text{CH}_2}$ ), 6.33 (d, 2H,  $J$  = 8.7 Hz, ArH), 7.12 (d, 2H,  $J$  = 8.6 Hz, ArH), 7.17 (d, 2H,  $J$  = 8.7 Hz, ArH), 7.92 (d, 2H,  $J$  = 8.6 Hz, ArH);  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 11.80, 11.88, 21.58, 22.50, 52.56, 77.63, 112.94, 127.22, 127.60, 130.90, 131.00, 131.58, 149.38, 166.83, 170.59; IR (solid state):  $\nu_{\text{max}}/\text{cm}^{-1}$  = 3353 (NH), 1715 (CO); TOF-MS ESI:  $m/z$  = 355 [ $\text{M}+\text{H}^+$ ]; CHN Anal.: (Found: C, 70.90; H, 7.40; N, 7.85;  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_3$  requires: C, 71.16; H, 7.39; N, 7.90 %).

**Methyl-4-[N-(4-N-propylamino)benzoyl)-N'-isobutylamido]-benzoate 7b**

Methyl-4-[N-(4-amino-benzoyl)-N'-isobutylamido]-benzoate (903 mg, 2.77 mmol), isobutylaldehyde (220  $\mu\text{L}$ , 3.05 mmol) and Pic-BH<sub>3</sub> (450 mg, 3.54 mmol) in methanol (8 mL), were stirred at room temperature for 20h. Purification by column chromatography (*Stationary Phase*: Silica, 50 g; *Mobile Phase*: 10% EtOAc in  $\text{CH}_2\text{Cl}_2$ ) isolated target material as a colourless crystalline solid. Yield: 814mg, 80%; m.p.: 90–91°C;  $R_F$ : 0.39 (10% EtOAc in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.98 (m, 9H,  $J$  = 6.6 Hz,  $\text{CH}_3$  x3), 1.60 (sext, 2H,  $J$  = 7.3 Hz,  $\text{CH}_2$ ), 1.99 (sept, 1H,  $J$  = 6.8 Hz, CH), 3.03 (t, 2H,  $J$  = 7.1 Hz,  $\text{CH}_2$ ), 3.83 (d, 2H,  $J$  = 7.5 Hz,  $\text{CH}_2$ ), 3.91 (s, 3H,

CO<sub>2</sub>Me), 6.32 (d, 2H,  $J = 8.7$  Hz, ArH), 7.12 (d, 2H,  $J = 8.7$  Hz, ArH), 7.16 (d, 2H,  $J = 8.7$  Hz, ArH), 7.91 (d, 2H,  $J = 8.7$  Hz, ArH); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): 11.97, 20.71, 22.92, 27.69, 45.58, 52.54, 57.47, 111.47, 123.75, 126.96, 127.16, 130.79, 131.65, 149.92, 150.34, 166.90, 171.16; IR (solid state):  $\nu_{\max}/\text{cm}^{-1} = 3368$  (NH), 2965, 2925, 2870 (alkyl CH), 1723 (CO); TOF-MS ESI:  $m/z = 369$  [M+H]<sup>+</sup>; CHN Anal.: (Found: C, 71.35; H, 7.70; N, 7.45; C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>O<sub>3</sub> requires: C, 71.71; H, 7.66; N, 7.60 %)

**Methyl-4-[[N-(4-nitrobenzoyl)-N-(4-N'-propylamido)benzoyl]-N'-propylamido]-benzoate 8a**

Methyl-4-[N-(4-N-propylamino)benzoyl]-N'-propylamido]-benzoate (914 mg, 2.58 mmol), *p*-nitrobenzoic acid (450 mg, 2.69 mmol) and dichlorotriphenylphosphorane (2.15 g, 6.45 mmol) in chloroform (10 mL), was stirred at reflux for 26 hours. Column chromatography (*Stationary Phase*: Silica, 55 g; *Mobile Phase*: 10% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>) isolated title product as a cream foam. Yield: 1.07 g, 83%; m.p. 45–47°C; R<sub>F</sub>: 0.47 (2% MeOH in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.83$  (2 x t, 6H,  $J = 7.3$  Hz, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.5 (m, 4H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.78 (m, 4H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.87 (s, 3H, CO<sub>2</sub>Me), 6.75 (d, 2H,  $J = 8.4$  Hz, ArH), 6.91 (d, 2H,  $J = 8.5$  Hz, ArH), 7.09 (d, 2H,  $J = 8.4$  Hz, ArH), 7.26 (d, 2H,  $J = 8.7$  Hz, ArH), 7.77 (d, 2H,  $J = 8.5$  Hz, ArH), 7.93 (d, 2H,  $J = 8.7$  Hz, ArH); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 11.65, 11.68, 21.23, 21.36, 52.26, 52.33, 52.85, 123.41, 127.52, 127.65, 128.80, 129.95, 130.45, 130.85, 135.25, 142.42, 144.16, 147.75, 148.46, 166.44, 168.26, 169.26$ ; IR (solid state):  $\nu_{\max}/\text{cm}^{-1} = 3073$  (NH), 2966, 2875 (aliphatic CH), 1721 (CO), 1641, (CO), 1603 (CO), 1526; HRMS-ESI  $m/z =$  Found: 526.1932 [M+Na<sup>+</sup>]; C<sub>28</sub>H<sub>29</sub>N<sub>3</sub>NaO<sub>6</sub> requires: 526.1949.

**Methyl-4-[[N-(4-nitrobenzoyl)-N-(4-N'-propylamido)benzoyl]-N'-isobutylamido]-benzoate 8b**

Methyl-4-[N-(4-N-propylamino)benzoyl]-N'-isobutylamido]-benzoate (810 mg, 2.20 mmol), *p*-nitrobenzoic acid (380 mg, 2.27 mmol) and dichlorotriphenylphosphorane (1.76 g, 5.28 mmol) in chloroform (15 mL), were heated at reflux for 24 h. Column chromatography (*Stationary Phase*: Silica, 70 g; *Mobile Phase*: 10% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>) isolated title product as a pale yellow foam. Yield: 893 mg, 79%; m.p.: 57–59°C; R<sub>F</sub>: 0.31 (10% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 0.90$  (t, 3H,  $J = 7.2$  Hz, CH<sub>3</sub>), 0.92 (d, 6H,  $J = 6.6$  Hz, CH<sub>3</sub>), 1.56 (sext, 2H,  $J = 7.5$  Hz, CH<sub>2</sub>), 1.88 (sept, 1H,  $J = 6.9$  Hz, CH), 3.79 (d, 2H,  $J = 7.5$  Hz, CH<sub>2</sub>), 3.82 (t, 2H,  $J = 7.6$  Hz, CH<sub>2</sub>), 3.94 (s, 3H, CO<sub>2</sub>Me), 6.83 (d, 2H,  $J = 8.4$  Hz, ArH), 6.99 (d, 2H,  $J = 8.5$  Hz, ArH), 7.15 (d, 2H,  $J = 8.4$  Hz, ArH), 7.33 (d, 2H,  $J = 8.7$  Hz, ArH), 7.83 (d, 2H,  $J = 8.5$  Hz, ArH), 8.00 (d, 2H,  $J = 8.7$  Hz, ArH); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): 11.26, 14.20, 20.14, 20.80, 27.07, 51.86, 52.46, 56.80, 123.02, 127.14, 128.24, 129.57, 129.98, 130.40, 135.04, 142.01, 143.67, 147.48, 148.05, 166.03, 167.86, 169.18; IR (solid state):  $\nu_{\max}/\text{cm}^{-1} = 2961, 2873$  (alkyl CH), 1721 (CO), 1646 (CO), 1602 (CO),

1524, 1509; TOF-MS ESI:  $m/z = 540 [M+Na]^+$ ; CHN Anal.: (Found: C, 66.85; H, 6.05; N, 8.00;  $C_{29}H_{31}N_3O_6$  requires: C, 67.30; H, 6.04; N, 8.12 %)

**Methyl-4- $\{N-(4\text{-aminobenzoyl})-N-(4\text{-}N'\text{-propylamido)benzoyl}\}-N'\text{-propylamido}\}$ -benzoate **9a****

Methyl-4- $\{N-(4\text{-nitrobenzoyl})-N-(4\text{-}N'\text{-propylamido)benzoyl}\}-N'\text{-propylamido}\}$ -benzoate (1.05 g, 2.08 mmol) was hydrogenated for 15 h. Target amine was isolated as cream crystalline solid. Yield: 883 mg, 90%; m.p. 75–77°C;  $R_F$ : 0.11 (20% EtOAc in  $CH_2Cl_2$ );  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta = 0.90$  (t, 3H,  $J = 7.4$  Hz,  $\underline{CH_3CH_2}$ ), 0.97 (t, 3H,  $J = 7.3$  Hz,  $\underline{CH_3CH_2}$ ), ~1.6 (m, 4H,  $CH_3\underline{CH_2}$ ), 3.80 (t, 2H,  $J = 7.7$  Hz,  $CH_2\underline{CH_2}$ ), 3.92 (t, 2H,  $J = 7.6$  Hz,  $CH_2\underline{CH_2}$ ), 3.96 (s, 3H,  $CO_2Me$ ), 6.39 (d, 2H,  $J = 8.5$  Hz, ArH), 6.86 (d, 2H,  $J = 8.5$  Hz, ArH), 7.01 (d, 2H,  $J = 8.6$  Hz, ArH), 7.04 (d, 2H,  $J = 8.6$  Hz, ArH), 7.16 (d, 2H,  $J = 8.5$  Hz, ArH), 7.90 (d, 2H,  $J = 8.6$  Hz, ArH);  $^{13}C$  NMR (300 MHz,  $CDCl_3$ ): 11.73, 21.42, 52.13, 52.36, 52.78, 113.74, 125.12, 127.31, 127.62, 128.04, 129.75, 131.01, 131.41, 134.00, 146.33, 148.15, 148.73, 166.89, 170.25, 170.46; IR (solid state):  $\nu_{max}/cm^{-1} = 3452, 3353$  (NH), 1701 (CO); HRMS-ESI  $m/z =$  Found: 474.2396  $[M+H]^+$ ;  $C_{28}H_{32}N_3O_4$  requires: 474.2387.

**Methyl-4- $\{N-(4\text{-aminobenzoyl})-N-(4\text{-}N'\text{-propylamido)benzoyl}\}-N'\text{-isobutylamido}\}$ -benzoate **9b****

Methyl-4- $\{N-(4\text{-nitrobenzoyl})-N-(4\text{-}N'\text{-propylamido)benzoyl}\}-N'\text{-isobutylamido}\}$ -benzoate (875 mg, 1.69 mmol) was hydrogenated for 16h. Target material isolated as a colourless solid. Yield: 493mg, 1.01mmol, 60%; M.p.: 191–193°C;  $R_F$ : 0.15 (20% EtOAc in  $CH_2Cl_2$ );  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta = 0.79$  (t, 3H,  $J = 7.4$  Hz,  $CH_3$ ), 0.86 (d, 6H,  $J = 6.7$  Hz,  $CH_3$ ), 1.47 (sext, 2H,  $J = 7.5$  Hz,  $CH_2$ ), 1.83 (sept, 1H,  $J = 6.8$  Hz, CH), 3.69 (t, 2H,  $J = 7.8$  Hz,  $CH_2$ ), 3.74 (d, 2H,  $J = 7.5$  Hz,  $CH_2$ ), 3.85 (s, 3H,  $CO_2Me$ ), 3.95 (broad s, 2H,  $NH_2$ ), 6.24 (d, 2H,  $J = 8.6$  Hz, ArH), 6.75 (d, 2H,  $J = 8.5$  Hz, ArH), 6.90 (d, 2H,  $J = 8.6$  Hz, ArH), 6.96 (d, 2H,  $J = 8.6$  Hz, ArH), 7.05 (d, 2H,  $J = 8.5$  Hz, ArH), 7.79 (d, 2H,  $J = 8.6$  Hz, ArH);  $^{13}C$  NMR (300 MHz,  $CDCl_3$ ): 11.75, 20.57, 21.35, 27.52, 52.36, 52.77, 57.03, 113.74, 125.12, 127.19, 127.34, 127.89, 129.69, 130.97, 131.40, 134.20, 146.26, 148.31, 148.74, 166.88, 170.48, 170.55; IR (solid state):  $\nu_{max}/cm^{-1} = 3458, 3352$  (NH), 1704 (CO); CHN Anal.: (Found: C, 70.85; H, 6.75; N, 8.45;  $C_{29}H_{33}N_3O_4$  requires: C, 71.44; H, 6.82; N, 8.45 %); HRMS-ESI  $m/z =$  Found: 488.2529  $[M+H]^+$ ;  $C_{29}H_{34}N_3O_4$  requires: 488.2544).

**Methyl-4- $\{N-(4\text{-}N'\text{propylaminobenzoyl})-N-(4\text{-}N'\text{-propylamido)benzoyl}\}-N'\text{-propylamido}\}$ -benzoate **2a****

Methyl-4- $\{N-(4\text{-aminobenzoyl})-N-(4\text{-}N'\text{-propylamido)benzoyl}\}-N'\text{-propylamido}\}$ -benzoate (398 mg, 0.84 mmol), propionaldehyde (65  $\mu$ L, 0.90 mmol) and Pic-BH<sub>3</sub> (110 mg, 1.03 mmol) in methanol (20 mL) was stirred at room temperature for 14 hours. Purification by column chromatography (*Stationary Phase*: Silica, 40g; *Mobile Phase*: 8% EtOAc in  $CH_2Cl_2$ ) isolated



target material as a colourless foam. Yield: 289 mg, 88 %; m.p.: 49–51°C; R<sub>F</sub>: 0.21 (10% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 0.86 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>), 0.93 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>), 0.99 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>), 1.54 (q, 2H, *J* = 7.5 Hz, CH<sub>2</sub>), 1.63 (m, 4H, CH<sub>2</sub>), 3.06 (t, 2H, *J* = 7.1 Hz, CH<sub>2</sub>), 3.76 (t, 2H, *J* = 7.6 Hz, CH<sub>2</sub>), 3.90 (t, 2H, *J* = 7.2 Hz, CH<sub>2</sub>), 3.91 (s, 3H, CO<sub>2</sub>Me), 4.15 (broad s, NH), 6.24 (d, 2H, *J* = 8.7 Hz, ArH), 6.84 (d, 2H, *J* = 8.4 Hz, ArH), 7.02 (t, 4H, *J* = 8.4 Hz, ArH), 7.14 (d, 2H, *J* = 8.4 Hz, ArH), 7.87 (d, 2H, *J* = 8.5 Hz, ArH); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): 11.33, 11.37, 11.59, 21.02, 22.56, 45.18, 51.75, 52.06, 52.31, 110.81, 122.97, 126.75, 127.19, 127.72, 129.41, 130.54, 131.19, 133.26, 146.24, 147.75, 149.90, 166.33, 169.85, 170.15; IR (solid state): ν<sub>max</sub>/cm<sup>-1</sup> = 3353 (NH), 2965, 2874 (alkyl CH), 1716 (CO); CHN Anal.: (Found: C, 71.45; H, 7.30; N, 8.05; C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>O<sub>4</sub> requires: C, 72.21; H, 7.23; N, 8.15 %); HRMS-ESI *m/z* = Found: 538.2688 [M+Na]<sup>+</sup>; C<sub>31</sub>H<sub>37</sub>N<sub>3</sub>NaO<sub>4</sub> requires: 538.2676.

**Methyl-4-[{*N*-(4-*N*'benzylaminobenzoyl)-*N*-(4-*N*'-propylamido)benzoyl)-*N*'-propylamido]-benzoate 2b**

Methyl-4-[{*N*-(4-aminobenzoyl)-*N*-(4-*N*'-propylamido)benzoyl)-*N*'-isobutylamido]-benzoate (321 mg, 0.66 mmol), benzaldehyde (70 μL, 0.69 mmol) and Pic-BH<sub>3</sub> (85 mg, 0.80 mmol) in methanol (20 mL) was stirred at room temperature for 14 hours. Purification by column chromatography (*Stationary Phase*: Silica, 25g; *Mobile Phase*: 8% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>) isolated target material as a colourless foam. Yield: 365mg, 0.63mmol, 95%; m.p.: 54–56°C; R<sub>F</sub>: 0.31 (10% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 0.79 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>), 0.87 (d, 6H, *J* = 6.6 Hz, CH<sub>3</sub>), 1.47 (m, 2H, CH<sub>2</sub>), 1.84 (m, 1H, CH), 3.70 (t, 2H, *J* = 7.6 Hz, CH<sub>2</sub>), 3.74 (m, 5H, CO<sub>2</sub>Me + CH<sub>2</sub>), 4.25 (s, 2H, CH<sub>2</sub>) ~4.5 (broad s, 1H, NH), 6.23 (d, 2H, *J* = 8.6 Hz, ArH), 6.77 (d, 2H, *J* = 8.4 Hz, ArH), 6.95 (d, 4H, *J* = 8.4 Hz, ArH), 7.06 (d, 2H, *J* = 8.4 Hz, ArH), 7.25 (m, 5H, ArH), 7.77 (d, 2H, *J* = 8.5 Hz, ArH); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): 11.36, 20.18, 20.98, 27.13, 47.60, 52.06, 52.25, 56.67, 111.16, 123.63, 127.05, 127.33, 127.35, 127.57, 128.65, 129.38, 130.48, 131.16, 132.27, 133.51, 138.77, 146.06, 147.91, 149.51, 166.34, 170.04, 170.13; IR (solid state): ν<sub>max</sub>/cm<sup>-1</sup> = 3348 (NH), 1722 (ester CO), 1632 (amide CO); HRMS-ESI *m/z* = (Found: 576.2855 [M-H]<sup>-</sup>; C<sub>36</sub>H<sub>38</sub>N<sub>3</sub>O<sub>4</sub> requires: 576.2868.

**4-[{*N*-(4-*N*'propylaminobenzoyl)-*N*-(4-*N*'-propylamido)benzoyl)-*N*'-propylamido]-benzoic acid 3a**

To a stirred solution of methyl-4-[{*N*-(4-*N*'propylaminobenzoyl)-*N*-(4-*N*'-propylamido)benzoyl)-*N*'-propylamido]-benzoate (147 mg, 0.29 mmol) in a water (3 mL)/ methanol (5 mL) mix was added 1M NaOH (3 mL). The reaction mixture was stirred at room temperature for 20 hours to completion. The mixture was acidified to pH 4 (1N HCl) and partitioned between dichloromethane

(2x20mL). The combined organic fractions were dried (MgSO<sub>4</sub>) and concentrated before final drying under vacuum. Product was isolated as a colourless crystalline solid. Yield: 128mg, 88%; m.p. 137–138°C; R<sub>F</sub>: 0.09 (4% MeOH in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, MeOD): δ = 0.76 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>), 0.83 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>), 0.91 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>), 1.41 (q, 2H, *J* = 7.5 Hz, CH<sub>2</sub>), 1.52 (q, 2H, *J* = 7.5 Hz, CH<sub>2</sub>), 1.59 (q, 2H, *J* = 7.5 Hz, CH<sub>2</sub>), 3.09 (t, 2H, *J* = 7.8 Hz, CH<sub>2</sub>), 3.70 (t, 2H, *J* = 7.5 Hz, CH<sub>2</sub>), 3.82 (t, 2H, *J* = 7.5 Hz, CH<sub>2</sub>), 6.74 (broad s, 2H, ArH), 6.89 (d, 2H, *J* = 8.4 Hz, ArH), 7.08 (q, 6H, *J* = 8.4 Hz, ArH), 7.78 (d, 2H, *J* = 8.5 Hz, ArH); <sup>13</sup>C NMR (300 MHz, MeOD): 11.83, 11.91, 22.11, 22.25, 22.30, 48.48, 50.18, 53.06, 53.27, 117.83, 128.88, 129.25, 130.49, 130.93, 132.07, 132.17, 136.09, 145.44, 146.41, 148.73, 169.23, 172.13; IR (solid state): ν<sub>max</sub>/cm<sup>-1</sup> = 3375 (br CO<sub>2</sub>H), 1707 (CO); HRMS-ESI *m/z* = Found: 500.2543 [M-H<sup>+</sup>] C<sub>35</sub>H<sub>36</sub>N<sub>3</sub>O<sub>4</sub> requires: 500.2555.

#### 4-*[N*-(4-*N'*benzylaminobenzoyl)-*N*-(4-*N'*propylamido)benzoyl)-*N'*-isobutylamido]-benzoic acid **3b**

To a stirred solution of methyl-4-*[N*-(4-*N'*benzylaminobenzoyl)-*N*-(4-*N'*propylamido)benzoyl)-*N'*-propylamido]-benzoate (205 mg, 0.36 mmol) in a water (3 mL)/ methanol (5 mL) mix was added 1M NaOH (3 mL, excess). The reaction mixture was stirred at room temperature for 20 hours to completion. The mixture was acidified to pH 4 (1N HCl) and partitioned between dichloromethane (2 x 20 mL). The combined organic fractions were dried (MgSO<sub>4</sub>) and concentrated before final drying under vacuum. Product was isolated as a colourless crystalline solid. Yield: 172 mg, 85%; m.p. 97-99°C; R<sub>F</sub>: 0.36 (10% MeOH in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, MeOD): δ = 0.86 (t, 3H, *J* = 7.4 Hz, CH<sub>3</sub>), 0.97 (d, 6H, *J* = 6.7 Hz, CH<sub>3</sub>), 1.51 (m, 2H, CH<sub>2</sub>), 1.84 (m, 1H, CH), 3.79 (t, 2H, *J* = 7.5 Hz, CH<sub>2</sub>), 3.86 (d, 2H, *J* = 7.4 Hz, CH<sub>2</sub>), 4.35 (s, 2H, CH<sub>2</sub>), 6.35 (d, 2H, *J* = 8.8 Hz, ArH), 6.93 (d, 2H, *J* = 8.8 Hz, ArH), 6.96 (d, 2H, *J* = 8.4 Hz, ArH), 7.17 (m, 5H, ArH), 7.31 (m, 4H, ArH), 7.86 (d, 2H, *J* = 8.6 Hz, ArH); <sup>13</sup>C NMR (300 MHz, MeOD): 11.91, 20.86, 22.15, 28.63, 48.11, 53.30, 57.96, 112.45, 123.75, 128.23, 128.49, 128.56, 129.13, 129.78, 130.40, 130.71, 132.07, 132.27, 135.66, 141.14, 147.19, 148.79, 152.26, 169.16, 172.64, 173.22; IR (solid state): ν<sub>max</sub>/cm<sup>-1</sup> = 3361 (NH), 2964 (CH), 1707 (CO), 1596 (CO); HRMS-ESI *m/z* = Found: 562.2713 [M-H]<sup>-</sup>; C<sub>35</sub>H<sub>36</sub>N<sub>3</sub>O<sub>4</sub> requires: 562.2711.

#### Cyclic Trimer **1a**

Methyl-4-*[N*-(4-*N'*propylaminobenzoyl)-*N*-(4-*N'*propylamido)benzoyl)-*N'*-propylamido]-benzoic acid (82 mg, 0.16 mmol) and dichlorotriphenylphosphorane (400 mg, 1.2 mmol) were stirred in chloroform (5mL) at reflux for 28 hours. The reaction mixture was concentrated and purified by column chromatography (*Stationary Phase*: Silica, 25g; *Mobile Phase*: 15% Et<sub>2</sub>O in CH<sub>2</sub>Cl<sub>2</sub>) to

reveal target macrocycle as a colourless solid. Yield: 72mg, 93%; m.p.: 193–194°C;  $R_F$ : 0.54 (15% EtOAc in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.93 (t, 9H,  $J$  = 7.3 Hz,  $\text{CH}_3$ ), 1.57 (m, 6H,  $\text{CH}_2$ ), 3.76 (d, 6H,  $J$  = 7.5 Hz,  $\text{CH}_2$ ), 6.81 (d, 6H,  $J$  = 8.1 Hz, ArH), 7.01 (d, 6H,  $J$  = 8.1 Hz, ArH);  $^{13}\text{C}$  NMR (500 MHz,  $\text{CDCl}_3$ ): 11.66, 21.27, 50.95, 128.50, 129.05, 136.46, 143.24, 171.04; IR (solid state):  $\nu_{\text{max}}/\text{cm}^{-1}$  = 2966, 2872, 1647 (CO), 1605 (CO); CHN Anal.: (Found: C, 74.35; H, 6.90; N, 8.45;  $\text{C}_{30}\text{H}_{33}\text{N}_3\text{O}_3$  requires: C, 74.51; H, 6.88; N, 8.69 %); HRMS-ESI  $m/z$  = Found: 484.2601 [ $\text{M}+\text{H}^+$ ]  $\text{C}_{30}\text{H}_{34}\text{N}_3\text{O}_3$  requires: 484.2595.

### Cyclic Trimer: 1b

4- $\{N$ -(4- $N'$ benzylaminobenzoyl)- $N$ -(4- $N'$ propylamido)benzoyl)- $N'$ -isobutylamido]-benzoic acid (158 mg, 0.28 mmol) and dichlorotriphenylphosphorane (400 mg, 1.2 mmol) were stirred in chloroform (5 mL) at reflux for 28 hours. The reaction mixture was concentrated and purified by column chromatography (*Stationary Phase*: Silica, 30g; *Mobile Phase*: 15%  $\text{Et}_2\text{O}$  in  $\text{CH}_2\text{Cl}_2$ ) to reveal target macrocycle as a colourless solid. Yield: 138 mg, 0.25 mmol, 89%; m.p.: 89–91°C;  $R_F$ : 0.28 (10% EtOAc in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.91 (t, 3H,  $J$  = 7.3 Hz,  $\text{CH}_3$ ), 0.95 (d, 6H,  $J$  = 6.6 Hz,  $\text{CH}_3$ ), 1.55 (m, 2H,  $\text{CH}_2$ ), 1.83 (m, 1H, CH), 3.66 (d, 2H,  $J$  = 7.4 Hz,  $\text{CH}_2$ ), 3.73 (t, 2H,  $J$  = 7.6 Hz,  $\text{CH}_2$ ), 4.97 (s, 2H,  $\text{CH}_2$ ), 6.60 (d, 2H,  $J$  = 8.2 Hz, ArH), 6.76 (d, 2H,  $J$  = 8.1 Hz, ArH), 6.82 (d, 2H,  $J$  = 8.2 Hz, ArH), 6.92 (d, 2H,  $J$  = 8.2 Hz, ArH), 6.98 (d, 2H,  $J$  = 8.1 Hz, ArH), 7.03 (d, 2H,  $J$  = 8.2 Hz, ArH), 7.24 (m, 5H, ArH);  $^{13}\text{C}$  NMR (500 MHz,  $\text{CDCl}_3$ ): 11.65, 20.51, 21.23, 27.28, 50.94, 53.01, 56.24, 128.18, 128.40, 128.58, 128.84, 129.00, 129.05, 129.18, 129.43, 135.83, 136.43, 136.53, 137.01, 142.94, 143.14, 143.69, 171.08, 171.30; IR (solid state):  $\nu_{\text{max}}/\text{cm}^{-1}$  = 3063, 2962, 2871, 1643 (CO), 1605 (CO); CHN Anal.: (Found: C, 76.25; H, 6.5; N, 7.45;  $\text{C}_{35}\text{H}_{35}\text{N}_3\text{O}_3$  requires: C, 77.04; H, 6.47; N, 7.70 %); HRMS-ESI  $m/z$  = Found: 568.2567 [ $\text{M}+\text{Na}^+$ ]  $\text{C}_{35}\text{H}_{35}\text{N}_3\text{O}_3\text{Na}$  requires: 568.2571.

### Crystal Structure Determination for 2a

Single crystals were grown by cooling a solution of wet solution of ether and methanol. X-ray diffraction data were collected at the University of Leeds.

**Crystal data.**  $\text{C}_{31}\text{H}_{39}\text{N}_3\text{O}_5$ ,  $M$  = 533.65, crystal size 0.33 x 0.165 x 0.16, triclinic,  $a$  = 10.3830(2),  $b$  = 12.3990(3),  $c$  = 12.8450(3) Å,  $\alpha$  = 104.730(1),  $\beta$  = 91.325(1),  $\gamma$  = 114.224(1)°,  $U$  = 1443.150 (57) Å<sup>3</sup>,  $T$  = 150(2), space group  $P$ -1,  $Z$  = 2,  $\mu(\text{MoK}\alpha)$  = 0.083 mm<sup>-1</sup>, 28977 reflections measured, 6611 unique ( $R_{\text{int}}$  = 0.0757), 4603 observed ( $I > 2\sigma(I)$ ). The final  $R_1$  was 0.0512 (observed reflections) and  $wR(F^2)$  was 0.1650 (all data) for 368 parameters.

### Crystal Structure Determination for **1a**

Single crystals of a 1:1 **1a**:toluene solvate were grown by slow evaporation of a solution of dichloromethane and toluene. X-ray diffraction data were collected at the microcrystal diffraction facility on station 16.2SMX of the Synchrotron Radiation Source, CCLRC Daresbury Laboratory, UK.

**Crystal data.**  $C_{37}H_{41}N_3O_3$ ,  $M = 575.73$ , crystal size  $0.13 \times 0.04 \times 0.02$ , monoclinic,  $a = 26.934(3)$ ,  $b = 9.8762(12)$ ,  $c = 47.994(6)$  Å,  $\beta = 94.712(1)^\circ$ ,  $U = 12723(3)$  Å<sup>3</sup>,  $T = 150(2)$  K, space group  $P2_1/c$  (no. 14),  $Z = 16$ ,  $\mu = 0.076$  mm<sup>-1</sup>,  $\lambda = 0.7977$  Å (synchrotron), 66070 reflections measured, 17528 unique ( $R_{\text{int}} = 0.0690$ ), 12870 observed ( $I > 2\sigma(I)$ ). The final  $R_1$  was 0.0674 (observed reflections) and  $wR(F^2)$  was 0.1831 (all data) for 1564 parameters.

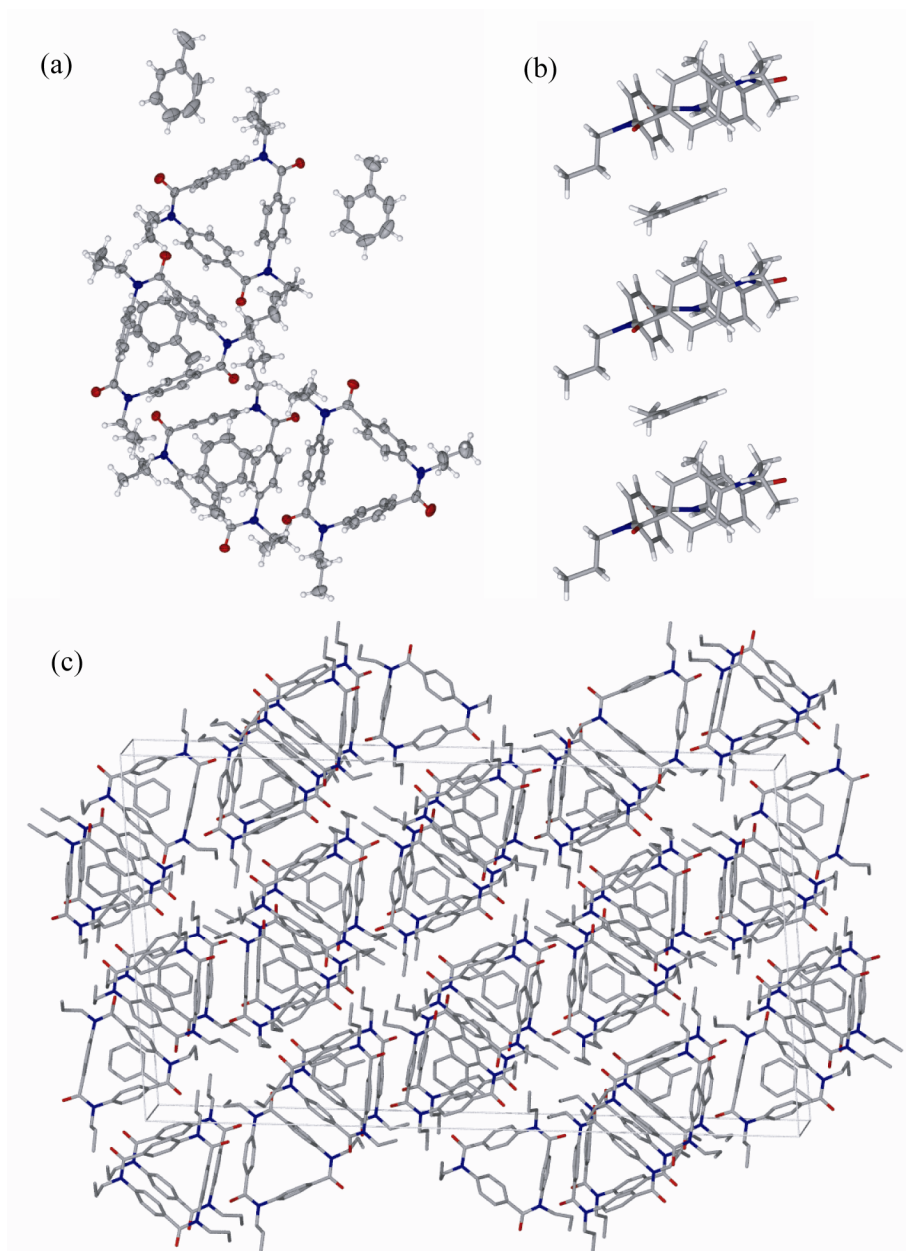


Figure S1. additional solid state representations of macrocycle **1a**  
(a) the asymmetric unit (b) columnar stacking of individual trimers via edge-to-face  $\pi$ - $\pi$  stacking with toluene (c) packing of columns

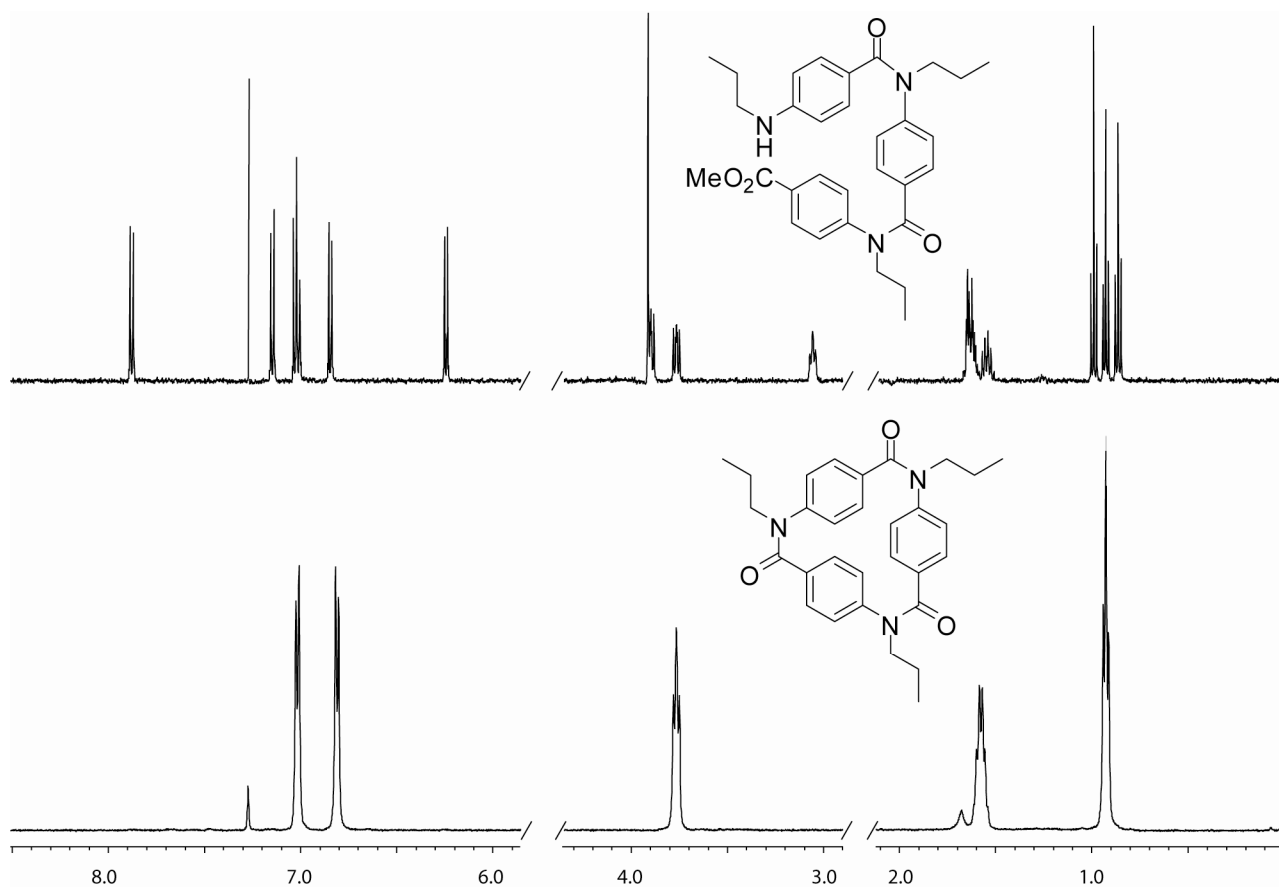


Figure S2. <sup>1</sup>H NMR Spectra (500 MHz, CDCl<sub>3</sub>) of acyclic trimer **2a** and cyclic trimer **1a**

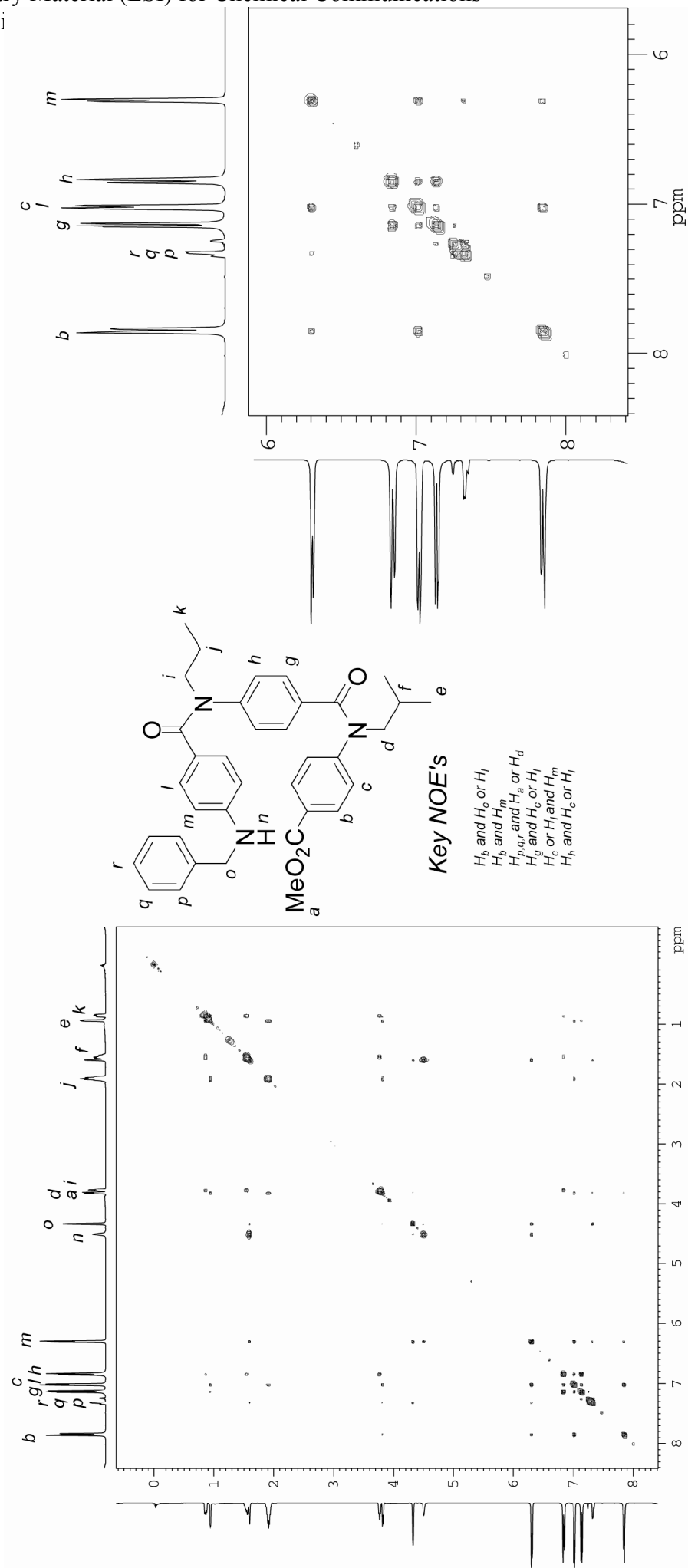


Figure S3. <sup>1</sup>H NOESY Spectra (500 MHz, CDCl<sub>3</sub>) of acyclic trimer **2b** and cyclic trimer **1b**

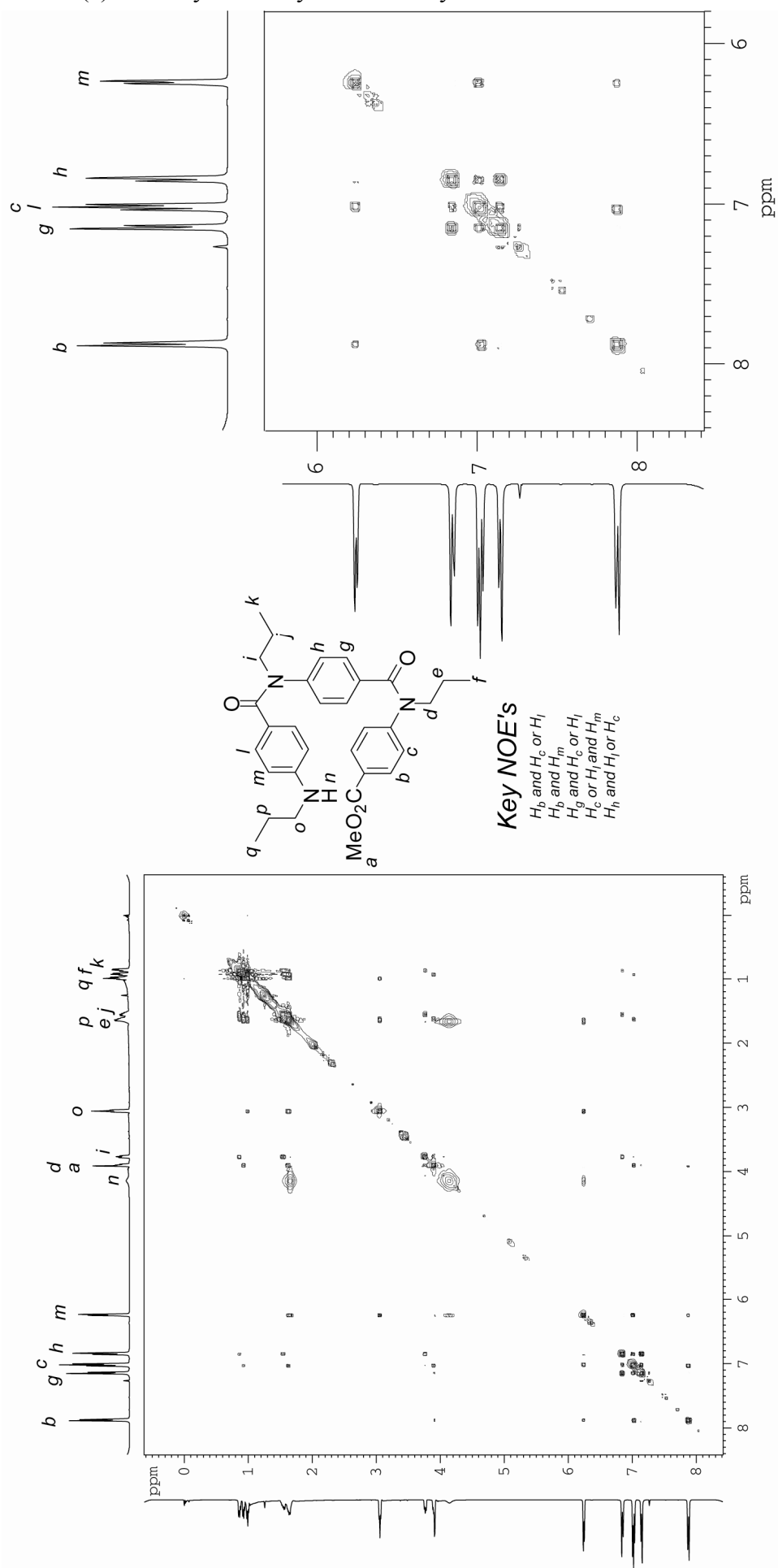


Figure S4. <sup>1</sup>H NOESY Spectra (500 MHz, CDCl<sub>3</sub>) of acyclic trimer **2a** and cyclic trimer **1a**