Non-Aggregational Aromatic Oligoamide Macrocycles

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I. Synthetic Procedures

**General Experimental.** Chemicals were purchased from commercial sources and used as received. Silica gel for analytical thin layer chromatography (TLC) and column chromatography (200–300 mesh) were purchased from Qingdao Haiyang Chemical Co., Ltd & SpeciaIl Silica Gel Factory. The $^1$H NMR spectra were recorded at 400 or 500 MHz and $^{13}$C NMR spectra were measured at 100 or 125 MHz on a Bruker AV400 spectrometer at ambient temperature. Chemical shifts are reported in parts per million downfield from TMS (tetramethylsilane). Coupling constant in $^1$H NMR are expressed in Hertz. MS (MALDI-TOF) spectra were performed on a Autoflex III instrument. EI mass spectra were performed on a ZAB-HS instrument. ESI mass spectra were performed on a Quattro micro$^{TM}$ API instrument. Elemental analyses were performed on a vario EL instrument. Melting points were measured on a microscope hot stage melting point apparatus and are uncorrected.

I-1. Synthesis of Macrocycles 2

![Synthesis of Macrocycles 2](image-url)
2,6-dimethoxy-3,5-dinitro-benzoic acid (2-1). 2,6-dimethoxybenzoic acid (9.1 g, 50 mmol) was dissolved in concentrated sulfuric acid (20 mL) and cooled to 0 °C in an ice bath. Then the mixture of sulfuric acid (15 mL) and nitric acid (63%, 7 mL) was added to the solution drop by drop in 1 h under vigorous stirring. The mixture was allowed to warm to room temperature for another 30 min, and then was poured into 30 g of crushed ice. The precipitate was collected by filtration and was dissolved in saturated sodium carbonate solution, then the solid was filtered off and the solution was acidified with conc. HCl till pH reached ca.1. Filtration and washing with water afforded the product as a faint yellow solid (11.2 g, 82.3%).

2,6-dimethoxy-3,5-dinitrobenzoyl chloride (2-2). 2-1 (13.6 g, 50 mmol) and phosphorus pentachloride (11.5 g, 55 mmol) were mixed in a round bottom flask under stirring at room temperature. When all the solid reacted into liquid, removed the resulting phosphoryl trichloride at reduced pressure. The residue was purified by column chromatography using petroleum ether/ethyl acetate (5:1) as the eluent, to afford the product as a yellow oil (10.6 g, 67.7%).

(S)-methyl 2-(2,6-dimethoxy-3,5-dinitrobenzamido)propanoate (2a-3). To a solution of L-alanine methyl ester hydrochloride (1.4 g, 10 mmol) and triethylamine
(4 mL) in dry methylene chloride (150 mL) was added 2,6-dimethoxy-3,5-dinitrobenzoyl chloride (2.9 g, 10 mmol) in dry methylene chloride (50 mL) at 0 °C. The mixture was allowed to warm to room temperature for 0.5 h, then most of the solvent was removed under reduced pressure. The resulting precipitate was filtered and afforded the product as a yellow crystal (3.2 g, 89.6 %); m.p. 173.5 °C. 1H NMR (400 MHz, CDCl3) δ 8.55 (s, 1H), 6.48 (d, J = 6.9, 1H), 4.80 (m, 1H), 4.05 (s, 6H), 3.81 (s, 3H), 1.56 (d, J = 6.9, 3H); 13C NMR (101 MHz, CDCl3) δ 172.46, 161.13, 155.69, 138.14, 129.37, 124.15, 64.38, 52.82, 48.89, 18.16; ESI-MS: 358.0 (M+H)+; EA (%): found N, 11.73; C, 43.79; H, 4.42, Calcd N, 11.76; C, 43.70; H, 4.23.

**Compound 2a-4.** 2a-3 (1 g, 2.8 mmol) was reduced in the presence of 10% Pd/C (100 mg) in 20 mL of methanol and 60 mL of THF under H2 (30 °C, 4 atm) for 2h. The mixture was filtered. After the solvent was removed under reduced pressure, dry THF was added to the residue, and then dry HCl gas was introduced for ca. 40 min. The precipitate was collected by filtration and washed with THF and petroleum ether to afford a white solid (0.65 g, 62.9%). 1H NMR (400 MHz, MeOD) δ 6.79 (s, 1H), 4.63 -4.68 (m, 1H), 3.81 (s, 6H), 3.77 (s, 3H), 1.48 (d, J = 7.3 Hz, 3H); 13C NMR (101 MHz, MeOD) δ 174.15, 166.72, 143.77, 130.64, 127.09, 111.36, 111.31, 62.45, 52.72, 17.33; ESI-MS: 298.3 (M+H+).

**2-(2-(isopentyloxy)ethoxy)ethanol (2-5).** To a solution of diethylene glycol (42.4 g, 0.4 mol) in THF (250 mL) was added NaH (1.5 g, 63 mmol) in an ice bath, followed by adding 1-bromo-3-methylbutane (10 mL, 20 mmol) dropwised. The mixture was refluxed for 12 h. After removal of the solvent, the residue was treated with water, extracted with ethyl acetate (200 mL × 3). The combined organic solvent was dried over anhydrous Na2SO4. The solvent was removed and provided the product as a colorless oil (3.2 g, 89.5 %), which was used for the next step without further purification.

**2-(2-(isopentyloxy)ethoxy)ethyl 4-methylbenzenesulfonate(2-6).** To a flask with
2-(2-(isopentyloxy)ethoxy)ethanol (3 g, 17 mmol) in THF (80 mL) at 0°C was added TsCl (3.2 g, 17 mmol) in 40 mL of THF. The mixture was stirred at room temperature for 2 h. After removal of the solvent, the residue was treated with water, extracted with ethyl acetate (200 mL × 3). The combined organic solvent was dried over anhydrous Na₂SO₄. After removing the solvent, the residue was purified by chromatography (petroleum ether/EtOAc, 4:1) to afford the product as a light yellow oil (3.7 g, 67.3%). ¹H NMR (400 MHz, CDCl₃) δ 7.80 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 4.16 (dd, J = 5.4, 4.4 Hz, 2H), 3.73 – 3.67 (m, 2H), 3.57 (dt, J = 4.5, 1.4 Hz, 2H), 3.51 (dt, J = 4.2, 1.4 Hz, 2H), 3.45 (t, J = 6.9 Hz, 2H), 2.45 (s, 3H), 1.73 – 1.59 (m, 1H), 1.52 – 1.41 (m, 2H), 0.89 (d, J = 6.6 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 144.75, 133.01, 129.79, 127.97, 70.79, 70.01, 69.89, 69.25, 68.67, 38.38, 25.04, 22.61, 21.64; MS(ESI): [M+H]⁺: 331.5.

4,6-dihydroxy-isophthalic acid (2-7). ¹ Resorcin (5 g, 45 mmol) and potassium bicarbonate (10.5 g, 105 mmol) were well mixed and ground before added to an autoclave. The reaction mixture was degassed with carbon dioxide. The mixture was then heated to 200°C for 4 hours. After cooling to room temperature, 30 mL of water was added to dissolve the reaction mixture. The solution was acidified with 6 N hydrochloric acid to pH 1. The resulting slurry was filtered and washed with water several times to give the product as white powders.

4,6-dihydroxy-isophthalic acid dimethyl ester (2-8). To a solution of 2-8 (20 g, 100 mmol) in methanol (350 mL) was added conc. sulfate acid (20 mL) slowly in 5 min at room temperature. The solution was refluxed for 60 hours. After cooling to room temperature, the white precipitate was collected and washed with methanol. The mother solution was concentrated and allowed to stand overnight at ca. 4°C. Then the white solid were combined and washed with methanol and afforded the product as a white solid (21.0 g, 93%).

4,6-bis-(3-methyl-butoxy)-isophthalic acid dimethyl ester (2a-9). A mixture of 2-8 (13.6 g, 60 mmol), 1-bromo-3-methyl-butane (17 mL, 132 mmol) and anhydrous potassium carbonate (20.7 g, 150 mmol) in DMF (200 mL) was heated at 100°C for 6
hours. The solid was filtered off and the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate (200 mL) and washed with NaHCO₃ solution and then water. The organic layer was pooled and dried over anhydrous sodium sulfate and evaporated to provide the product as a yellow solid (15.3 g, 70%).

\(^1\)H NMR (CDCl₃, 400 MHz) \(\delta\) 8.46 (s, 1H), 6.45 (s, 1H), 4.12 (t, \(J = 6.5\) Hz, 4H), 3.85 (s, 6H), 1.96~1.95 (m, 2H), 1.80 (q, \(J = 6.5\) Hz, 4H), \(\delta\) 1.00 (d, \(J = 6.5\) Hz, 12H); \(^{13}\)C NMR (CDCl₃, 101 MHz) \(\delta\) 165.4, 163.7, 137.1, 111.6, 97.2, 67.5, 51.7, 37.6, 24.9, 22.6; MS(EI) \(m/z\) 366 [M\(^+\), (58)], 277 (53), 265 (31), 207 (61), 194 (100), 162 (69), 43 (82); Anal.Calcd for \((C_{20}H_{30}O_6)\): N, 0.00; C, 65.55; H, 8.25; found N, 0.00; C, 65.55; H, 8.15.

4,6-bis(3-methyl-butoxy)-isophthalic acid (2a-10). To a solution of 2a-9 (3.7 g, 10 mmol) in MeOH (30 mL) was added 2 M NaOH (20 mL, 40 mmol) at room temperature. The mixture was heated to refluxed for 5 h. After evaporating most of the methanol, the mixture was acidified with 3 N hydrochloric acid to pH 2. The precipitate was filtered to afford the product as a white solid (3.26 g, 97.6%). \(^1\)H NMR (CDCl₃, 400 MHz) \(\delta\) 9.89 (brs, 2H), 8.86 (s, 1H), 6.55 (s, 1H), 4.30 (t, \(J = 6.0\) Hz, 4H), 1.83~1.91 (m, 6H), 1.02 (d, \(J = 6.0\) Hz, 12H); \(^{13}\)C NMR(CDCl₃, 101 MHz) \(\delta\) 165.1, 162.9, 140.0, 111.7, 96.9, 69.2, 37.5, 25.1, 24.5; MS (ESI) \(m/z\) 339.4 (M + H); Anal.Calcd for \((C_{18}H_{26}O_6)\): N, 0.00; C, 63.89; H, 7.74; found N, 0.00; C, 63.70; H, 7.54.

dimethyl 4,6-bis(2-(2-(isopentyloxy)ethoxy)ethoxy)isophthalate (2b-9). Prepared analogously as described above for compound 2a-9. Colorless oil, 76.4 %. \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 8.46 (s, 1H), 6.57 (s, 1H), 4.24 (w, 4H), 3.94 (w, 4H), 3.85 (s, 6H), 3.80~3.72 (m, 4H), 3.64~3.55 (m, 4H), 3.48 (t, \(J = 6.9\) Hz, 4H), 1.69-1.64 (m, 2H), 1.48 (q, \(J = 7.0\) Hz, 4H), 0.89 (d, \(J = 6.6\) Hz, 12H); \(^{13}\)C NMR (101 MHz, CDCl₃) \(\delta\) 165.16, 163.32, 137.00, 112.22, 98.47, 71.15, 70.15, 69.88, 69.40, 69.12, 51.74, 38.39, 25.06, 22.63; MS(ESI): [M+H]\(^+\): 543.7.

4,6-bis(2-(2-(isopentyloxy)ethoxy)ethoxy)isophthalic acid (2b-10). Prepared
analogously as described above for compound \textbf{2a-10}. White solid, 94.5 %; m.p. 92.4 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.88 (s, 1H), 6.65 (s, 1H), 4.49 – 4.37 (m, 4H), 4.02 – 3.91 (m, 4H), 3.73 (dd, $J$ = 5.6, 3.5 Hz, 4H), 3.62 (dd, $J$ = 5.6, 3.5 Hz, 4H), 3.48 (t, $J$ = 7.0 Hz, 4H), 1.70 – 1.59 (m, 2H), 1.51 – 1.35 (m, 4H), 0.88 (d, $J$ = 6.6 Hz, 12H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.74, 162.35, 139.44, 112.44, 98.44, 70.86, 70.03, 69.93, 69.70, 68.66, 38.30, 25.05, 22.62; MS(ESI): [M+Na]$^+$: 537.6.

**Compound 2a-11.** \textbf{2a-10} (3.4 g, 10 mmol) was dissolved in 3 mL of thionyl chloride. The mixture was refluxed for 30 min. Then the solvent was evaporated at reduced pressure to provide the product as a white solid, which was dissolved in dry dichloromethane (80 mL), then 2a-4 (1.5 g, 4 mmol) in dry dichloromethane (50 mL) and triethylamine (0.5 mL) were added. The mixture was stirred for another 1h at 0°C. Then several drops of water were added. When the solvent was evaporated, the residue was subjected to chromatography (CHCl$_3$ : MeOH : HCOOH, 30:1:0.5) to provide the product as a white solid (1.4 g, 36.5 %). m.p. 258.6 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.80 (s, 2H), 9.42 (s, 1H), 9.15 (s, 2H), 6.76 (d, $J$ = 7.5 Hz, 1H), 6.59 (s, 2H), 4.83–4.89 (m, 1H), 4.41 – 4.24 (m, 8H), 3.84 (s, 6H), 3.79 (s, 3H), 1.97 – 1.77 (m, 12H), 1.55 (d, $J$ = 7.2 Hz, 3H), 1.01-1.04 (m, 24H); $^{13}$C NMR (101 MHz, DMSO) $\delta$ 172.43, 165.91, 163.41, 162.42, 161.57, 160.44, 142.45, 135.75, 127.32, 125.11, 114.76, 113.62, 112.93, 98.38, 68.47, 67.30, 61.82, 51.78, 47.86, 37.19, 36.84, 24.63, 24.37, 22.35, 16.72; ESI-MS: 939.4 (M+H$^+$).

**Compound 2b-11.** Prepared analogously as described above for compound \textbf{2a-11}. Yellow oil, 42.5 %. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.90 (s, 2H), 9.29 (s, 1H), 9.07 (s, 2H), 6.76 (s, 2H), 4.87 – 4.79 (m, 1H), 4.49 (w, 4H), 4.40 (w, 4H), 3.99 (w, 4H), 3.94 (w, 4H), 3.85 (s, 6H), 3.79 (s, 3H), 3.76 – 3.67 (m, 8H), 3.66 – 3.57 (m, 4H), 3.58 – 3.41 (m, 8H), 3.37 (t, $J$ = 7.0 Hz, 4H), 1.72 – 1.55 (m, 4H), 1.53 (d, $J$ = 7.2 Hz, 3H), 1.45 (dd, $J$ = 14.2, 7.3 Hz, 4H), 1.34 (q, $J$ = 7.0 Hz, 4H), 0.88 (d, $J$ = 6.6 Hz, 12H), 0.83 (d, $J$ = 6.6 Hz, 12H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 173.02, 164.49, 164.26, 161.53, 161.36, 160.99, 143.72, 138.88, 128.13, 123.72, 116.98, 116.56, 112.08,
Compound 6a. 2a-10 (1.4 g, 4 mmol) was dissolved in 3 mL of thionyl chloride. The mixture was refluxed for 30 min. Then the solvent was evaporated to provide the product as a white solid, which was dissolved in dry dichloromethane (50 mL), then was dropped slowly into a stirred solution of 2a-4 (3.8 g, 10 mmol) in dry dichloromethane (80 mL) at 0°C in the presence of triethyl amine (0.5 mL). The mixture was stirred for another 1 h. Then the solvent was evaporated, the residue was subjected to chromatography (CHCl₃ : MeOH, 40:1) to provide the product as a white solid with the protection of nitrogen for the next coupling step (1.4 g, 39.8%).

1H NMR (400 MHz, CDCl₃) δ 9.99 (s, 2H), 9.12 (s, 1H), 8.13 (s, 2H), 6.76 (d, J = 7.6 Hz, 2H), 6.58 (s, 1H), 4.86 (p, J = 7.2 Hz, 2H), 4.32 (t, J = 6.8 Hz, 4H), 3.80 (s, 6H), 3.79 (s, 6H), 3.77 (s, 6H), 2.03 – 1.75 (m, 6H), 1.54 (d, J = 7.2 Hz, 6H), 0.99 (d, J = 6.4 Hz, 12H); 13C NMR (101 MHz, CDCl₃) δ 173.13, 164.51, 162.13, 160.27, 139.61, 138.79, 137.92, 136.73, 129.13, 123.82, 115.65, 109.81, 96.76, 68.65, 62.55, 61.38, 52.45, 48.32, 37.35, 25.13, 22.52, 18.36.

Compound 6b. Prepared analogously as described above for compound 6a. Yellow solid, 54.2%.

Compound 2a. To a solution of 2a-12 (187.6 mg, 0.2 mmol) in dry dichloromethane (20 mL) was added several drops of thionyl chloride. The mixture was refluxed for 30 min. The solvent was evaporated at reduced pressure. The residue was dissolved in dry dichloromethane (50 mL), and transferred to a 100 mL round-bottomed flask with two neck, under nitrogen protection cooled to 0°C, followed by addition of 6a (179.3 mg, 0.2 mmol) in dry dichloromethane (20 mL) in the presence of several drops of triethyl amine by a syringe within 30 min. The mixture was stirred for another 1 h. After the removal of the solvent, the residue was subjected to chromatography (CHCl₃ : MeOH, 20:1) to give the desired product as a white solid (56.1 mg, 15.6%); m.p. 294.3°C. 1H NMR (400 MHz, MeOD) δ 9.00 (s, 1H), 8.91 (s, 1H), 6.42 (s, 1H), 6.83 (w, 1H), 4.57 -4.54 (w, 2H), 4.29 (w, 2H), 4.04 (s, 3H), 3.96 (s, 3H), 3.82 (s, 3H), 2.02 – 1.90 (m,
6H), 1.59 (d, $J = 7.2$ Hz, 3H), 1.15 (w, 12H); $^{13}$C NMR (101 MHz, DMSO) $\delta$ 172.48, 163.56, 162.25, 160.07, 143.11, 136.78, 126.94, 124.97, 116.98, 114.79, 98.05, 68.53, 61.87, 51.79, 47.87, 37.05, 24.60, 22.36, 16.73; MS(MALDI): [M+Na]$^+$: 1822.3.

**Compound 2b.** Prepared analogously as described above for compound 2a. Yellow solid, 14.8 %. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.68 (s, 2H), 9.43 (s, 1H), 9.39 (s, 1H), 6.68 (s, 1H), 4.90 – 4.79 (m, 1H), 4.45 (w, 3H), 4.00 (w, 4H), 3.89 (w, 6H), 3.79 (w, 4H), 3.71 (w, 4H), 3.51 (w, 4H), 3.42 – 3.26 (w, 4H), 1.67 – 1.43 (m, 6H), 1.34 (d, $J = 7.0$ Hz, 3H), 0.83 (d, $J = 6.5$ Hz, 12H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 172.04, 163.21, 161.44, 159.33, 142.80, 137.86, 127.17, 122.74, 117.38, 114.69, 96.93, 69.77, 69.00, 68.65, 68.15, 61.61, 51.35, 47.27, 45.76, 37.10, 24.00, 21.58, 17.02; MS(MALDI): [M+Na]$^+$: 2349.9.

### I-2. Synthesis of 3 and 4

![Chemical structure and reaction scheme](image)

**4,6-bis-(3-methyl-butoxy)-isophthalic acid monomethyl ester (3-1).** To a solution of 2a-9 (3.7 g, 10 mmol) in MeOH (30 mL) was added 1 M NaOH (8 mL, 8 mmol, 0.8 eq) at room temperature. The mixture was refluxed for 4 h. After evaporating most of the methanol, the mixture was acidified with 3 N hydrochloric acid to pH 2. The precipitate was filtered and then was subjected to flash column chromatography (petroleum ether/aceton 5:1) to give the product as a white solid (2.3 g, 63.8%). $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ 8.42 (s, 1H), 6.86 (s, 1H), 4.32 (t, $J = 6.5$ Hz, 2H), 4.24 (t, $J = 7.0$ Hz, 2H), 3.71 (w, 4H), 3.63 (w, 4H), 3.51 (w, 4H), 3.42 – 3.26 (w, 4H), 1.67 – 1.43 (m, 6H), 1.34 (d, $J = 7.0$ Hz, 3H), 0.83 (d, $J = 6.5$ Hz, 12H).
\[ J = 6.4 \text{ Hz}, 2\text{H}) \], 3.81 (s, 3H), 1.90–1.99 (m, 2H), 1.77 (q, \( J = 6.8 \text{ Hz}, 2\text{H}) \), 1.71-1.73 (m, 2H), 0.98-1.02 (m, 12H); \( ^{13}\text{C NMR(CDCl}_3, 101 \text{ MHz}) \) \( \delta \) 164.8, 164.5, 164.2, 161.6, 138.4, 114.4, 109.7, 95.8, 69.0, 67.9, 51.8, 37.6, 37.5, 25.1, 24.9, 22.5, 22.4; ESI-MS: 353.0 (M+H\(^+\)).

**Compound 3.** 2a-4 (0.7 g, 2 mmol) was dissolved in CH\(_2\)Cl\(_2\) (50 mL) and triethylamine (0.5 mL) was added followed by the addition of acid chloride, prepared from 3-1 (1.4 g, 4 mmol) based on the general procedure (2a-11). The solution was stirred for 1h at 0°C. After the removal of the solvent, the residue was subjected to flash column chromatography (petroleum ether/acetone 3:1) to give the product as a white solid(1.7g, 86.9%). \(^1\text{H NMR (400 MHz, CDCl}_3\) \( \delta \) 10.00 (s, 2H), 9.61 (s, 1H), 8.95 (s, 2H), 6.66 (d, \( J = 6.9 \text{ Hz}, 1\text{H}) \), 6.52 (s, 2H), 4.92 – 4.82 (m, 1H), 4.30 (t, \( J = 6.5 \text{ Hz}, 4\text{H}) \), 4.13 (t, \( J = 6.6 \text{ Hz}, 4\text{H}) \), 3.86 (s, 6H), 3.84 (s, 6H), 3.80 (s, 3H), 1.97 – 1.76 (m, 12H), 1.54 (d, \( J = 7.2 \text{ Hz}, 3\text{H}) \), 1.00 (d, \( J = 2.36 \text{ Hz}, 24\text{H}) \); \( ^{13}\text{C NMR (101 MHz, CDCl}_3\) \( \delta \) 172.96, 165.15, 164.09, 163.16, 162.12, 160.81, 143.27, 137.91, 128.65, 123.28, 117.23, 113.93, 113.30, 96.89, 68.39, 67.74, 62.52, 52.48, 51.64, 48.40, 37.64, 37.41, 25.12, 24.96, 22.56, 18.29; ESI-MS: 989.2(M+Na\(^+\)).

**Compound 4.** The couple of 6a (358.6 mg, 0.4 mmol) and the acid chloride of 3-1 (0.35 g, 1 mmol) based on the similar procedure with 3 afforded the desired product as a white solid( 218.5 mg, 34.9%). \(^1\text{H NMR (400 MHz, CDCl}_3\) \( \delta \) 9.88 (s, 2H), 9.82 (s, 2H), 9.37 (s, 2H), 9.27 (s, 1H), 8.90 (s, 2H), 6.68 (d, \( J = 7.6 \text{ Hz}, 2\text{H}) \), 6.61 (s, 1H), 6.53 (s, 2H), 4.90 – 4.81 (m, 2H), 4.31 (m, 8H), 4.13 (t, \( J = 6.5 \text{ Hz}, 4\text{H}) \), 3.88 – 3.80 (m, 18H), 3.79 (s, 6H), 1.97 – 1.75 (m, 18H), 1.54 (d, \( J = 7.1 \text{ Hz}, 6\text{H}) \), 1.00-1.03 (m, 36H); \( ^{13}\text{C NMR (101 MHz, CDCl}_3\) \( \delta \) 171.91, 164.21, 163.20, 162.08, 161.17, 161.09, 159.83, 159.28, 142.92, 137.38, 136.71, 127.49, 127.39, 122.42, 117.08, 114.90, 113.13, 112.52, 96.23, 95.92, 67.62, 67.50, 66.85, 61.36, 61.34, 51.32, 50.59, 47.46, 36.71, 36.51, 36.49 ,24.17, 24.00, 21.54, 21.49, 17.16; MS(MALDI): [M+Na\(^+\)]: 1587.6.
II. NMR and Mass Spectra

Compound 2a-3
Compound 2a-4

\[
\text{\begin{align*}
\text{MeO} & \quad \text{NH}_2 \\
\text{H}_2\text{N} & \quad \text{NH}_2
\end{align*}}
\]
Compound 2b-9

\[
\begin{array}{c}
\text{MeOOC} \\
\text{COOMe}
\end{array}
\]
Compound 2a-11

[Chemical structure and spectra image]
Compound 2b-11

Electronic Supplementary Material (ESI) for Chemical Communications
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Compound 6a
Compound 2a
Compound 3

MALDI-TOF, CCA, WXX-G16, 2010, 11, 08

Electronic Supplementary Material (ESI) for Chemical Communications
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Compound 4
III. MALDI spectrum of the reaction mixture of attempted preparation of macrocycle 2a based on the one-pot reaction of monomeric diacid chloride and monomeric diamine

Explanation of peak labels: numbers indicate the degree of oligomerization (number of residues); peaks labeled in blue correspond to cyclic oligomers; peaks labeled in pink correspond to non-cyclic oligomeric diamines; peaks labeled in red correspond to non-cyclic oligomeric diacids.

IV. $^1$H NMR Spectra of 2a and 2b in Different Solvents
IV-1. Concentration dependent $^1$H NMR spectra of 2a in CDCl$_3$

IV-2. $^1$H NMR spectrum of 2a in CD$_3$OD
IV-3. $^1$H NMR spectrum of 2a in DMSO-$d_6$

IV-4. Concentration dependent $^1$H NMR spectra of 2b in CDCl$_3$
V. Concentration-dependent $^1$H NMR spectra of 2b + GuaCl (1:1) in CDCl$_3$

The signals of b, c and those of NH$_2$ were assigned based on this HSQC spectrum.
VII. ROESY Spectrum of 2b/GuaCl (1:1, 2 mM) in CDCl₃

Partial ROESY spectrum of 2b/GuaCl (1/1) (2 mM in CDCl₃, 298 K, mixing time: 0.4s).

VIII. Determination of the Association Constants of 2b•GuaCl Complex

The association constants \(K_a\) of 2b and guanidine hydrochloride were determined by \(^1\)H NMR study over the concentration range about 0.1 to 5 mM. The binding constants \(K_a\) were obtained by nonlinear regression analysis using 1stOpt Program based on the following equation and the measured concentration vs chemical shift data.

\[
\delta = \delta_s + \Delta \delta \{1 + (K_a/2C_0) - [(K_a/2C_0)^2 - (K_a/C_0)]^{1/2}\}
\]

\(\delta = \) the complexation-induced shift of the amide proton c of 2b

\(\Delta \delta = \) complexation induced shift;

\(K_a = \) Association constants;

\(C_0 = \) concentration of the host.

Four values of \(K_a\) (±10%) were obtained from CDCl₃ containing 5%, 10%, 15%, and 20% CD₃OD. The \(K_a\) value in CDCl₃ \((2.2 \pm 0.2) \times 10^6 \text{ M}^{-1}\) was obtained by extrapolating these \(K_a\) values to 0% CD₃OD.

<table>
<thead>
<tr>
<th>The ratio of MeOH in CDCl₃</th>
<th>5%</th>
<th>10%</th>
<th>15%</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>(K_a) (M(^{-1}))</td>
<td>1.9\times10^6</td>
<td>1.3\times10^6</td>
<td>1.1\times10^6</td>
<td>9.0\times10^5</td>
</tr>
</tbody>
</table>
Four values of \( K_a \) (±10%) were obtained from CDCl\(_3\) containing 5%, 10%, 15%, and 20% DMSO-\(d_6\). The \( K_a \) value in CDCl\(_3\) (\((1.2 \pm 0.1) \times 10^6 \text{ M}^{-1}\)) was obtained by extrapolating these \( K_a \) values to 0% DMSO-\(d_6\).

<table>
<thead>
<tr>
<th>The ratio of DMSO-(d_6) in CDCl(_3)</th>
<th>5%</th>
<th>10%</th>
<th>15%</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>( K_a (\text{M}^{-1}) )</td>
<td>(9.6 \times 10^5)</td>
<td>(6.8 \times 10^5)</td>
<td>(3.3 \times 10^5)</td>
<td>(1.8 \times 10^5)</td>
</tr>
</tbody>
</table>

**IX. Determination of Crystal Structures**

Data were collected on a Bruker APEX diffractometer with a CCD detector.\(^2\) Absorption corrections were made with the program SADABS.\(^3\) The crystallographic package SHELXTL\(^4\) and PLATON\(^5\) was used for all calculations.