Supplementary Material for:

Highly Selective One-Pot Synthesis of H-Bonded Pentagon-Shaped Circular Aromatic Pentamers

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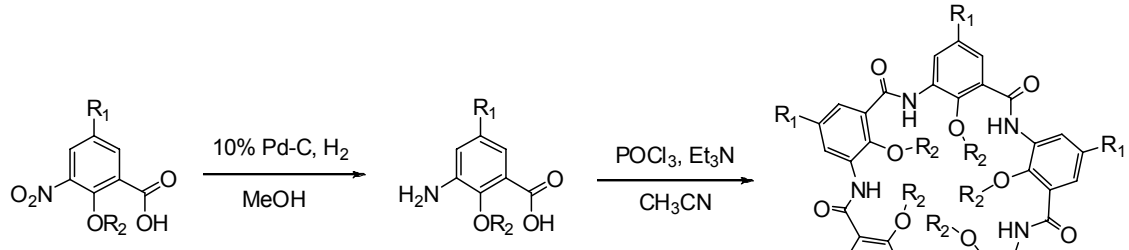
Table of Contents

General Remarks

All the reagents were obtained from commercial suppliers and used as received unless otherwise noted. Aqueous solutions were prepared from distilled water. The organic solutions from all liquid extractions were dried over anhydrous Na_2SO_4 for a minimum of 15 minutes before filtration. Reactions were monitored by thin-layer chromatography (TLC) on silica gel precoated glass plates (0.25 mm thickness, 60F-254, E. Merck). Flash column chromatography was performed using pre-coated 0.2 mm silica plates from Selecto Scientific. Chemical yields refer to pure isolated substances. Melting points were obtained either using Büchi Melting Point-B540. Mass spectra were obtained using the Instrumentation includes Finnigan MAT95XL-T and Micromass VG7035. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker ACF-300 (300 MHz) or AVF500 spectrometers (500 MHz). In addition, key compounds were characterized by X-ray Diffraction. The solvent signal of $CDCl_3$ was referenced at δ = 7.26. Coupling constants (*J* values) are reported in Hertz (Hz). ^{1}H NMR data are recorded in the order: chemical shift value, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), number of protons that gave rise to the signal and coupling constant, where applicable. ^{13}C spectra are proton-decoupled and recorded on Bruker ACF300 (300 MHz) and ACF500 spectrometers (500 MHz). The solvent, $CDCl_3$, was referenced at δ = 77 ppm and d_6-DMSO was referenced at δ = 39.5. $CDCl_3$ (99.8%-Deuterated) and d_6-DMSO (99.8%-Deuterated) was purchased from Aldrich and used without further purification.

Melting points were obtained either using Büchi Melting Point-B540.

Scheme S1. Synthetic Routes for 1a-7a and Circular Pentamers 1-7

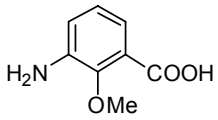


1f R_1 = H, R_2 = Me
2c R_1 = O*n*-C_8H_{17}, R_2 = Me
3b R_1 = OMe, R_2 = Me
4b R_1 = O*iso*-Pr, R_2 = Me
5b R_1 = Me, R_2 = Me
6b R_1 = H, R_2 = Et
7b R_1 = OMe, R_2 = Et

1a R_1 = H, R_2 = Me
2a R_1 = O*n*-C_8H_{17}, R_2 = Me
3a R_1 = OMe, R_2 = Me
4a R_1 = O*iso*-Pr, R_2 = Me
5a R_1 = Me, R_2 = Me
6a R_1 = H, R_2 = Et
7a R_1 = OMe, R_2 = Et

1 R_1 = H, R_2 = Me
2 R_1 = O*n*-C_8H_{17}, R_2 = Me
3 R_1 = OMe, R_2 = Me
4 R_1 = O*iso*-Pr, R_2 = Me
5 R_1 = Me, R_2 = Me
6 R_1 = H, R_2 = Et
7 R_1 = OMe, R_2 = Et

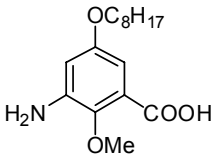
Synthetic Procedure & Characterization Data for 1a-7a and Pentamers 1-7



1a

3-amino-2-methoxybenzoic acid (1a)

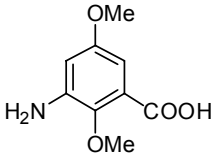
1f (3.94 g, 20.0 mmol, m.p. 198-200 °C) was reduced by catalytic hydrogenation in MeOH (100 mL) at 40 °C, using Pd-C (0.39 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the crude product, which was recrystallized from ether to give the pure product **1a** as a white solid, m.p. 104-105 °C. Yield: 3.14 g, 94 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.03-6.93 (m, 1H), 6.18 (s, 1H), 3.88 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.75, 146.89, 140.49, 124.84, 122.66, 121.64, 121.00, 60.89. HRMS-EI: calculated for $[M]^+$ ($C_8H_9NO_3^+$): m/z 167.0582, found: m/z 167.0582.



2a

3-amino-2-methoxy-5-(octyloxy)benzoic acid (2a)

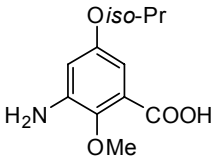
2c (6.5 g, 20.0 mmol, m.p. 72-73 °C) was reduced by catalytic hydrogenation in MeOH (100 mL) at 40 °C, using Pd-C (0.65 g, 10%) as the catalyst for 3 h. The reaction mixture w as then filtered and the solvent removed in *vacuo* to give the crude product, which was recrystallized from ether to give the pure product **2a** as a gray solid, m.p. 54-55 °C. Yield: 5.66 g, 96%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, *J* = 2.9 Hz, 1H), 6.51 (d, *J* = 2.9 Hz, 1H), 3.89 (t, *J* = 6.6 Hz, 2H), 3.84 (s, 3H), 1.75-1.68 (m, 2H), 1.44-1.36 (m, 2H), 1.34-1.22 (m, 9H), 0.86 (dd, *J* = 8.8, 5.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.68, 155.96, 141.12, 141.03, 122.49, 108.12, 105.43, 68.32, 61.13, 31.69, 29.21, 29.12, 29.08, 25.88, 22.54, 13.97. HRMS-ESI: calculated for $[M+Na]^+$ ($C_{16}H_{24}NO_4$+Na^+): *m/z* 318.1676, found: *m/z* 318.1681.



3a

3-amino-2,5-dimethoxybenzoic acid (3a)

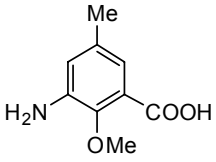
3b (2.27 g, 10.0 mmol, m.p. 186-187 °C) was reduced by catalytic hydrogenation in MeOH (50 mL) at 40 °C, using Pd-C (0.23 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the crude product, which was recrystallized from ether to give the pure product **1a** as a gray oily solid. Yield: 1.81 g, 92%.^{1}H NMR (500 MHz, $CDCl_3$) *δ* 6.91 (d, *J* = 3.0 Hz, 1H), 6.51 (d, *J* = 3.0 Hz, 1H), 6.02 (s, 2H), 3.85 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.51, 156.42, 141.18, 122.60, 107.64, 104.62, 61.18, 55.52; HRMS-EI: calculated for $[M]^+$ ($C_{10}H_{13}NO_4^+$): *m/z* 211.0845, found: *m/z* 211.0842.



4a

3-amino-5-isopropoxy-2-methoxybenzoic acid (4a)

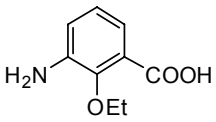
4b (2.55 g, 10.0 mmol, m.p. 117-119 °C) was reduced by catalytic hydrogenation in MeOH (50 mL) at 40 °C, using Pd-C (0.26 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the crude product, which was recrystallized from ether to give the pure product **4a** as a gray oily solid. Yield: 2.07 g, 92%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, J = 2.8 Hz, 1H), 6.51 (d, J = 2.9 Hz, 1H), 6.09 (s, 3H), 4.48 (dt, J = 12.1, 6.0 Hz, 1H), 3.85 (s, 3H), 1.28 (d, J = 6.0 Hz, 6H). ^{13}C NMR (125 MHz, CDCl3) δ 168.00, 154.68, 141.37, 141.08, 122.80, 109.48, 107.01, 70.43, 61.19, 21.98. HRMS-ESI: calculated for $[M+Na]^+$ ($C_{11}H_{15}NO_4$+Na^+): m/z 248.0893, found: m/z 248.0892.



5a

3-amino-2-methoxy-5-methylbenzoic acid (5a)

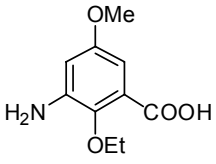
5b (1.27 g, 6.0 mmol, m.p. 180-182 °C) was reduced by catalytic hydrogenation in MeOH (100 mL) at 40 °C, using Pd-C (0.13 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the crude product, which was recrystallized from ether to give the pure product **4a** as a light yellow oily solid. Yield: 0.92 g, 85%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.25 (m, 1H), 6.82 (d, J = 1.6 Hz, 1H), 5.93 (s, 2H), 3.92 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.21, 144.51, 139.80, 135.23, 122.36, 121.96, 121.81, 61.03, 20.82. HRMS-ESI: calculated for $[M+Na]^+$ ($C_9H_{11}NO_3$+Na^+): m/z 204.0631, found: m/z 204.0635.



6a

3-amino-2-ethoxybenzoic acid (6a)

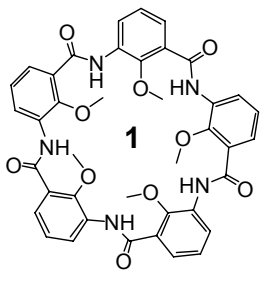
6b (4.22 g, 20.0 mmol, m.p. 96-97 °C) was reduced by catalytic hydrogenation in MeOH (100 mL) at 40 °C, using Pd-C (0.42 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the crude product, which was recrystallized from ether to give the pure product **6a** as a gray solid, m.p. 107-108 °C. Yield: 3.44 g, 95%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J = 6.6 Hz, 1H), 7.03 (t, J = 7.8 Hz, 1H), 6.97 (dd, J = 7.8, 1.6 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 1.46 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.28, 145.37, 140.34, 125.12, 122.73, 121.84, 121.09, 77.25, 77.00, 76.74, 69.97, 15.45. HRMS-EI: calculated for $[M]^+$ ($C_9H_{11}NO_3^+$): m/z 181.0739, found: m/z 181.0737.



7a

3-amino-2-ethoxy-5-methoxybenzoic acid (7a)

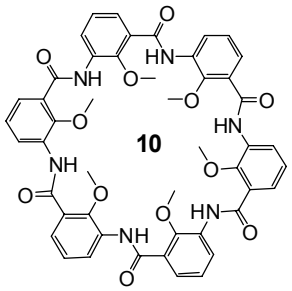
6b (2.41 g, 10.0 mmol, m.p. 143-145 °C) was reduced by catalytic hydrogenation in MeOH (50 mL) at 40 °C, using Pd-C (0.24 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the crude product, which was recrystallized from ether to give the pure product **6a** as a gray solid, m.p. 128-129 °C. Yield: 1.90 g, 90%.^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 (s, 1H), 6.52 (d, J = 3.0 Hz, 1H), 4.09 (q, J = 7.0 Hz, 2H), 3.77 (s, 3H), 1.46 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.93, 156.73, 140.95, 139.67, 122.72, 108.06, 104.60, 70.40, 55.63, 15.37. HRMS-EI: calculated for $[M]^+$ ($C_{10}H_{13}NO_4^+$): m/z 211.0845, found: m/z 811.0842.


1

Circular Pentamer 1

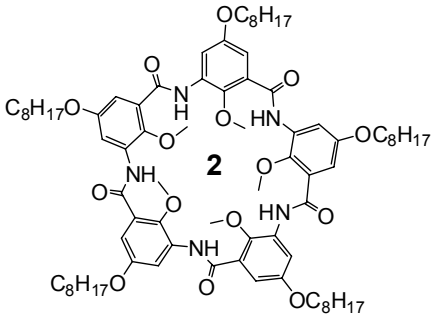
To a solution of amino acid **1a** (33.4 mg, 0.2 mmol) in CH_3CN (2.0 mL) was added $POCl_3$ (38 uL, 0.4 mmol) at room temperature. The solution was vigorously stirred. After 10 min, Et_3N (84 uL, 0.6 mmol) was added into the reaction mixture. The solution was stirred for 12 h. The reaction was concentrated *in vacuo*. The residue was purified by flash column

chromatography (ethyl acetate:dichloromethane = 1:10) to afford circular pentamer **1** as a white solid, m.p. 345 °C (Decomposed). Yield: 13.7 mg, 46%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.91 (s, 5H), 9.02 (d, *J* = 7.9 Hz, 5H), 8.04 (d, *J* = 7.7 Hz, 5H), 7.46 (t, *J* = 8.0 Hz, 5H), 4.12 (s, 15H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.27, 146.50, 132.85, 126.56, 126.18, 125.62, 124.33, 63.32. HRMS-ESI: exact mass calculated for $[M\text{-}H]^-$ ($C_{40}H_{35}N_5O_{10}$-H^-): *m/z* 744.2311, found: *m/z* 744.2314.



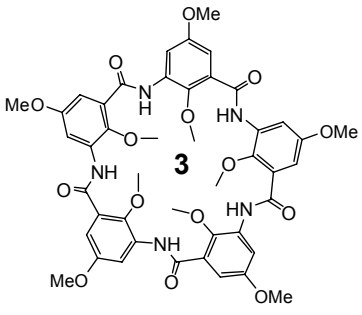
Circular Hexamer 10

White solid, m.p. 400 °C (Decomposed), yield: 1.8 mg, 6%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.68 (s, 6H), 8.77 (d, *J* = 7.0 Hz, 6H), 8.04-7.89 (m, 6H), 7.43 (t, *J* = 8.0 Hz, 6H), 4.02 (s, 18H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.39, 147.56, 131.90, 127.20, 126.68, 126.34, 125.94, 63.19.HRMS-ESI: calculated for $[M\text{-}H]^-$ ($C_{48}H_{41}N_6O_{12}^-$): *m/z* 893.2788, found: *m/z* 893.2825.



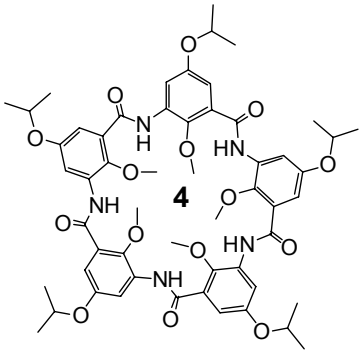
Circular Pentamer 2

To a solution of amino acid **2a** (59.0 mg, 0.2 mmol) in CH_3CN (2.0 mL) was added $POCl_3$ (38 uL, 0.4 mmol) at room temperature. The solution was vigorously stirred. After 10 min, Et_3N (84 uL, 0.6 mmol) was added into the reaction mixture. The solution was stirred for 12 h. The reaction was concentrated *in vacuo*. The residue was purified by flash column chromatography (ethyl acetate:dichloromethane = 1:8) to afford Circular pentamer **2** (**8a**) as a white solid, m.p. 202-204 °C. Yield: 23.3 mg, 42%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.96 (s, 5H), 8.61 (d, *J* = 2.9 Hz, 5H), 7.50 (d, *J* = 2.9 Hz, 5H), 4.10 (t, *J* = 6.4 Hz, 10H), 4.04 (s, 15H), 1.92-1.77 (m, 10H), 1.56-1.46 (m, 10H), 1.35 (dd, *J* = 13.1, 6.5 Hz, 40H), 0.93 (t, *J* = 6.8 Hz, 15H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.20, 156.88, 140.34, 133.45, 125.75, 111.05, 110.48, 68.73, 63.38, 31.81, 29.32, 29.23, 29.17, 25.98, 22.65, 14.08. HRMS-ESI: calculated for $[M\text{-}H]^-$ ($C_{80}H_{114}N_5O_{15}^-$): *m/z* 1384.8317, found: *m/z* 1384.8313.



Circular Pentamer 3

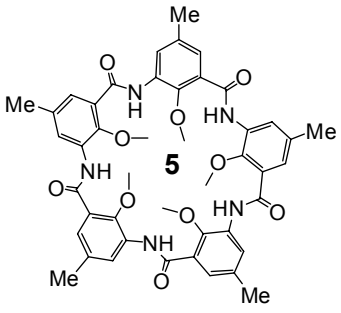
To a solution of amino acid **3a** (39.4 mg, 0.2 mmol) in CH_3CN (2.0 mL) was added $POCl_3$ (38 uL, 0.4 mmol) at room temperature. The solution was vigorously stirred. After 10 min, Et_3N (84 uL, 0.6 mmol) was added into the reaction mixture. The solution was stirred for 12 h. The reaction was concentrated *in vacuo*. The residue was purified by flash column chromatography (ethyl acetate:dichloromethane = 1:10) to afford circular pentamer **3** as a white solid, m.p. 342 °C (Decomposed). Yield: 16.2 mg, 45%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.97 (s, 5H), 8.65 (d, *J* = 3.1 Hz, 5H), 7.53 (d, *J* = 3.1 Hz, 5H), 4.05 (s, 15H), 3.96 (s, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.18, 157.37, 140.52, 133.53, 125.84, 110.59, 110.02, 63.43, 55.96. HRMS-ESI: calculated for $[M+Na]^+$ ($C_{45}H_{45}N_5O_{15}$+Na^+): *m/z* 918.2804, found: *m/z* 918.2780.



Circular Pentamer 4

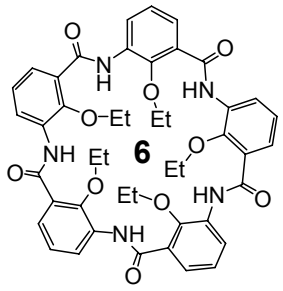
To a solution of amino acid **4a** (45.0 mg, 0.2 mmol) in CH_3CN (2.0 mL) was added $POCl_3$ (38 uL, 0.4 mmol) at room temperature. The solution was vigorously stirred. After 10 min, Et_3N (84 uL, 0.6

mmol) was added into the reaction mixture. The solution was stirred for 12 h. The reaction was concentrated *in vacuo*. The residue was purified by flash column chromatography (ethyl acetate:hexane = 1:5) to afford circular pentamer **4** as a white solid, m.p. 334-335 ^{o}C. Yield: 12.8 mg, 31%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.93 (s, 5H), 8.61 (d, *J* = 2.8 Hz, 5H), 7.51 (d, *J* = 2.7 Hz, 5H), 4.72 (m, 5H), 4.03 (s, 15H), 1.42 (d, *J* = 6.0 Hz, 30H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.21, 155.72, 140.29, 133.54, 125.88, 112.35, 112.04, 70.84, 63.36, 22.02. HRMS-FAB: calculated for $[M+H]^+$ ($C_{55}H_{65}N_5O_{15}$+H^+): *m/z* 1036.4550, found: *m/z* 1036.4506.



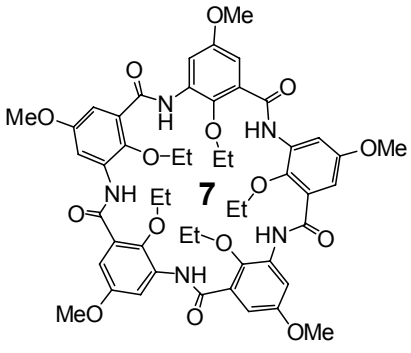
Circular Pentamer 5

To a solution of amino acid **5a** (36.2 mg, 0.2 mmol) in CH_3CN (2.0 mL) was added $POCl_3$ (38 uL, 0.4 mmol) at room temperature. The solution was vigorously stirred. The solution was stirred for 12 h. The reaction was concentrated *in vacuo*. The residue was purified by flash column chromatography (ethyl acetate:dichloromethane = 1:10) to afford circular pentamer **5** as a white solid, 380 ^{o}C (Decomposed) .Yield: 7.8 mg, 24%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.85 (s, 5H), 8.83 (s, 5H), 7.81 (s, 5H), 4.04 (s, 15H), 2.50 (s, 15H). ^{13}C NMR (125 MHz, D6-DMSO) δ 162.29, 144.67, 136.02, 132.61, 131.02, 125.96, 125.06, 124.53, 63.44, 22.57. HRMS-ESI: calculated for $[M-H]^-$ ($C_{45}H_{44}N_5O_{10}^-$): *m/z* 814.3094, found: *m/z* 814.3087.



Circular Pentamer 6

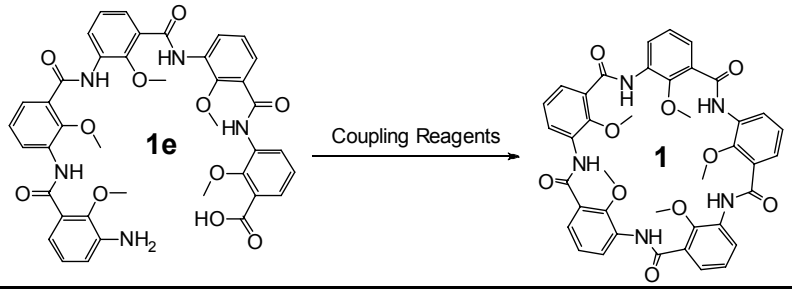
To a solution of amino acid **6a** (36.2 mg, 0.2 mmol) in CH_3CN (2.0 mL) was added $POCl_3$ (38 uL, 0.4 mmol) at room temperature. The solution was vigorously stirred. After 10 min, Et_3N (84 uL, 0.6 mmol) was added into the reaction mixture. The solution was stirred for 12 h. The reaction was concentrated *in vacuo*. The residue was purified by flash column chromatography (ethyl acetate:dichloromethane = 1:10) to afford circular pentamer **6** as a white solid, m.p. 327-329 ^{o}C. Yield: 10.4 mg, 32%.^{1}H NMR (500 MHz, $CDCl_3$) δ 10.40 (s, 5H), 8.94 (d, *J* = 8.1 Hz, 5H), 8.01-7.88 (m, 5H), 7.43 (t, *J* = 8.0 Hz, 5H), 4.20 (q, *J* = 7.0 Hz, 10H), 1.43 (t, *J* = 7.1 Hz, 15H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.99, 144.80, 133.16, 127.24, 126.14, 125.99, 123.79, 72.37, 15.00. HRMS-ESI: calculated for $[M-H]^-$ ($C_{55}H_{65}N_5O_{15}$+H^+): *m/z* 814.3094, found: *m/z* 814.3056.



Circular Pentamer 7

To a solution of amino acid **7a** (42.2 mg, 0.2 mmol) in CH_3CN (2.0 mL) was added $POCl_3$ (38 uL, 0.4 mmol) at room temperature. The solution was vigorously stirred. After 10 min, Et_3N (84 uL, 0.6 mmol) was added into the reaction mixture. The solution was stirred for 12 h. The reaction was concentrated *in vacuo*. The residue was purified by flash column chromatography (ethyl acetate:dichloromethane = 1:10) to afford circular pentamer **7** as a white solid, m.p. 320-321 ^{o}C. Yield: 10.1 mg, 26%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.42 (s, 5H), 8.54 (d, *J* = 3.1 Hz, 5H), 7.40 (d, *J* = 3.1 Hz, 5H), 4.11 (q, *J* = 6.7 Hz, 10H), 3.91 (s, 15H), 1.37 (t, *J* = 7.0 Hz, 15H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.91, 157.09, 138.63, 133.81, 127.47, 110.15, 109.91, 72.35, 55.92, 14.85.HRMS-ESI: calculated for $[M+H]^+$ ($C_{50}H_{55}N_5O_{15}$+Na^+): *m/z* 988.3587, found: *m/z* 988.3566.

Table S1. Searching Suitable Conditions[a] for Synthesizing Circular Pentamer 1 via Intramolecular Cyclization of Acyclic Pentamer 1e



Entry	Coupling Reagent	Base	Solvent (ratio)	Yield (%)[b]
1	DCC[c]	NA	DMF/DCM(1:1)	ND
2	CDI[c]	NA	DCM	ND
3	HATU[c]/HOBt[c]	NA	DCM	Trace
4	$P(OPh)_3$	Py[c]	NMP	Trace
5	Ph_3PCl_2	NA	$CHCl_3$	ND
6	PyBOP[c]	DMAP[c]	DMF/DCM(1:1)	22
7	BOP[c]	DIEA	DCM	72
8	$POCl_3$	Et_3N	DCM	70[d]
9	$POCl_3$	Et_3N	CH_3CN	76[d]

[a] Reaction conditions: **1e** (0.2 mmol), coupling reagent (2.0 equiv.), base (3.0 equiv.), room temerature, 12 hrs. [b] Isolated yield by flash column chromatography. [c] Abbeviation: N,N'-Dicyclohexylcarbodiimide (DCC), N,N'-Carbonyldiimidazole (CDI), 2-(1H-7-Azabenzotriazol-1-yl)--1,1,3,3-tetramethyl uronium hexafluorophosphate (HATU), N-Hydroxybenzotriazole (HOBt), Benzotriazole-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate (PyBOP), N,N-Diisopropylethylamine (DIEA).Benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (BOP), Pyridine (Py), 4-Dimethylaminopyridine (DMAP). [d] This work.

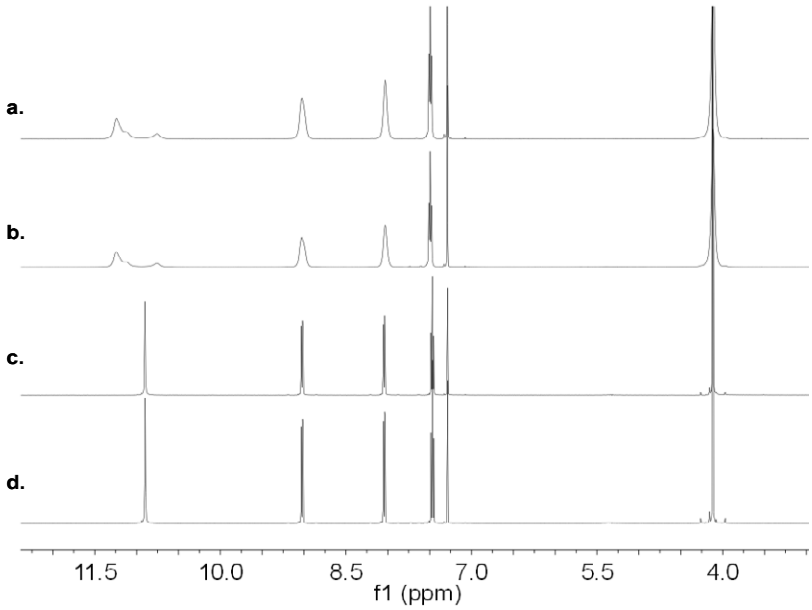


Figure S1. ^{1}H NMR spectra (5.0 mM, $CDCl_3$, 500 MHz) of circular pentamer **1**. (a) and (b) were recorded at 223 K; (c) and (d) were recorded at 298 K. **1** in (a) and (c) was made by the stepwise construction reported by us previously (*Org. Lett.* **2008**, *10*, 5127) while **1** in (b) and (d) was made by one-step cyclization reaction as reported in this work. These comparisons show that **1** made by two different routes are identical.

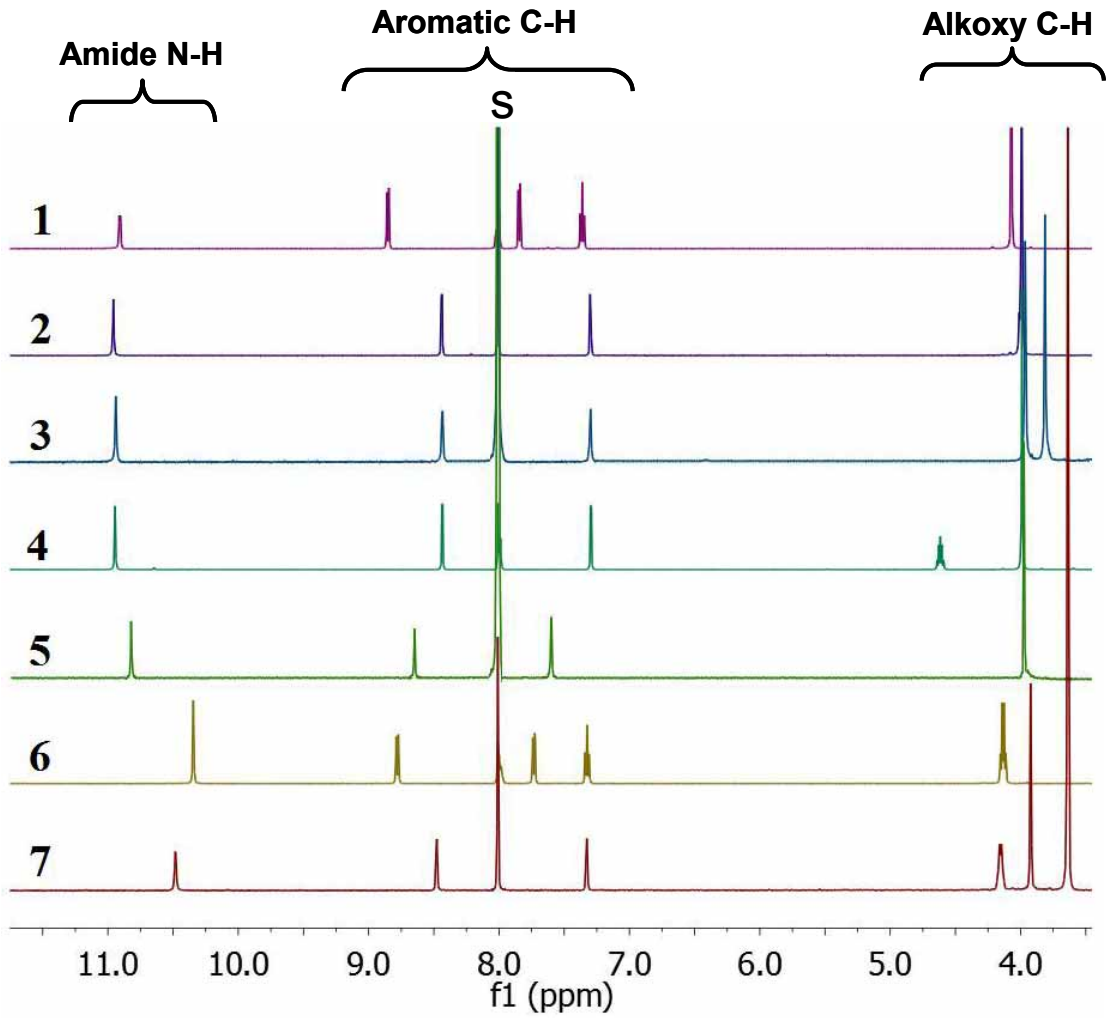


Figure S2. ^{1}H NMR spectra of pentamers **1**-**7** (500 MHz, 50% $CDCl_3$/50% DMSO-d_6, 298K). The ^{1}H NMR spectra of **1** and **6** in $CDCl_3$ showed four sets of proton signals corresponding to the aromatic and amide protons. Similarly, two sets of aromatic protons and one set of amide protons were observed for **2**-**5** and **7**. The observation of these single sets of ^{1}H NMR signals is in accord with the highly symmetrical nature of **1**-**7**. In particular, the amide protons of **1**-**7**, resonating at the very low field (> 10 ppm over a concentration range of 1-20 mM), are a diagnostic indicator of the presence of strong H-bonding interactions, consisting of both S(5) and S(6) type intramolecular H-bonds that cause the rigidification of the amide linkages and a circularly folded aromatic backbone in **1**-**7**. **S** refers to the solvent signal from $CDCl_3$.

Figure S3-S7: Aggregation Study of Pentamers 1, 2, 3, 6, and 7

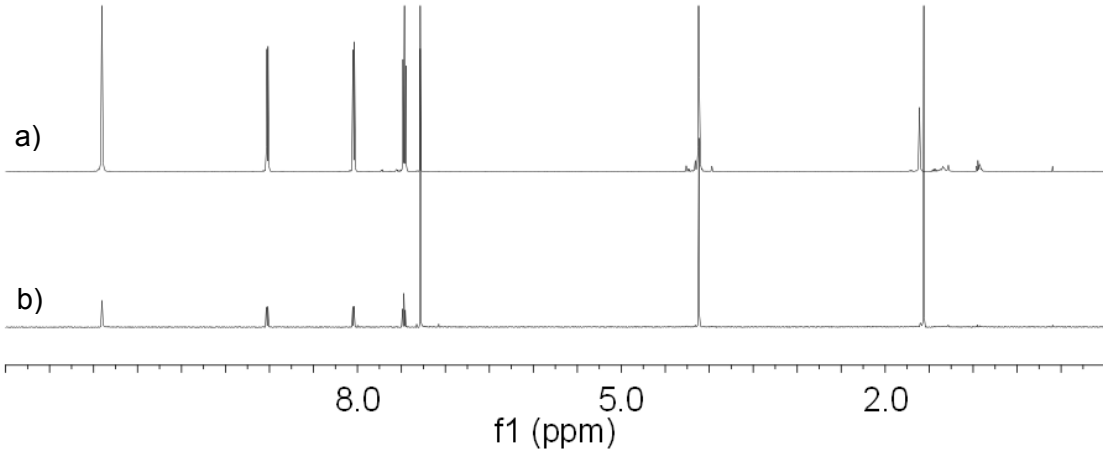


Figure S3. ^{1}H NMR spectra ($CDCl_3$, 500 MHz, 298 K) of pentamer **1** at (a) 20 mM and (b) 1.0 mM.

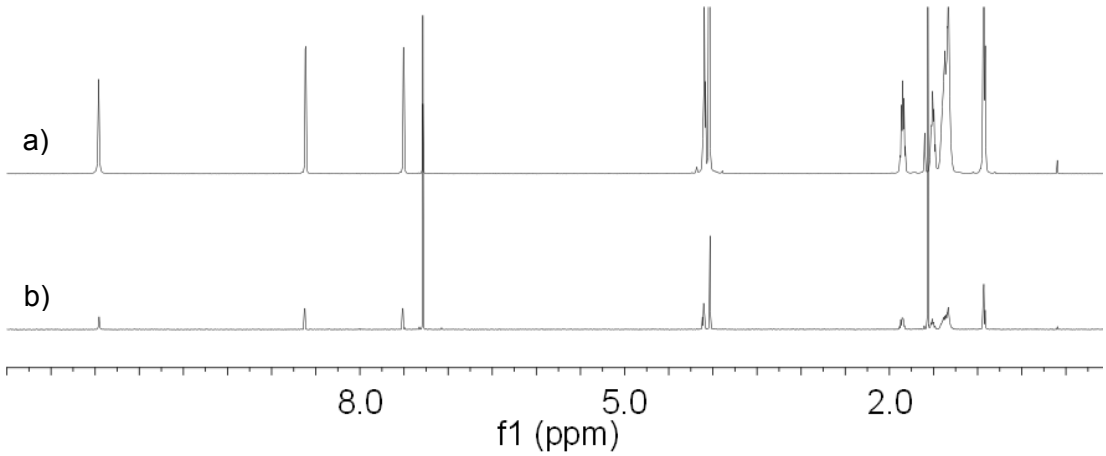


Figure S4. ^{1}H NMR spectra ($CDCl_3$, 500 MHz, 298 K) of pentamer **2** at (a) 20 mM and (b) 1.0 mM.

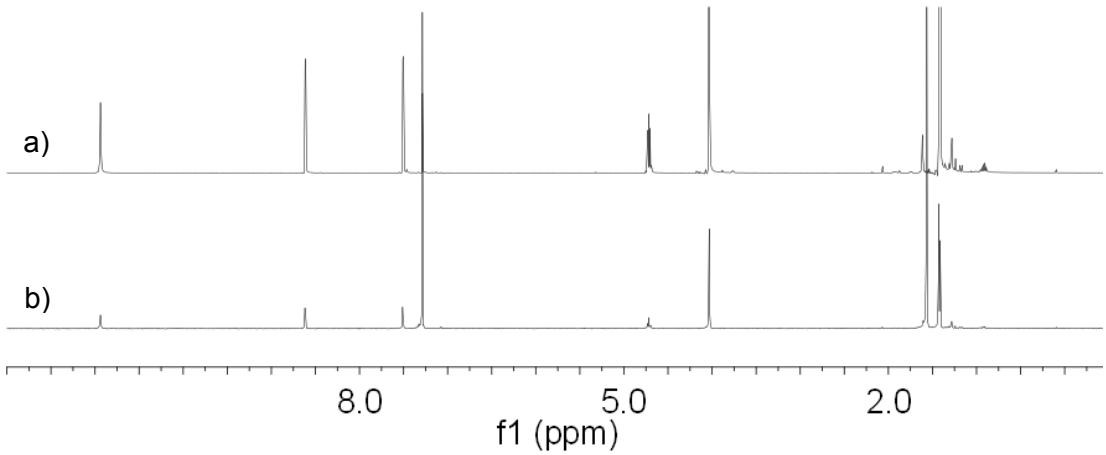


Figure S5. ^{1}H NMR spectra ($CDCl_3$, 500 MHz, 298 K) of pentamer **3** at (a) 20 mM and (b) 1.0 mM.

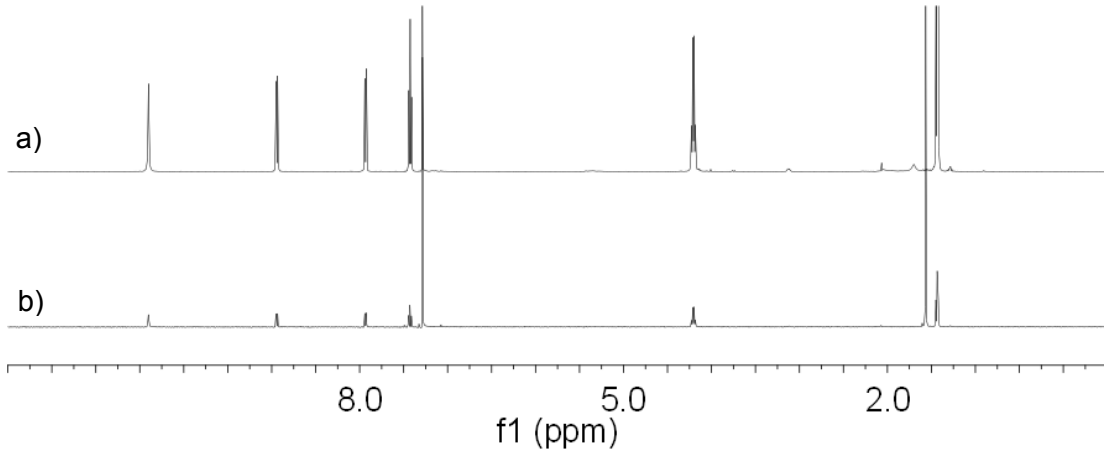


Figure S6. ^{1}H NMR spectra ($CDCl_3$, 500 MHz, 298 K) of pentamer **6** at (a) 20 mM and (b) 1.0 mM.

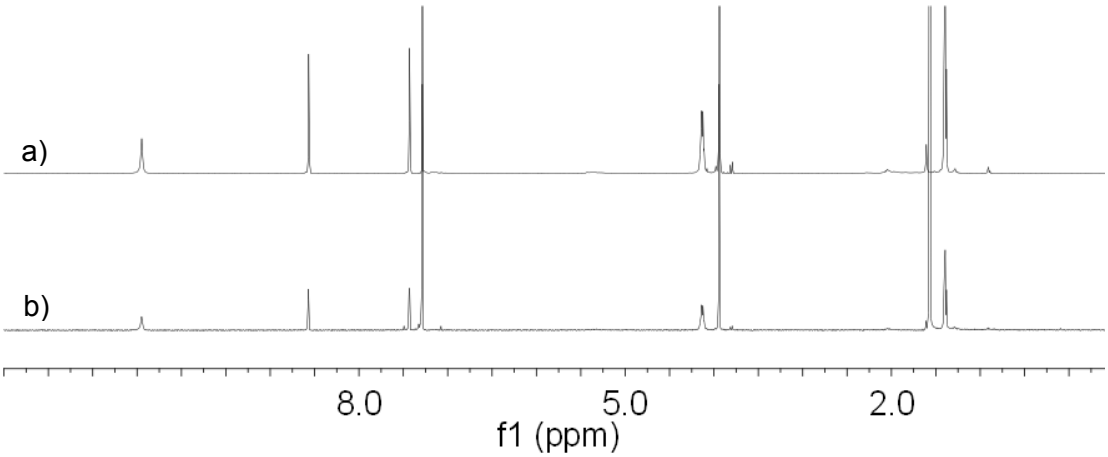


Figure S7. ^{1}H NMR spectra ($CDCl_3$, 500 MHz, 298 K) of pentamer **7** at (a) 20 mM and (b) 1.0 mM.

***Ab Initio* Molecular Modeling**: All the calculations were carried out by utilizing the Gaussian03 program package.[170] The geometry optimizations were performed at the density functional theory (DFT) level, and the Becke's three parameter hybrid functional with the Lee-Yang-Parr correlation functional (B3LYP) [171] method was employed to do the calculations. The 6-31G*[172, 173] basis from the Gaussian basis set library has been used in all the calculations. All the trimers and hexamers were relaxed fully without any symmetry constraints. The harmonic vibrational frequencies and zero-point energy corrections were calculated at the same level of theory. Single point energy were obtained at the B3LYP level in conjunction with the 6-311+G (2d,p) basis set with use of the above optimized geometries, i.e., B3LYP/6-311+G (2d,p) //B3LYP/6-31G (d).

Table S2. Computationally derived relative energy[a,b] per aromatic repeating unit among circularly folded aromatic macrocycles in gas phase, dichloromethane and acetonitrile.

Entry	Circular aromatic foldamer	Relative energy per unit (kcal/mol)		
		Gas phase	CH_2Cl_2	CH_3CN
1	Circular tetramer	12.52	4.54	4.56
2	Circular pentamer **1**	**0.00**	**0.00**	**0.00**
3	Circular hexamer	7.96	0.50	0.52
4	Circular heptamer	9.03	1.09	1.00

[a] Density functional theory at the B3LYP/6-31G* level with the single point energy calculated at the level of B3LYP/6-311+G**.
[b] The relative energy per repeating unit from entries 1-4 anis normalized against pentamer **1**, respectively.

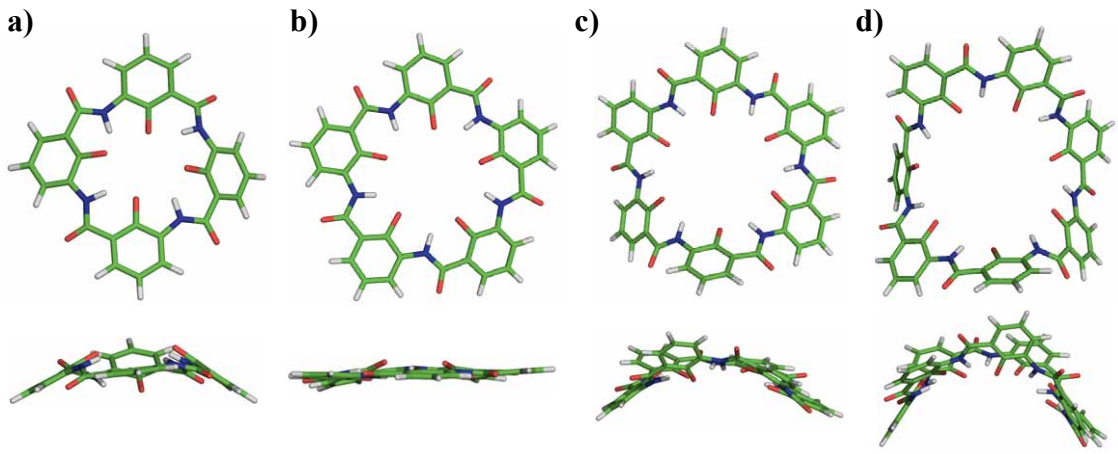


Figure S8. Top and side views of a*b initio*-optimized structures of circularly folded (a) tetramer, (b) pentamer **1**, (c) hexamer and (d) heptamer in acetonitrile at the B3LYP/6-31G* level. The computationally derived relative energy per repeating unit among these circular foldamers is normalized based on pentamer **1** in acetonitrile. The computationally derived planar backbone and geometry in **1** are nearly identical to those found in the crystal structure. For clarity of view, all the interior methyl groups in (a)-(d) were removed.

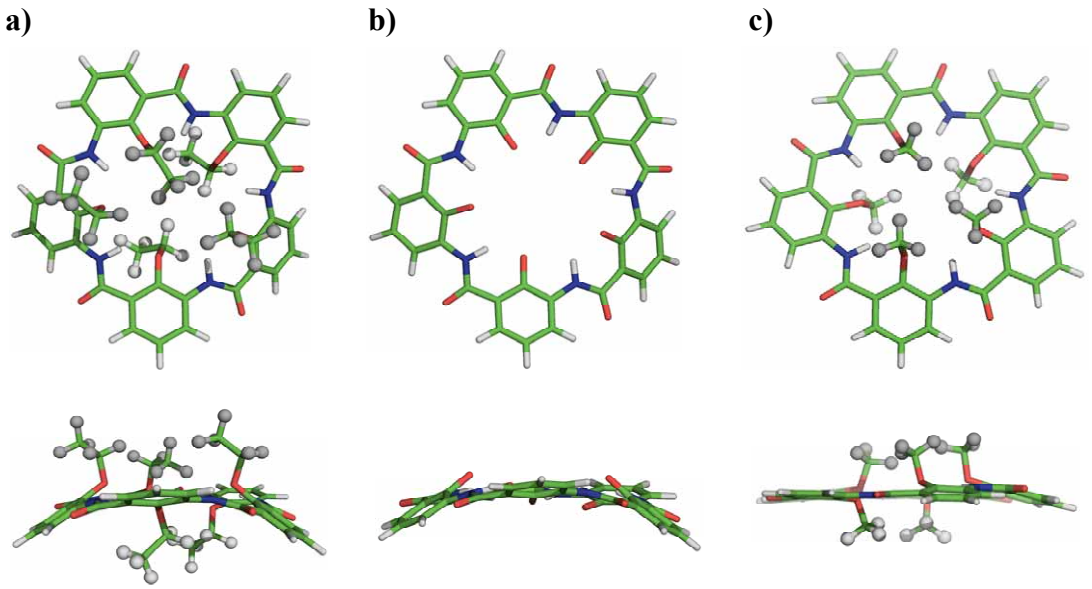
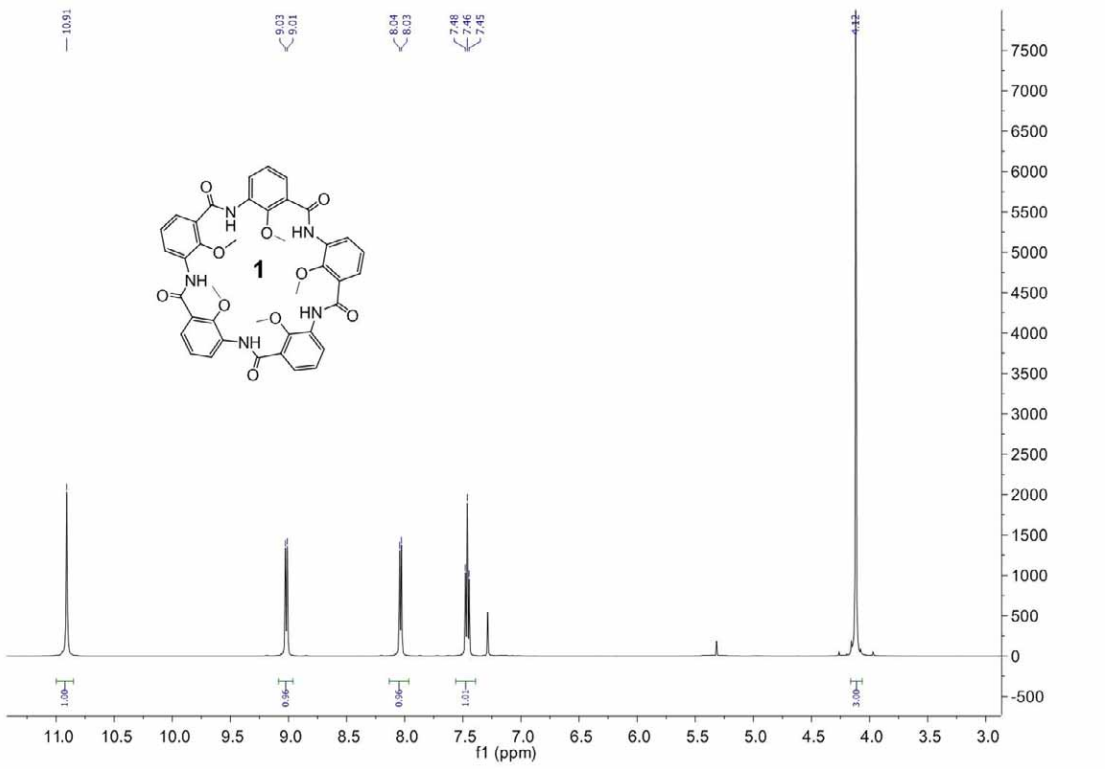


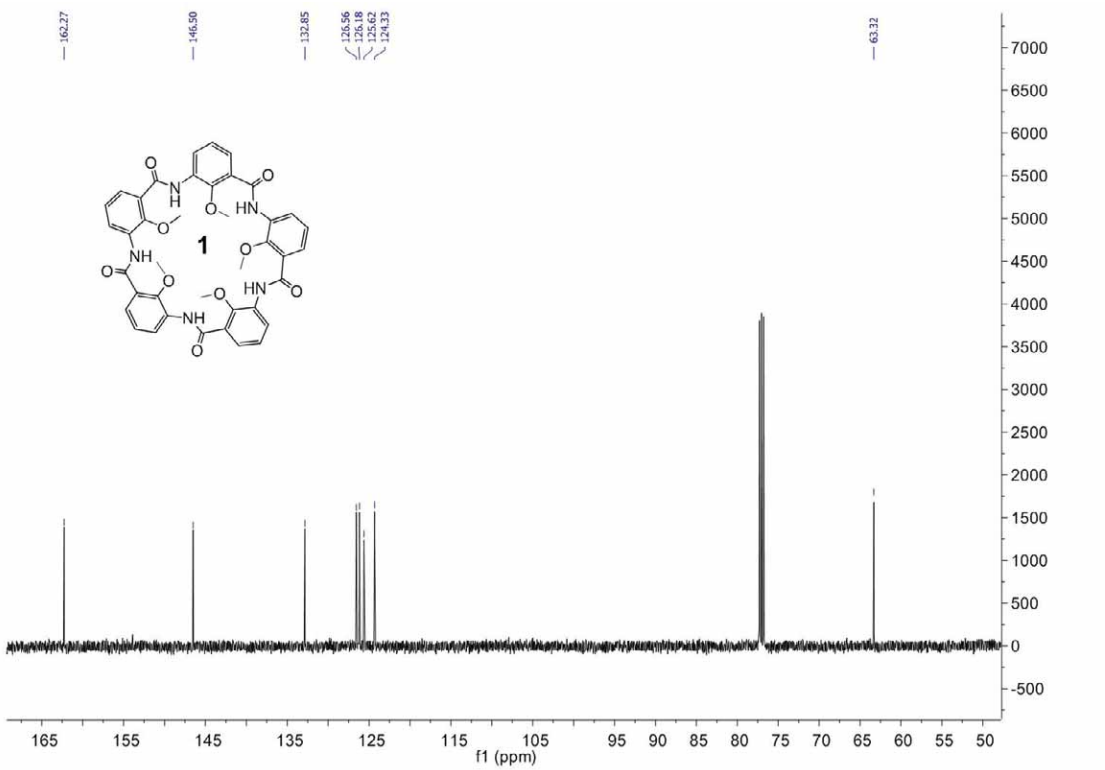
Figure S9. Both (a) and (b) show the top and side views of ab initio-optimized structure of circular pentamer **6**, carrying five ethoxy groups in its interior. For comparison, shown in (c) are the top and side vies of circular pentamer **1** that contains five smaller methoxy groups in its interior. It can be seen that the backbone in **6** is much more distorted than that in **1**. In (b), the interior ethyl groups were removed for clarity of view.

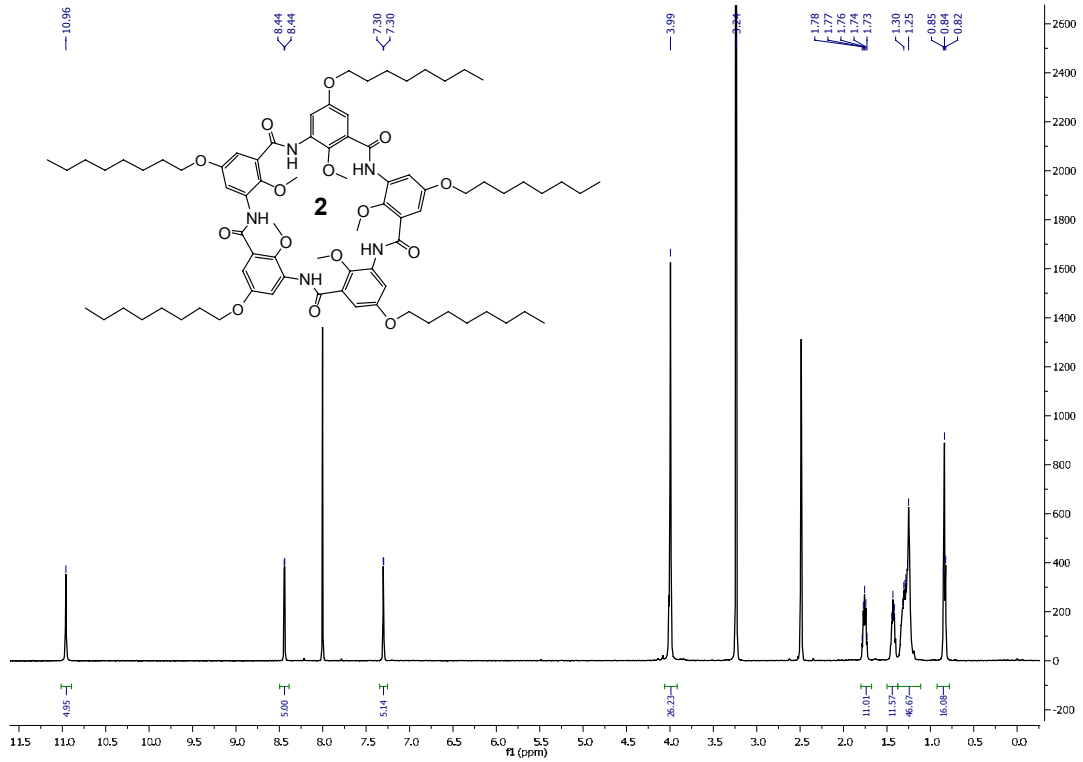
Experimental Conditions for Amide Hydrogen-Deuterium Exchange Experiments

Solutions of circular pentamers **1-7** (2.0 or 0.20 mM) were prepared by dissolving the compounds into 50% DMSO-d_6 in $CDCl_3$ (total volume: 0.95 mL) and the spectra were recorded at room temperature as the reference spectra at $t = 0$. The H-D exchange experiment was initiated by adding 0.05 mL of D_2O into the samples, which resulted in a solution in a mixed solvent of D_2O/DMSO-d_6/$CDCl_3$ (2:19:19 v/v). The resultant spectra were then recorded (500 MHz) at appropriate time intervals, based on which the time dependent peak areas of the amide protons were obtained and fitted into the pseudo-first-order reaction rate equation of $(I_t - I_\infty)/ (I_o - I_\infty) = e^{-kt}$, where I_t, I_∞, and I_0, correspond to the integrated area of the corresponding proton at $t = t$, $t = \infty$, $t = 0$; k is the decay rate constant. The half-life $T_{1/2}$ is related to k by $T_{1/2} = \ln 2/k$. Thus, the half-life $T_{1/2}$ was obtained by fitting the time-dependent peak areas into the above equation [$(I_t - I_\infty)/ (I_o - I_\infty) = e^{-kt}$] with Origin 7.7 program.

^{1}H and ^{13}C NMR Spectra of 1-7



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7.30
7.30
3.99
3.24
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1.76
1.74
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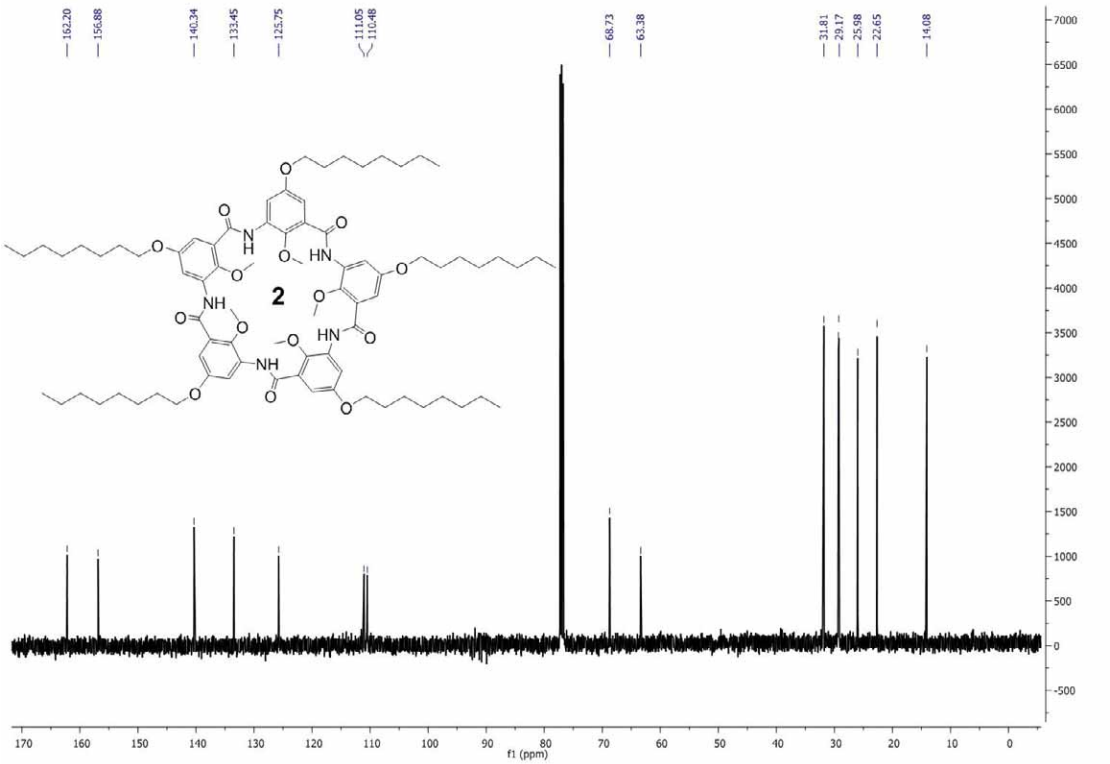
1.30
1.25
0.85
0.84
0.82
2
f1 (ppm)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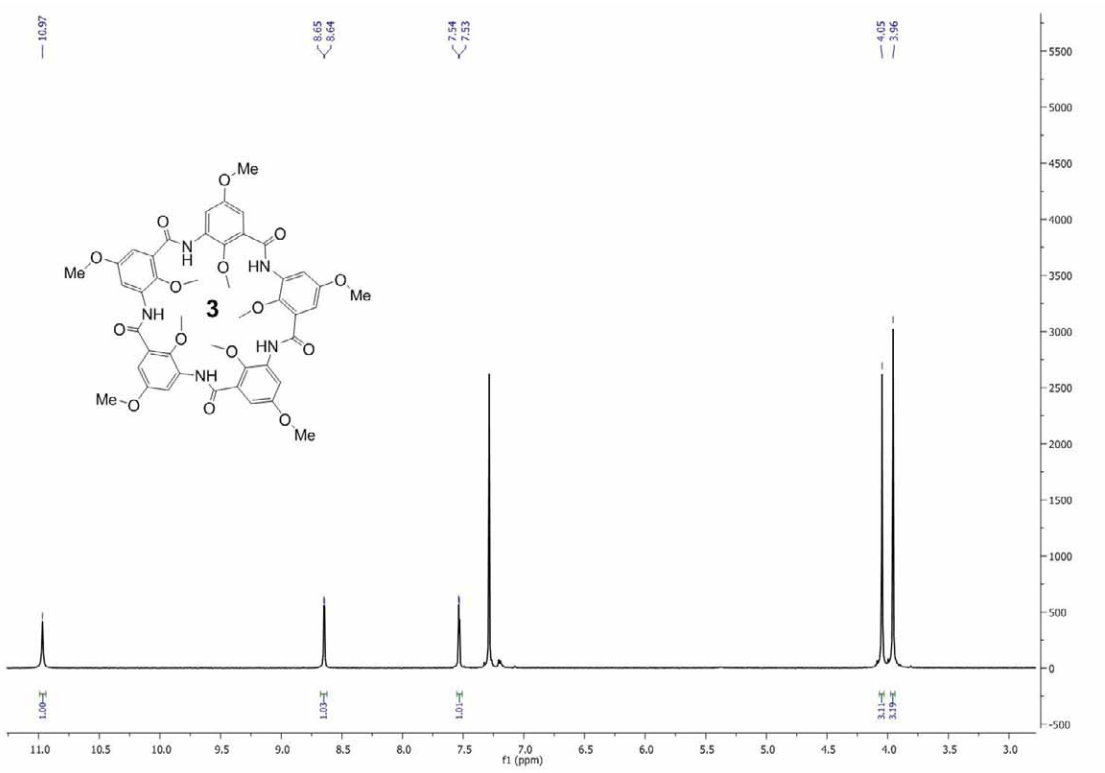
22.65
14.08
2
f1 (ppm)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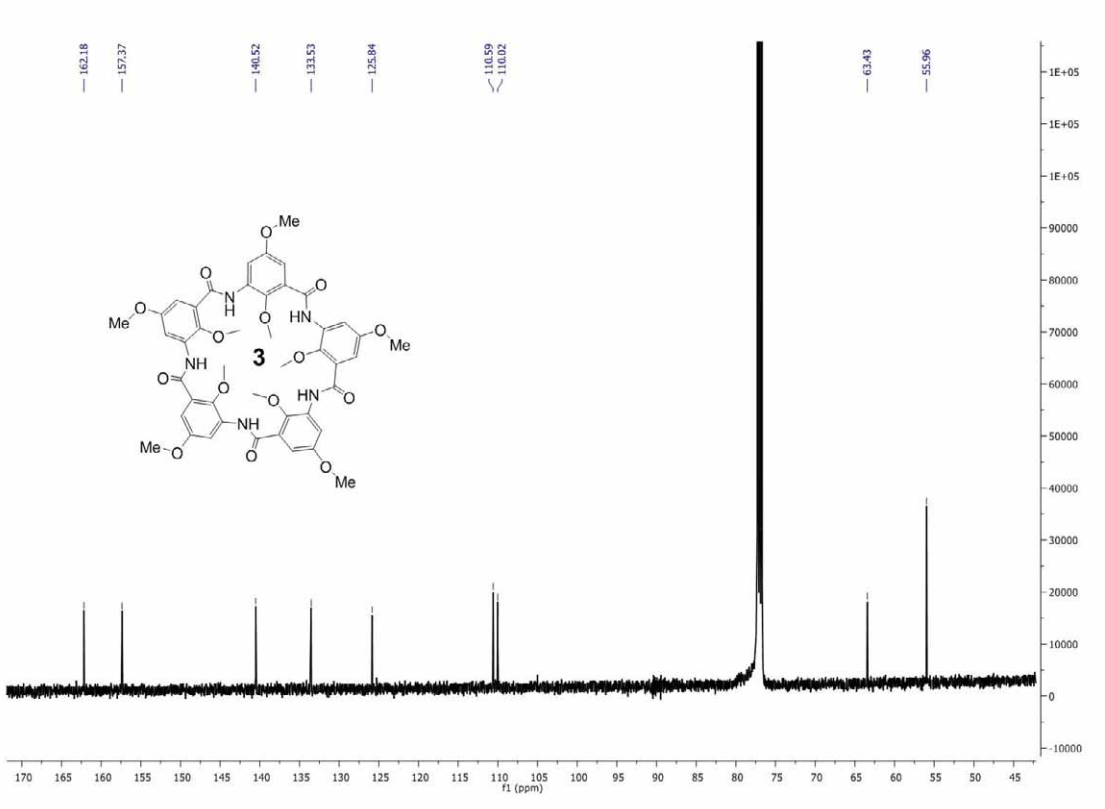
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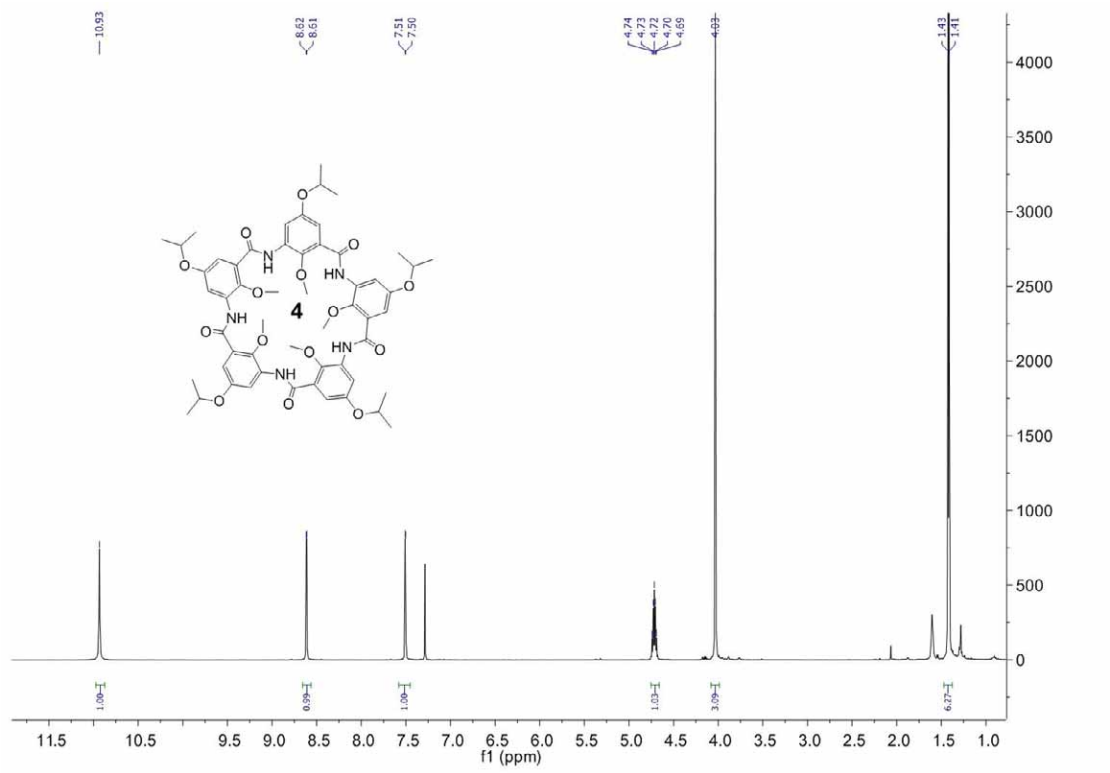
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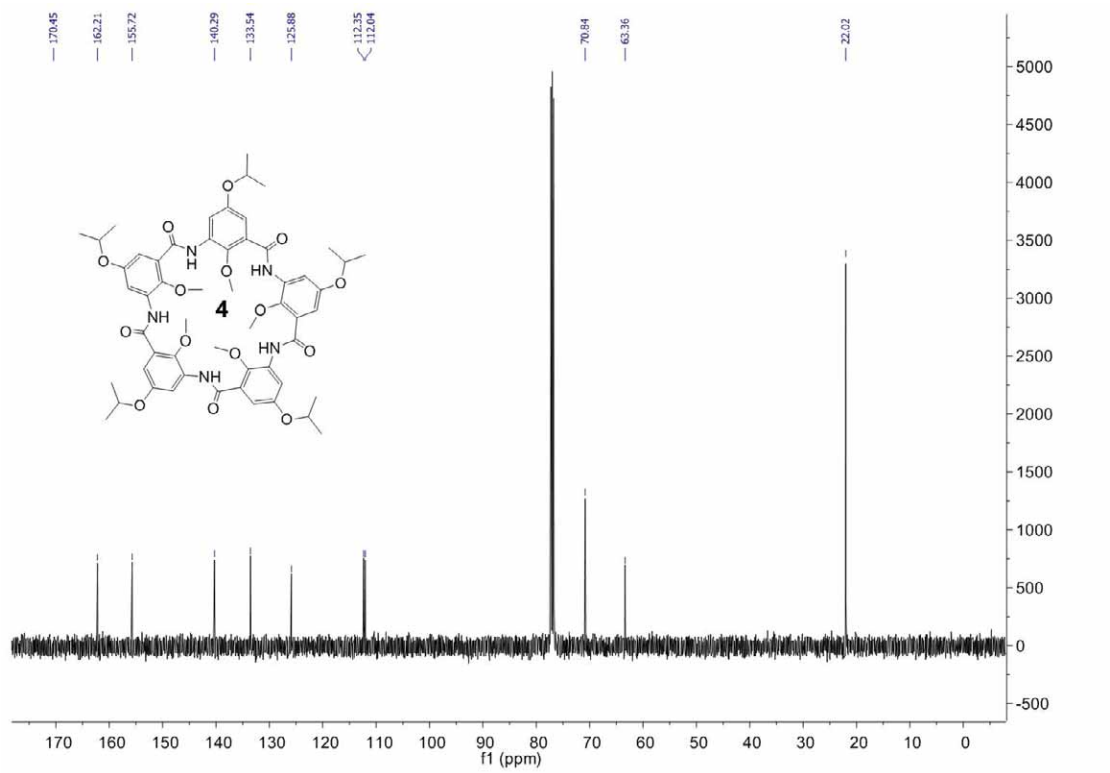
f1 (ppm)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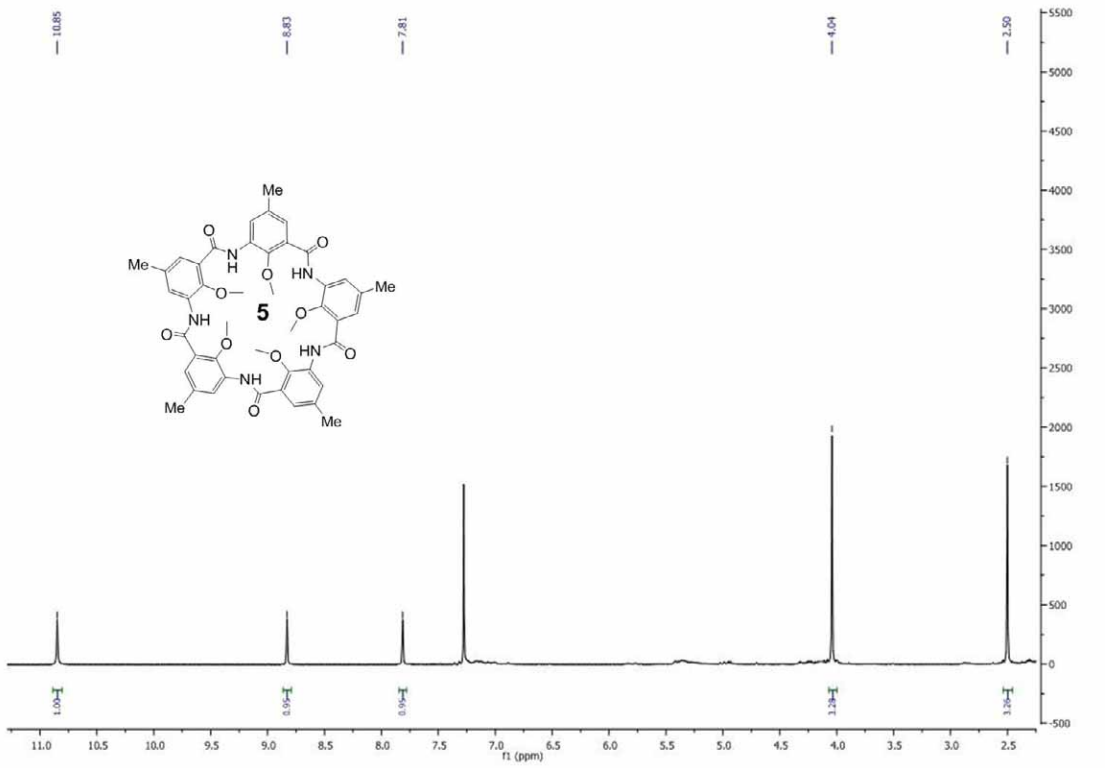
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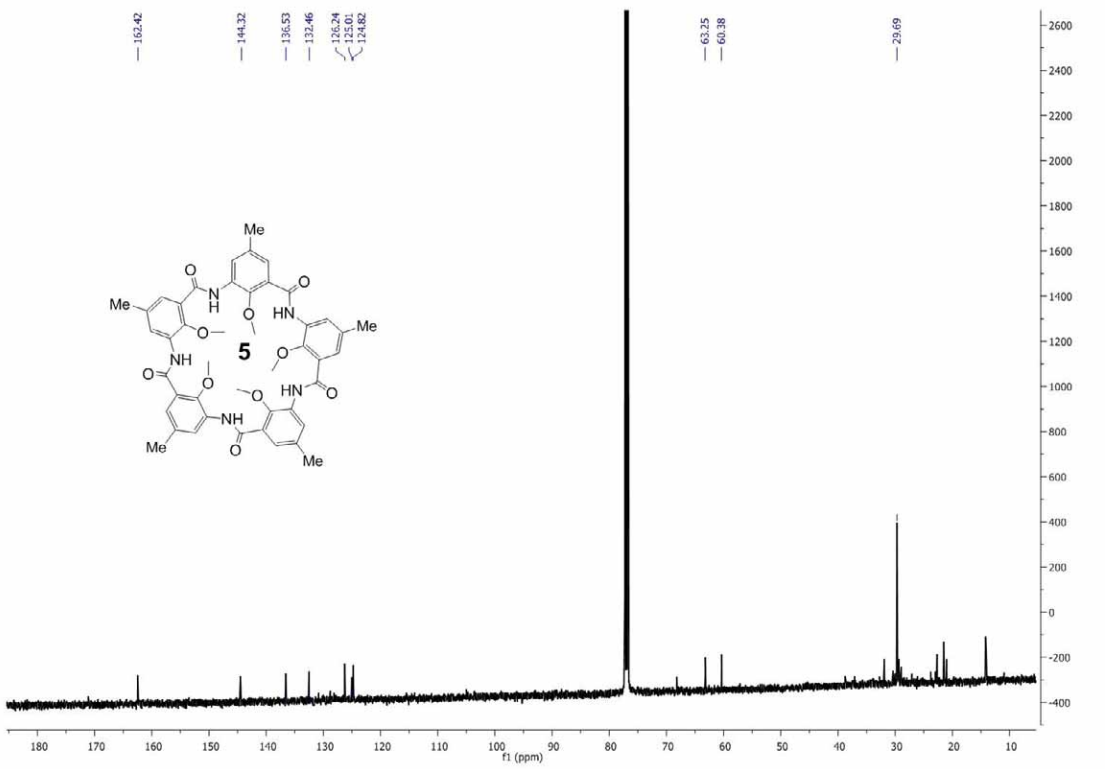
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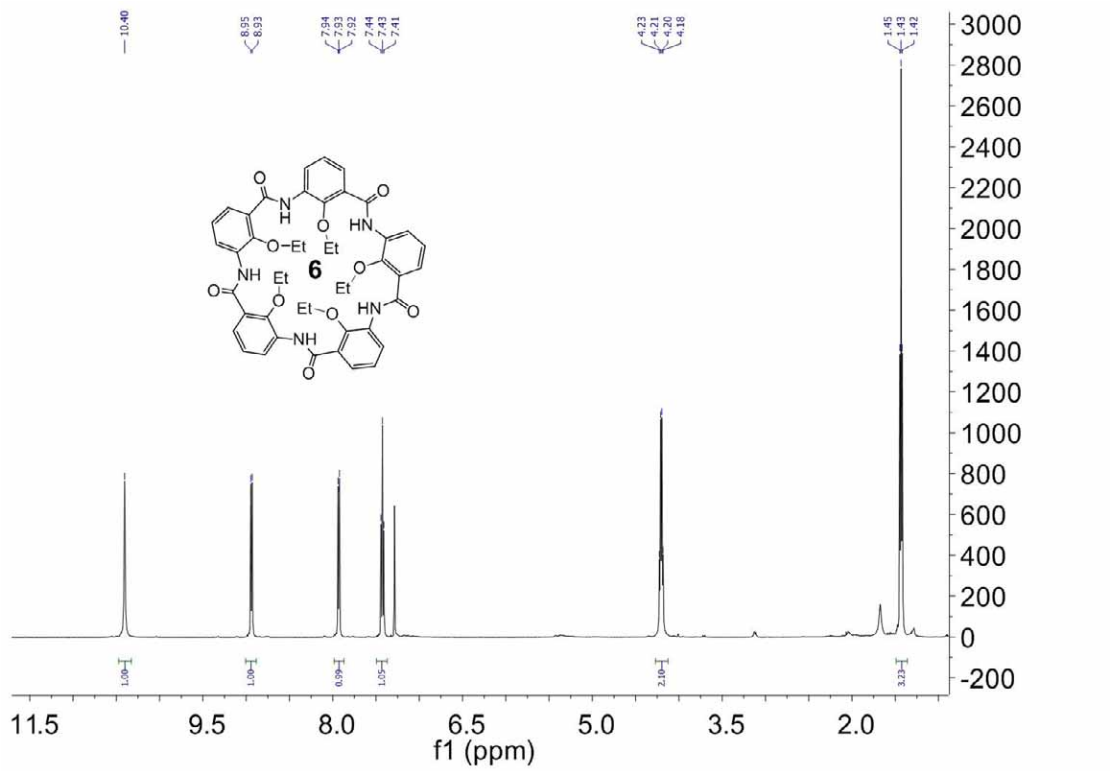
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1.00
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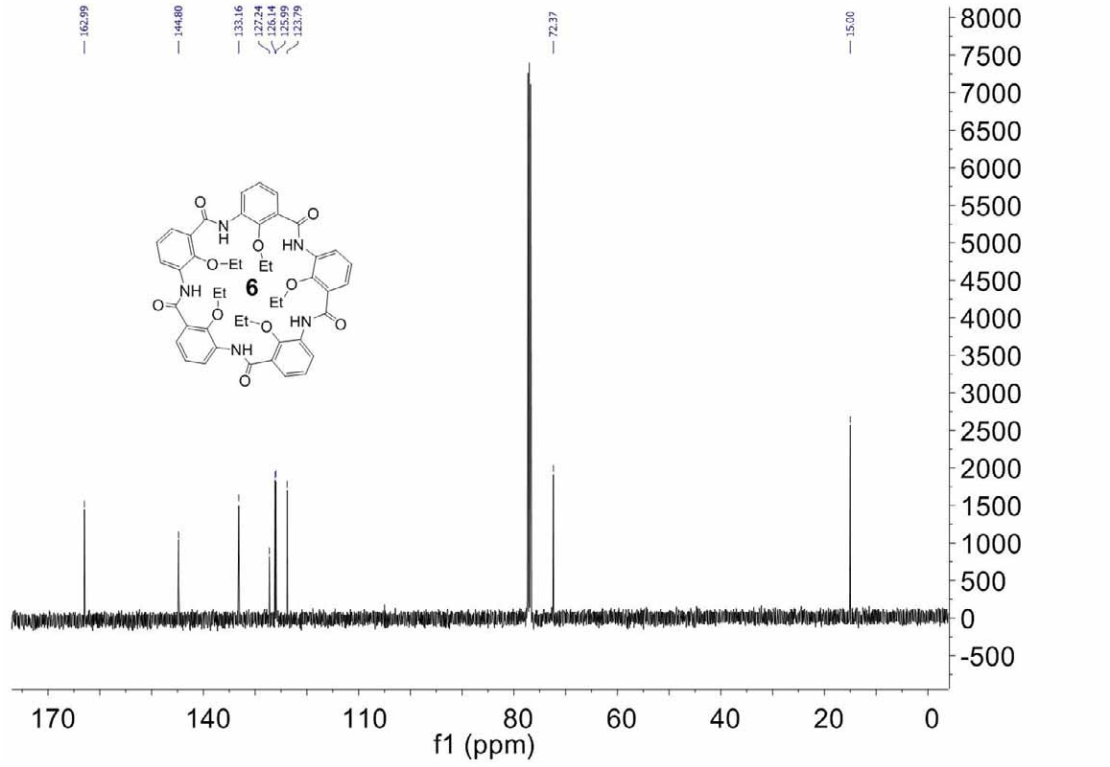
2.0
f1 (ppm)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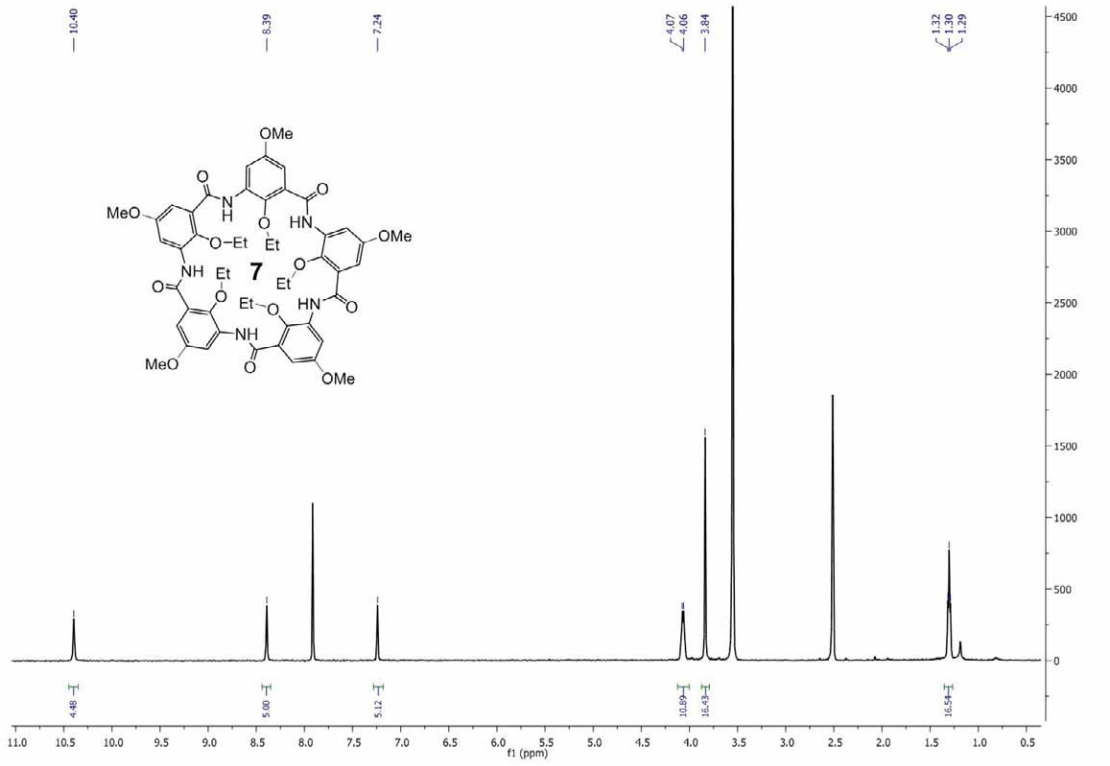
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1.30
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NH
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MeO
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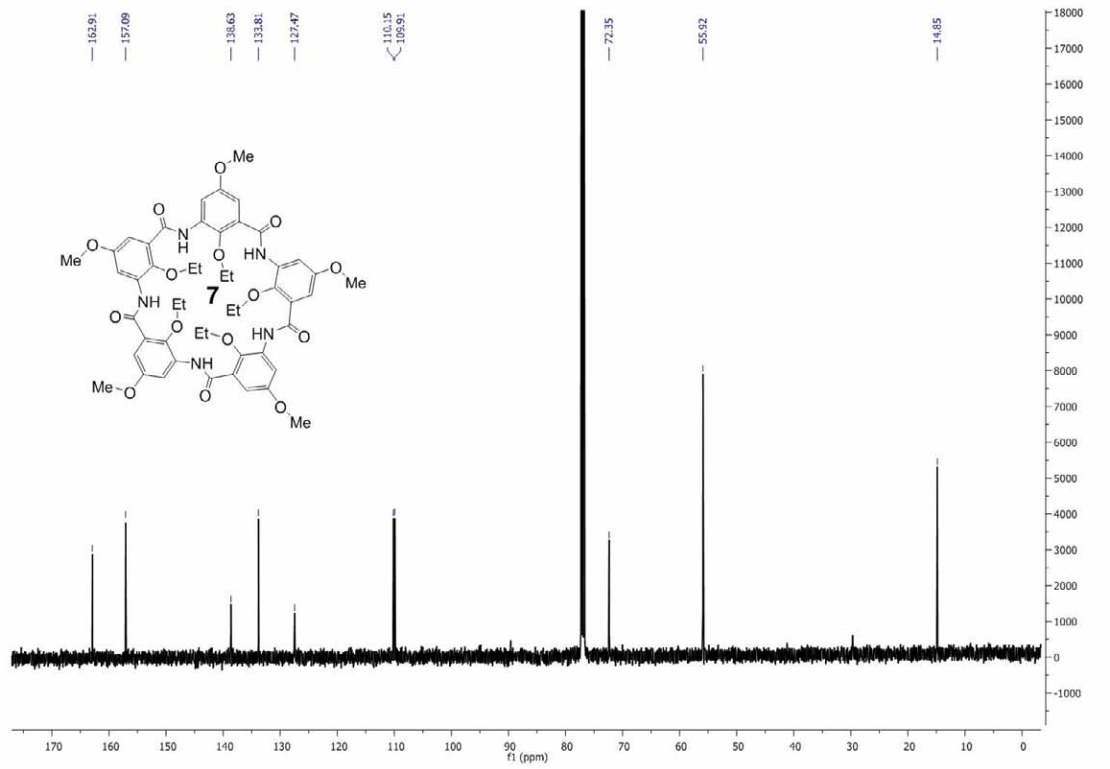
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f1 (ppm)