Supplementary Material for:

Computational Prediction and Experimental Verification of Pyridine-Based Helical Oligoamides Containing Four Repeating Units per Turn

Wei Qiang Ong,^a Huaiqing Zhao,^a Zhiyun Du,^b Jared Ze Yang Yeh,^a Changliang Ren,^a Leon Zhen Wei Tan,^a Kun Zhang,^b and Huaqiang Zeng^{*a}

^a Department of Chemistry, National University of Singapor, 3 Science Drive 3, Singapore. Fax: (+) 65-6779-1691; Tel: (+) 65-6516-2683; E-mail: chmzh@nus.edu.sg

^b Faculty of Chemical Engineering and Light Industry, Guang Dong University of Technology, Guang Dong, 510006, China. Tel: (+) 86-20-3932-2883; E-mail: zhiyundu@gdut.edu.cn; kzhang@gdut.edu.cn

Corresponding Author: chmzh@nus.edu.sg

1.	General Remarks	S2
2.	Scheme S1. Synthetic Route that Affords Pentamer 5	S3
3.	Scheme S2. Synthetic Route that Affords Trimer 3a	S4
4.	Synthetic Procedures & Characterization	S5
5.	Figure S1–S4. 2D NOESY Spectra of Compounds 3b, 4 and 5	.S15
6.	Figure S5. Aggregation Study of Pentamer 5	.S19
7.	Figure S6. <i>Ab Initio</i> Molecular Modeling	.S20
8.	Figure S7. IR Spectra of Compounds 3b, 4 and 5	.S21
9.	X-Ray Crystal Data for Compounds 2, 3a, 4 and 5	.S22
10.	¹ H and ¹³ C NMR spectra of Compounds 2d, 2, 3a, 3b, 4 and 5	.S26

1. General Remarks

All the reagents were obtained from commercial suppliers and used as received unless otherwise stated. Aqueous solutions were prepared from distilled water. The organic solutions from all liquid extractions were dried over anhydrous sodium sulphate for a minimum of 15 minutes before filtration. Reactions were monitored by thin-layer chromatography (TLC) on silica gel pre-coated glass plates (0.25 mm thickness, 60F-254, E., Merck). Chemical yields refer to pure isolated substances. Melting point (mp) of the compounds was measured using Büchi Melting point B540. Infrared (IR) spectra were acquired using a Varian 3100 FTIR spectrometer with values reported as wavenumbers. Mass spectra were obtained using instrumentation which includes Finnigan MAT95XL-T and Micromass VG7035. ¹H and ¹³C NMR spectra were recorded on a Bruker AMX500 (500 MHz) spectrometer. In addition, key compounds were characterized by 2D NOESY and X-Ray Diffraction. The solvent signal of CDCl₃ and DMSO-d₆ in ¹H NMR were referenced at δ = 7.26 ppm and δ = 2.50 ppm respectively. Coupling constants (J values) are reported in Hertz (Hz). ¹H NMR data are recorded in the order: chemical shift value, multiplicity (s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; br: broad), coupling constant and number of protons that gave rise to the signal, where applicable. ¹³C NMR spectra are proton-decoupled and the solvent peaks of CDCl₃ and DMSO-d₆ were referenced at $\delta = 77.0$ ppm and 39.5 ppm respectively. 2D NMR experiments were recorded on a Bruker DRX500 (500 MHz) spectrometer, unless otherwise stated. $CDCl_3$ and $DMSO-d_6$ were purchased from Cambridge Isotope Laboratories, Inc. and used without further purification unless otherwise stated. Single crystal X-ray diffraction study was recorded on Bruker-AXS Smart Apex CCD single crystal diffractometer.

2. Scheme S1. Synthetic Route that Affords Pentamer 5.



Electronic Supplementary Material (ESI) for Chemical Communications This journal is The Royal Society of Chemistry 2011

3. Scheme 2. Synthetic Route that Affords Trimer 3a



4. Synthetic Procedures & Characterization

Compound 2b:

Concentrated sulphuric acid (5ml) was added dropwise to pyridine-2,6-dicarboxylic acid (**2a**) (5.49 g, 32.9 mmol) in methanol (120ml). The solution was refluxed for 48 hrs and thereafter, the solvent was removed in *vacuo*. Dichloromethane (CH₂Cl₂) was added and the product was washed with water and aqueous sodium hydroxide. Removal of CH₂Cl₂ yielded the pure product as a white solid (Yield: 6.16 g, 96%; mp: 122–124 °C). ¹H NMR (500 MHz, CDCl₃): δ 8.28 (q, *J* = 3.8 Hz, 2H), 7.89–8.02 (m, 1H), 3.99 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ 164.98, 148.17, 138.29, 127.94, 53.09. HRMS-EI: calculated for [M]⁺ (C₉H₉NO₄): *m/z* 195.0532, found: *m/z* 195.0535.

Compound 2c:

Solid potassium hydroxide (1.72 g, 30.7 mmol) was dissolved in minimal amount of water and was added to compound **2b** (6.00 g, 30.7 mmol) in methanol (30 ml). The mixture was stirred at room temperature for 12 hrs and thereafter the solvent was removed in *vacuo*. The crude product was then dissolved in water and extracted with CH_2Cl_2 twice to remove any starting material. The aqueous layer was acidifed with 1M HCl and extracted with ethyl acetate five times. Removal of the solvent in *vacuo* yielded the pure product as a white solid (Yield: 4.35 g, 78%; mp: 148–150 °C). ¹H NMR (500 MHz, DMSO-*d*₆): δ 8.22–8.25 (m, 2H), 8.17 (t, *J* = 7.9 Hz, 1H),

3.91 (s, 3H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ 165.62, 147.57, 139.06, 127.86, 55.61. HRMS-ESI: calculated for [M-H]⁻ (C₈H₆NO₄): *m/z* 180.0291, found: *m/z* 180.0296.

Compound 2d:

Compound 2c (0.18 g, 1.0 mmol) was dissolved in THF / DMF (3 ml / 2 ml) and the solution was cooled to -5 °C to -10 °C using an ice-salt bath. Ethyl chloroformate (0.12 ml, 1.2 mmol) and *N*-methylmorpholin (0.12 ml, 1.2 mmol) was added to the cooled solution and stirred for 15 mins. Sodium azide (0.10 g, 1.5 mmol), which was dissolved in minimal amount of water, was added to the cooled solution and the solution was allowed to stirred for 30mins. THF in the solution was then removed in *vacuo* and CH₂Cl₂ was then added to the remaining solution. The organic layer was washed twice with water to remove any salts and the remaining DMF. The solvent was then removed in vacuo to yield a yellow solid. The yellow solid was dissolved in 5ml of toluene and benzyl alcohol (0.11 ml, 1.1 mmol) was added into it. The solution was heated at 120 °C for 30 hrs. The solvent was then removed in *vacuo* and the crude product was dissolved in CH₂Cl₂ and washed with water. Removal of the solvent yielded the crude product which was recrystalized with methanol to give the pure product as a white solid (Yield: 0.17 g, 65 %; mp: 101–102 °C). ¹H NMR (500 MHz, CDCl₃): δ 8.19 (d, J = 2.6 Hz, 1H), 8.02 (s, 1H), 7.78–7.82 (m, 2H), 7.29–7.37 (m, 5H), 5.20 (s, 2H), 3.93 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 165.07, 152.96, 151.46, 145.90, 139.19, 135.62, 128.51, 128.27, 127.89, 120.29, 116.11, 67.10, 52.78. HRMS-ESI: calculated for $[M+Na]^+$ (C₁₅H₁₄N₂O₄²³Na): *m/z* 309.0846, found: *m/z* 309.0851.

H₃COOC

Compound 2e:

Compound **2d** (0.29 g, 1.0 mmol) underwent catalytic hydrogenation in THF (10 ml) at 50 °C for 3 hrs using Pd/C (0.03 g, 10 wt%) as the catalyst. The reaction was then filtered and the solvent was removed *in vacuo* to give the product **2e**. The compound was used directly in the next step without further purification. (Yield: 0.15 g, 98 %; mp: 78–80 °C). ¹H NMR (500 MHz, DMSO-d₆): δ 7.51 (t, *J* = 7.9 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 6.50 (d, *J* = 8.2 Hz, 1H), 6.29 (s, 2H), 3.79 (s, 3H). ¹³C NMR (125 MHz, DMSO-d₆): δ 165.79, 159.70, 145.70, 137.69, 113.20, 112.24, 51.88. HRMS-EI: calculated for [M]⁺ (C₇H₈N₂O₂): *m/z* 152.0586, found: *m/z* 152.0583.



Compound 2f:

Solid NaOH (0.16 g, 4.0 mmol) was dissolved in minimal amount of deionized water and was then added into the rbf containing compound **2d** (0.57 g, 2.0 mmol) in dioxane (10 ml). The mixture was stirred at room temperature overnight and the solvent was then removed *in vacuo*. Water (20 ml), MeOH (20 ml) and solid KHSO₄ (0.54 g, 4.0 mmol) was then added. The suspension was then filtered, washed and the residue obtained was dried to give a pure product as a white solid (Yield: 0.48 g, 88 %; mp: 268–270 °C, decompose). ¹H NMR (500 MHz, DMSO-d₆): δ 10.56 (s, 1H), 8.04 (d, *J* = 8.9 Hz, 1H), 7.94 (t, *J* = 7.9 Hz, 1H), 7.69–7.71 (m, 1H), 7.37–7.43 (m, 4H), 7.31–7.34 (m, 1H), 5.19 (s, 2H). ¹³C NMR (125 MHz, DMSO-d₆): δ 165.95,

153.70, 152.09, 147.20, 139.30, 132.36, 128.42, 127.92, 127.64, 115.85, 112.44, 65.82. HRMS-ESI: calculated for [M-H]⁻ (C₁₄H₁₁N₂O₄): *m/z* 271.0724, found: *m/z* 271.0720.



Dimer 2:

Compound 2f (0.27 g, 1 mmol) was dissolved in THF / DMF (3 ml/2 ml) in a rbf and was cooled in an ice bath. 4-methylmorpholin (0.1 ml, 1.0 mmol) and ethyl chloroformate (0.1 ml, 1.0 mmol) were added to the rbf and stirred for 30 mins while maintaining the temperature at -5 °C to -10 ^oC. Compound 2e (0.15 g, 1.0 mmol) was dissolved in THF (2 ml) and DMF (2 ml) and the solution was then added into the rbf. The ice bath was then removed and the mixture was then stirred at 90 °C overnight. The solvents were then removed in vacuo, DCM (25 ml) was added and the product was washed with water (2 x 10ml), 1M HCl (2 x 10ml) and 1M NaOH (2 x 10ml). The solvent was then removed *in vacuo* to yield the crude compound which was recrystallized with MeOH to yield the pure product as a white solid (Yield: 0.21 g, 52 %; mp: 160-161 °C). ¹H NMR (500 MHz, DMSO-d₆): δ 10.35 (s, 1H), 8.63 (t, J = 4.3 Hz, 1H), 8.20 (d, J =8.2 Hz, 1H), 7.95 (d, J = 7.7 Hz, 1H), 7.85–7.89 (m, 3H), 7.74 (s, 1H), 7.32–7.44 (m, 5H), 5.28 (s, 2H), 4.00 (s, 3H). ¹³C NMR (125 MHz, DMSO-d₆): δ 165.23, 162.26, 152.85, 151.14, 150.19, 146.99, 146.21, 139.98, 139.31, 135.63, 128.60, 128.36, 127.95, 121.24, 117.71, 117.58, 115.78, 67.29, 52.90. HRMS-ESI: calculated for $[M+Na]^+$ (C₂₁H₁₈N₄O₅²³Na): m/z 429.1169, found: m/z429.1163.

Dimer 2g:

Solid NaOH (0.16 g, 4.0 mmol) was dissolved in minimal amount of deionized water and was then added into the rbf containing dimer **2** (0.81 g, 2.0 mmol) in dioxane (10 ml). The mixture was stirred at room temperature overnight and the solvent was then removed *in vacuo*. Water (20 ml), MeOH (20 ml) and solid KHSO₄ (0.54 g, 4.0 mmol) was then added. The suspension was then filtered, washed and the residue obtained was dried to give a pure product as a white solid (Yield: 0.69 g, 84 %). ¹ H NMR (500 MHz, DMSO-d₆): δ 10.94 (s, 1H), 10.45 (s, 1H), 8.50 (s, 1H), 7.88–8.48 (m, 3H), 7.82–7.86 (m, 2H), 7.33–7.45 (m, 5H), 5.24 (s, 2H). ¹³C NMR (125 MHz, DMSO-d₆): δ 162.67, 162.33, 153.49, 151.26, 150.48, 147.54, 146.88, 140.88, 140.57, 139.92, 136.37, 128.64, 128.26, 128.07, 121.08, 121.07, 118.78, 117.12, 116.14, 66.38. HRMS-ESI: calculated for [M-H]⁺ (C₂₀H₁₅N₄O₅): *m/z* 391.1048, found: *m/z* 391.1049.



Trimer 3a:

Trimer **3b** (0.53 g, 1.0 mmol) underwent catalytic hydrogenation in DMF (50 ml) at room temperature using Pd/C (0.05 g, 10 wt%) as the catalyst. After stirring the reaction overnight, the

catalyst was filtered and the filtrate was poured into a rbf. Triethylamine (0.28 ml, 2.0 mmol) was added into the rbf, followed by the addition of Moz-Cl (0.30 ml, 2.0 mmol) and the reaction was stirred for 2 hr at room temperature and thereafter, the solvent was removed *in vacuo*. DCM (25ml) was added to the crude product and was washed with water (2 x 10ml), 1M HCl (2 x 10ml) and 1M NaOH (2 x 10ml). The solvent was removed *in vacuo* to give the crude product and the flash column chromatography was used to afford the pure product as a white solid (Yield: 0.06 g, 11 %). ¹H NMR (500 MHz, CDCl₃): δ 10.41 (s, 1H), 10.27 (s, 1H), 8.70–8.73 (m, 1H), 8.67 (d, *J* = 8.2 Hz, 1H), 8.29 (d, *J* = 8.6 Hz, 1H), 8.06 (d, *J* = 6.9 Hz, 1H), 7.91–8.01 (m, 6H), 7.36 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 1H), 5.19 (s, 2H), 3.92 (s, 3H), 3.81 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 165.29, 162.59, 162.44, 159.87, 153.07, 151.40, 150.67, 150.06, 147.35, 147.07, 146.19, 140.02, 139.98, 139.44, 130.26, 127.71, 121.41, 118.83, 118.08, 117.85, 117.53, 116.02, 114.00, 67.35, 55.28, 52.95. HRMS-ESI: calculated for [M+Na]⁺ (C₂₈H₂₄M₆O₇²³Na): *m/z* 579.1599, found: *m/z* 579.1604.



Trimer 3b:

Dimer 2g (0.39 g, 1.0 mmol) was dissolved in dry DCM (10ml) in a rbf. DMF (0.1 ml) was added, followed by the dropwise addition of oxalyl chloride (0.3 ml, 2.0 mmol) into the rbf. The reaction mixture was stirred for 2 hrs and the solvent and excess oxalyl chloride were removed *in*

vacuo and dry DCM (10 ml) was added to the acid chloride in nitrogen atmosphere. Minimal amount of dry DCM was added to a mixture containing compound **2e** (0.15 g, 1.0 mmol) and triethylamine (0.28 ml, 2.0 mmol) and the mixture was injected into the acid chloride. The mixture was allowed to stir for 1 hr at room temperature and after the reaction, the product was washed with water (2 x 10ml), 1M HCl (2 x 10ml) and 1M NaOH (2 x 10ml). The solvent was removed *in vacuo* to give the crude product and the flash column chromatography was used to afford the pure product as a white solid (Yield: 0.21 g, 39 %; mp: 232–234 °C). ¹H NMR (500 MHz, CDCl₃): δ 10.31 (s, 1H), 10.17 (s, 1H), 8.61–8.68 (m, 2H), 8.25 (d, *J* = 8.1 Hz, 1H), 7.95–8.00 (m, 3H), 7.84–7.90 (m, 4H), 7.30–7.41 (m, 5H), 5.23 (s, 2H), 3.87 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 165.14, 162.44, 162.27, 152.87, 151.29, 150.52, 149.94, 147.26, 147.02, 146.10, 139.87, 139.84, 139.28, 135.51, 128.50, 128.34, 128.29, 121.29, 118.74, 117.96, 117.84, 117.41, 115.91, 67.40, 52.78. HRMS-ESI: calculated for [M+Na]⁺ (C₂₇H₂₂N₆O₆²³Na): *m/z* 549.1492.



Tetramer 4:

Solid NaOH (0.16 g, 4.0 mmol) was dissolved in minimal amount of deionized water and was then added into the rbf containing Trimer **3a** (1.05 g, 2.0 mmol) in dioxane (10 ml). The mixture

was stirred at room temperature overnight and the solvent was then removed in vacuo. Water (20 ml), MeOH (20 ml) and solid KHSO₄ (0.54 g, 4.0 mmol) was then added. The suspension was then filtered, washed and the residue obtained was dried to give the acid intermediate. The acid intermediate (0.51 g, 1.0 mmol) was dissolved in dry DCM (10ml) in a rbf. DMF (0.1 ml) was added, followed by the dropwise addition of oxalyl chloride (0.3 ml, 2.0 mmol) into the rbf. The reaction mixture was stirred for 2 hrs and the solvent and excess oxalyl chloride were removed in vacuo and dry DCM (10 ml) was added to the acid chloride in nitrogen atmosphere. Minimal amount of dry DCM was added to a mixture containing compound 2e (0.15 g, 1.0 mmol) and triethylamine (0.28 ml, 2.0 mmol) and the mixture was injected into the acid chloride. The mixture was allowed to stir for 1 hr at room temperature and after the reaction, the product was washed with water (2 x 10ml), 1M HCl (2 x 10ml) and 1M NaOH (2 x 10ml). The solvent was removed *in vacuo* to give the crude product and the flash column chromatography was used to afford the pure product as a white solid (Yield: 0.29 g, 46 %). ¹H NMR (500 MHz, CDCl₃): δ 10.44 (s, 1H), 10.34 (s, 1H), 10.27 (s, 1H), 8.59–8.64 (m, 3H), 8.32 (br, 1H), 8.23 (d, *J* = 7.5 Hz, 1H), 7.88–8.03 (m, 6H), 7.75–7.79 (m, 2H), 7.08-7.20 (m, 5H), 5.02 (s, 2H), 3.81 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 164.97, 162.48, 162.45, 162.36, 153.00, 151.28, 150.63, 150.02, 149.89, 147.33, 147.28, 147.13, 145.95, 139.96, 139.32, 135.30, 128.37, 128.17, 127.69, 121.15, 118.78, 118.71, 117.83, 117.70, 117.49, 116.10, 67.11, 52.80. HRMS-ESI: calculated for $[M+Na]^+$ (C₃₃H₂₆N₈O₇²³Na): *m/z* 669.1817, found: *m/z* 669.1843.



Pentamer 5:

Solid NaOH (0.16 g, 4.0 mmol) was dissolved in minimal amount of deionized water and was then added into the rbf containing tetramer 4 (1.29 g, 2.0 mmol) in dioxane (20 ml). The mixture was stirred at room temperature overnight and the solvent was then removed in vacuo. Water (20 ml), MeOH (20 ml) and solid KHSO₄ (0.54 g, 4.0 mmol) was then added. The suspension was then filtered, washed and the residue obtained was dried to give the acid intermediate. The acid intermediate (0.63 g, 1.0 mmol) was dissolved in dry DCM (10ml) in a rbf. DMF (0.1 ml) was added, followed by the dropwise addition of oxalyl chloride (0.3 ml, 2.0 mmol) into the rbf. The reaction mixture was stirred for 2 hrs and the solvent and excess oxalyl chloride were removed in vacuo and dry DCM (20 ml) was added to the acid chloride in nitrogen atmosphere. Minimal amount of dry DCM was added to a mixture containing 2-aminopyridine (0.19 g, 2.0 mmol) and triethylamine (0.28 ml, 2.0 mmol) and the mixture was injected into the acid chloride. The mixture was allowed to stir for 1 hr at room temperature and after the reaction, the product was washed with water (2 x 10ml), 1M HCl (2 x 10ml) and 1M NaOH (2 x 10ml). The solvent was removed in vacuo to give the crude product and the flash column chromatography was used to afford the pure product as a white solid (Yield: 0.26 g, 37 %; mp: 261–263 °C, decompose). ¹H NMR (500 MHz, CDCl₃): δ 10.47 (s, 1H), 10.42 (s, 1H), 10.40 (s, 1H), 10.36 (s, 1H), 8.75 (t, J =

8.1 Hz, 2H), 8.67 (d, J = 7.5 Hz, 1H), 8.40 (d, J = 7.9 Hz, 1H), 8.13 (d, J = 7.1 Hz, 1H), 8.03 (q, J = 7.4 Hz, 2H), 7.95–7.99 (m, 2H), 7.92 (d, J = 7.5 Hz, 2H), 7.87–7.89 (m, 2H), 7.76 (t, J = 7.9 Hz, 1H), 7.63–7.67 (m, 2H), 7.54 (s, 1H), 7.13–7.19 (m, 3H), 7.06–7.08 (m, 2H), 6.69 (t, 1H, J = 6.3 Hz), 5.01 (s, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 162.60, 162.50, 162.38, 161.97, 152.31, 150.92, 150.26, 150.15, 149.84, 147.48, 147.37, 147.33, 147.18, 146.79, 140.23, 140.14, 140.08, 139.63, 138.52, 135.31, 128.35, 128.10, 127.67, 119.70, 118.98, 118.94, 118.55, 117.88, 117.66, 117.60, 117.14, 115.72, 113.71, 67.28. HRMS-ESI: calculated for [M+Na]⁺ (C₃₇H₂₈N₁₀O₆²³Na): *m/z* 731.2085, found: *m/z* 731.2104.

Electronic Supplementary Material (ESI) for Chemical Communications This journal is The Royal Society of Chemistry 2011

5. 2D NOESY Spectra of Compounds 3b, 4 and 5



Figure S1. Full 2D NOESY spectrum containing NOE contacts seen in **3b** as revealed by 2D NOESY study (5 mM, 263 K, CDCl₃, AMX 500 MHz, mixing time = 500 ms).



Figure S2. Full 2D NOESY spectrum containing NOE contacts seen in **4** as revealed by 2D NOESY study (10 mM, 298 K, CDCl₃, 500 MHz, mixing time = 500 ms).

Electronic Supplementary Material (ESI) for Chemical Communications This journal is o The Royal Society of Chemistry 2011



Figure S3. Full 2D NOESY spectrum containing NOE contacts seen in 5 as revealed by 2D NOESY study (10 mM, 298 K, $CDCl_3$, 500 MHz, mixing time = 500 ms).



Figure S4. Expanded NOESY spectra of 3b, 4 and 5 showing the various end-to-end contacts. The closest interatomic distances shown in the figure are taken from the respective crystal structure, except for 3b where its distances were obtained from crystal 3a. Double headed arrows in pink indicate the NOE cross peaks observed.

6. Aggregation Study of Pentamer 5



Figure S5. ¹H NMR spectra (CDCl₃, 500 MHz, 298 K) of pentamer **5** at (a) 10 mM, (b) 5.0 mM and (c) 1.0 mM. This shows that the aggregation of **5** in chloroform can be neglected and thus the NOEs seen from NOESY spectrum of **5** are not due to the intermolecular aggregation.

7. Ab Initio Molecular Modeling

All the calculations were carried out by utilizing the either the Gaussian 03^1 or Gaussian 09^2 program package. 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 $(B3LYP)^3$ method was employed to do the calculations. Unless otherwise stated, the 6-31G*⁴ basic from the Gaussian basis set library has been used in all the calculations. 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 conjuction with the 6-311+G (2d, p) basis set with the use of the above optimized geometries, i.e., B3LYP/6-311+G(2d,p)//B3LYP/6-31G. For dimer **1f** – **1l**, the harmonic vibrational frequencies and zero-point energy corrections were calculated using the 6-311+G (2d, p) basis set from the Gaussian basis set library directly.



Figure S6. Ab initio modeling of dimers 1f - 1l. The values in parenthesis shown below the structures are the relative energy in kcal/mol computed and normalized against the most stable conformer 1f.

¹ Frisch, M. J.; et al. *Gaussian 03*; Gaussian , Inc.: Wallingford CT, 2004.

² Frisch, M. J.; et al. *Gaussian 09*; Gaussian , Inc.: Wallingford CT, 2009.

³ Becke, A. D. J. Chem. Phys. 1993, 98, 5648.

⁴ Petersson, G. A.; Al-Laham, M. A. J. Chem. Phys. 1991, 94, 6081; Petersson, G. A.; Bennett, A.;

Tensfeldt, T. G.; Al-Laham, M. A.; Shirley, W. A.; Mantzaris, J. J. Chem. Phys. 1988, 89, 2193.

8. IR spectra of Compounds 3b, 4 and 5

Figure S7. IR spectra of (a) trimer 3b, (b) tetramer 4 and (c) pentamer 5.

9. X-Ray Crystal Data for Compound 2, 3a, 4 and 5

(i) Crystal data and structure refinement for dimer 2:

CCDC Deposition Number	817347		
Empirical formula	$C_{20}H_{16}N_4O_4$		
Formula weight	376.37		
Temperature	223(2) K		
Wavelength	0.71073 Å		
Crystal system	Monoclinic		
Space group	C2/c		
Unit cell dimensions	a = 34.441(2) Å	<i>α</i> = 90°.	
	b = 5.2810(3) Å	β=90.6040(10)°.	
	c = 19.1556(12) Å	$\gamma = 90^{\circ}$.	
Volume	3483.9(4) Å ³		
Z	8		
Density (calculated)	1.435 Mg/m ³		
Absorption coefficient	0.103 mm ⁻¹		
F(000)	1568		
Crystal size	0.70 x 0.10 x 0.08 mm ³		
Theta range for data collection	2.13 to 27.48°.		
Index ranges	-44<=h<=42, -6<=k<=6, -24<=l<=22		
Reflections collected	11784		
Independent reflections	3989 [R(int) = 0.0331]		
Completeness to theta = 27.48°	99.8 %		
Absorption correction	Sadabs, (Sheldrick 2001)		
Max. and min. transmission	0.9918 and 0.9314		
Refinement method	Full-matrix least-squares on F ²		
Data / restraints / parameters	3989 / 0 / 262		
Goodness-of-fit on F ²	1.041		
Final R indices [I>2sigma(I)]	R1 = 0.0469, wR2 = 0.1086		
R indices (all data)	R1 = 0.0614, $wR2 = 0.1154$		
Largest diff. peak and hole	0.215 and -0.212 e.Å ⁻³		

(ii) Crystal data and structure refinement for Trimer 3a:

CCDC Deposition Number	817348			
Empirical formula	$C_{29.50} \ H_{27} \ N_6 \ O_{7.50}$			
Formula weight	585.57			
Temperature	100(2) K			
Wavelength	0.71073 Å			
Crystal system	Monoclinic			
Space group	P2(1)/n			
Unit cell dimensions	a = 11.0265(11) Å	<i>α</i> = 90°.		
	b = 7.7675(8) Å	$\beta = 96.551(3)^{\circ}$.		
	c = 32.872(3) Å	$\gamma = 90^{\circ}$.		
Volume	2797.1(5) Å ³			
Ζ	4			
Density (calculated)	1.391 Mg/m ³			
Absorption coefficient	0.103 mm ⁻¹			
F(000)	1224			
Crystal size	0.20 x 0.14 x 0.06 mm ³			
Theta range for data collection	2.48 to 25.00°.			
Index ranges	-13<=h<=12, -9<=k<=9	, -30<=l<=39		
Reflections collected	15771			
Independent reflections	4903 [R(int) = 0.0492]			
Completeness to theta = 25.00°	99.7 %			
Absorption correction	Semi-empirical from equ	uivalents		
Max. and min. transmission	0.9939 and 0.9798	0.9939 and 0.9798		
Refinement method	Full-matrix least-squares	Full-matrix least-squares on F ²		
Data / restraints / parameters	4903 / 3 / 417			
Goodness-of-fit on F ²	1.326			
Final R indices [I>2sigma(I)]	R1 = 0.1146, wR2 = 0.2346			
R indices (all data)	R1 = 0.1271, wR2 = 0.24	R1 = 0.1271, $wR2 = 0.2414$		
Largest diff. peak and hole	0.791 and -0.403 e.Å ⁻³	0.791 and -0.403 e.Å ⁻³		

(iii) Crystal data and structure refinement for Tetramer 4:

CCDC Deposition Number	817349	817349		
Empirical formula	$C_{34}H_{28}Cl_2N_8O_7$	$C_{34}H_{28}Cl_2N_8O_7$		
Formula weight	731.54	731.54		
Temperature	223(2) K	223(2) K		
Wavelength	0.71073 Å	0.71073 Å		
Crystal system	Monoclinic			
Space group	P2(1)/n			
Unit cell dimensions	a = 14.2827(5) Å	<i>α</i> = 90°.		
	b = 18.5948(8) Å	β= 101.1340(10)°.		
	c = 25.6428(10) Å	$\gamma = 90^{\circ}$.		
Volume	6682.1(5) Å ³			
Ζ	8			
Density (calculated)	1.454 Mg/m ³	1.454 Mg/m ³		
Absorption coefficient	0.257 mm ⁻¹	0.257 mm ⁻¹		
F(000)	3024	3024		
Crystal size	0.60 x 0.26 x 0.26 mm ³	0.60 x 0.26 x 0.26 mm ³		
Theta range for data collection	1.52 to 27.50°.	1.52 to 27.50°.		
Index ranges	-18<=h<=17, -24<=k<=	-18<=h<=17, -24<=k<=23, -33<=l<=29		
Reflections collected	47121	47121		
Independent reflections	15349 [R(int) = 0.0469]	15349 [R(int) = 0.0469]		
Completeness to theta = 27.50°	99.9 %	99.9 %		
Absorption correction	Semi-empirical from eq	Semi-empirical from equivalents		
Max. and min. transmission	0.9361 and 0.8609	0.9361 and 0.8609		
Refinement method	Full-matrix least-square	Full-matrix least-squares on F ²		
Data / restraints / parameters	15349 / 0 / 953	15349 / 0 / 953		
Goodness-of-fit on F ²	1.100			
Final R indices [I>2sigma(I)]	R1 = 0.0738, $wR2 = 0.1$	R1 = 0.0738, $wR2 = 0.1488$		
R indices (all data)	R1 = 0.1085, wR2 = 0.1	R1 = 0.1085, wR2 = 0.1644		
Largest diff. peak and hole	0.475 and -0.417 e.Å ⁻³	0.475 and -0.417 e.Å ⁻³		

(iv) Crystal data and structure refinement for Pentamer 5:

CCDC Deposition Number	817350	817350		
Empirical formula	$C_{37}H_{32}N_{10}O_8$	$C_{37}H_{32}N_{10}O_8$		
Formula weight	744.73	744.73		
Temperature	100(2) K	100(2) K		
Wavelength	0.71073 Å	0.71073 Å		
Crystal system	Monoclinic			
Space group	P2(1)/n			
Unit cell dimensions	a = 8.0823(7) Å	$\alpha = 90^{\circ}$.		
	b = 16.6905(14) Å	β=97.306(2)°.		
	c = 25.880(2) Å	$\gamma = 90^{\circ}$.		
Volume	3462.8(5) Å ³			
Ζ	4			
Density (calculated)	1.428 Mg/m ³			
Absorption coefficient	0.104 mm ⁻¹			
F(000)	1552			
Crystal size	0.44 x 0.26 x 0.12 mm ³			
Theta range for data collection	1.59 to 27.49°.			
Index ranges	-10<=h<=10, -21<=k<=21, -25<=l<=33			
Reflections collected	24661			
Independent reflections	7945 [R(int) = 0.0336]	7945 [R(int) = 0.0336]		
Completeness to theta = 27.49°	99.9 %			
Absorption correction	Semi-empirical from equivalents			
Max. and min. transmission	0.9749 and 0.8267	0.9749 and 0.8267		
Refinement method	Full-matrix least-squares	Full-matrix least-squares on F ²		
Data / restraints / parameters	7945 / 116 / 572	7945 / 116 / 572		
Goodness-of-fit on F ²	1.065	1.065		
Final R indices [I>2sigma(I)]	R1 = 0.0542, wR2 = 0.13	R1 = 0.0542, $wR2 = 0.1351$		
R indices (all data)	R1 = 0.0722, wR2 = 0.14	R1 = 0.0722, $wR2 = 0.1437$		
Largest diff. peak and hole	0.608 and -0.506 e.Å ⁻³	0.608 and -0.506 e.Å ⁻³		

