Supporting Information for

Solvent dependence of helix stability in aromatic oligoamide foldamers

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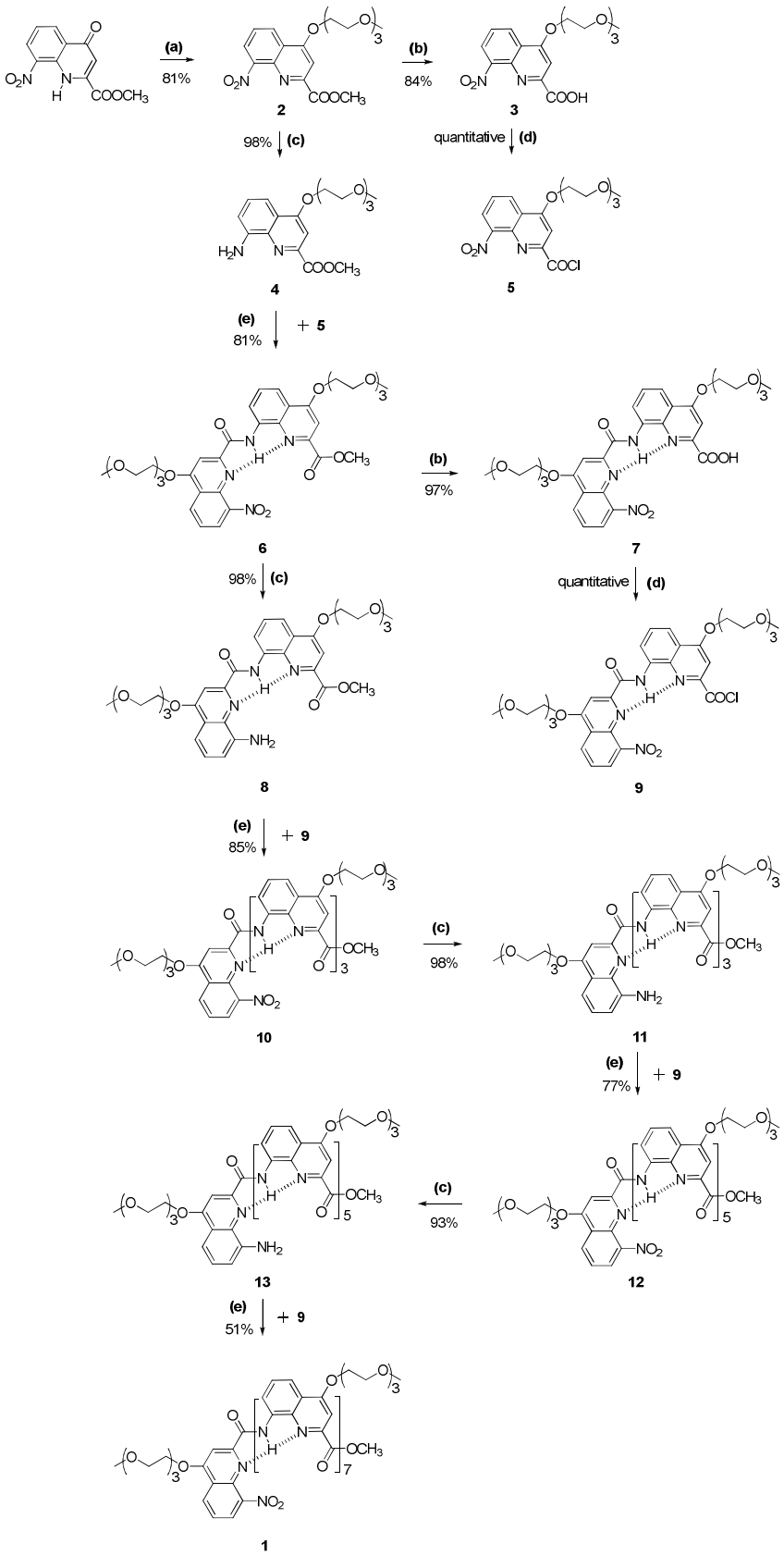

Scheme 1 (a) $CH_3(OCH_2CH_2)_3OH$, DIAD, PPh_3, THF; (b) KOH, 1,4-dioxane/H_2O; (c) Pd/C, H_2, EtOAc; (d) 1-Chloro-*N*,*N*,2-trimethyl-1-propenylamine, DCM; (e) DIPEA, DCM.

Experimental section

Reactions requiring anhydrous conditions were carried out under an dry nitrogen atmosphere. Commercial reagents were purchased from Sigma-Aldrich or Alfa-Aesar and were used without further purification. Tetrahydrofurane (THF) and dichloromethane (DCM) were dried over alumina column; N,N-diisopropylethylamine (DIPEA) was distilled from calcium hydride (CaH_2) prior to use. Methyl 8-nitro-(1H)-4-quinolinone-2-carboxylate[1] was synthesized according to the literature. Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel 60-F254 plates and observed under UV light. Column chromatography was carried out on Merck GEDURAN Si60 (40-63 μm). ESI mass spectra were obtained on an LCT premier spectrometer. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded in deuterated solvents on 300 MHz spectrometers. Chemical shifts are reported in parts per million (ppm, δ) relative to the signal of the NMR solvent used. ^{1}H NMR splitting patterns with observed first-order coupling are designated as singlet (s), doublet (d) or triplet (t). Coupling constants (J) are reported in hertz. Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m). ^{13}C NMR spectra were recorded on 75 or 100 MHz spectrometers. Chemical shifts are reported in ppm (δ) relative to carbon resonances of the NMR solvent.

Monomer ester (2). A mixture of methyl 8-nitro-(1H)-4-quinolinone-2-carboxylate[1] (5 g, 20.2 mmol) and triphenylphosphine (5.55 g, 1.05 equiv.), triethylene glycol monomethyl ether (3.55 mL, 1.1 equiv.) in anhydrous THF (45 mL) under nitrogen, was cooled down to 0°C. Diisopropyl azodicarboxylate (5.95 mL, 1.5 equiv.) was slowly added and the mixture was stirred at 0°C for 30 min, then at room temperature for 16 h. The solvent was removed and the crude solid was recrystallized cold MeOH (−18 °C) (10 mL) to afford the pure product as yellow crystals that were filtered and washed twice with cold MeOH (−18 °C, 5 mL). Yield 6.4 g (81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ *:* 8.51 (dd, J = 8.5, 1.4 Hz, 1H), 8.11 (dd, J = 7.5, 1.4 Hz, 1H), 7.69 (s, 1H), 7.65 (dd, J = 8.5, 7.5 Hz, 1H), 4.49 (dd, J = 5.3, 3.9 Hz, 2H), 4.06 – 4.02 (m, 5H), 3.83 – 3.76 (m, 2H), 3.74 – 3.63 (m, 4H), 3.57 – 3.51 (m, 2H), 3.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ*:* 165.71, 162.70, 151.36, 148.44, 140.16, 126.73, 126.10, 125.30, 123.30, 102.42, 72.03, 71.15, 70.81, 70.76, 69.23, 69.04, 59.18, 53.52.

General method for the saponification of methyl esters. The monomer **2** or dimer **6** was dissolved in a mixture of 1,4-dioxane and H_2O. KOH powder (2.5 equiv.) was added, and the solution was stirred at room temperature overnight. The reaction was monitored by TLC (silica gel, 95:5 (v/v) CH_2Cl_2/MeOH). After the reaction was completed, the solution was acidified to pH ≈ 5 using a citric acid aqueous solution (5% (w/w)). Solvents were evaporated and the crude product dissolved in acetone followed by filtration of the suspension. The solvent of the filtrate was removed and the solid was dissolved in toluene. The solution was dried over $MgSO_4$ and evaporated to afford the corresponding acid.

Monomer acid (3). Monomer **2** (2g, 5.08 mmol) was saponified according to the general procedure, KOH (711 mg, 12.7 mmol) was used in a mixture of 1,4-dioxane (70 mL) and H_2O (1 mL). The reaction was acidified using 30 mL of citric acid aqueous solution (5% (w/w)). The reaction yielded 1.6 g (84%) of a yellow solid which was checked by NMR and used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ : 8.60 (dd, J = 8.5, 1.4 Hz, 1H), 8.26 (dd, J = 7.5, 1.4 Hz, 1H), 7.80 (s, 1H), 7.75 (dd, J = 8.5, 7.6 Hz, 1H), 4.58 – 4.55 (m, 2H), 4.12 – 4.03 (m, 2H), 3.85 – 3.77 (m, 2H), 3.74 – 3.66 (m, 4H), 3.60 – 3.52 (m, 2H), 3.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.13, 163.70, 149.40, 147.05, 138.38, 127.51, 126.64, 126.36, 123.57, 100.56,

71.96, 71.09, 70.72, 70.67, 69.53, 69.11, 59.10.

Dimer acid (7). Dimer **6** (550 mg, 0.76 mmol), was saponified according to the general procedure in a mixture of 1,4-dioxane (10 mL) and H_2O (0.5 mL), using KOH (106 mg, 1.89 mmol). The resulting solution was acidified with 8 mL of a citric acid aqueous solution (5% (w/w)). After workup 526 mg (97%) of a yellow solid was obtained which was characterized by NMR and used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 11.50 (s, 1H), 8.96 (d, *J* = 7.2 Hz, 1H), 8.27 (d, *J* = 7.2 Hz, 1H), 8.15 (d, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 7.9 Hz, 1H), 7.81 (s, 1H), 7.63 – 7.55 (m, 2H), 7.47 – 7.42 (m, 1H), 4.51 – 4.48 (m, 2H), 4.41 (s, 2H), 4.13 – 4.02 (m, 2H), 3.97 (s, 2H), 3.84 – 3.81 (m, 2H), 3.78 – 3.73 (m, 4H), 3.72 – 3.63 (m, 6H), 3.58 – 3.52 (m, 4H), 3.39 (s, 3H), 3.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) *δ:* 164.65, 163.45, 163.14, 161.85, 153.09, 146.95, 146.59, 138.99, 138.29, 133.91, 128.31, 127.45, 126.08, 125.63, 123.08, 122.55, 119.27, 117.15, 100.25, 100.00, 71.95, 71.94, 71.08, 71.01, 70.73, 70.70, 70.65, 70.64, 69.22, 69.13, 68.92, 59.08.

General procedure for the hydrogenation of nitro groups. The nitro precursor **2**, **6**, **10** or **12** was dissolved in EtOAC and 10% Pd/C catalyst was added to the solution. The resulting suspension was placed under a hydrogen atmosphere (balloon) and stirred vigorously for 16 h at room temperature. Completion of the reaction was monitored by NMR. The solution was then filtered through Celite, and the solvent was evaporated. The product was characterized by ^{1}H NMR and used without further purification.

Monomer amine (4). Monomer **2** (1.54 g, 3.91 mmol) was reduced according to the general procedure of hydrogenation, using 10% Pd/C catalyst (154 mg, 10% (w/w)), in 40 mL EtOAc. After evaporation of the solvent, 1.39 g (98%) of a yellow solid was obtained. ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 7.57 – 7.49 (m, 2H), 7.43 – 7.33 (m, 1H), 6.96 (dd, *J* = 7.5, 1.2 Hz, 1H), 5.12 (s, 2H), 4.50 – 4.39 (m, 2H), 4.12 – 3.97 (m, 5H), 3.87 – 3.78 (m, 2H), 3.76 – 3.64 (m, 4H), 3.57 – 3.54 (m, 2H), 3.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) *δ:* 166.28, 162.30, 145.69, 144.92, 138.38, 128.73, 122.86, 110.94, 109.69, 100.86, 71.94, 71.09, 70.71, 70.63, 69.32, 68.29, 59.06, 52.84.

Dimer amine (8). Dimer **6** (313 mg, 0.43 mmol) was reduced according to the general procedure of hydrogenation, using 10% Pd/C catalyst (31 mg, 10% (w/w)), in 10 mL EtOAc to yield to 288 mg (98%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 12.69 (s, 1H), 9.05 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.96 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.78 (s, 1H), 7.67 (t, *J* = 8.1 Hz, 1H), 7.60 (s, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.44 – 7.34 (m, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 5.53 (s, 2H), 4.56 – 4.41 (m, 4H), 4.10 (s, 3H), 4.07 – 4.04 (m, 4H), 3.84 – 3.81 (m, 4H), 3.76 – 3.61 (m, 8H), 3.59 – 3.51 (m, 4H), 3.37 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) *δ:* 165.37, 163.15, 163.12, 162.85, 148.31, 146.86, 144.96, 139.74, 137.54, 135.37, 128.73, 128.46, 123.07, 122.23, 117.41, 115.95, 111.16, 109.79, 101.63, 98.41, 72.16, 72.14, 71.30, 70.94, 70.86, 69.59, 69.47, 68.69, 68.58, 59.28, 53.17.

Tetramer amine (11). According to the general procedure of hydrogenation, tetramer **10** (210 mg, 0.15 mmol) was reduced using 10% Pd/C catalyst (76 mg, 36% (w/w)), in 10 mL EtOAc to afford 201 mg (98%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 12.44 (s, 1H), 11.95 (s, 1H), 11.80 (s, 1H), 9.03 (dd, *J* = 7.6, 1.0 Hz, 1H), 8.44 (dd, *J* = 7.6, 1.0 Hz, 1H), 8.04 (dd, *J* = 5.2, 1.1 Hz, 1H), 8.02 (dd, *J* = 5.9, 1.2 Hz, 1H), 7.98 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.86 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.77 (s, 1H), 7.76 – 7.69 (m, 1H), 7.66 (t, *J* = 8.1 Hz, 1H), 7.52 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.39 – 7.29 (m, 2H), 7.12 – 7.03 (m, 1H), 6.89 (s, 1H), 6.69 (s, 1H), 5.98 (dd, *J* = 7.5, 0.9 Hz, 1H), 4.60 (s, 4H), 4.32 – 4.22 (m, 4H), 4.22 – 4.14 (m, 4H), 4.09 – 4.03 (m, 4H), 3.91 – 3.87 (m, 8H), 3.79 – 3.77 (m, 10H), 3.75 – 3.69 (m, 8H), 3.62 – 3.56 (m, 8H), 3.53 (s, 3H), 3.40 (m, 12H). ^{13}C

NMR (75 MHz, $CDCl_3$) *δ:* 163.83, 163.64, 163.40, 162.87, 162.70, 162.02, 161.48, 160.70, 150.73, 149.49, 148.42, 145.16, 143.17, 139.09, 138.97, 137.90, 136.30, 134.72, 134.03, 133.68, 128.00, 127.59, 127.49, 127.34, 122.74, 121.78, 121.72, 121.63, 117.10, 116.53, 116.46, 116.42, 116.07, 115.55, 109.91, 100.38, 98.57, 98.53, 97.96, 72.00, 71.24, 71.17, 71.11, 70.82, 70.80, 70.73, 70.70, 70.68, 69.43, 69.33, 69.26, 69.23, 68.81, 68.66, 68.49, 68.35, 59.11, 52.37.

Hexamer amine (13). The hexamer **12** (140 mg, 0.07 mmol) was converted to the amine according to the procedure of hydrogenation using 10% Pd/C catalyst (50 mg, 36% (w/w)), in 10 mL EtOAc to give 128 mg (93%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ : 11.89 (s, 1H), 11.75 (s, 1H), 11.66 (s, 1H), 11.45 (s, 1H), 11.43 (s, 1H), 8.63 (d, *J* = 7.4 Hz, 1H), 8.22 (d, *J* = 7.1 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 17.5 Hz, 1H), 7.50 (d, *J* = 14.1 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.39 – 7.30 (m, 2H), 7.28 (s, 1H), 7.03 (s, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 15.2 Hz, 2H), 6.52 (d, *J* = 4.1 Hz, 2H), 5.82 (d, *J* = 7.4 Hz, 1H), 4.86 – 4.60 (m, 4H), 4.50 – 4.23 (m, 10H), 4.23 – 4.03 (m, 12H), 4.03 – 3.89 (m, 10H), 3.89 – 3.53 (m, 38H), 3.52 – 3.28 (m, 18H), 3.17 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) *δ:* 163.62, 163.41, 162.89, 162.74, 162.70, 162.43, 161.84, 161.66, 161.41, 161.12, 160.60, 159.07, 150.16, 149.49, 148.97, 148.01, 145.19, 142.97, 138.89, 138.36, 138.12, 137.74, 137.65, 136.05, 133.79, 133.77, 133.58, 133.43, 132.81, 127.76, 127.31, 127.28, 127.15, 126.81, 126.74, 122.66, 122.38, 121.78, 121.77, 121.43, 121.42, 116.97, 116.94, 116.74, 116.30, 116.27, 116.00, 115.86, 115.82, 115.45, 109.91, 109.71, 100.22, 99.52, 98.37, 98.13, 97.74, 97.37, 72.08, 72.05, 72.01, 71.98, 71.30, 71.27, 71.25, 71.15, 71.12, 70.95, 70.88, 70.85, 70.83, 70.81, 70.80, 70.77, 70.75, 70.72, 70.68, 69.45, 69.32, 69.20, 68.76, 68.69, 68.26, 68.06, 59.16, 59.15, 52.09.

General procedure for coupling an amine and an acid. The nitro quinoline acid monomer **3** or dimer **7** was dissolved in anhydrous DCM under nitrogen. "Ghosez reagent" (1-Chloro-*N*,*N*,2-trimethyl-1-propenylamine, 1.1 equiv.) was added at 0°C. The reaction was then warmed up to room temperature under nitrogen and stirred for 2 hours. Completion of the acid chloride formation was monitored by NMR. Solvents were removed under reduced pressure to yield the corresponding moisture sensitive nitro-quinoline acid chloride monomer of dimer as a yellow solid. This solid was then dissolved in dry DCM and slowly added at 0°C to a solution of the amino quinoline methyl ester **4**, **8**, **11** or **13** (1 equiv.) and N,N-diisopropylethylamine (5.5 equiv.) in dry DCM under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 12 h. Solvents were evaporated and the crude material purified by flash chromatography with CH_2Cl_2/MeOH as eluent to yield the pure compound as yellow solid.

Monomer acid chloride (5). ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 8.51 (dd, *J* = 8.5, 1.2 Hz, 1H), 8.13 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.72 (dd, *J* = 8.4, 7.6 Hz, 1H), 7.59 (s, 1H), 4.52 – 4.49 (m, 2H), 4.18 – 4.00 (m, 2H), 3.91 – 3.75 (m, 3H), 3.75 – 3.62 (m, 5H), 3.55 – 3.52 (m, 2H), 3.36 (s, 3H).

Dimer acid chloride (9). ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 11.82 (s, 1H), 9.11 (dd, *J* = 7.8, 1.0 Hz, 1H), 8.56 (dd, *J* = 8.4, 0.9 Hz, 1H), 8.17 (dd, *J* = 7.4, 0.9 Hz, 1H), 8.03 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.99 (s, 1H), 7.73 (t, *J* = 8.1 Hz, 1H), 7.70 – 7.62 (m, 1H), 7.56 (s, 1H), 4.65 – 4.52 (m, 2H), 4.52 – 4.41 (m, 2H), 4.15 – 3.99 (m, 4H), 3.88 – 3.77 (m, 4H), 3.77 – 3.62 (m, 8H), 3.56 – 3.53 (m, 4H), 3.37 (s, 6H).

Dimer (6). Monomer acid **3** (115 mg, 0.3 mmol), was activated with 1-Chloro-*N*,*N*, 2-trimethyl-1-propenylamine (0.044 mL, 0.33 mmol), and reacted according to the general coupling procedure with the monomer amine **4** (100 mg, 0.27 mmol), in presence of

N,N-diisopropylethylamine (0.26 mL, 1.51 mmol) in 10 mL anhydrous DCM. The crude product was purified by flash chromatography using CH_2Cl_2/MeOH (100/1 (v/v)) as eluent to yield 162 mg (81%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 11.75 (s, 1H), 8.95 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.04 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.71 – 7.62 (m, 2H), 4.54 – 4.43 (m, 2H), 4.13 (s, 3H), 4.08 – 4.01 (m, 2H), 3.86 – 3.79 (m, 2H), 3.76 – 3.63 (m, 4H), 3.58 – 3.51 (m, 2H), 3.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) *δ:* 166.87, 163.09, 162.58, 162.46, 153.97, 148.35, 147.84, 139.83, 139.46, 134.91, 128.01, 127.07, 125.64, 125.58, 123.37, 122.24, 118.93, 116.98, 101.65, 100.38, 72.01, 71.16, 71.11, 70.79, 70.78, 70.73, 70.73, 69.36, 69.24, 69.05, 68.62, 59.15, 53.77. MS (ESI) (m/z) : 727.6 $[M+H]^+$, 749.6 $[M+Na]^+$, 1453.1 $[2M+H]^+$, 1475.1 $[2M+Na]^+$. (calculated for $C_{35}H_{42}N_4O_{13}$: 726.3).

Tetramer (10). Dimer acid **7** (100 mg, 0.14 mmol) was activated and coupled according to the general procedure using 1-Chloro-*N*,*N*, 2-trimethyl-1-propenylamine 0.02 mL, 0.15 mmol), the dimer amine **8** (89 mg, 0.13 mmol), and N,N-diisopropylethylamine (0.12 mL, 0.69 mmol) in 10 mL of anhydrous DCM. The crude product was flash chromatographed with CH_2Cl_2/MeOH (60/1 (v/v)) as eluent to yield 150 mg (85%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 12.29 (s, 1H), 11.92 (s, 1H), 11.65 (s, 1H), 9.13 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.58 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.39 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.15 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.01 (dd, *J* = 3.2, 1.2 Hz, 1H), 7.99 (dd, *J* = 3.2, 1.2 Hz, 1H), 7.92 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.87 (s, 1H), 7.79 – 7.72 (m, 1H), 7.65 – 7.60 (m, 2H), 7.51 – 7.45 (m, 2H), 7.38 – 7.31 (m, 1H), 6.86 (s, 1H), 6.70 (s, 1H), 4.67 (s, 2H), 4.62 – 4.59 (m, 2H), 4.32 – 4.18 (m, 6H), 4.16 – 4.13 (m, 2H), 4.10 – 4.02 (m, 4H), 3.95 – 3.84 (m, 8H), 3.84 – 3.75 (m, 8H), 3.75 – 3.68 (m, 8H), 3.62 – 3.52 (m, 8H), 3.47 (s, 3H), 3.40 (s, 3H), 3.40 (s, 3H), 3.39 (s, 3H), 3.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) *δ:* 163.96, 163.35, 163.13, 162.99, 162.93, 162.16, 161.53, 160.66, 153.60, 151.11, 149.00, 145.61, 145.22, 139.29, 139.18, 139.11, 138.31, 135.29, 134.09, 133.80, 128.34, 128.16, 127.73, 127.17, 126.38, 124.92, 123.71, 122.02, 121.94, 121.85, 117.89, 117.03, 116.96, 116.85, 116.44, 116.19, 100.66, 100.21, 98.95, 97.68, 72.08, 71.31, 71.24, 71.21, 70.91, 70.89, 70.80, 69.46, 69.37, 69.35, 69.33, 68.97, 68.86, 68.77, 68.62, 59.21, 59.19, 52.55. MS (ESI) (m/z) : 1391.9 $[M+H]^+$, 1413.9 $[M+Na]^+$. (calculated for $C_{69}H_{82}N_8O_{23}$: 1390.5).

Hexamer (12). Dimer acid **7** (69 mg, 0.097 mmol)was activated and coupled according to the general procedure using 1-Chloro-*N*,*N*, 2-trimethyl-1-propenylamine (0.014 mL, 0.11 mmol), the tetramer amine **11** (120 mg, 0.088 mmol) and N,N-diisopropylethylamine (0.08 mL, 0.48 mmol) in 10 mL of anhydrous DCM. The crude product was flash chromatographed with CH_2Cl_2/MeOH (30/1 (v/v)) as eluent to yield 140 mg (77%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) *δ :* 11.84 (s, 1H), 11.61 (s, 1H), 11.57 (s, 1H), 11.41 (s, 1H), 11.34 (s, 1H), 8.54 (dd, *J* = 7.6, 1.0 Hz, 1H), 8.41 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.23 (ddd, *J* = 7.6, 2.5, 1.1 Hz, 2H), 8.09 (dd, *J* = 7.7, 1.0 Hz, 1H), 8.06 (dd, *J* = 6.0, 1.2 Hz, 1H), 8.03 (dd, *J* = 5.9, 1.1 Hz, 1H), 7.98 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.93 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.78 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.55 – 7.30 (m, 7H), 7.24 – 7.21 (m, 1H), 7.16 (s, 1H), 6.75 (d, *J* = 20.5 Hz, 2H), 6.51 (d, *J* = 2.9 Hz, 2H), 4.78 – 4.64 (m, 2H), 4.55 – 4.05 (m, 20H), 4.04 – 3.90 (m, 10H), 3.89 – 3.54 (m, 40H), 3.50 – 3.33 (m, 18H), 3.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ :* 163.45, 162.97, 162.72, 162.70, 162.61, 162.36, 161.63, 161.02, 160.93, 160.53, 159.96, 159.75, 152.85, 150.36, 149.12, 148.65, 148.53, 145.04, 144.58, 138.70, 138.63, 138.19, 138.17, 137.89, 137.49, 133.95, 133.70, 133.47, 132.52, 127.95, 127.54, 127.23, 127.21, 126.71, 126.18, 126.14, 124.40, 123.31, 122.33, 121.96, 121.64, 121.35, 121.25, 116.86, 116.61, 116.51, 116.38, 116.29, 115.99, 115.83, 115.55, 100.12,

99.64, 99.50, 97.78, 97.58, 97.39, 71.94, 71.90, 71.86, 71.18, 71.16, 71.11, 70.98, 70.95, 70.78, 70.76, 70.72, 70.70, 70.61, 70.56, 69.33, 69.22, 69.18, 69.04, 69.00, 68.62, 68.58, 68.53, 68.50, 68.44, 68.12, 58.99, 51.98. TOF-MS (ESI) (m/z) : 2078.60 $[M+Na]^+$, 1050.78 $[M+2Na]^{2+}$. (calculated for C103H122N12O33: 2054.82).

Octamer (1). Dimer acid **7** (50 mg, 0.07 mmol) was activated with 1-Chloro-*N*,*N*, 2-trimethyl-1-propenylamine (0.01 mL, 0.077 mmol) according to the procedure of coupling reaction, and coupled to the hexamer amine **8** (128 mg, 0.063 mmol), in presence of N,N-diisopropylethylamine (0.06 mL, 0.35 mmol) in 10 mL of anhydrous DCM. The crude product was purified by flash chromatography with CH_2Cl_2/MeOH (40/1 (v/v)) as eluent to afford 88 mg (51%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ : 11.48 (s, 1H), 11.34 (s, 1H), 11.23 (s, 1H), 11.09 (s, 1H), 11.04 (s, 1H), 11.03 (s, 2H), 8.32 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.21 (d, *J* = 7.5 Hz, 1H), 8.12 – 8.06 (m, 4H), 7.99 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.87 (dd, *J* = 3.3, 1.1 Hz, 1H), 7.86 – 7.79 (m, 2H), 7.73 (dd, *J* = 4.7, 1.2 Hz, 1H), 7.70 (dd, *J* = 4.7, 1.1 Hz, 1H), 7.64 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.52 – 7.28 (m, 10H), 7.08 (d, *J* = 7.6 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.65 (s, 1H), 6.63 (s, 1H), 6.49 (s, 1H), 6.46 (s, 1H), 6.40 (s, 1H), 6.09 (s, 1H), 4.53 – 4.35 (m, 8H), 4.29 – 4.20 (m, 8H), 4.17 – 4.01 (m, 18H), 3.93 – 3.90 (m, 8H), 3.87 – 3.64 (m, 44H), 3.63 – 3.53 (m, 10H), 3.50 – 3.35 (m, 24H), 3.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 163.42, 162.55, 162.50, 162.47, 162.33, 162.27, 162.19, 161.58, 160.81, 160.54, 160.38, 159.90, 159.48, 159.15, 159.13, 152.93, 149.87, 149.03, 148.95, 148.67, 148.62, 148.06, 144.85, 144.41, 138.61, 138.59, 137.96, 137.65, 137.52, 137.32, 133.95, 133.54, 133.42, 133.19, 132.70, 132.61, 132.56, 127.94, 127.71, 127.20, 127.05, 126.58, 126.16, 126.00, 124.38, 123.31, 122.22, 122.14, 122.00, 121.99, 121.42, 121.20, 121.06, 117.20, 116.91, 116.72, 116.57, 116.23, 116.20, 116.03, 115.97, 115.88, 115.87, 115.77, 115.48, 100.01, 99.57, 99.18, 98.65, 98.30, 97.59, 97.42, 97.31, 72.06, 71.98, 71.94, 71.32, 71.23, 71.14, 71.11, 71.10, 71.07, 71.02, 70.93, 70.86, 70.81, 70.78, 70.75, 70.69, 70.65, 69.31, 69.24, 69.20, 69.15, 69.10, 69.07, 68.56, 68.46, 68.37, 68.25, 68.09, 59.15, 59.10, 59.07, 51.90. TOF-MS (ESI) (m/z) : 1371.98 $[M+H+Na]^{2+}$, 1382.95 $[M+2Na]^{2+}$. (calculated for C137H162N16O43: 2719.10).

Investigation of helix handedness inversion, HPLC and kinetic measurements. HPLC separations were performed by using a stainless-steel CHIRALPAK IA column (250 mm x 4.6 mm I.D., 5 μm particle-size) [Daicel Chemical Industries, Ltd., Tokyo, Japan]. HPLC-grade solvents were supplied by Wako Pure Chemical, Inc. (Kyoto, Japan). The HPLC system consisted of a JASCO 980 (JASCO, Tokyo, Japan) pump equipped with a Rheodyne injector (Rohnert Park, CA, USA), a 20-μL sample loop and the column temperature was controlled in the refrigerated circulator (NESLAB Instruments, Inc. USA). The chromatograms were detected with a JASCO Model CD2095 Plus chiral detector and JASCO Model MD2010 multi-wavelength UV detector. Chiral separation of the oligoamide **1** was carried out with a chloroform/2-propanol (25/75, vol/vol) mixture as a mobile phase (flow rate: 0.5 mL min^{-1}, temperature: -5 °C). This ratio was optimized for optimal separation of oligoamide 1. The initial stock solutions were prepared in a chloroform, in which the oligoamide **1** is more soluble than in the eluting solvent. The racemic oligomer was dissolved in this solvent and the solution was injected into HPLC. The fraction of right-handed helical conformer (*P*) was collected and the solvent was evaporated at -5 ˚C under vacuum. The *P*-**1** was then dissolved in various organic solvents listed in Table 1. The racemization of *P*-1 at 30 ˚C was monitored by CD spectroscopic measurements. UV spectra of *P*-**1** were measured before and after monitoring of racemization to confirm that no precipitation

took place during racemization. The racemization rate constant (k_{rac}) of *P*-**1** was obtained by curve fitting to an exponential decay (Equation 1) where t is the aging time.

$$\frac{[M]}{[M]_0} = \frac{1}{2}e^{(-2k_{rac}t)} + \frac{1}{2} \qquad \text{(Equation 1)}$$

Half-lives ($t_{1/2}$) were calculated following Equation (2):

$$t_{1/2} = -\frac{\ln(1/2)}{2k_{rac}} \qquad \text{(Equation 2)}$$

Crystallography. X-ray quality crystals of **6** were obtained from MeOH. Data collection was performed at the IECB X-ray facility on a Bruker AXS X8-Proteum rotating anode at the copper k_α wavelength at 213K. The crystal was mounted on a cryo-loop after quick soaking on Paratone-N oil from Hampton research and flash-frozen. The crystal structure of compound **6** was solved using the charge flipping algorithm implemented in the SUPERFLIP software[2]. The structure was refined using SHELXL-97.[3] Full-matrix least-squares refinement was performed on F^2 for all unique reflections, minimizing $w(Fo^2 - Fc^2)^2$, with anisotropic displacement parameters for non-hydrogen atoms. The positions of hydrogen atoms were located on a subsequent differential electron-density map. Hydrogen atoms were mostly spotted in Fourier differences but included in idealized positions and refined with a riding model, with U_{iso} constrained to 1.2 U_{eq} value of the parent atom (1.5 U_{eq} when CH_3). The positions and isotropic displacement parameters of the remaining hydrogen atoms were refined freely. Data statistics are reported in the "note" section of the manuscript and in the cif file.

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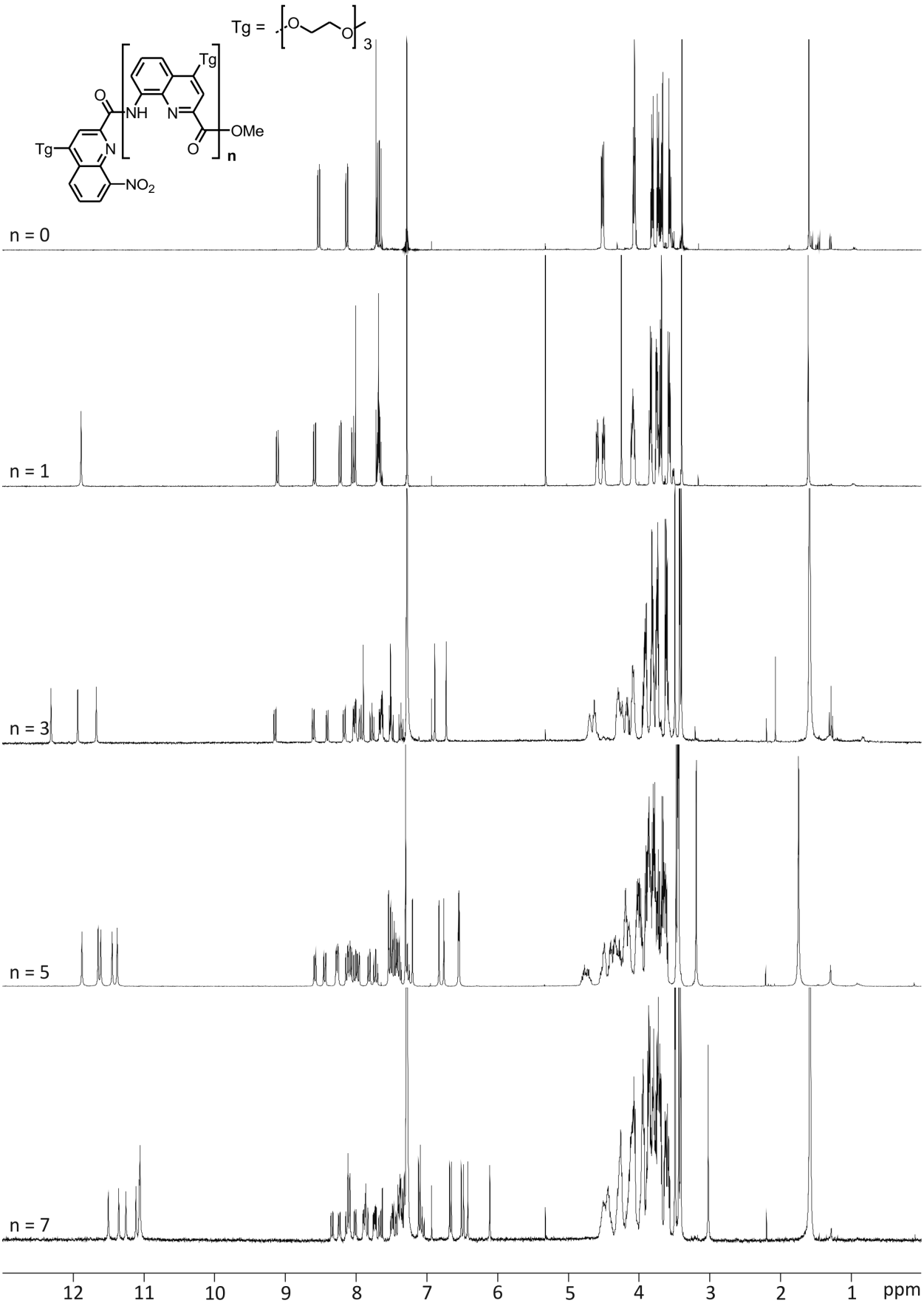

Figure S1 : ^{1}H-NMR spectra in CDCl3 of the oligomer serie : monomer **2** (n=0), dimer **6** (n=1), tetramer **10** (n=3), hexamer **12** (n=5) and octamer **1** (n=7)

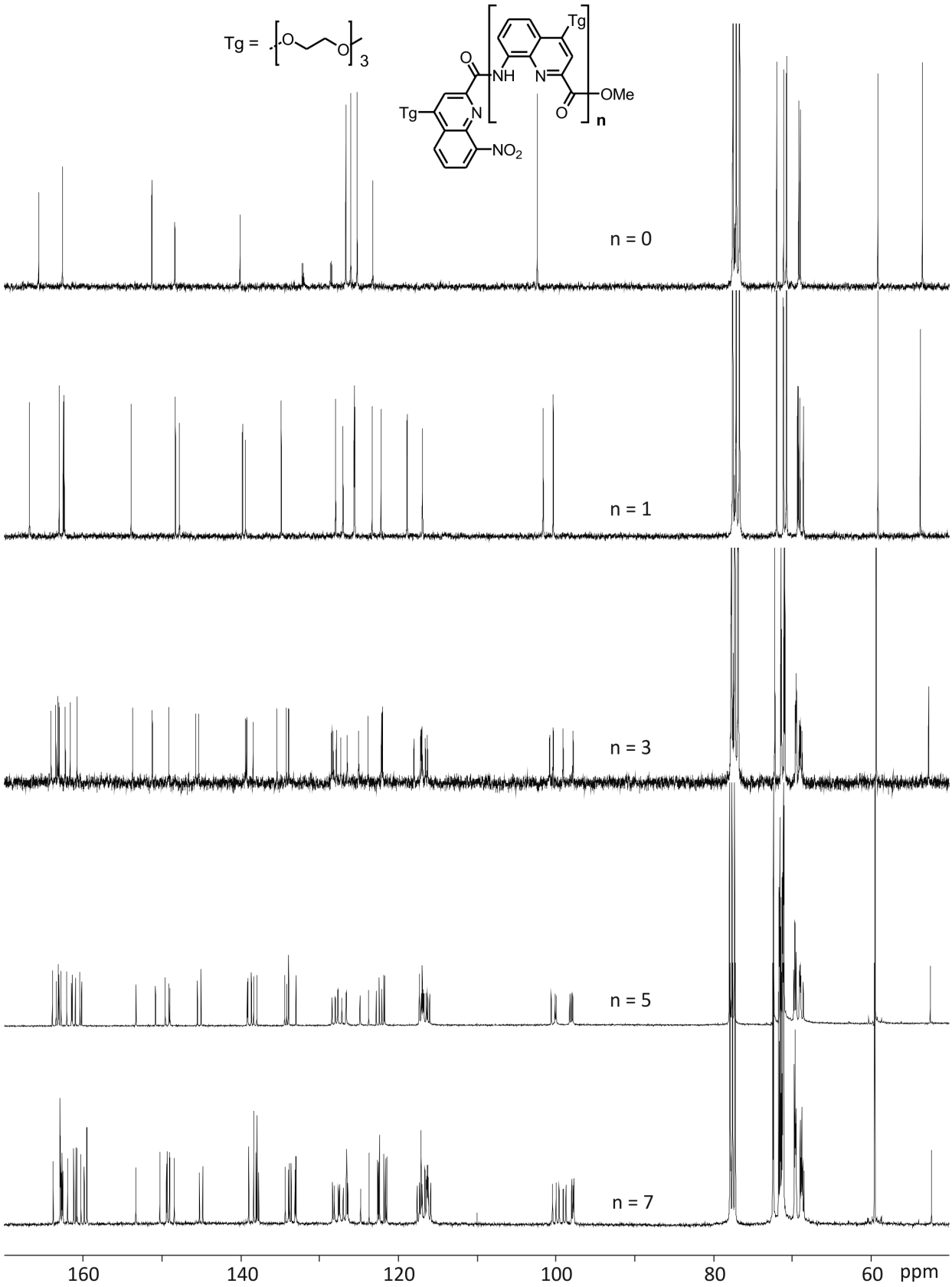

Figure S2 : ^{13}C-NMR spectra in CDCl3 of the oligomer serie : monomer **2** (n=0), dimer **6** (n=1), tetramer **10** (n=3), hexamer **12** (n=5) and octamer **1** (n=7)