Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Aromatic Oligoamides with Increased Backbone Flexibility: Improved Synthetic Efficiencies, Solvent-Dependent Folding and Cooperative Conformational Transitions

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Supplementary Information

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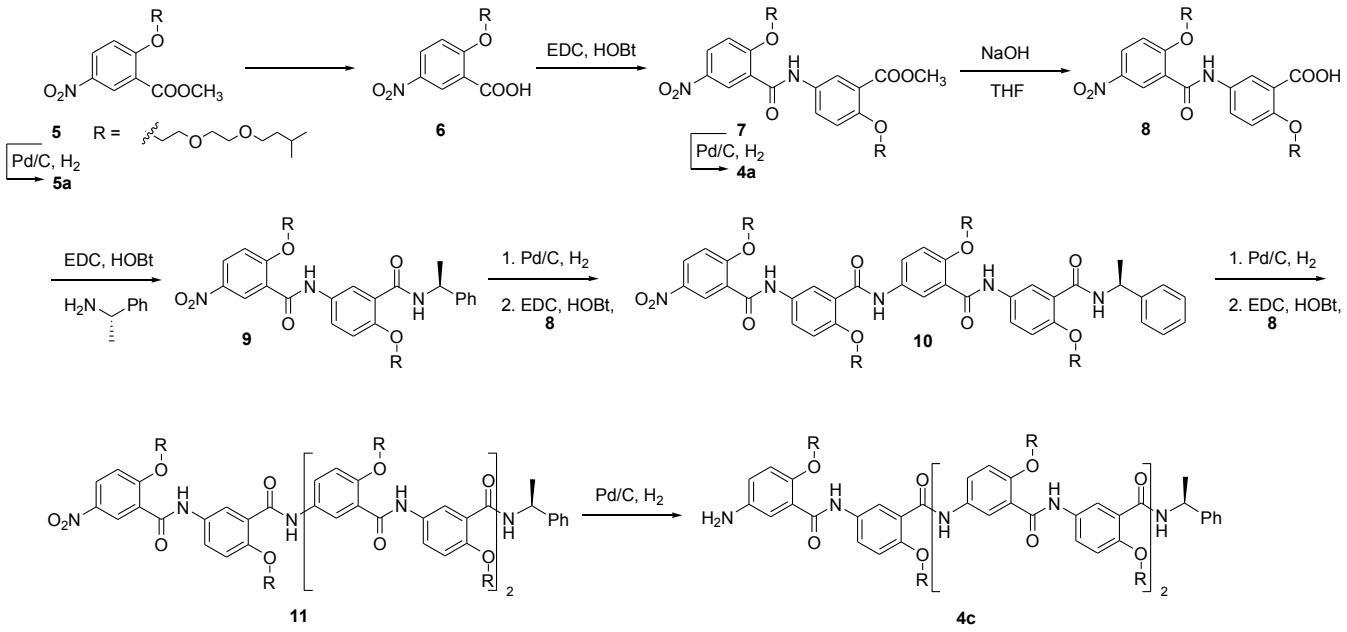
1. Synthesis



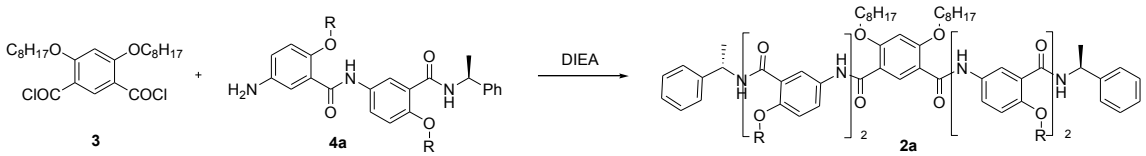
Compound (**7**): To a solution of **6** [1](2.44 g, 7.2 mmol), EDC (1.66 g, 10.7 mmol) and HOBt (1.06 g, 7.9 mmol) in CH_2Cl_2 (50 mL) was added the amine **5a** [1] (2.33 g, 7.2 mmol) in CH_2Cl_2 (30 mL). The reaction was allowed to proceed for 4 hours. The mixture was washed with diluted HCl and solvent was removed in vacuum. Purification was accomplished by chromatography on silica gel by using hexane/acetone to afford **7** (3.82 g, 82%) as light yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 9.15 (d, *J* = 2.9 Hz, 1H), 8.34 (dd, *J* = 9.1, 2.7 Hz, 1H), 8.03 (dd, *J* = 8.9, 2.7 Hz, 1H), 7.97 (d, *J* = 2.7 Hz, 1H), 7.10 (d, *J* = 9.1 Hz, 1H), 7.01 (d, *J* = 9.0 Hz, 1H), 4.50 – 4.40 (m, 2H), 4.21 (t, *J* = 5.0 Hz, 2H), 4.07–4.05 (m, 2H), 3.94 – 3.90 (m, 2H), 3.88 (s, 3H), 3.80 – 3.74 (m, 4H), 3.64 – 3.57 (m, 2H), 3.57 –3.52(m, 2H), 3.49 (t, *J* = 5.0 Hz, 2H), 3.34 (t, *J* = 4.2 Hz, 2H), 1.75 – 1.63 (m, 1H), 1.62 – 1.45 (m, 3H), 1.33 (q, *J* = 6.9 Hz, 2H), 0.92 – 0.77 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.25, 160.86, 160.58, 155.27, 142.28, 131.41, 128.62, 128.17, 125.99, 123.70, 123.13, 120.82, 114.74, 112.92, 71.07, 70.72, 70.17, 69.99, 69.92, 69.64, 69.50, 68.98, 68.67, 52.06, 51.97, 38.44, 38.29, 25.09, 25.04, 22.64. ESI-MS: 671.6 $(M + Na)^+$.

Compound (**8**): Compound **7** (1.4 g, 2.1 mmol) was dissolved in THF (100 mL) at room temperature. A solution of 1M NaOH (21 mL) was added under stirring. The mixture was warmed up to 40˚C until all the methyl ester was consumed. THF was removed in vacuum and then diluted HCl was added. The precipitate was filtered off and recrystallized in ethyl acetate/hexane to give the white solid (1.1 g, 79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.10 (s, 1H), 10.00 (s, 1H), 9.05 (s, 1H), 8.41 (d, *J* = 7.5 Hz, 1H), 8.31 (d, *J* = 7.2 Hz, 1H), 7.98 (s, 1H), 7.13 (d, *J* = 9.0 Hz, 1H), 7.07 (d, *J* = 9.0 Hz, 1H), 4.51– 4.45 (m, 2H), 4.44– 4.35 (m, 2H), 4.15–4.12 (m, 2H), 4.00– 3.85 (m, 4H), 3.75– 3.70 (m, 2H), 3.64–3.55 (m, 4H), 3.49 (t, *J* = 6.6 Hz, 2H), 3.36 (d, *J* = 6.9 Hz, 2H), 1.80 – 1.24 (m, 6H), 0.90 (d, *J* = 6.6 Hz, 6H), 0.82 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.91, 160.87, 160.70, 153.72, 141.97, 133.18, 128.34, 128.27, 127.00, 124.50, 122.53, 118.47, 114.20, 113.00, 70.81, 70.29, 70.05, 69.90, 69.73, 69.54, 69.23, 68.63, 38.34, 38.26, 25.02, 24.97, 22.60, 22.54. ESI-MS: 657.4 $(M+Na)^+$.

Compound (**9**): An equimolar ratio of the compound **8** (0.70 g, 1.1mmol) and (*s*)-1-phenyl ethylamine (0.13 g, 1.1 mmol), 1.3 eq. of EDC (0.22 g, 1.4 mmol) and 1.1 eq. of HOBt (0.16 g, 1.2 mmol) were dissolved in dichloromethane. The solution was stirred overnight. Water (30mL) was added to the mixture and the aqueous layer was extracted with CH_2Cl_2 (3×40 mL). The organic layer was collected and concentrated in vacuum to provide the crude product. The crude was purified by silica gel column chromatography to give the product as a white solid (0.75 g, 91 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.95 (s, 1H), 9.10 (m, 1H), 8.48 (d, *J* = 7.8 Hz, 1H), 8.35 (dd, *J* = 9.0, 2.7 Hz, 1H), 8.29 (dd, *J* = 9.0, 2.9 Hz, 1H), 7.92 (d, *J* = 2.7 Hz, 1H), 7.45 – 7.20 (m, 5H), 7.07 (d, *J* = 9.1 Hz, 1H), 6.95 (d, *J* = 9.0 Hz, 1H), 5.33 (p, *J* = 7.0 Hz, 1H), 4.56 – 4.38 (m, 2H), 4.31 – 4.19 (m, 2H), 4.09 – 3.95 (m, 2H), 3.91 – 3.76 (m, 4H), 3.67 – 3.52 (m, 2H), 3.52 – 3.36 (m, 6H), 3.28 (t, *J* = 7.0 Hz, 2H), 1.73 – 1.36 (m, 7H), 1.34 – 1.21 (m, 2H), 0.85 (d, *J* = 6.6 Hz, 6H), 0.78 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.53, 160.84, 160.74, 153.33, 144.03, 142.10, 132.18, 128.47, 128.08, 126.97, 126.14, 125.10, 123.95, 123.07, 122.02, 113.03, 112.89, 70.98, 70.56, 70.23, 70.07, 69.91, 69.69, 69.34, 69.25, 68.65, 68.25, 49.00, 38.35, 38.27, 25.04, 25.00, 22.60, 22.56, 22.43. ESI-MS: 760.5 $(M+Na)^+$.

Tetramer (**10**): A solution of compound **9** (0.82 g, 1.1 mmol) in CH_2Cl_2 /MeOH (1:1, v/v) and Pd/C (10%) was shaken under a hydrogen atmosphere for 2 hours, and then catalyst was filtered. The filtrate was evaporated in vacuum, yielding the corresponding amine **4a**. The coupling reaction of compound **8** and the freshly made amine was performed using similar synthetic procedure of **9.** The crude product was recrystallized in ethyl acetate / hexane to give the 4mer as a white solid (1.23g, 84%).^{1}H NMR (300 MHz, $CDCl_3$) δ 10.26 (s, 1H), 10.23 (s, 1H), 10.00 (s, 1H), 9.12 (d, *J* = 2.9 Hz, 1H), 8.48 (d, *J* = 7.8 Hz, 1H), 8.38 (dd, *J* = 9.0, 2.7 Hz, 1H), 8.36 – 8.25 (m, 3H), 8.12 (d, *J* = 2.7 Hz, 1H), 8.03 (d, *J* = 2.8 Hz, 1H), 7.99 (d, *J* = 2.8 Hz, 1H), 7.48 – 7.19 (m, 5H), 7.09 (d, *J* = 9.2 Hz, 1H), 7.05 – 6.97 (m, 2H), 6.95 (d, *J* = 9.0 Hz, 1H), 5.36 (p, *J* = 6.9 Hz, 1H), 4.52 – 4.44 (m, 2H), 4.42 – 4.32 (m, 4H), 4.31 – 4.22 (m, 2H), 4.15 – 4.06 (m, 2H), 4.06 – 3.97 (m, 4H), 3.94 – 3.76 (m, 8H), 3.61 – 3.28 (m, 18H), 1.89 – 1.24 (m, 15H), 0.96 – 0.73 (m, 24H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.69, 162.60, 162.47, 160.87, 160.75, 153.14, 152.95, 152.84, 144.07, 142.07, 133.03, 132.86, 132.46, 128.46, 128.09, 126.94, 126.15, 125.48, 125.44, 125.01, 123.98, 123.88, 123.01, 122.22, 122.19, 122.01, 113.46, 113.36, 113.01, 112.78, 71.01, 70.87, 70.57, 70.30, 70.23, 70.07, 69.91, 69.75, 69.68, 69.28, 69.14, 68.77, 68.24, 48.96, 38.33, 25.00, 22.60, 22.42. ESI-MS: 1346.9 $(M+Na)^+$;

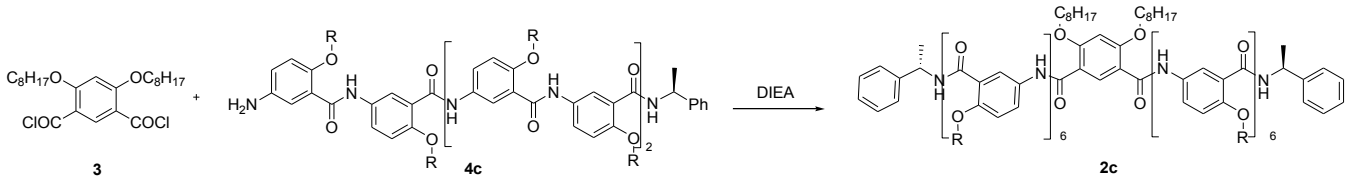
Hexamer (**11**): Prepared analogously as described above for compound **10**. The crude was recrystallized in ethyl acetate / hexane to give the 6mer as a white solid (0.33 g, 72%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.28 (s, 3H), 10.23 (s, 1H), 10.01 (s, 1H), 9.13 (d, *J* = 2.9 Hz, 1H), 8.60 – 8.17 (m, 7H), 8.17 – 7.90 (m, 5H), 7.50 – 7.19 (m, 5H), 7.16 – 6.83 (m, 6H), 5.36 (d, *J* = 7.0 Hz, 1H), 4.60 – 4.44 (m, 2H), 4.44 – 4.30 (m, 6H), 4.30 – 4.18 (m, 2H), 4.15 – 3.96 (m, 8H), 3.92 – 3.77 (m, 12H), 3.62 – 3.22 (m, 30H), 1.75 – 1.23 (m, 23H), 0.94 – 0.71 (m, 36H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.70, 162.65, 162.49, 160.88, 160.75, 153.15, 152.94, 152.80, 144.07, 142.09, 133.13, 133.06, 132.89, 132.47, 128.46, 128.09, 126.94, 126.16, 125.49, 125.03, 124.00, 123.95, 123.03, 122.22, 122.03, 113.38, 113.00, 112.79, 71.02, 70.89, 70.57, 70.32, 70.24, 70.07, 69.91, 69.76, 69.68, 69.33, 69.28, 69.17, 68.78, 68.69, 68.24, 48.95, 38.34, 25.00, 22.60, 22.40. MS(MALDI): $(M+Na)^+$: 1934.3.



3 4a 2a

Compound **2a**: Hydrogenation of **9** based on the similar procedures as described above gives the crude product **4a**, which was used directly for the next step without further purification. Diacid chloride **3** was prepared by adding thionyl chloride into a solution of 4,6-bis(octyloxy)isophthalic acid (220 mg, 0.52 mmol) in dichloromethane. The solvent was removed at reduced pressure after 3 hrs. The residue was dissolved in CH_2ClCH_2Cl (7 mL). The resulting solution was slowly added into a mixture of **2a** (642 mg, 1.04 mmol) and DIEA (141 mg, 1.09 mmol) in CH_2ClCH_2Cl (58 mL). The reaction was kept at room temperature for 1 hour, and then the reaction mixture is heated under reflux for 24 hrs. After removal of the solvent, the residue was purified by silica gel column chromatography using $CHCl_3/CH_3OH$ (60/1, v/v) as the eluant. The product was further recrystallized in ethyl acetate / hexane to give the pure sample as a white solid (497 mg, 53%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.26 (s, 2H), 9.71 (s, 2H), 9.08 (s, 1H), 8.48 (d, *J* = 7.7 Hz, 2H), 8.38 (d, *J* = 8.9 Hz, 2H), 8.31 (d, *J* = 8.9 Hz, 2H), 8.04 – 7.91 (m, 4H), 7.49 – 7.13 (m, 10H), 7.01 (d, *J* = 9.0 Hz, 2H), 6.95 (d, *J* = 9.0 Hz, 2H), 6.46 (s, 1H), 5.37 (p, *J* = 6.9 Hz, 2H), 4.44 – 4.30 (m, 4H), 4.26 (m, 4H), 4.20 (t, *J* = 6.2 Hz, 4H), 4.01 – 3.91 (m, 4H), 3.86 (m, 4H), 3.81 – 3.73 (m, 4H), 3.59 – 3.38 (m, 16H), 3.31 (t, *J* = 6.9 Hz, 4H), 2.07 – 1.84 (m, 4H), 1.76 – 1.16 (m, 38H), 0.91 – 0.86 (m, 10H), 0.85 – 0.76 (m, 20H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.71, 162.57, 162.03, 160.16, 152.89, 152.74, 144.12, 137.31, 132.97, 128.45, 126.92, 126.16, 125.04, 124.97, 123.88, 122.94, 122.15, 122.01, 114.95, 113.64, 112.79, 96.57, 70.83, 70.55, 70.21, 70.06, 69.91, 69.66, 69.30, 69.14, 68.77, 68.22, 48.94, 38.35, 31.78, 29.68, 29.24, 29.08, 26.15, 25.04, 25.00, 22.60, 22.44, 14.11. MS(MALDI): $(M+Na)^+$: 1825.2.

Compound **2b**: The same procedure which was described above for **2a** was followed. A white solid (53 mg, 47%) was collected after recrystallization in ethyl acetate/ hexane. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.31 (s, 2H), 10.28 (s, 2H), 10.25 (s, 2H), 9.74 (s, 2H), 9.14 (s, 1H), 8.52 – 8.26 (m, 10H), 8.04 (s, 4H), 7.97 (s, 4H), 7.49 – 7.20 (m, 10H), 7.11 – 6.89 (m, 8H), 6.52 (s, 1H), 5.63 – 5.08 (m, 2H), 4.46 – 4.32 (m, 12H), 4.25 (m, 8H), 4.08 – 3.94 (m, 14H), 3.92 – 3.70(m, 18H), 3.62 – 3.07 (m, 40H), 2.19 – 1.89 (m, 4H), 1.85 – 1.12 (m, 50H), 1.00 – 0.55 (m, 54H).^{13}C NMR (75 MHz, $CDCl_3$) δ 163.71, 162.68, 162.13, 160.19, 152.94, 152.81, 144.07, 133.17, 132.98, 132.92, 128.46, 126.94, 126.16, 125.55, 125.36, 125.06, 124.01, 123.93, 123.07, 122.21, 122.04, 115.28, 113.76, 113.44, 112.81, 70.89, 70.57, 70.32, 70.24, 70.07, 69.92, 69.76, 69.69, 69.29, 69.20, 68.80, 68.25, 48.95, 38.34, 31.77, 29.69, 29.23, 29.12, 26.18, 25.01, 22.60, 22.40, 14.11. MS(MALDI): $(M+Na)^+$: 2999.0.

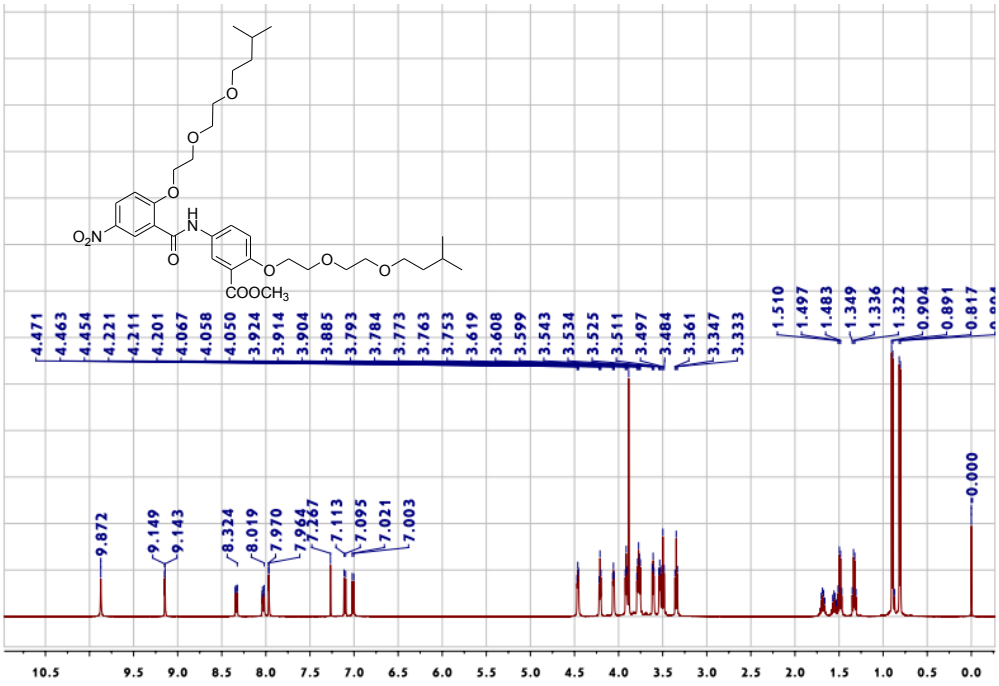


3 4c 2c

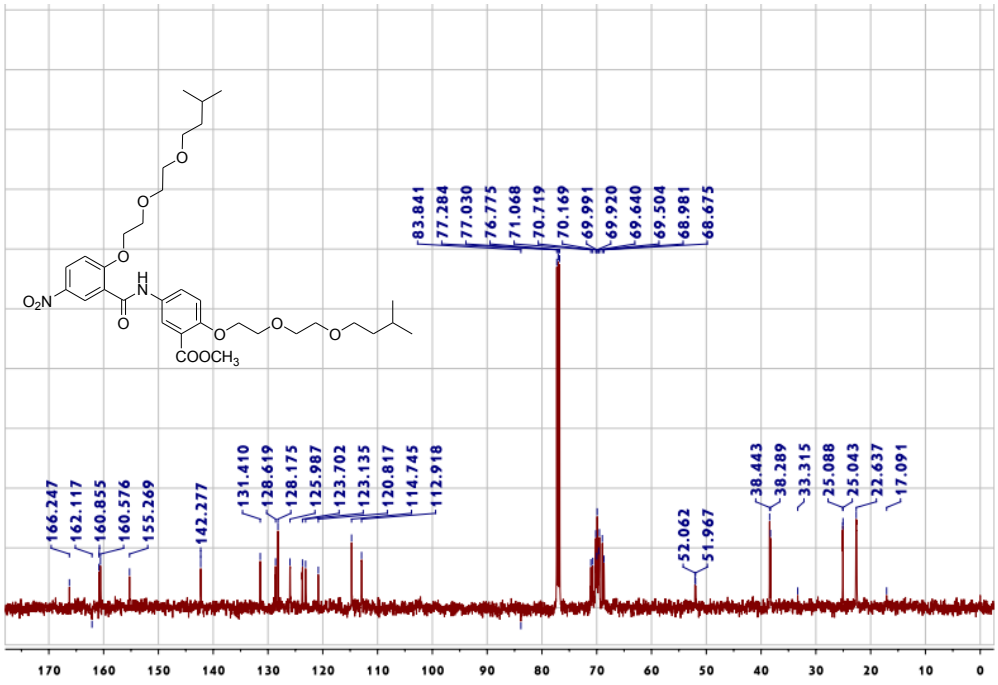
Compound **2c**: The same procedure which was described above for **2a** was followed to provide a white solid (16 mg, 27%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.39 – 10.20 (m, 10H), 9.75 (s, 2H), 9.15 (s, 1H), 8.52 – 8.29 (m, 14H), 8.09 (s, 8H), 8.03 – 7.93 (m, 4H), 7.41 (d, *J* = 7.4 Hz, 4H), 7.34 (t, *J* = 7.6 Hz, 4H), 7.24 (d, *J* = 7.3 Hz, 2H), 7.08 – 6.99 (m, 10H), 6.95 (d, *J* = 9.0 Hz, 2H), 6.53 (s, 1H), 5.35 (dd, *J* = 14.4, 7.2 Hz, 2H), 4.47 – 4.31 (m, 20H), 4.29 – 4.12 (m, 8H), 4.09 – 3.95 (m, 20H), 3.93 – 3.73 (m, 24H), 3.63 – 3.52 (m, 20H), 3.52 – 3.27 (m, 32H), 2.04 (m, 4H), 1.73 – 1.50 (m, 10H), 1.49 – 1.40(m, 10H), 1.40 – 1.12 (m, 42H), 0.90 – 0.77 (m, 78H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.75, 162.75, 162.71, 162.18, 160.23, 152.98, 152.84, 144.08, 133.21, 133.17, 133.00, 132.92, 128.48, 126.99, 126.23, 126.15, 125.60, 125.41, 125.10, 124.08, 124.02, 123.98, 122.26, 122.07, 115.34, 113.47, 112.84, 71.02, 70.94, 70.83, 70.61, 70.45, 70.35, 70.26, 70.18, 70.09, 70.04, 69.95, 69.87, 69.80, 69.72, 69.32, 69.23, 68.84, 68.28, 55.80, 48.95, 38.38, 31.80, 29.71, 29.25, 27.32, 26.21, 25.04, 22.66, 22.61, 22.43, 14.11. MS(MALDI): $(M+Na)^+$: 4171.9.

(1) Wu, X. X.; Liang, G. X.; Ji, G.; Fun, H. K.; He, L.; Gong, B. *Chem. Commun.* **2012**, *48*, 2228.

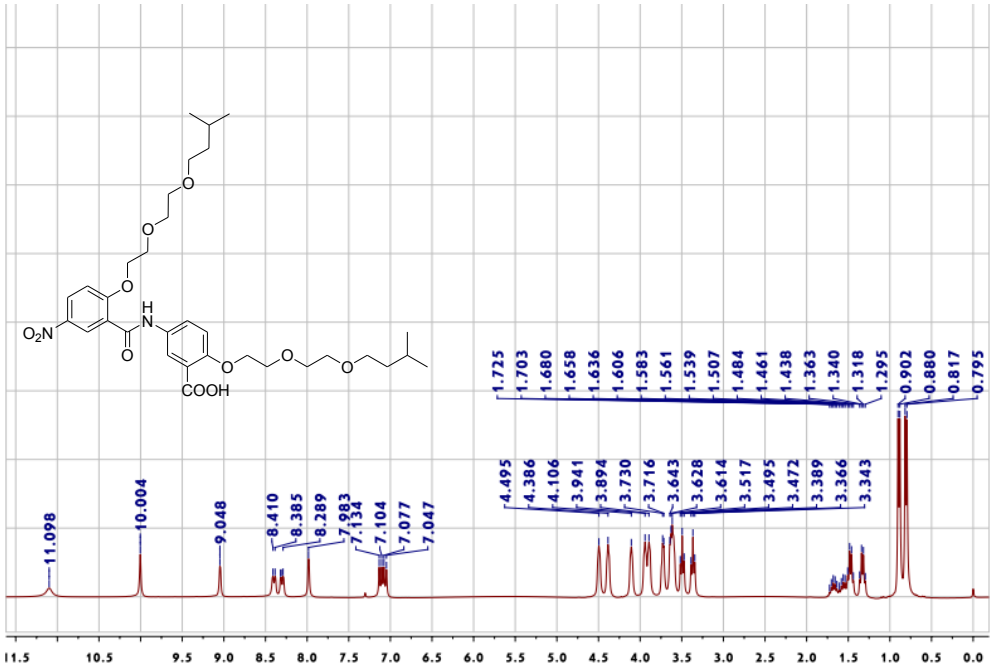
2. NMR and MS Spectra



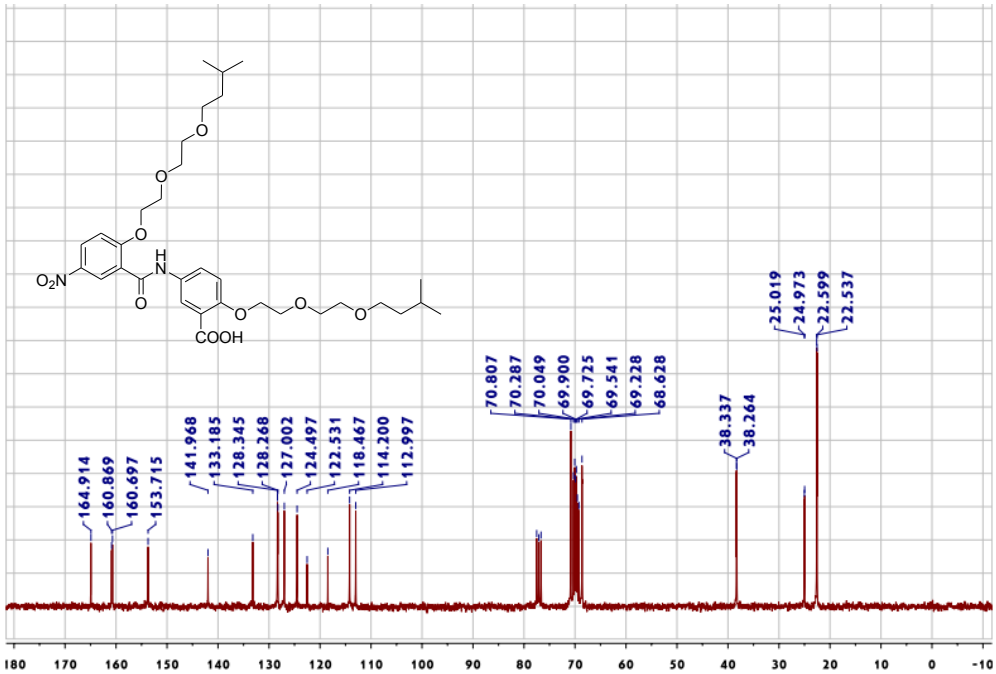
^{1}H NMR spectrum of **7** (11 mM, $CDCl_3$, 298K)



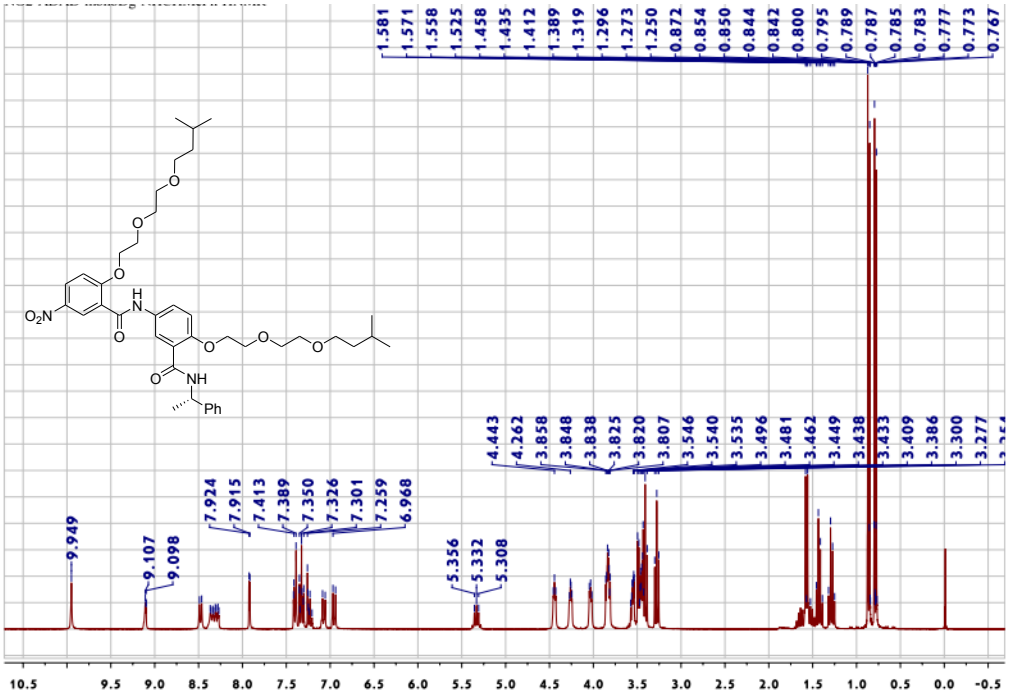
^{13}C NMR spectrum of **7** (11 mM, $CDCl_3$, 298K)



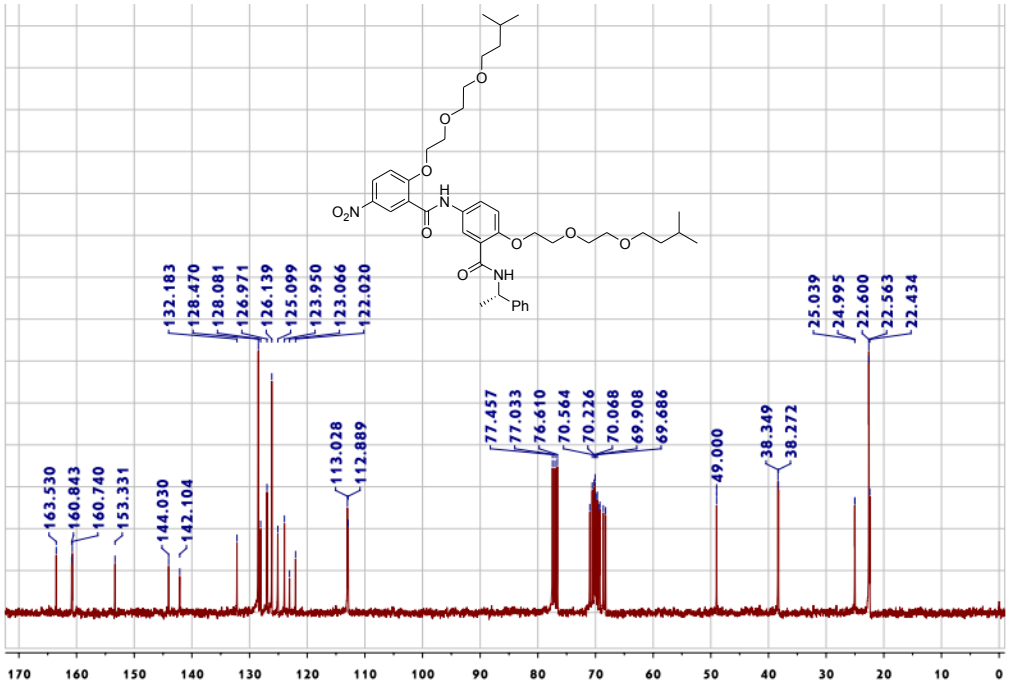
^{1}H NMR spectrum of **8** in $CDCl_3$ at 298K (20 mM, $CDCl_3$, 298K)



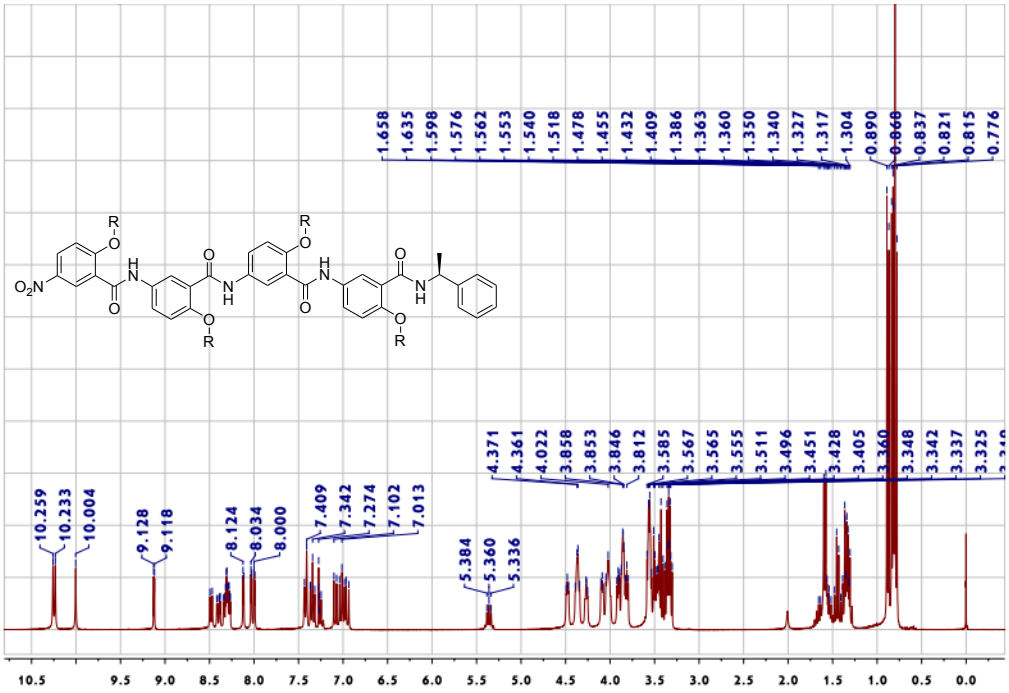
^{13}C NMR spectrum of **8** (20 mM, $CDCl_3$, 298K)



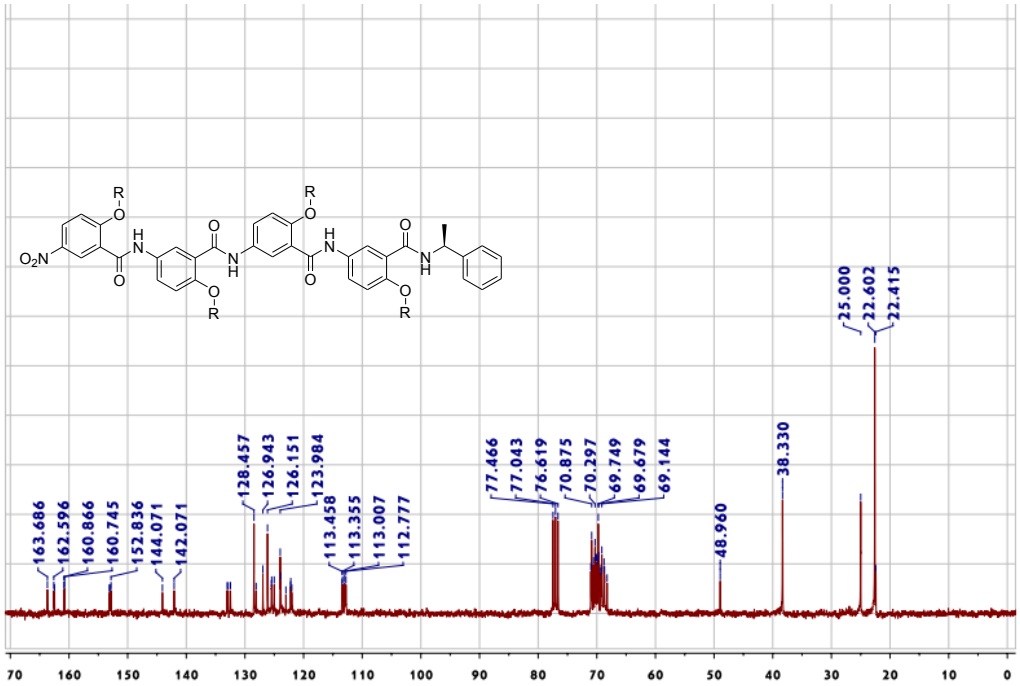
^{1}H NMR spectrum of **9** (12 mM, $CDCl_3$, 298K)



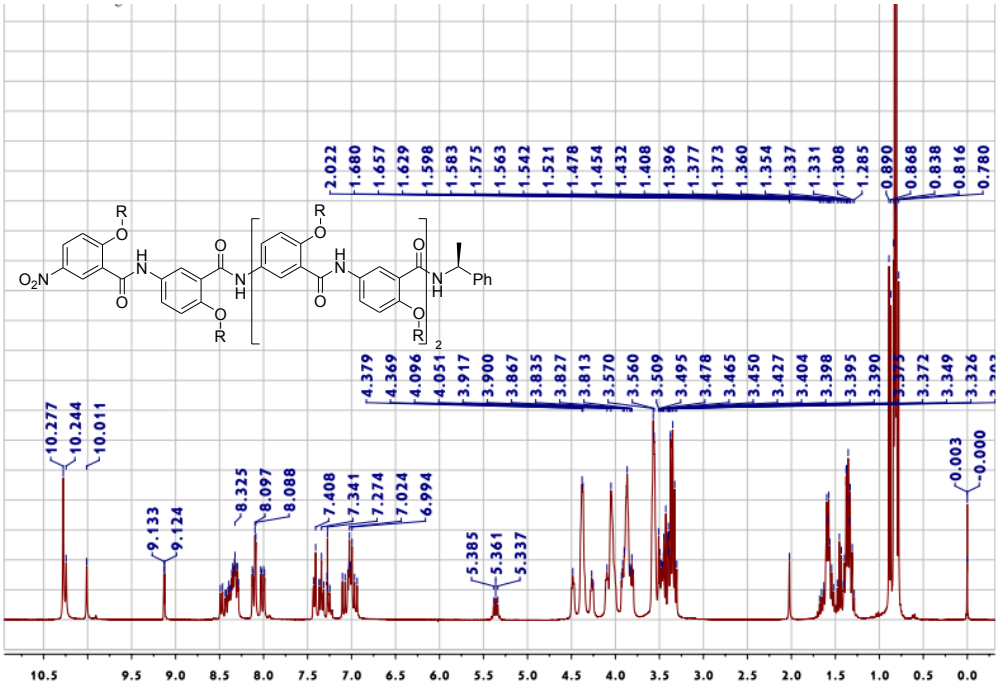
^{13}C NMR spectrum of **9** (12 mM, $CDCl_3$, 298K)



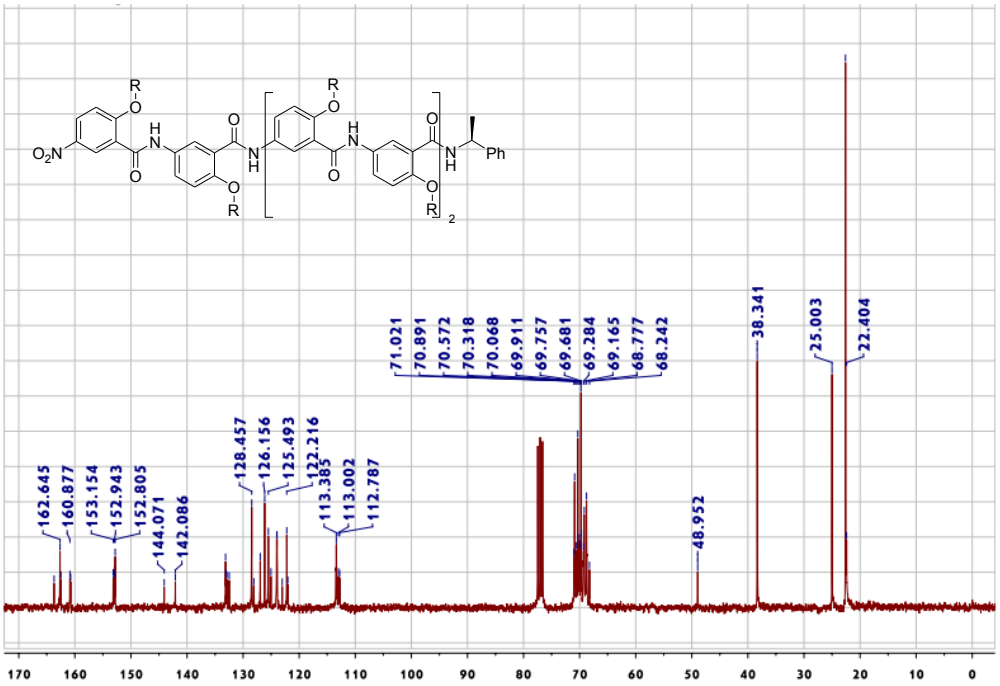
^{1}H NMR spectrum of **10** (10 mM, $CDCl_3$, 298K)



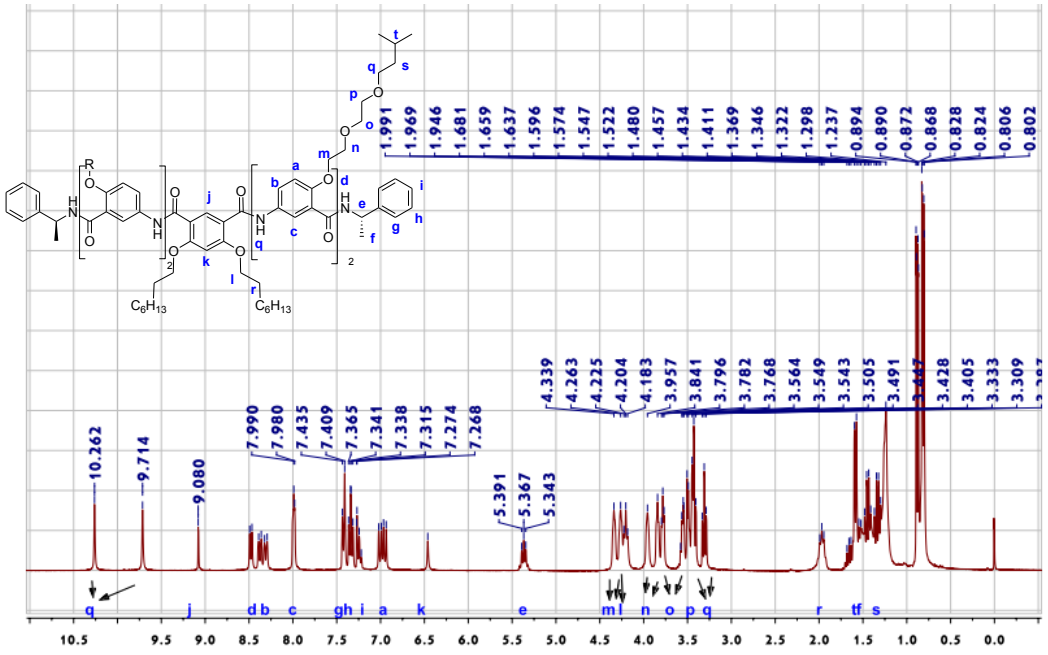
^{13}C NMR spectrum of **10** (10 mM, $CDCl_3$, 298K)



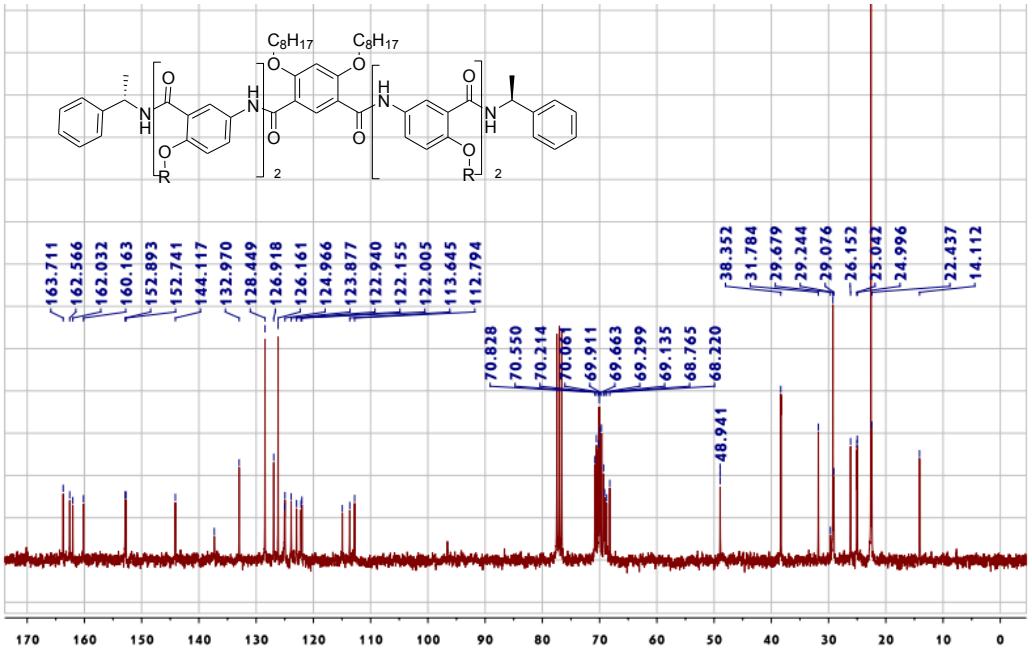
^{1}H NMR spectrum of **11** (10 mM, $CDCl_3$, 298K)



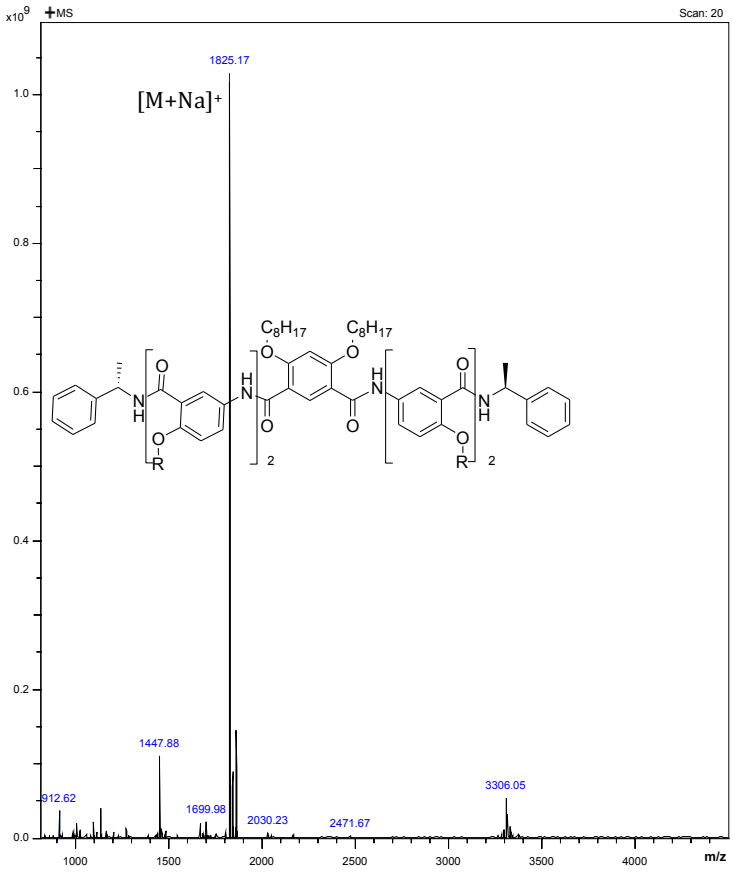
^{13}C NMR spectrum of **11** (10 mM, $CDCl_3$, 298K)



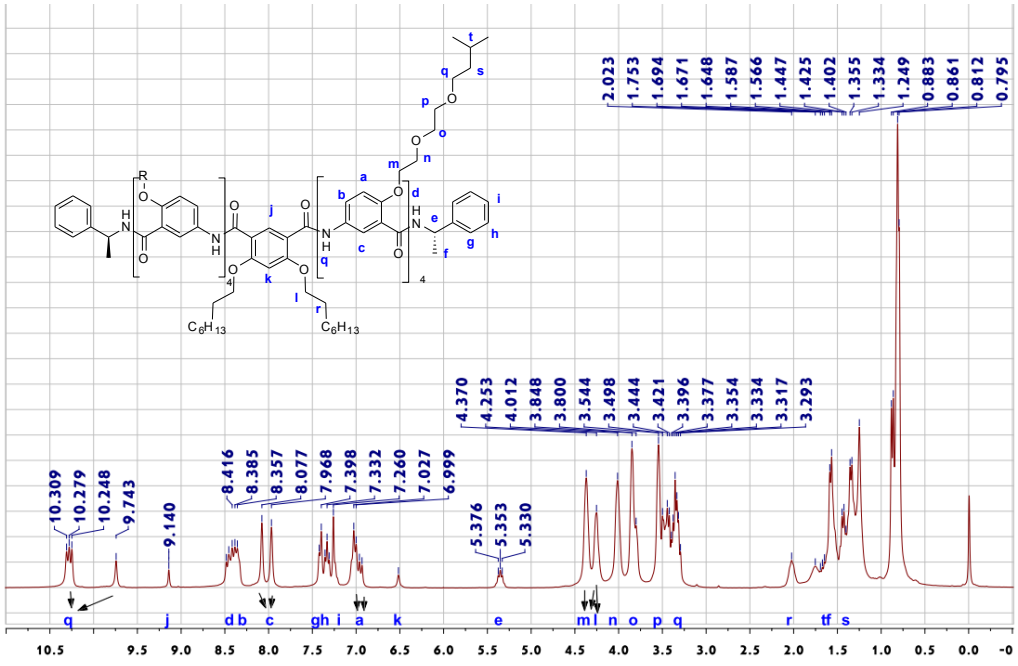
^{1}H NMR spectrum of **2a** (15 mM, $CDCl_3$, 298K)



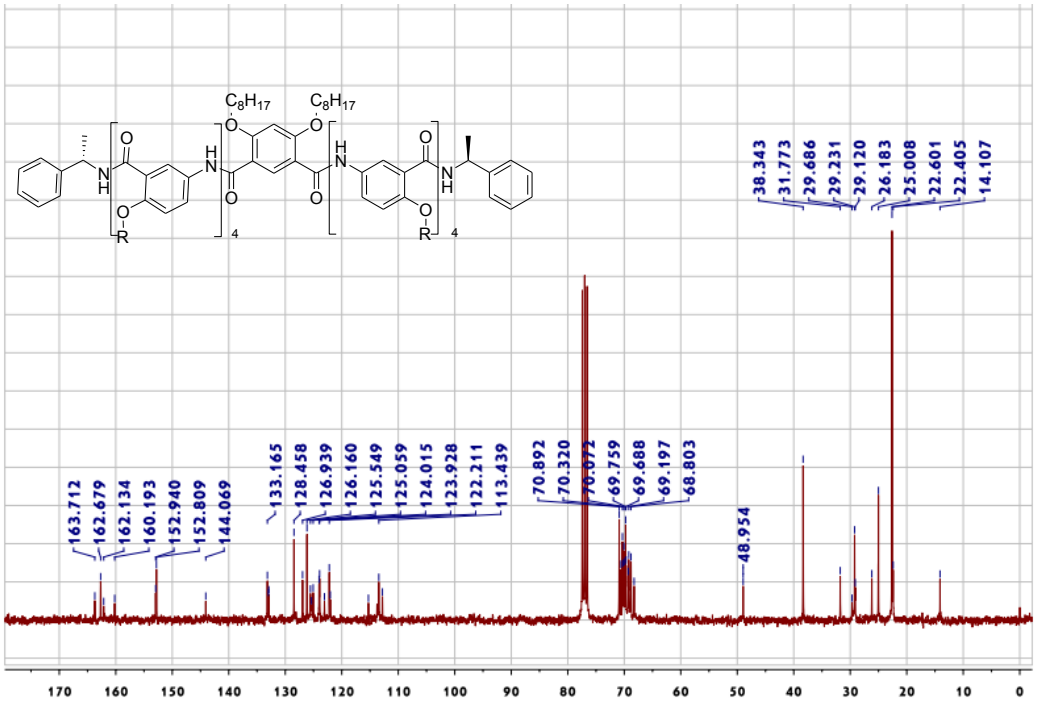
^{13}C NMR spectrum of **2a** (15 mM, $CDCl_3$, 298K)



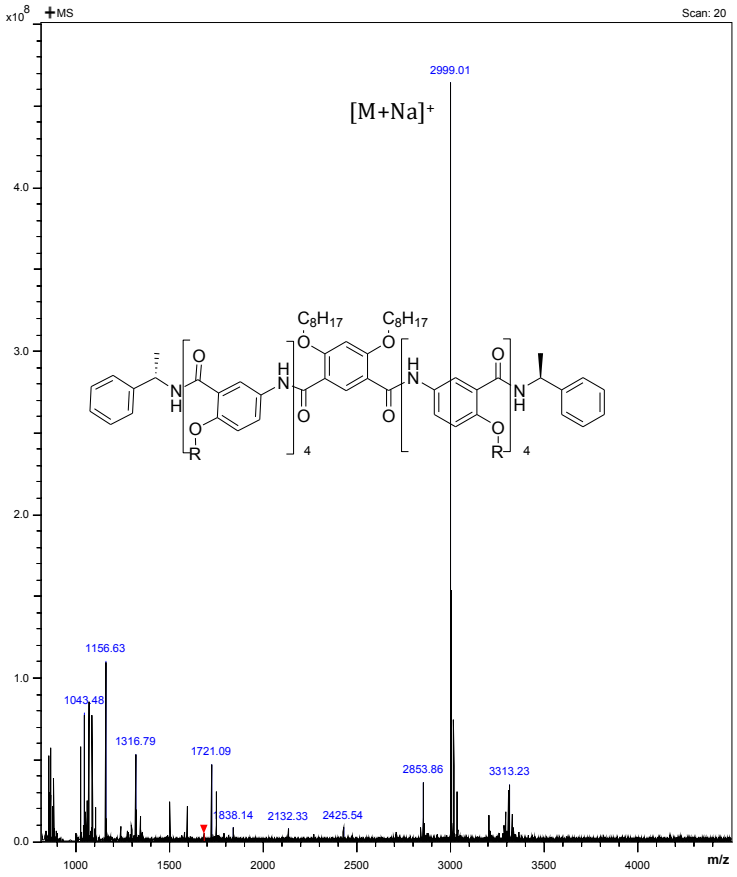
The MALDI spectrum of **2a**



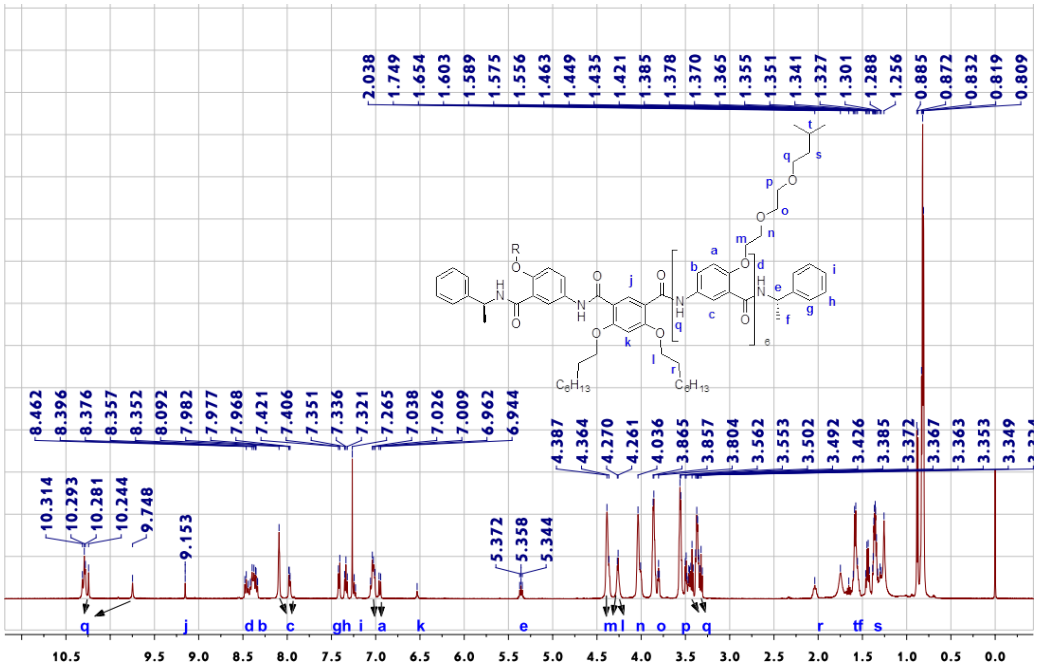
^{1}H NMR spectrum of **2b** (10 mM, $CDCl_3$, 298K)



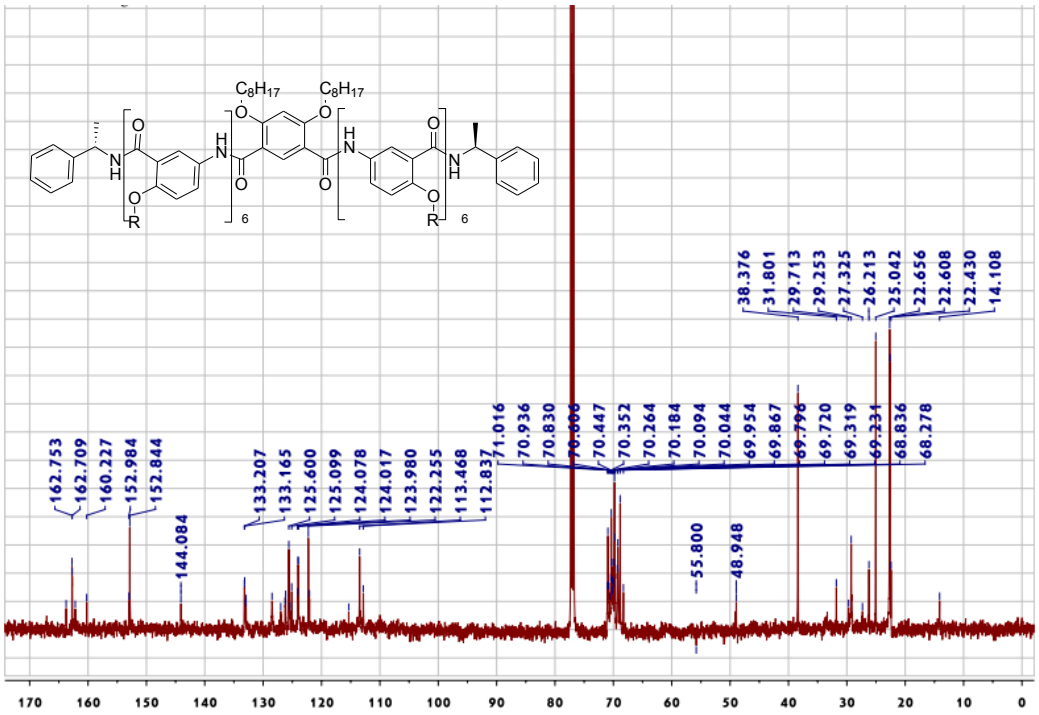
^{13}C NMR spectrum of **2b** (10 mM, $CDCl_3$, 298K)



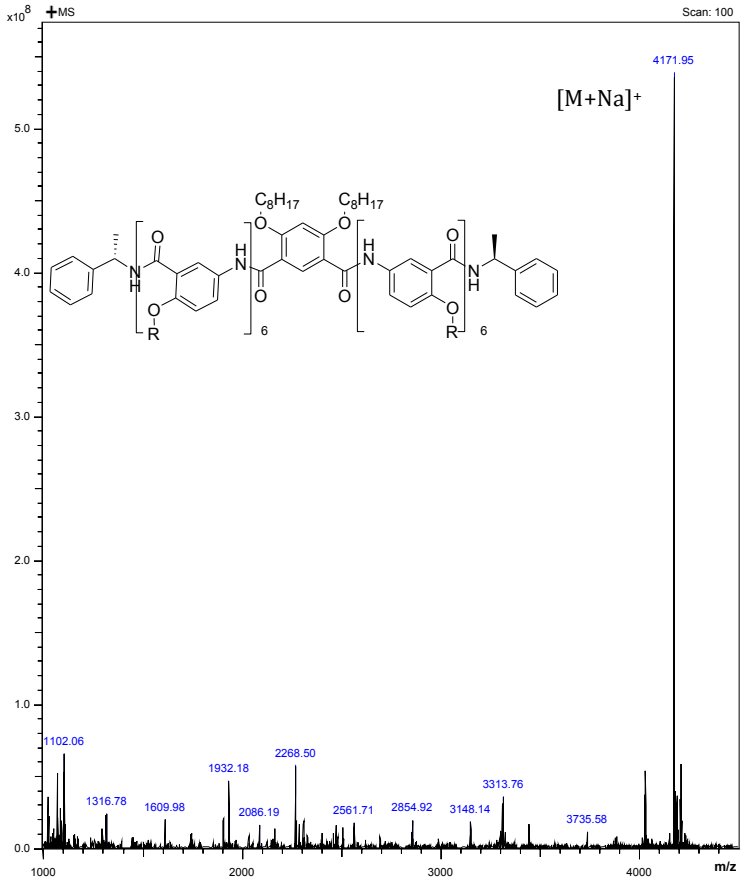
The MALDI spectrum of **2b**



^{1}H NMR spectrum of **2c** (6 mM, $CDCl_3$, 298K)

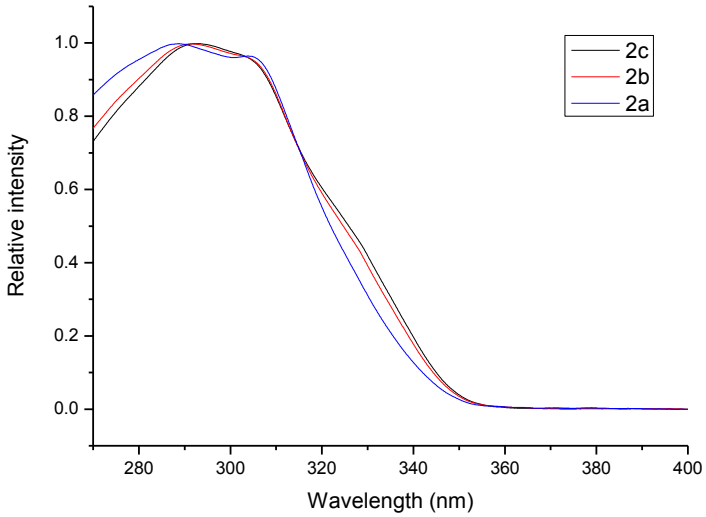


^{13}C NMR spectrum of **2c** (6 mM, $CDCl_3$, 298K)

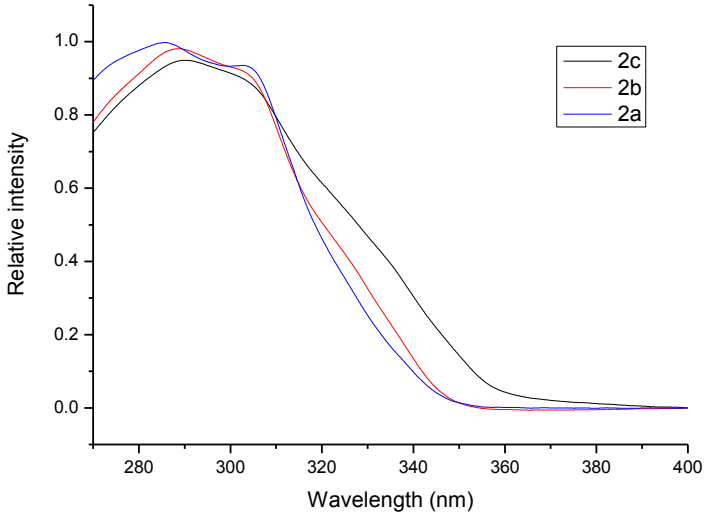


The MALDI spectrum of **2c**

3. UV Spectra of 2a, 2b and 2c



Normalized UV spectra of **2a-c** in chloroform (8 μM). The peak maxima are around 290 nm.



Normalized UV spectra of **2a-c** in ethyl acetate (8 μM). The peak maxima are around 290 nm.

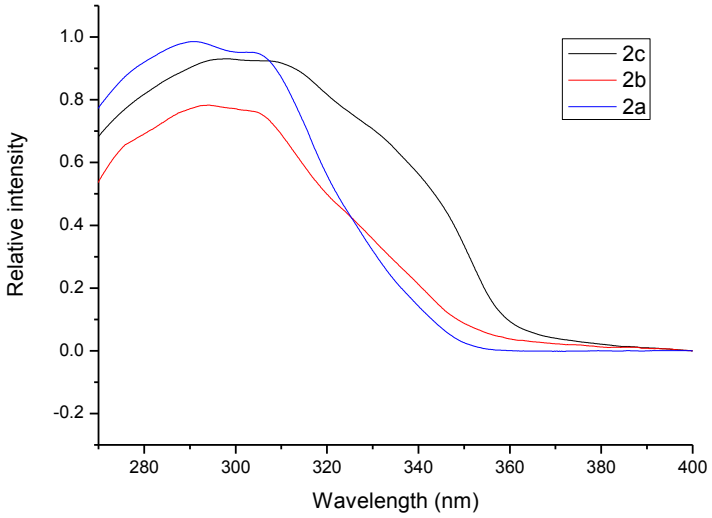
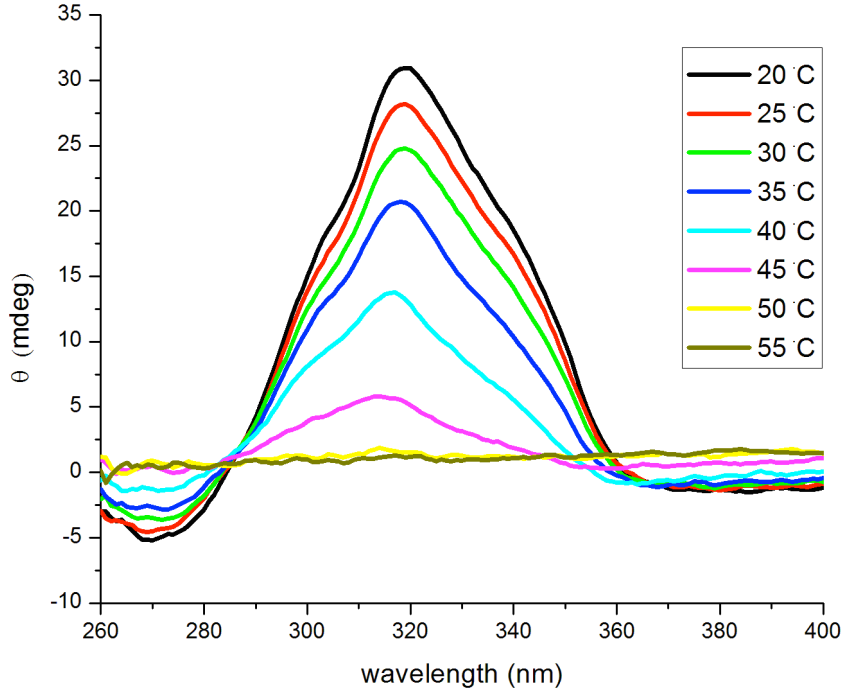
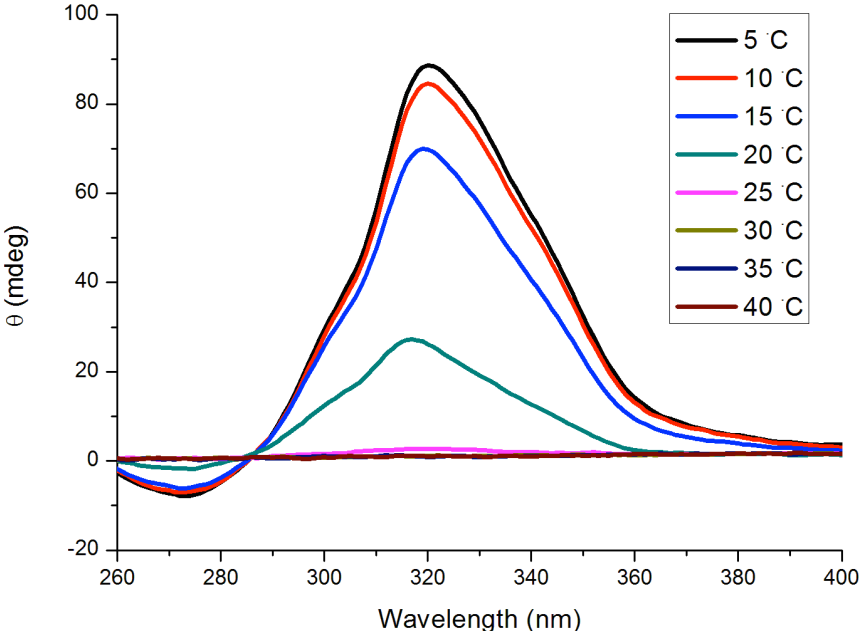


Fig. 3 Normalized UV spectra of **2a-c** in CCl_4 (8 μM). The peak maxima are around 290 nm.

4. Temperature-dependent CD spectra of 2c



CD spectra of **2c** in CCl_4 (1.6 μM) recorded at different temperatures.



CD spectra of **2c** in ethyl acetate (3.2 μM) recorded at different temperatures.