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PAPER

Hydrogen bonded supramolecular polymers in protic solvents: role of multitopicity†

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We describe the synthesis of macromolecular amphiphiles of various molar masses containing well-defined hydrophobic groups incorporating urea moieties. All compounds have the same proportion of associative hydrophobic groups and solubilising POE chains. However, a strong influence of both the number of associative groups per chain and the polydispersity is demonstrated. In water, where the interactions between stickers are strong, the monomer (bearing a single sticker) self-assembles into filaments, but all other compounds with more than one sticker per chain are insoluble. In methanol, where the interactions between stickers are weaker, neither the monomer nor the monodispersed dimer is assembled, whereas polydispersed chains with an average number of 2 or 3 stickers per chain self-assemble into filaments, leading to macroscopic gelation.

Introduction

Hydrogen bonding interactions in aqueous media are often very weak because of the competition from water molecules, but they can still have a decisive effect on self-assemblies when used in combination with other interactions. DNA and RNA duplex formation is a well-known example where the fine control of the assembly derives from the directionality and specificity of base pairing, even though the energetic contribution from hydrogen bonds is much weaker than that from base stacking interactions.[1] The combination of hydrogen bonding and stacking interactions has also been used in synthetic heterocyclic systems to assemble columnar architectures with unprecedented structural control.[2] In the case of amphiphiles with a hydrophobic part made from flexible alkyl chains, the introduction of hydrogen bonds within the hydrophobic domains through urea groups has been shown to dramatically increase the viscosity of aqueous solutions,[3,4] and to enable self-sorting between amphiphiles of distinct structures.[5] The rheological properties of these low molar mass compounds result from the formation of well structured worm-like micelles that become entangled at high enough concentrations (Fig. 1a).

Another popular approach to synthesise viscous solutions or gels consists in decorating water soluble high molar mass polymers with hydrophobic groups.[6] In this case, useful rheological properties are obtained when the hydrophobic groups assemble into spherical micelles creating physical intermolecular cross-links (Fig. 1b).

Our aim is to investigate the properties of systems combining both design elements, *i.e.* macromolecules with hydrophobic groups able to form very long anisotropic hydrophobic domains (Fig. 1c). In this article, we report the synthesis of macromolecular amphiphiles of various molar masses containing well-defined hydrophobic groups that incorporate urea moieties. The water solubility of these polymers is unfortunately not sufficient to test the proposed concept, however a strong effect of the

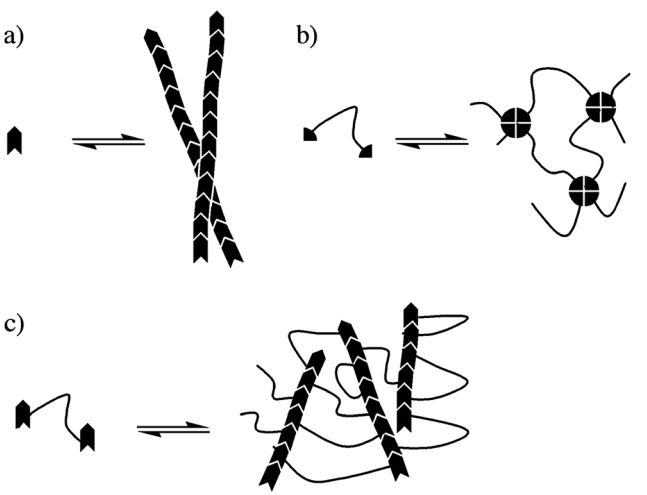

Fig. 1 Schematic assemblies formed by some amphiphiles: low molar mass compounds incorporating hydrogen bonds within a single hydrophobic group (a); polymers bearing multiple hydrophobic groups (b); polymers bearing multiple hydrophobic groups incorporating hydrogen bonds (c).

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multitopicity is revealed in polar organic solvents such as methanol.

Experimental part

Synthesis

11-*tert*-Butoxycarbonylamino-undecanoic acid (1). Adapted from Leigh:[7] to a stirred solution of 11-aminoundecanoic acid (30.4 g, 151 mmol) in a mixture THF–H_2O (400 mL/400 mL) was added NaOH (9.0 g, 225 mmol). After 10 min, di-*tert*-butyl dicarbonate (40.4 g, 185 mmol) was added and the reaction mixture was stirred overnight at room temperature. The solution was reduced in volume and acidified with 1 N HCl which led to a white precipitate. The solution was taken up with CH_2Cl_2 (400 mL) and washed with 1 N HCl (3 × 200 mL). The organic layer was then dried over $MgSO_4$, filtered and the filtrate evaporated to obtain a colorless crystalline solid (**1**, 45.3 g, 99%); m.p.: 69 °C; ^{1}H NMR (200 MHz, $CDCl_3$) 4.53 (br, 1H, N*H*), 3.10 (br, 2H, NH-CH_2), 2.34 (t, J = 7.4 Hz, 2H, CH_2-CO), 1.65–1.24 (m, 25H, C(CH_3)$_3$ and CH_2); ^{13}C NMR (50 MHz, $CDCl_3$) 179.4 (*C*OOH), 156.1 (NH-*C*O-O), 79.1 (*C*(CH$_3$)$_3$), 40.8 (NH-*C*H$_2$), 34.1, 30.1, 29.5, 29.4, 29.3, 29.2, 29.1, 28.6 (C(*C*H$_3$)$_3$), 26.9, 24.8.

11-*tert*-Butoxycarbonylamino-undecanoyl-[poly(ethyleneglycol) 350-monomethylether]-ester (2a). In a 250 mL round-bottom flask, 11-*tert*-butoxycarbonylamino-undecanoic acid (**1**, 18.1 g, 60.0 mmol), *N*,*N*′-dicyclohexylcarbodiimide (DCC) (11.1 g, 53.8 mmol) and dimethylaminopyridine (DMAP) (2.0 g, 16.1 mmol) were stirred in 80 mL of dry dichloromethane under nitrogen. To the solution was added 18.5 g (52.8 mmol) of poly(ethylene glycol)-monomethyl ether (M_n *ca.* 350) and the reaction mixture was stirred overnight. After filtration to remove the dicyclohexylurea, the filtrate was concentrated and purified by column chromatography (silica gel, gradient from CH_2Cl_2 to CH_2Cl_2–ethanol 9 : 1 v/v) to obtain a transparent oil (**2**, 31.16 g, 93%); ^{1}H NMR (200 MHz, $CDCl_3$) 4.52 (br, 1H, N*H*), 4.21 (br, 2H, CH_2O-CO), 3.8–3.5 (br, 30H, OCH_2), 3.37 (s, 3H, OCH_3), 3.08 (q, J = 6.5 Hz, 2H, NH-CH_2), 2.31 (t, J = 7.5 Hz, 2H, CH_2-CO), 1.65–1.23 (m, 25H, C(CH_3)$_3$ and CH_2); ^{13}C NMR (50 MHz, $CDCl_3$) 174.0 (*C*OOH), 72.0–63.5 (O*C*H$_2$), 59.2 (O*C*H$_3$), 40.7 (NH-*C*H$_2$), 34.3, 30.2, 29.6, 29.5, 29.4, 29.3, 29.2, 28.6 (C(*C*H$_3$)$_3$), 26.9, 25.0; MALDI-TOF [M + Na$^+$] = 689.93 ± n × 44 (calcd: 690.5 ± n × 44).

11-Aminoundecanoyl-[poly(ethyleneglycol)350-monomethyl-ether]-ester (2b). To 30.9 g of product **2** placed under nitrogen and cooled to 0 °C was added 40 mL of a 4 M HCl solution in dioxane. The solution was stirred at 0 °C for 1 h and then at room temperature for 2 h. The solvent was evaporated (NaOH trap) to yield 27.9 g (100%) of the product as its hydrochloric salt, which was used without further purification; ^{1}H NMR (200 MHz, $CDCl_3$) 7.96 (br, 3H, NH_3^+), 4.11 (br, 2H, CH_2O-CO), 3.7–3.3 (br, 34H, OCH_2), 3.23 (s, 3H, OCH_3), 2.73 (q, J = 6.9 Hz, 2H, CH_2N), 2.29 (t, J = 7.3 Hz, 2H, CH_2-CO), 1.52 (m, 4H, CH_2CH$_2$CO and CH_2CH$_2$N), 1.24 (br, 12H, CH_2); ^{13}C NMR (50 MHz, $CDCl_3$) 174.0 (*C*OOH), 72.0–63.5 (O*C*H$_2$), 59.2 (O*C*H$_3$), 40.2 (NH-*C*H$_2$), 34.4, 30.2, 29.4, 29.3, 29.2, 29.1, 27.7, 26.7, 25.1; MALDI-TOF [M + Na$^+$] = 546.23 ± n × 44 (NH_2 form, calcd: 546.4 ± n × 44).

Di-(11-*tert*-butoxycarbonylaminoundecanoyl-ester)[poly(ethyleneglycol)600] (3a). Same procedure as **2a**: product **1** (20.9 g, 69.5 mmol), DCC (13.8 g, 66.7 mmol) and DMAP (1.9 g, 15.4 mmol) in 100 mL of dry CH_2Cl_2, and poly(ethylene glycol) (M_n *ca.* 600) were added to 20 mL of dry CH_2Cl_2. Purification of the product by column chromatography (silica gel, gradient from CH_2Cl_2 to CH_2Cl_2–ethanol 9 : 1 v/v) yielded 22.9 g (65%) of a white wax; ^{1}H NMR (250 MHz, $CDCl_3$) 4.52 (br, 2H, N*H*), 4.21 (br, 4H, CH_2O-CO), 3.8–3.5 (br, 57H, OCH_2), 3.08 (q, J = 6.6 Hz, 4H, NH-CH_2), 2.31 (t, J = 7.5 Hz, 4H, CH_2-CO), 1.7–1.2 (m, 50H, C(CH_3)$_3$ and CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$) 174.0 (*C*OOH), 70.7, 69.3, 63.5 (O*C*H$_2$), 40.7 (NH-*C*H$_2$), 34.3, 30.2, 29.6, 29.5, 29.4, 29.3, 29.2, 28.6 (C(*C*H$_3$)$_3$), 26.9, 25.0; MALDI-TOF [M + Na$^+$] = 1223.91 ± n × 44 (calcd: 1223.8 ± n × 44).

Di-(11-aminoundecanoyl-ester)[poly(ethyleneglycol)600] (3b). Same procedure as **2b**: **3a** (22.9 g, 19.6 mmol) in 30 mL of a 4 M HCl solution in dioxane yielded 20.3 g of a yellowish wax; ^{1}H NMR (250 MHz, $CDCl_3$) 8.13 (br, 6H, NH_3^+), 4.21 (br, 4H, CH_2O-CO), 3.8–3.5 (br, 57H, OCH_2), 2.96 (br, 4H, NH-CH_2), 2.32 (t, J = 7.4 Hz, 4H, CH_2-CO), 1.75–1.61 (m, 8H, CH_2CH$_2$CO and CH_2CH$_2$N), 1.26 (br, 24H, CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$) 174.0 (*C*OOH), 70.6, 69.3, 63.5 (O*C*H$_2$), 40.1 (NH-*C*H$_2$), 34.3, 29.3, 29.2, 29.1, 27.7, 26.7, 25.0; MALDI-TOF [M + Na$^+$] = 1023.79 ± n × 44 (NH_2 form, calcd: 1023.8 ± n × 44).

Oligomers B1*, B2, B3, B5 and B9. In a round-bottom flask, products **2b** and **3b** were weighed in adequate proportions (see Table S1†) and dissolved in dry dichloromethane under nitrogen. To these solutions, triethylamine (TEA) and toluene-2,4-diisocyanate (TDI) were added and stirred overnight. FT-IR measurements confirmed the absence of isocyanate functions. Solutions were washed with 20 mL of water (with a few drops of ethanol to break the emulsion if necessary) to remove triethylamine salts. The organic layer was evaporated and dried under vacuum to obtain products as yellowish waxes or solids. Oligomers **B2**, **B3**, **B5** and **B9** were characterized by NMR†, SEC (Fig. 2) and MALDI-TOF (Fig. 3).

The monomer **B1*** was further purified using column chromatography (silica gel, gradient eluent from CH_2Cl_2 to CH_2Cl_2–ethanol 9 : 1 v/v) to give a white wax (1.04 g, 45%); ^{1}H NMR (200 MHz, d_6-DMSO) 8.27 and 7.47 (s, 2H, Ar-N*H*), 7.70 (d, J = 2.1 Hz, 1H, Ar-*H*), 7.11 (dd, J = 8.2 and 2.1 Hz, 1H, Ar-*H*), 6.90 (d, J = 8.4 Hz, 1H, Ar-*H*), 6.50 and 5.94 (br, 2H, CH$_2$-N*H*), 4.11 (br, 4H, CH_2O-CO), 3.6–3.3 (br, 52H, OCH_2), 3.23 (s, 6H, OCH_3), 3.04 (br, 4H, CH_2-NH), 2.28 (t, J = 7.2 Hz, 4H, CH_2-CO), 2.07 (s, 3H, Ar-CH_3), 1.6–1.2 (br, 32H, CH_2); ^{13}C NMR (50 MHz, d_6-DMSO) 172.9 (O*C*=O), 155.2 (NH*C*ONH), 138.6, 138.2, 127.6, 118.8, 109.7 (Ar), 71.3, 69.8, 68.3, 63.1 (O*C*H$_2$), 58.1 (O*C*H$_3$), 33.4, 29.8, 29.0, 28.9, 28.8, 28.7, 28.5, 26.5, 24.5 (*C*H$_2$), 17.2 (Ar-*C*H$_3$); MALDI-TOF [M + Na$^+$] = 1199.83 ± n × 44 (calcd: 1199.81 ± n × 44); Anal. calcd for $C_{59.2}H_{108.4}N_4O_{19.1}$: C, 60.2; H, 9.2; N, 4.7%, found: C, 59.6; H, 9.3; N, 4.6%.

2-{11-[Poly(ethyleneglycol)350-monomethylether-amido-undecanoyl]-ureido},4-nitro-toluene (4). To a solution of triphosgene (0.253 g, 0.85 mmol) in dry dichloromethane (20 mL) placed under nitrogen and room temperature was added, using a syringe

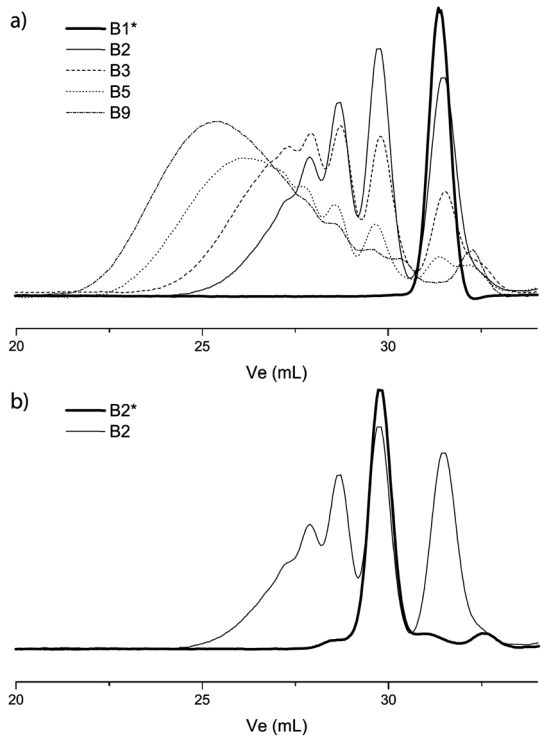


Fig. 2 SEC traces for oligomers (a) and dimer **B2*** (b).

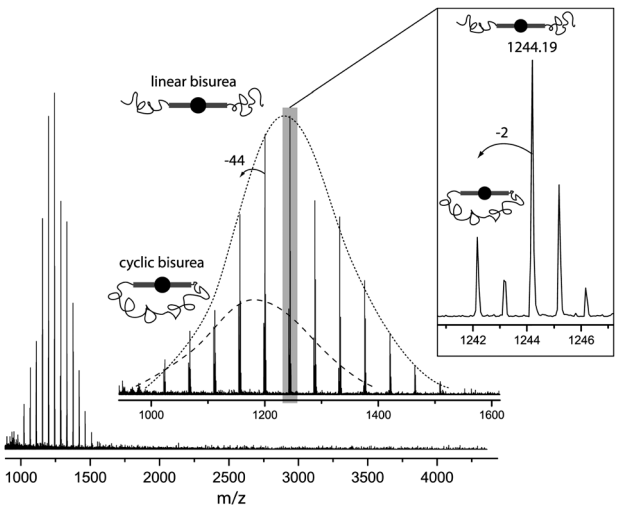


Fig. 3 MALDI-TOF spectrum for oligomer **B3**.

pump (5 mL h^{-1}), a solution of 2-methyl-5-nitroaniline (0.391 g, 2.57 mmol) and diisopropylethylamine (DIEA) (0.47 mL, 2.72 mmol) in 20 mL dry CH_2Cl_2. 90 min after the addition, a solution of **2b** (1.71 g, 2.9 mmol) and TEA (0.79 mL, 5.65 mmol) in dry CH_2Cl_2 (20 mL) was rapidly added to the flask and stirred overnight. FT-IR measurements confirmed the absence of isocyanate functions (~2265 cm^{-1}). The solution was washed with water and a few drops of ethanol (to break the emulsion). The organic layer was evaporated and purified by flash chromatography (Reveleris Flash System (Grace), silica 40 μm, column 40 g, flow 25–30 mL min^{-1}) using a gradient eluent from CH_2Cl_2 to CH_2Cl_2–ethanol 9 : 1 v/v (Rf ~ 0.6 at CH_2Cl_2–ethanol 5 : 1 v/v) to obtain an oil (1.79 g, 95%); ^{1}H NMR (200 MHz, d_6-DMSO) 8.96 (d, $J = 2.4$ Hz, 1H, Ar-*H*), 7.96 (s, 1H, Ar-N*H*), 7.70 (dd, $J = 8.3$ Hz and 2.4 Hz, 1H, Ar-*H*), 7.38 (d, $J = 8.3$ Hz, 1H, Ar-*H*), 6.83 (t, $J = 5.4$ Hz, 1H, CH_2-N*H*), 4.11 (br, 2H, CH_2-OCO), 3.3–3.6 (br, 35H, CH_2-O), 3.23 (s, 3H, CH_3-O), 3.11 (q, $J = 6.0$ Hz, 2H, CH_2-NH), 2.29 (s and t, 5H, Ar-CH_3 and CH_2-CO), 1.2–1.6 (br, 16H, CH_2); ^{13}C NMR (50 MHz, d_6-DMSO) 172.9 (O*C*=O), 154.9 (NH*C*ONH), 146.1, 139.5, 133.3, 130.9, 115.6, 112.7 (Ar), 71.3, 69.8, 68.3, 63.1 (O*C*H_2), 58.1 (O*C*H_3), 39.0 (*C*H_2-NH), 33.4, 29.6, 29.0, 28.9, 28.8, 28.7, 28.5, 26.5, 24.5 (*C*H_2), 18.2 (Ar-*C*H_3); MALDI-TOF [M + Na^+] = 768.39 ± n × 44 (calcd: 768.6 ± n × 44).

2-{11-[Poly(ethyleneglycol)350-monomethylether-amido-undecanoyl]-ureido},4-amino-toluene (5). A solution of **4** (1.71 g, 2.34 mmol), cyclohexene (2 mL, 19.7 mmol) and palladium (10% on carbon) (0.08 g, 2.28 mmol) in isopropanol (10 mL) was stirred under reflux for 5 days, filtered on Celite and evaporated before flash chromatography (Reveleris Flash System (Grace), silica 40 μm, column 40 g, flow 30 mL min^{-1}) with a gradient eluent from CH_2Cl_2 to CH_2Cl_2–ethanol 8 : 2 v/v (Rf ~ 0.45 at CH_2Cl_2–ethanol 8 : 2 v/v) to produce a yellowish wax (0.532 g, 32%); ^{1}H NMR (200 MHz, d_6-DMSO) 7.28 (s, 1H, Ar-N*H*), 7.12 (d, $J = 2.3$ Hz, 1H, Ar-*H*), 6.72 (d, $J = 8.2$ Hz, 1H, Ar-*H*), 6.41 (t, $J = 5.6$ Hz, 1H, CH_2-N*H*), 6.10 (dd, $J = 7.9$ Hz and 2.3 Hz, 1H, Ar-*H*), 4.71 (s, 2H, NH_2), 4.11 (br, 2H, CH_2-OCO), 3.3–3.6 (br, 34H, CH_2-O), 3.23 (s, 3H, CH_3-O), 3.04 (q, $J = 6.0$ Hz, 2H, CH_2-NH), 2.29 (t, $J = 7.3$ Hz, 2H, CH_2-CO), 1.99 (s, 3H, Ar-CH_3), 1.2–1.6 (br, 16H, CH_2); ^{13}C NMR (50 MHz, d_6-DMSO) 172.9 (O*C*=O), 155.3 (NH*C*ONH), 146.8, 138.5, 130.1, 113.6, 108.1, 106.7 (Ar), 71.3, 69.8, 68.3, 63.1 (O*C*H_2), 58.1 (O*C*H_3), 39.0 (*C*H_2-NH), 33.4, 29.8, 29.0, 28.9, 28.8, 28.7, 28.5, 26.5, 24.5 (*C*H_2), 17.1 (Ar-*C*H_3); MALDI-TOF [M + Na^+] = 694.36 ± n × 44 (calcd: 694.4 ± n × 44).

Dimer **B2***. To a solution of triphosgene (73 mg, 0.24 mmol) in dry dichloromethane (~10 mL) placed under nitrogen and room temperature was added, using a syringe pump (5 mL h^{-1}), a solution of **5** (0.516 g, 0.74 mmol) and DIEA (130 μL, 0.76 mmol) in 20 mL dry CH_2Cl_2. 2 h after the addition, a solution of **3b** (0.335 g, 0.32 mmol) and TEA (205 μL, 1.47 mmol) in dry CH_2Cl_2 (20 mL) was rapidly added into the flask. After 3 h, FT-IR measurements confirmed the absence of isocyanate functions (~2265 cm^{-1}). The solution was washed with water (no $MgSO_4$ drying), reduced in volume, and then purified by flash chromatography (Reveleris Flash System (Grace), silica 40 μm, column 12 g, flow 25–30 mL min^{-1}) using a gradient eluent from CH_2Cl_2 to CH_2Cl_2–ethanol 8 : 2 v/v (Rf ~ 0.3 at CH_2Cl_2–ethanol 5 : 1 v/v) to give a brown wax (0.697 g, 80%); ^{1}H NMR (250 MHz, d_6-DMSO) 8.25 (s, 2H, Ar-N*H*), 7.70 (d, $J = 2.1$ Hz, 2H, Ar-*H*), 7.46 (s, 2H, Ar-N*H*), 7.12 (dd, $J = 8.2$ Hz and 2.1 Hz, 1H, Ar-*H*), 6.90 (d, $J = 8.4$ Hz, 2H, Ar-*H*), 6.49 (t, $J = 5.6$ Hz, 2H, CH_2-N*H*), 5.95 (t, $J = 5.7$ Hz, 2H, CH_2-N*H*), 4.11 (br, 8H, CH_2-OCO), 3.3–3.6 (br, 130H, CH_2-O), 3.23 (s, 6H, CH_3-O), 3.04 (br, 8H, CH_2-NH), 2.28 (t, $J = 7.3$ Hz, 8H, CH_2-CO), 2.07 (s, 6H, Ar-CH_3), 1.2–1.6 (br, 64H, CH_2); ^{13}C NMR (62.5 MHz, d_6-DMSO) 172.9 (O*C*=O), 155.2 and 155.3 (NH*C*ONH), 138.7, 138.3, 129.9, 118.8, 111.5, 109.8 (Ar), 71.3, 69.8, 68.3, 63.0 (O*C*H_2), 58.1 (O*C*H_3), 39.0 (*C*H_2-NH), 33.4, 29.8, 29.0, 28.9, 28.8, 28.7, 28.5, 26.4, 24.5 (*C*H_2), 17.2 (Ar-*C*H_3); MALDI-TOF [M + Na^+] = 2418.61 ± n × 44 (calcd: 2418.4 ± n × 44).

Analyses

Size exclusion chromatography (SEC). Measurements were performed in a 1 g L^{-1} LiBr solution in dimethylformamide (DMF) at a flow rate of 0.8 mL min^{-1} using a Waters HPLC 515 pump, a Viscotek VE 5200 automatic injector and two columns thermostatted at 60 °C (PSS GRAM, 1000 Å, 10 μm, 8 mm × 300 mm and PSS GRAM, 30 Å, 10 μm, 8 mm × 300 mm). Polymers were detected by refractive index, viscosimetry (Viscotek Dual Model 250) and light scattering (Wyatt Technology MiniDAWN). Molar masses were computed with Omnisec v4.1 software, based on a polyethylene oxide (Polymer Laboratories) calibration curve.

NMR analysis. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 200 or ARX 250 spectrometer operating at proton frequencies of 200 MHz and 250 MHz respectively. $CDCl_3$ was suitable for most compounds except for final products, which required the use of d_6-DMSO to avoid aggregation of bis-urea moieties.

MALDI TOF spectrometry. 10 μL of the polymer solution (5 g L^{-1} in THF) was mixed with 20 μL of the matrix solution (1,8-dihydroxy-9[10*H*]-anthracenone (dithranol), 25 g L^{-1} in THF), and 10 μL of sodium iodide solution (20 g L^{-1} in THF). A 1 μL portion of the final solution was deposited onto the sample target. The MALDI mass spectra represent averages over 256 consecutive laser shots. Standards (polystyrenes of known structure, $M_n = 1500$ and 3280 g mol^{-1} purchased from Polymer Standards Service) were used to calibrate the mass scale. Samples were analysed with an Autoflex III Smartbeam (Bruker) using the flexControl V3 software. The data were treated with the flexAnalysis V3 software.

Solubility tests. Samples were prepared by weighing the product and solvent directly into vials, which were gently warmed for 2–5 min with a hair-dryer and shaken on an oscillating table for at least 24 h at room temperature.

Viscosimetry. Solutions were filtered on PTFE membranes (0.45 μm porosity). Measurements were performed with an automatic Anton-Paar AMVn viscometer (capillary internal diameter 1.8 mm; ball diameter 1.5 mm), tilted at an angle of 50°, and repeated 6 times.

Small angle neutron scattering (SANS). Measurements were made at the LLB (Saclay, France) on the Pace instrument, at several distance–wavelength combinations to cover at least the 2.4×10^{-3} to 0.37 $Å^{-1}$ q-range, where the scattering vector q is defined as usual, assuming elastic scattering, as $q = (4\pi/\lambda)\sin(\theta/2)$, where θ is the angle between incident and scattered beam. Data were corrected for the empty cell signal and the solute and solvent incoherent background. A light water standard was used to normalize the scattered intensities to cm^{-1} units.

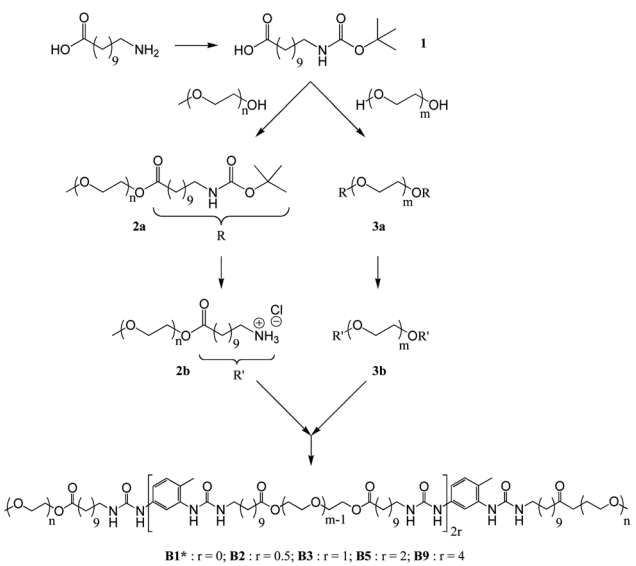
Cryogenic transmission electron microscopy (cryoTEM). Samples were fast frozen in liquid ethane. The cryoTEM images were recorded using a JEOL JEM2100F equipped with a GATAN Ultrascan 4000 camera. The image acquisition was performed with a low electron beam intensity (10 electron $Å^{-2}$ s^{-1}).

Results and discussion

Synthesis

In a first step, polyethylene glycol connected to one or two amino groups through a hydrophobic spacer was prepared by esterification of a boc-protected amino acid (Scheme 1). In a second step, both amines were reacted together with toluene diisocyanate to afford bis-urea oligomers, the molar mass of which was varied by changing the ratio of monoamine **2b** to diamine **3b** (r = [**2b**]/[**3b**]), while maintaining the stoichiometry between amine and isocyanate functions ([NH_2]/[NCO] = 1). The resulting oligomers were characterized by NMR, SEC and MALDI-TOF mass spectrometry. ^{1}H and ^{13}C NMR spectra are in agreement with the expected structures† and the integration of the aromatic protons relative to the POE methyl protons affords the average number of bis-urea moieties per chain (Table 1). SEC confirms the expected increase in molar mass when the monoamine to diamine ratio r is reduced (Fig. 2a). In addition, a peak at an elution volume larger than for bisurea **B1*** is detected. The absence of unreacted amine and the MALDI-TOF results (see below) indicate that this peak is due to the presence of a low amount of cyclic species.[8] A typical MALDI-TOF spectrum obtained for oligomer **B3** is shown in Fig. 3. Although only the low molar mass fraction of the sample is detected, the agreement between calculated and measured masses allows confirmation of the structure of the linear monomer bearing one hydrophobic bisurea group and two methoxy-terminated POE groups and of the cyclic monomer bearing one hydrophobic bisurea group and one POE group.

In order to evaluate the influence of polydispersity, a dimer was also prepared, starting from 2-amino-4-nitrotoluene (Scheme 2), following a strategy previously established for non-symmetrical bis-ureas.[9] NMR and MALDI TOF confirm the structure of dimer **B2*** and SEC (Fig. 2b) shows that the



Scheme 1 Oligomer synthesis.

Table 1 Molar masses of oligomers[a]

	n_{theo}	n_{NMR}	M_n (g mol^{-1})	M_w (g mol^{-1})	M_w/M_n
B1*	1.0	1.0	1190	1200	1.01
B2*	2.0	1.8	2130	2410	1.13
B2	2.0	1.9	2420	3930	1.63
B3	3.0	3.0	3245	6000	1.85
B5	5.0	4.9	4640	10 200	2.19
B9	9.1	9.0	5750	14 000	2.44

[a] n_{theo} (resp. n_{NMR}): number of bis-urea moieties per chain, based on reactant ratio (resp. on NMR analysis); molar masses determined by SEC in DMF.

Table 2 Solubility data[a]

	Water	Acetonitrile	Methanol	Ethanol
B1*	S	S	S	S
B2*	I	G	S	S
B2	I	PG	G	PS
B3	I	PG	G	PS
B5	I	I	PS	I
B9	I	I	PS	I

[a] S: fluid solution; PS: partially soluble (fluid solution with solid deposit); G: homogeneous gel; PG: partial gel (gel with solid deposit).

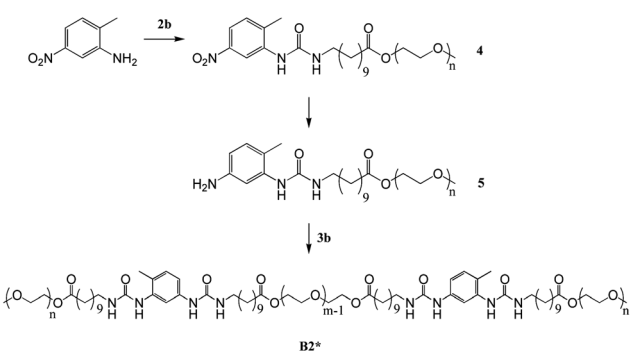
polydispersity of **B2*** is much narrower than that of sample **B2** obtained by statistical condensation.

Solubility

The solubility of the oligomers was tested at a concentration of 1% (w/w) in various polar solvents (Table 2 and Fig. 4). The monomer **B1*** dissolves readily in water: a clear solution forms within a few minutes of shaking at room temperature. In contrast, none of the polymers could be dissolved in water, even after a prolonged period of heating, of sonicating or by using a low amount of co-solvent (tetrahydrofuran). The hydrophilic/hydrophobic balance of all the samples is the same, therefore the insolubility of the oligomers must be a consequence of the presence of several associating groups per chain. A decreasing solubility with an increasing molar mass is a well-known entropic effect in polymer science, however in the present case, the influence of the number of stickers per chain is drastic because the dimer **B2** is already insoluble. In order to check if this low solubility is due to polydispersity, *i.e.* the presence of macromolecules with more than 2 stickers per chain, dimer **B2*** was also tested. Its insolubility unambiguously establishes that the presence of 2 stickers per chain hinders the solubility in water. In contrast, the solubility of the oligomers is significantly improved in polar organic solvents. In particular, the dimer **B2*** is soluble in methanol and oligomers **B2** and **B3** form gels after gentle heating. Therefore further characterization was performed in methanol and compared to the results for monomer **B1*** in water and methanol.

Self-assembly in water

Capillary viscosity measurements show that aqueous solutions of bis-urea **B1*** are significantly viscous ($\eta/\eta_0 = 5$) at a concentration of 1% (w/w). Therefore the presence of large anisotropic self-assemblies is expected.[3–5] This was confirmed by cryoTEM and SANS analyses. Fig. 5 shows the presence of micrometer long filaments. In fact, close inspection of the images reveals the presence of two populations of filaments: closely packed filaments with a diameter of 8.8 ± 0.5 nm and isolated filaments with a diameter of 11.0 ± 0.8 nm. The solutions were also analysed by SANS (Fig. 6): the low angle region of the scattered intensity shows perfect q^{-1} dependence over more than a decade, which is characteristic for long and rigid fibrillar objects. In principle, the characteristic dimensions of the scattering objects can be deduced from a fit to a form factor calculated according to a suitable geometrical model. In the present case, the use of a form factor taking into account two populations of infinitely long rigid filaments with a uniform scattering length density profile and a circular cross-section[10] afforded an excellent fit over the whole q range. The parameters deduced from the fit are 41% of thin filaments (with a cross-section diameter of 5.6 nm and a mass per unit length corresponding to 3.0 molecules in the cross-section) and 59% of thicker filaments (with a cross-section diameter of 7.5 nm and a mass per unit length corresponding to 5.4 molecules in the cross-section). However, one has to note that the use of a form factor for infinitely long rigid filaments with an elliptical cross-section[4] also affords an excellent fit over the whole q range. The exact determination of the fine structure of the filaments would therefore require further investigation. Nevertheless, the SANS and cryoTEM results are coherent and show that the solutions contain very long filaments with a cross-section diameter that is



Scheme 2 Dimer **B2*** synthesis.

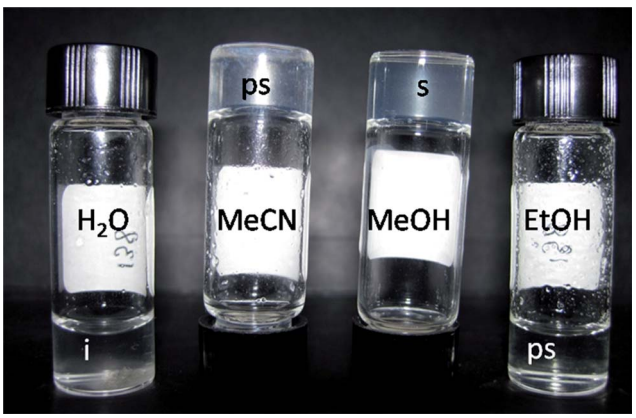


Fig. 4 Solubility tests for solutions of oligomer **B2** (1%).

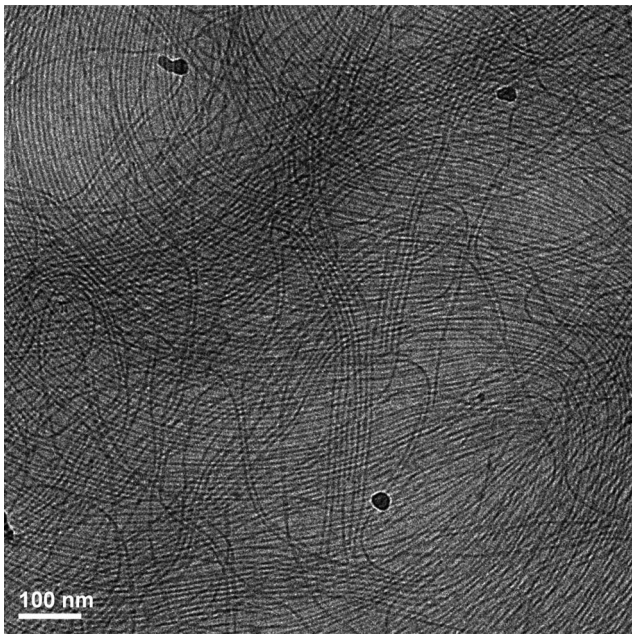


Fig. 5 CryoTEM for monomer **B1*** solution (0.25% in water).

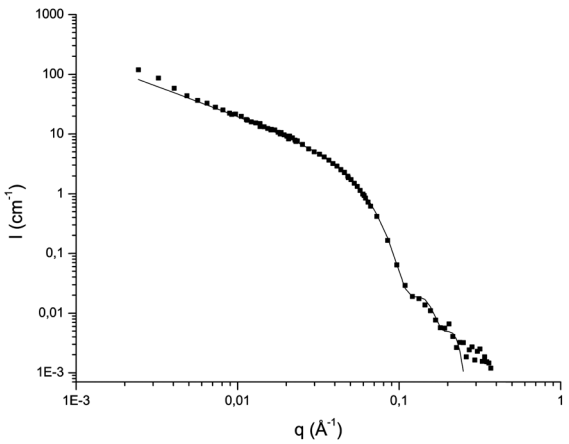


Fig. 6 SANS intensity (*I*) *versus* scattering vector (*q*) for monomer **B1*** solution in D_2O at 10 g L^{-1} and 25 °C. The plain curve is a fit according to a model for two populations of long rigid filaments with a circular cross-section (respective cross-section diameters: 5.6 and 7.5 nm).

close to the largest dimension of a **B1*** molecule in a fully extended conformation (8.5 nm). Based on these microscopic and scattering data, it is reasonable to assume a self-assembled structure similar to related systems where hydrophobic interactions induce aggregation (both in the direction of the filament and within the cross-section), which is reinforced by hydrogen bonds along the filament direction.[4]

Self-assembly in methanol

The better solubility of the samples in methanol allows a more straightforward comparison of the effect of the macromolecular structure. The bis-urea monomer **B1*** and the dimer **B2*** form clear and fluid ($\eta/\eta_0 < 1.05$) solutions at 1% in methanol, whereas the polydisperse dimer **B2** and trimer **B3** form slightly turbid gels

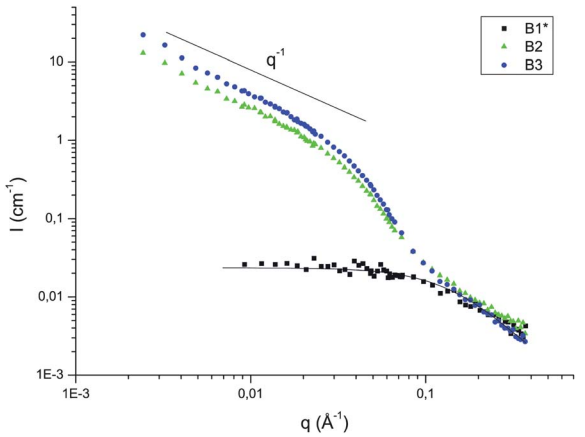


Fig. 7 SANS intensity (*I*) *versus* scattering vector (*q*) for monomer **B1*** and oligomers **B2** and **B3** solutions in CD_3OD at 10 g L^{-1} and 25 °C.

(Fig. 4), and the longer oligomers **B5** and **B9** are only partially soluble. The strong influence of the macromolecular structure on the supramolecular structure is confirmed by SANS (Fig. 7). First of all, monomer **B1*** displays a low scattering intensity which is characteristic of a low molar mass structure. A fit to a Gaussian chain form factor yields a molar mass of 690 g mol^{-1} and a radius of gyration of 1.1 nm indicating that the monomer **B1*** is virtually not assembled in methanol. There is thus a strong solvent effect: in methanol the solvophobic interactions are probably much weaker than in water so that the assembly formed by monomer **B1*** in water is not stable in methanol at the same concentration. In contrast, short oligomers **B2** and **B3** display a strong scattering intensity, with q^{-1} dependence typical of long and rigid objects. Even though the stickers on **B1*** and **B2** are the same, the weakness of the interaction is apparently compensated in the case of **B2** by the fact that several stickers are present on each chain. A possible explanation involves the probably cooperative growth of the filaments. Indeed, it is well-known that worm-like micelles display a cooperative growth, in the sense that the amphiphilic monomers assemble only above a critical micellar concentration (cmc).[11] The growth of bis-urea based supramolecular polymers is also cooperative: formation of a dimer is less favoured than elongation of an existing oligomer.[12] Therefore, the growth of these objects is possible only above a certain concentration where small nuclei become stable. In the present case, one can assume that when more than 2 stickers are present on a macromolecule, the local concentration of stickers is large enough for a stable nucleus to form,[13] which in turn allows formation of long filaments, whereas the monomer present at the same macroscopic concentration cannot assemble.

Conclusion

We have described the synthesis of macromolecular amphiphiles of various molar masses containing well-defined hydrophobic groups incorporating urea moieties. All compounds have the same proportion of associative hydrophobic groups and solubilising POE chains. However, a strong influence of both the number of associative groups per chain and the polydispersity has been demonstrated. In water, where the interactions between stickers are strong, the monomer self-assembles into filaments,

but all other compounds with more than one sticker per chain are insoluble. In methanol, where the interactions between stickers are weaker, neither the monomer nor the monodispersed dimer is assembled, whereas polydispersed chains with an average number of stickers per chain of 2 or 3 self-assemble into filaments, leading to macroscopic gelation.

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