Supplementary Material (ESI) for Chemical Communications

Supporting information

Synthesis of star-shaped poly(ε-caprolactone) *via* 'click' chemistry and 'supramolecular click' chemistry

*Richard Hoogenboom, Brian C. Moore and Ulrich S. Schubert**

Materials and instrumentation

All compounds were used without further purification. Solvents were purchased from Biosolve. Stannous octoate, ε-caprolactone, 5-hexyn-1-ol sodium ascorbic acid, copper(II) sulphate, 3,6-di(pyridine-2-yl)-1,2,4,5-tetrazine and *tetrakis*acetonitrilecopper(I) hexafluorophosphate were obtained from Aldrich. *Heptakis*-azido-β-cyclodextrin was bought from Acros.

^{1}H-NMR and ^{13}C-NMR were recorded on a Varian Mercury 400 spectrometer or a Varian Gemini 300 spectrometer. Chemical shifts are given in ppm relative to TMS or solvent signals for proton and carbon spectra. MALDI-TOF-MS was performed on a Voyager-DE™ PRO Biospectrometry™ Workstation (Applied Biosystems) time-of-flight mass spectrometer using linear mode for operation. The spectra were obtained in the positive ion mode and ionization was performed with a 337 nm pulsed nitrogen laser, whereby dithranol was used as matrix. Gel Permeation Chromatography (GPC) was measured on a Shimadzu system with a SCL-10A system controller, a LC-10AD pump, a RID-6A refractive index detector, a SPD-10A UV detector and a PLgel 5 μm Mixed-D column, whereby chloroform:triethylamine:2-propanol (94:4:2) was used as eluent at 1 mL/min and the column oven was set to 50 ºC. The molecular weights were calculated against polystyrene standards. GPC of the β-cyclodextrin containing compounds was performed on a Shimadzu system with a SCL-10A system controller, a LC-10AD pump, a RID-10A refractive index detector, a SPD-10A UV detector and both a PSS Gram30 and a PSS Gram1000 column in series, whereby *N,I*-dimethylacetamide with 5 mmol LiCl was used as eluent at 1 mL/min and the column oven was set to 60 ºC. The molecular weights were calculated against poly(methyl methacrylate) standards.

Microwave-assisted synthesis was performed utilizing an Emrys Liberator microwave synthesizer (Biotage) utilizing capped reaction vials. All microwave reactions were performed with temperature control (IR sensor).

Acetylene terminated poly(ε-caprolactone) (1)

1-Hexyn-5-ol (65.4 mg, 0.67 mmol) was dissolved in ε-caprolactone (1.5 g, 13.1 mmol) and heated to 110 ºC. After addition of one drop of tin octoate, the solution was stirred for 3 hours at 110 ºC. The obtained solid was dissolved in CH_2Cl_2 and precipitated in methanol:water (2:1) resulting in the acetylene terminated poly(ε-caprolactone) **1**, as white solid (1.28 g, 82%).

^{1}H-NMR ($CDCl_3$): δ 4.06 (t, *J* = 6.7 Hz, 40H, C$\underline{H}_2$OC=O), 3.65 (t, *J* = 6.5 Hz, 2H, C$\underline{H}_2$OH), 2.31 (t, *J* = 7.5 Hz, 40H, OC=OC$\underline{H}_2$), 2.24 (dt, *J* = 7.0, 2.6 Hz, 2H, C≡CC$\underline{H}_2$), 1.97 (t, *J* = 2.6 Hz, 1H, $\underline{H}$C≡C), 1.78-1.72 (m, 4H, C≡CCH$_2$C$\underline{H}_2$C$\underline{H}_2$), 1.70-1.55 (m, 85H, OC=OCH$_2$C$\underline{H}_2$CH$_2$C$\underline{H}_2$), 1.38 (quintet, *J* = 7.5 Hz, 41H, OC=OCH$_2$CH$_2$C$\underline{H}_2$).

GPC [chloroform:triethylamine:isopropanol (94:4:2); PS calibration]: RI-detector: M_n = 4,460 Da, PDI = 1.19. MALDI-TOF-MS: M_n = 2,200 Da, PDI = 1.03. ^{1}H-NMR: M_n = 2,380 Da.

***Heptakis*-poly(ε-caprolactone)-*β*-cyclodextrin 3**

Poly(ε-caprolactone) **1** (200 mg, 90 μmol), *heptakis*-azido-*β*-cyclodextrin **2** (13,1 mg, 10 μmol), sodium ascorbate (10 mg, 50 μmol) and copper(II) sulphate (2 mg, 8 μmol) were dissolved *N,N*-dimethylformamide (2 mL). This reaction mixture was stirred for 15 minutes at 100 ºC under microwave irradiation. The crude reaction mixture was precipitated in methanol and, subsequently, purified by preparative size exclusion chromatography (Biobeads SX-1 in dichloromethane).

^{1}H-NMR (DMSO-*d6*): δ 7.65 (s, 7H, $CH_{triazine}$), 6.09-5.90 (br, 14H, *β*-CD), 5.09-5.10 (br, 7H, *β*-CD), 4.33 (t, *J* = 5.2, 7H, *β*-CD), 3.97 (t, *J* = 5.9 Hz, 303H, C$\underline{H}_2$OC=O), 2.26 (t, *J* = 6.5 Hz, 319H, OC=OC$\underline{H}_2$), 1.62-1.40 (m, 636H, CCH$_2$C$\underline{H}_2$C$\underline{H}_2$, OC=OCH$_2$C$\underline{H}_2$CH$_2$C$\underline{H}_2$), 1.28 (quintet, *J* = 6.5 Hz, 324H, OC=OCH$_2$CH$_2$C$\underline{H}_2$). The remaining *β*-CD signals and the C$\underline{H}_2$OH were covered by the water signal (3.5-3.1 ppm).

GPC [*N,N*-dimethylacetamide with 5 mmol LiCl; PMMA calibration]: RI-detector: M_n = 27,900 Da, PDI = 1.12. ^{1}H-NMR: M_n = 19,200 Da.

3,6-Di(pyridine-2-yl)-4-poly(ε-caprolactone)pyridazine (3)

A solution of the acetylene terminated poly(ε-caprolactone) **2** (200 mg, 0.084 mmol) and 3,6-di(pyridine-2-yl)-1,2,4,5-tetrazine (47.2 mg, 0.2 mmol) in CH_2Cl_2 (2.0 mL) was heated to 150 ºC for 150 minutes under microwave irradiation. After evaporation of the solvent, the crude product was purified by column chromatography (silica, chloroform with 1% methanol) and preparative size exclusion chromatography (Biobeads SX-1, CH_2Cl_2) resulting in the 3,6-di(2-pyridyl)-4-poly(ε-caprolactone)pyridazine (**3**), as white solid (158 mg, 73%).

^{1}H-NMR ($CDCl_3$): δ 8.73-8.66 (m, 3H, H-3'',6,6''), 8.45 (s, 1H, H-5'), 8.11 (d, *J* = 7.9 Hz, 1H, H-3), 7.86 (dt, *J* = 7.9, 1.8 Hz, 2H, H-4,4''), 7.37 (dt, *J* = 4.7, 1.2 Hz, 2H, H-5,5''), 4.01 (t, *J* = 6.7 Hz, 41H, C$\underline{H_2}$OC=O), 3.59 (t, *J* = 6.5 Hz, 2H, C$\underline{H_2}$OH), 3.10 (t, *J* = 7.5 Hz, 2H, CC$\underline{H_2}$), 2.26 (t, *J* = 7.5 Hz, 41H, OC=OC$\underline{H_2}$), 1.68-1.50 (m, 86H, $CCH_2C\underline{H_2}C\underline{H_2}$, $OC{=}OCH_2C\underline{H_2}CH_2C\underline{H_2}$), 1.40-1.27 (quintet, *J* = 7.5 Hz, 42H, $OC{=}OCH_2CH_2C\underline{H_2}$).

GPC (chloroform): UV-detector: M_n = 4,800 Da, PDI = 1.23 RI-detector: M_n = 4,660 Da, PDI = 1.21. MALDI-TOF-MS: M_n = 2,450 Da, PDI = 1.03. ^{1}H-NMR: M_n = 2,590 Da.

UV-vis titration experiments

A stock solution (3.0 mL) of DPP pεCL **5** in dichloromethane ($0.5 \cdot 10^{-4}$ M) was transferred into a quartz UV-cuvet. Small portions (25 µL) of a stock solution of *tetrakis*acetonitrilecopper(I) hexafluorophosphate in dichloromethane (0.45 mg/mL) were added stepwise to this solution and the mixture was shaken for several seconds. After each addition, an UV-Vis spectrum was recorded.