ELECTRRONIC SUPPLEMENTARY INFORMATION

Applying "click" chemistry to polyurethanes: a straightforward approach for glycopolymer synthesis

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Materials

Polytetramethylene oxide (PTMO - TERATHANE® 1000 polyether glycol), hexamethylene diisocyanate (HDI), 3-allyloxy-1,2-propane-diol, 1-thio-ß-D-glucose tetraacetate and 1-thio-ß-D-galactose tetraacetate were obtained from Sigma-Aldrich. HDI was purified by distillation; PTMO and 3-allyloxy-1,2-propane-diol (AOPD) were dried at 40 °C under reduced pressure until the water content was below 70 ppm as it was determined using a Karl Fischer Coulometer (Mettler Toledo DL 32).
The other chain extender 2,2-di(prop-2-ynyl)propane-1,3-diol (DPPD) was synthesized according to literature.[1]

Synthesis and characterization of starting materials, model complexes and polymers

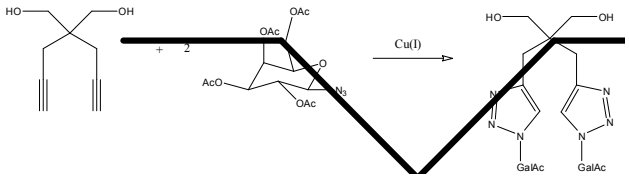
(1) Synthesis of azido-glucose-tetraacetate

Preparation according to literature procedure:[2]
Bromo glucosyl tetraacetate (2 g, 411.20 g/mol, 0.00486 mol) was dissolved in 10 mL dry DMF. Sodium azide (0.47 g, 65.01 g/mol) was added and the mixture was stirred at room temperature for 10 hours. Water was added to quench the reaction, and the mixture was extracted several times with diethyl ether. The combined organic layers were dried over Na_2SO_4. After filtration, the solvent was evaporated. The addition of a small amount of diethyl ether provoked the precipitation of the pure desired product.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.22 (t, 1H, CH), 5.10 (t, 1 H, CH), 4.96 (t, 1H, CH), 4.61 (d, 1H, CH), 4.26 (dd, 1H, *C*H), 4.15 (dd, 1H, CH), 3.79 (m, 1H, CH), 2.10 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.01 (s, 3H, CH_3)

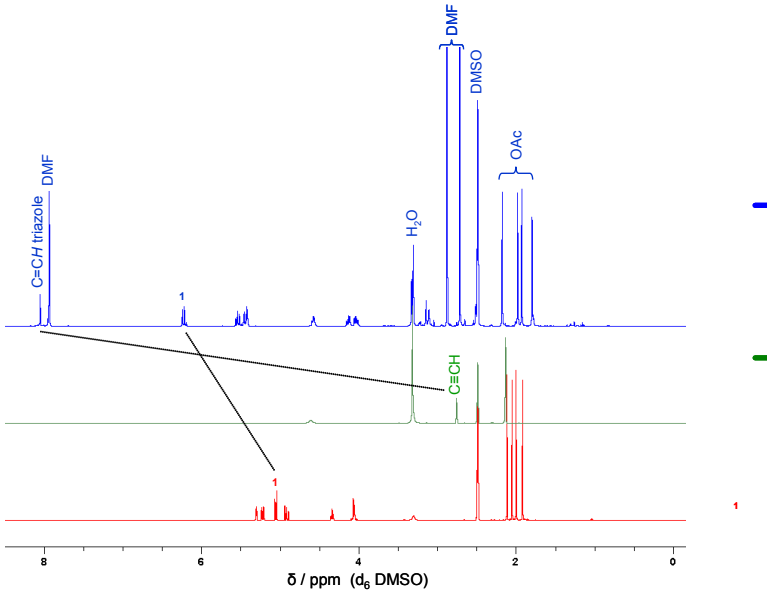
(2) Synthesis of azido-galactose-tetraacetate

Preparation according to literature procedure:[3]
4 g galactose pentaacetate (4g, 411.20 g/mol) were dissolved in 40 mL dry DCM. Afterwards, 1.8 g trimethylsilyl azide (115.21 g/mol; 1.5 exc.) and 0.5 mL Sn(IV) chloride were added to the solution. The mixture was stirred at ambient temperatures for 12 hours. The solvent was removed and the crude residue was purified by flash column chromatography (SiO_2, ethyl acetate/petroleum ether 1:1). The residue was recystallized from ethanol and dried under reduced pressure yielding the desired product.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.43 (dd, 1H, CH), 5.17 (dd, 1H, CH), 5.04 (dd, 1H, CH), 4.61 (d, 1H, CH), 4.19 (dd, 1H, CH), 4.14 (dd, 1H, CH), 4.01 (ddd, 1H, CH), 2.18 (s, 3H, CH_3), 2.11 (s, 3 H, CH_3), 2.07 (s, 3H, CH_3), 1.99 (s, 3H, CH_3).

(3) Click reaction of azido-galactose tetraacetate and DPPD



DPPD (50 mg, M = 152,18 g/mol) and 1-azido-ß-D-galactose tetraacetate (270 mg, 373,32 g/mol) were dissolved in 1 mL DMSO and the catalyst CuBr/PMDETA (1:1) was added to the mixture. The reaction mixture was stirred at 50 °C for 5 hours. Afterwards, 20 mL of water was added and the mixture was extracted twice with DCM (2 × 50 mL). The organic layers were combined and dried over Na_2SO_4. The excess of galactose starting material was removed by column chromatography with EtOAc/petrolether 1:1). The desired model compound was eluted from the column material after adding methanol. The solvent was revoved *in vacuo*.
^{1}H NMR (400 MHz, DMSO): δ = 8.07 (s, 2H, C=C*H* triazole), 6.22 (m, 2H, CH), 5.53 (m, 2H, CH), 5.42 (m, 2H, CH), 4.58 (m, 2H, CH), 4.13 - 4.04 (m, 6H, $CHCH_2$), 3.34 (s, 4H, CH_2-OH), 3.15 (m, 4H, CH_2), 2.18 (s, 6H, CH_3), 1.98 (s, 6H, CH_3), 1.92 (s, 6H, CH_3), 1.80 (s, 6H, CH_3).



(4) General synthesis procedure of the polyurethanes

In a beaker were introduced 1 equiv. of HDI, 1.05 equiv. of chain extender and polyol and a catalytic amount of dibutytin dilaurate (DBTL). The mixture was stirred thoroughly with a spatula until it became viscous. Afterwards, the polymers were cured in an oven at 75 °C for 5 hours.
GPC (THF, DPPD-PU): M_n = 38,400 g/mol, PDI = 1.76.
GPC (THF, AOPD-PU): M_n = 36,700 g/mol, PDI = 2.62.

DPPD-based polyurethane:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.2 - 4.6 (m, 2H, N*H*), 4.20 - 3.95 (m, 4H, CH_2O_{DPPD}), 3.65 - 3.24 (m, 4H, $CH_2CH_2O_{PTMO}$), 3.23 - 3.00 (m, 4H, CH_2NHCO), 2.45 - 2.30 (m, 4H, CH_2C≡CH), 2.04 (s, 2H, CH_2C≡C*H*), 1.80 - 1.55 (m, 4H, O-CH_2(CH_2)$_2$-CH_2-O), 1.55 – 1.25 (m, 8H, NH-CH_2(CH_2)$_4$-CH_2-NH).

AOPD-based polyurethane:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.82 (q, 1H, C*H*=CH_2), 5.23 (dd, 2H, CH=CH_2), 5.15 – 4.6 (m, 2H, N*H*), 4.25 – 3.63 (m, 7H, C*H*, CH_2 AOPD), 3.62 - 3.24 (m, 4H, $CH_2CH_2O_{PTMO}$), 3.23 - 3.00 (m, 4H, CH_2NHCO), 1.80 - 1.55 (m, 4H, O-CH_2(CH_2)$_2$-CH_2-O), 1.55 – 1.25 (m, 8H, NH-CH_2(CH_2)$_4$-CH_2-NH).

(5) Click reaction of azido-glucose/galactose tetraacetate to polyurethane

The reactions were performed according to the description of the model complex **(3)**. The polymers were dissolved in DMSO, azido-glucose/galactose tetraacetate and the catalyst (CuBr and PMDETA) were added. The mixture was stirred at 65 °C overnight.

(6) General procedure for the deacetylation of the carbohydrates[4]

The protected glucose/galactose-containing polyurethanes were dissolved in chloroform and a predetermined amount of sodium methanolate(0.1 M solution in dry MeOH) was added dropwise to the solution. The solution was stirred for 1 hour at room temperature before it was precipitated twice into ice-cold diethyl ether to give the desired glycopolymer.

glucose-functionalized polyurethane:
^{1}H NMR (400 MHz, d_6-DMSO): δ = 8.04 (s, 2H, C=C*H* triazole), 5.38 - 4.20 (m, 7H, C*H*-OH & CH_2-OH glucose), 4.23 – 2.48 (m, 12H, CH_2O$_{DPPD}$, CH$_2$CH_2O$_{PTMO}$, CH_2NHCO$_{HDI}$), 1.75 – 0.93 (m, 12H, O-CH$_2$(CH_2)$_2$-CH$_2$-O, NH-CH$_2$(CH_2)$_4$-CH$_2$-NH).

galactose functionalized polyurethane:
^{1}H NMR (400 MHz, d_6-DMSO): δ = 8.03 (s, 2H, C=C*H* triazole), 5.50 - 4.60 (m, 7H, C*H*-OH & CH_2-OH galactose), 4.20 – 2.50 (m, 12H, CH_2O$_{DPPD}$, CH$_2$CH_2O$_{PTMO}$, CH_2NHCO$_{HDI}$), 1.75 – 0.95 (m, 12H, O-CH$_2$(CH_2)$_2$-CH$_2$-O, NH-CH$_2$(CH_2)$_4$-CH$_2$-NH).

(7) Click reaction of thio-glucose/galactose tetraacetate to polyurethane

The alkene-functionalized polyurethane was dissolved in chloroform. Thiol-functionalized glucose/galactose and photoinitiator (Irgacure 651) were added to the mixture. The solution was irradiated for 1h at 365nm.

glucose tetraacetate-functionalized polyurethane:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.25 – 3.63 (m, 16H, C*H*-OAc & CH_2-OAc glucose, N*H*, C*H*, CH_2 AOPD), 3.62 - 3.01 (m, 8H, CH$_2$CH_2O$_{PTMO}$, CH_2NHCO), 2.69 (m, 2H, GalAc-S-CH_2), 2.11 – 1.89 (m, 12H, CH_3COO), 1.74 (m, 2H, GalAc-S-CH$_2$CH_2), 1.70 – 1.55 (m, 4H, O-CH$_2$(CH_2)$_2$-CH$_2$-O), 1.55 – 1.26 (m, 8H, NH-CH$_2$(CH_2)$_4$-CH$_2$-NH).

galactose tetraacetate-functionalized polyurethane:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.40 – 3.63 (m, 16H, C*H*-OAc & CH_2-OAc galactose, N*H*, C*H*, CH_2 AOPD), 3.62 - 3.01 (m, 8H, CH$_2$CH_2O$_{PTMO}$, CH_2NHCO), 2.69 (m, 2H, GalAc-S-CH_2), 2.20 – 1.85 (m, 12H, CH_3COO), 1.74 (m, 2H, GalAc-S-CH$_2$CH_2), 1.70 – 1.55 (m, 4H, O-CH$_2$(CH_2)$_2$-CH$_2$-O), 1.55 – 1.26 (m, 8H, NH-CH$_2$(CH_2)$_4$-CH$_2$-NH).

IR-spectra

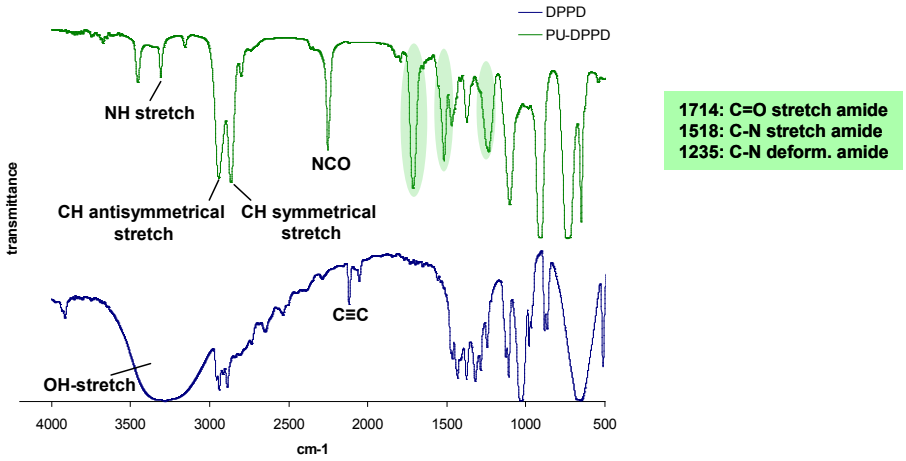


Figure 1: IR-spectra of DPPD chain extender (blue) and DPPD-PU (green).

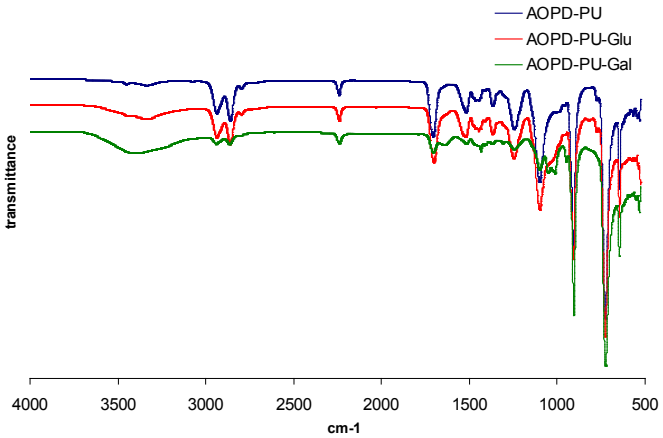


Figure 2: IR-spectra of AOPD-PU (blue) and the corresponding materials modified with glucose (red) and galactose (green).

Characterization techniques

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker 400 MHz spectrometer at room temperature using deuterated chloroform ($CDCl_3$) and dimethylsulfoxide (DMSO) as solvents. Chemical shifts are reported in ppm from external tetramethylsilane.

Gel permeation chromatography (GPC) was performed on a Waters associates liquid chromatograph equipped with differential refractometer and 3× mixed C and 1 mixed E PLgel column (each 7.5 × 30 mm^2) from polymer laboratories. Tetrahydrofuran (flow rate of 1.0 mL/min) was used as eluent at 22 ± 2 °C. The columns were calibrated with narrow polydispersity polystyrene standards (polymer laboratories).

FTIR spectra were recorded at room temperature on a Nicolet 6700 FTIR spectrophotometer (Thermo Fisher Scientific).

X-ray photoelectron spectroscopy (XPS) analysis was performed using an AXIS Ultra DLD spectrometer (Kratos Analytical Inc., Manchester, UK) with a monochromated Al K_α source at a power of 45 W (15 kV × 3 mA), a hemispherical analyser operating in the fixed analyser transmission mode and the standard aperture (0.3 mm × 0.7 mm slot) The total pressure in the main vacuum chamber during analysis was typically 10^{-8} mbar. Each specimen was analysed at an emission angle of 0° as measured from the surface normal. Assuming typical values for the electron attenuation length of relevant photoelectrons in organic compounds the XPS analysis depth (from which 95 % of the

detected signal originates) ranges between 5 and 10 nm. Data processing was performed using CasaXPS processing software version 2.3.15 (Casa Software Ltd., Teignmouth, UK). To obtain information about chemical structure, oxidation states etc., high resolution spectra were recorded from individual peaks at 40 eV pass energy (yielding a typical peak width for polymers of 1.0 – 1.1 eV). Binding energies were referenced to the aliphatic hydrocarbon peak at 285.0 eV.

Sample preparation for spin-casted films: Glass slides were cleaned with 2% v/v RBS 35 concentrate in water (2 % ethanol) and with ultrasound for 1 hour. Afterwards, they were rinsed extensively with Milli-Q water, dipped into ethanol and blown dry under nitrogen stream. The polymers were then dissolved in a $CHCl_3$ / DMF (1:1) solution and spin-casted onto the glass slide (3 layers, 1500 rpm). The polymer films were subsequently dried overnight at 50 °C. (Films which were used for XPS measurements were additionally washed with ethanol and PBS.)

Contact angle measurements were performed on a CAM 2008 (KSV Instruments). The CAM includes a FireWire video camera, an adjustable sample stage and a LED light source. The LEDs are in a reflective sphere which integrates the light and directs it towards the sample. The light is monochromatic. 30, 60 or 100 photos per second (fps) are recorded on the FireWire camera. The resolution used is 512 × 480 pixels. The objective lens provided with the camera is telecentric with a 55 mm focus length.

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[1] G. Eglinton and A. R. Galbraith; J. Chem. Soc. 1959, 889-896.

[2] A. Hasneen, S. J. Kim and H.-J. Paik; Macromol. Res. 2007, *15*, 541-546.
[3] J. Geng, J. Lindqvist, G. Mantovani, G. Chen, C. T. Sayers, G. J. Clarkson and D. M. Haddleton; QSAR Comb. Sci. 2007, *26*, 1220-1228.
[4] C. R. Becer, K. Babiuch, D. Pilz, S. Hornig, T. Heinze, M. Gottschaldt and U. S. Schubert; Macromolecules 2009, *42*, 2387-2394.