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A “click-chemistry” approach to cellulose-based hydrogels

Andreas Koschella[a], Matthias Hartlieb[a], Thomas Heinze[a,b,*]

[a] *Friedrich Schiller University of Jena, Institute for Organic Chemistry and Macromolecular Chemistry, Center of Excellence for Polysaccharide Research, Humboldtstraße 10, D-07743 Jena, Germany*
[b] *Åbo Akademi University, Fibre and Cellulose Technology, Porthansgatan 3, FI-20500 Åbo, Finland*

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ABSTRACT

Cellulose derivatives bearing azide- and alkyne moieties were prepared by conversion of cellulose *p*-toluenesulphonic acid ester with sodium azide, on one hand, and propargylamine, on the other. The products obtained were carboxymethylated to yield water soluble multifunctional cellulose derivatives. Elemental analysis, FTIR- and NMR spectroscopy were applied to prove the structure of the polymers. SEC of the hydrogel components revealed values of the degree of polymerization (DP) between 43 and 200 that are acceptable values after this multi-step reaction starting from celluloses with DP 600. The copper(I)-catalyzed 1,3-dipolar cycloaddition reaction (Huisgen-reaction) was applied for the cross-linking. Gel formation occurred within 55 and 1600 s after mixing of the aqueous solutions of both components and copper(I) catalyst. The gelation time was found to depend on both the degree of functionalization and the amount of copper(I) catalyst. FTIR spectroscopy revealed incomplete conversion of the reactive sites. The gels contain up to 98.4% water. Freeze-drying led to spongy materials with a porous structure as visualised by SEM.

1. Introduction

Hydrogels are three-dimensional networks of hydrophilic polymers that are cross-linked either chemically via covalent bonds or physically by ionic-, van der Waals-, hydrophobic, or hydrogen bond interactions (Yu & Ding, 2008). Their most important property is the capability of remarkable solvent uptake. Such materials play an enormous role in our daily lives as, e.g., superabsorbers in diapers and other hygiene products (Buchholz, 1996). Due to their high water content and tissue like structure, hydrogels are valuable materials for advanced applications in fields where biocompatible devices in chemical and biochemical applications are needed (Bajpai, Shukla, Bhanu, & Kankane, 2008; Calvert, 2009; Lee & Mooney, 2001; Park & Park, 1996; Yu & Ding, 2008).

Due to its inherent hydrophilicity the renewable resource cellulose is a valuable starting material for hydrogels. It is already reported that physical gels from hydroxypropylmethyl cellulose, methyl cellulose, and hydroxypropyl cellulose possess thermoresponsive properties and are therefore only stable above the lower critical solution temperature (LCST). Moreover, chemical cross-linking can be achieved by either difunctional molecules (e.g. divinyl sulphone) or by radical cross-linking with high-energy irradiation. It is also possible to prepare hydrogels from solutions of unmodified cellulose (Chang & Zhang, 2011). Yang et al. dissolved cellulose in an ionic liquid followed by coagulation with water yielding a gel that is physically cross-linked by hydrogen bonds (Li, Lin, Yang, Wan, & Cui, 2009). Zhang et al. prepared gels by dissolving cellulose in an aqueous 6 wt% NaOH solution with 4 wt% urea and subsequent cross-linking with epichlorohydrin (Zhou, Chang, Zhang, & Zhang, 2007). Most of the cellulose-based hydrogels are hybrid systems. Biocompatibile cellulose and cellulose derivatives are combined with a variety of synthetic polymers, e.g., poly(acrylonitrile) (Pourjavadi, Zohuriaan-Mehr, Ghasempoori, & Hossienzadeh, 2007), poly(*N*-isopropylacrylamide) (pNIPAAm) (Ma, Zhang, Fan, Xu, & Liang, 2008), and poly(vinyl alcohol) (Alupei, Popa, Hamcerencu, & Abadie, 2002) in order to tune the properties. The disadvantage of most of these gels is that hazardous cross-linking agents like epichlorohydrin or glutaraldehyde have to be used (Shang, Shao, & Chen, 2008).

An alternative preparation method would be the cross-linking by 1,3-dipolar cycloaddition reaction of alkynes and azides. One example is a gel composed of 6-azido-6-deoxy cellulose and pNIPAAm-co-hydroxyethylmethacrylate (HEMA). The HEMA block is modified with an alkyne moiety and the gelation is accomplished by the 1,3-dipolar cycloaddition (Zhang, Xu, Wu, Zhang, & Zhuo,

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* Corresponding author at: Friedrich Schiller University of Jena, Institute for Organic Chemistry and Macromolecular Chemistry, Center of Excellence for Polysaccharide Research, Humboldtstraße 10, D-07743 Jena, Germany.
Tel.: +49 3641 948270; fax: +49 3641 948272.
E-mail address: Thomas.heinze@uni-jena.de (T. Heinze).

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2009). Because of the LCST of pNIPAAm, the gels produced are thermo-sensitive.

It was interesting to study hydrogels solely composed of cellulose derivatives that can be prepared in aqueous solution. This paper describes the synthesis of water-soluble cellulose derivatives capable of undergoing the copper-catalyzed 1,3-dipolar cycloaddition reaction. Hydrogels were prepared and characterized regarding their cross-linking- and swelling behaviour as well as their morphology in the dried state.

2. Experimental

2.1. Materials

Spruce sulphite pulp was purchased from Fluka. Other chemicals were supplied by Aldrich, Merck and Fluka. Cellulose was dried in vacuum at 100 °C for 2 d over KOH and LiCl was dried in vacuum for 1 d at 150 °C.

2.2. Measurements

FTIR spectra were recorded on a Nicolet Avatar 370 spectrometer using the KBr-technique. The ^{1}H- and ^{13}C-NMR spectra were acquired on a Bruker AVANCE 400 spectrometer in dimethyl sulphoxide (DMSO)-d_6 or D_2O at 70 °C. For ^{1}H-NMR spectra up to 200 scans and for ^{13}C-NMR spectra up to 26,000 scans were accumulated.

Elemental analysis was performed with a Vario EL III from Elementaranalysensysteme Hanau (Germany). The DS values were calculated from the elemental composition by an inhouse software. Both the calculated composition based on the DS values and found values are given in the experimental part.

Size exclusion chromatography in aq. 0.1 mol/L Na_2HPO_4 containing 0.1% NaN_3 was measured with a JASCO SEC system (degasser DG 980-50, pump PU 980, UV detector 975 working at $\lambda = 254$ nm, refractive index detector 930, columns Suprema 1000 and Suprema 30 from Kromatek, Great Dunmow, Essex, UK, with eluent flow rate of 1.000 mL/min). The eluent DMSO/LiBr was used in combination with the columns Novema 3000 and Novema 300 (Polymer Standards Service, Mainz, Germany). Pullulan- and dextran standards (for $M < 10^4$ g/mol) were used for calibration. Weight average ($\bar{M}_w$) and number average molecular mass ($\bar{M}_n$) as well as polydispersity index (PDI) were calculated.

Scanning electron microscopic images were obtained from a LEO-1450 VP with Cryo-Transfer (BAL-TEC-VCT 100), X-ray-microanalysis (Oxford-Link Isis) and a resolution of 4 nm. The samples were freeze dried gels with the volume of 1 mL.

Rheological measurements were performed on a HAAKE Mars rheometer with cone and plate geometry at room temperature. The measurement parameter were $\tau = 10000$ Pa and $f = 1\ s^{-1}$.

Ascorbic acid (0.2 mL, 0.1 M) was mixed with 0.2 mL aqueous $CuSO_4$ solution (0.02, 0.03, and 0.04 M). The polymer solution (0.2 mL, 5%, w/w) was mixed with 0.2 mL of the catalyst solution and 0.2 mL of the mixture were rapidly transferred to the rheometer. The time given in Fig. 2 and Table 2 includes the time starting from mixing the solutions, transfer to the rheometer and start of the measurement. The time dependence of the storage modulus (G') and the loss modulus (G'') was recorded.

For the determination of the degree of swelling, gels were prepared from 1 mL reaction mixture. Immediately after preparation, the wet gels were placed in tubes equipped with fritted glass plate. The hydrogels were allowed to swell in a water bath for 48 h at a temperature of 25 °C. Excess of water was wiped off and the tubes were centrifuged for 2 min at 2200 rpm and weighed to obtain m_s. The swollen hydrogels were dried for 24 h at 60 °C and weighed to obtain m_d. The maximum water content Q_{eq} was calculated according to Eq. (1).

$$Q_{eq} = \frac{m_s - m_d}{m_s} \times 100\% \qquad (1)$$

Q_{eq}: maximum water content; m_s: mass of the swollen sample; m_d: mass of the dried sample.

The gel fraction F_p was calculated according to Eq. (2).

$$F_p = \frac{m_{th}}{m_d} \times 100\% \qquad (2)$$

F_p: gel fraction; m_{th}: theoretical mass of the polymer in the gel (based on the stock solutions used); m_d: mass of the dried sample.

The degree of substitution (DS) of carboxymethyl groups was determined by HPLC after hydrolysis of the polymer with perchloric acid according to a previously published method (Heinze & Pfeiffer, 1999).

2.3. Methods

2.3.1. Synthesis of tosyl cellulose **2**

The synthesis was carried out according to (Rahn, Diamantoglou, Klemm, Berghmans, & Heinze, 1996).

Yield: 41.1 g (133.8 mmol, 91.6%).
Degree of substitution of tosyl groups, DS_{Tos}: 0.94 (based on elemental analysis).
Degree of substitution of 6-deoxy-6-chloro groups, DS_{Cl}: 0.06 (based on elemental analysis).
Elemental analysis: 48.21% C, 5.17% H, 9.76% S, 0.7% Cl.
FTIR (KBr): 3479 (ν OH), 2887 (ν CH_2), 1359 (ν_{as} SO_2), 1173 (ν_s SO_2) cm^{-1}.

2.3.2. 6-Azido-6-deoxy cellulose (**4**)

Tosyl cellulose **2** (12.01 g, 39 mmol, DS_{Tos} 0.94) was dissolved in 400 mL *N,N*-dimethyl formamide (DMF) under stirring. Sodium azide (12.03 g, 185 mmol, 4.8 mol/mol anhydroglucose unit, AGU) was added to the viscous solution. The reaction mixture was allowed to react for 24 h at 100 °C under stirring. After cooling down to room temperature, the solution was poured into 3 L of ice water. The precipitate was filtered off, washed with water (4 × 1 L) and ethanol (3 × 500 mL). The white powder was dried in vacuum at 40 °C.

Yield: 6.84 g (37.3 mmol, 95.6%).
Degree of substitution of 6-azido-6-deoxy groups, DS_{Azide}: 0.81 (based on elemental analysis).
DS_{Tos}: 0.01 (based on elemental analysis).
SEC: $\bar{M}_n$ 53,278 g/mol, $\bar{M}_w$ 216,140 g/mol, PDI 4.06.
Number average degree of polymerization, DP_n: 291.
Elemental analysis: 38.42% C, 4.81% H, 18.51% N, 0.12% S. [theoretical data: 39.65% C, 5.03% H, 18.52% N, 0.17% S].
^{1}H-NMR: (DMSO-d_6/LiCl) δ: 7.8–7.4 (H_{aryl}-Tosyl), 5.00–3.14 (H_{AGU}) ppm.
^{13}C-NMR (DMSO-d_6/LiCl) δ: 103.3 (C1), 79.6 (C4), 75.6–72.3 (C2, 3, 5), 60.1 (C6′), 51.5 (C6) ppm.
FTIR (KBr): 3441 (ν OH), 2920 (ν CH_2), 2108 (ν azide), 1373 (ν_{as} SO_2), 1161 (ν_s SO_2) cm^{-1}.

2.4. Carboxymethyl-6- azido -6-deoxy cellulose (**6**)

6-Azido-6-deoxy cellulose **4** (6.01 g, 32.8 mmol, DS_{Azide} 0.81) was stirred with 100 mL DMSO for 2 h at room temperature. Isopropanol (150 mL) was added to the swollen polymer under stirring. A solution of 7.8 g (195.5 mmol, 6 mol/mol AGU) NaOH in 30 mL water was added to the suspension and the