Advanced Industrial and Engineering Polymer Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Advanced Industrial and Engineering Polymer Research

journal homepage: http://www.keaipublishing.com/aiepr

Synthesis and structure characterization of novel polyampholytes based on cellulose

Annett Pfeifer, Agnes Kemmer, Thomas Heinze*

Friedrich Schiller University of Jena, Institute of Organic Chemistry and Macromolecular Chemistry, Centre of Excellence for Polysaccharide Research, Humboldtstraße 10, D-07743, Jena, Germany

ARTICLE INFO

Article history:
Received 18 March 2021
Received in revised form
1 June 2021
Accepted 8 June 2021

Keywords:
Amino cellulose
Sultone
Polyelectrolyte
Polybetaine
NMR spectroscopy

ABSTRACT

Sulfobetainic polymers were synthesized by polymeranalogous reaction of new amino celluloses starting from cellulose tosylate. To obtain different amino celluloses as starting building blocks, a comprehensive study with a selection of asymmetric and symmetric *N*-alkylated diamines was performed. For reaction with asymmetric diamines, it turned out that the primary amino moiety reacts preferably. Derivatives thus obtained consist in a neutral main structural unit and a cationic side structural unit, which is not described up to now. In order to investigate the reactivity of the amino celluloses 6-deoxy-6-(*N*,*N*,*N*′,*N*′-tetramethylethylenediamino) cellulose was used as uniform starting material for the design of novel polyampholytes by conversion with 1,3-propansultone. Detailed structure characterization was implemented by means of 1D and 2D-NMR spectroscopy.

1. Introduction

Polyampholytes are polymers containing both positively and negatively charged repeating units. A particular case exists for polyzwitterions or synonymously polybetains that bear the same number of anionic and cationic moieties located in the same monomer [1,2]. Polyampholytes and in particular zwitterionic polymers are very important naturally occurring macromolecules (e.g., proteins) that play a key role of life. Various synthetic and natural polyampholytes are applied for commercial purposes, e.g., for protein separation, desalination, binding of metal ions, enhanced oil recovery, and antifouling coatings [3]. Coatings of zwitterionic polymers gain increasing interest in the field of non-fouling surfaces, i.e., layer that do not show nonspecific absorption of proteins [4,5]. They are also promising in combination with antimicrobial properties [6,7]. Even nanoparticles could be obtained by a one-step synthesis via distillation-precipitation polymerization of various methacrylic monomers. The nanoparticles are useful in membranes for dye removal [8]. Moreover, stimuli-responsive nanostructures [9] and hydrogels based on amino acid components [10] are reported in literature. Like the first developed poly(sulfo)betaines [11,12], structurally most mentioned polybetaines contain quaternary pyridinium [13] and imidazolium groups prepared by polymerization of respective vinyl compounds [14] and other *N*-heterocyclic cationic moieties [15,16]. Further, (meth)acrylate or (meth)acrylamide based (co)polymers are widespread described [17].

Not only from a synthetic point of view, it is an implication to design the structure of the ionic polymers but also environmental and sustainability aspects give rise to develop such functional polymers based on biopolymers. In this context, the chemical modification of polysaccharides seems to be a useful approach to design polyzwitterionic structures. Compared to synthetic polymers, an improved solubility was found for zwitterionic cellulose derivatives like 6-deoxy-6-aminocelluloses [18]. 6-Imidazolyl-6-deoxycellulose derivative was allowed to react with 1,3-propane sultone to yield regioselectively substituted zwitterionic cellulose derivatives [19]. Chitosan derivatives with cationic *N*-functionalization are comparable to synthetic polybetains [20]. Zwitterionic cellulose derivatives were obtained by heterogeneous conversion of the biopolymer with aspartic anhydrides *N*-protected with either trifluoroacetyl or carbobenzyloxy in an aqueous reaction medium [21]. Moreover, zwitterionic celluloses were prepared by reacting cellulose with *N*-(3-triethoxysilylpropyl)-*N*-(3-sulfobutyl) amine or *N*-[3-(trimethoxysilyl) propyl] diethylenetriamine-*N*-(7-sulfobutyl) amine [22].

* Corresponding author. Fax: +49 3641 948272.
E-mail address: thomas.heinze@uni-jena.de (T. Heinze).

https://doi.org/10.1016/j.aiepr.2021.06.001

A promising path for the structure design of cellulose is the nucleophilic substitution reaction of cellulose sulfonic acid esters, in particular tosylates, with amines in addition to the modification of the remaining hydroxyl groups. A broad variety of novel bio-based polymers could be designed that found applications in the bio-medical field, e.g., in biosensors, nanoparticles, or biocidal polymers [23–25]. The nucleophilic substitution reaction of cellulose tosylate with 2-aminosuccinic acid, 4-aminobutyric acid, or 3-aminopropyl sulfonic acid yields ampholytic cellulose derivatives that possess negligible cytotoxicity and may be used in pharmaceutical and biomedical applications [26].

Here we report an alternative path to synthesize cellulose based polyzwitterionic polymers by modification of amino celluloses, which can be easily obtained from cellulose tosylates, with a very broad structural diversity as discussed in detail in Ref. [23]. A variety of novel amino celluloses were synthesized applying diamines and characterized in detail by means of NMR spectroscopy. Polyzwitterionic cellulose derivatives were designed by the reaction of 6-deoxy-6-(*N,N,N′,N′*-tetramethylethylenediamino) cellulose with 1,3-propane sultone.

2. Experimental

2.1. Materials

Cellulose *p*-toluenesulfonic acid esters (cellulose tosylates) were prepared according to procedures reported in the literature [27]. Cellulose (microcrystalline cellulose, Lehmann & Voss & Co. KG, $M_w = 67.900$, $M_n = 23.200$ g mol^{-1}) and lithium chloride (LiCl, Sigma Aldrich) were dried in vacuum at 105 °C over potassium hydroxide. Triethylamine (Sigma Aldrich) was distilled from calcium hydride prior to use. *p*-Toluenesulfonyl chloride, dimethyl sulfoxide (DMSO, 99.7%, dry over molecular sieve), and *N,N*-dimethyl acetamide (DMA, 99.5%, dry over molecular sieve), *N,N*-dimethylethylendiamine (DMEDA **3a**), *N,N*-dimethyl-1,3-propanediamine (DMPDA **3b)**, *N,N,N′*-trimethylethylenediamine (TriMEDA **3c**), and *N,N,N′,N′*-tetramethylethylenediamine (TetraMEDA **3d**), as well as ion exchange resin IRA-410 (Cl_2-form) were purchased from Sigma Aldrich and used as received. 1,3-propane sultone (97%) was purchased from Acros Organics. Acetone, ethanol, and 2-propanol used were technical grade.

2.2. Measurements

The content of C, H, N, and S [%] were determined with a Vario EL III (Elementaranalysensysteme, Hanau, Germany). The chlorine content was determined after combustion and potentiometric titration according to Schöniger's method. The degree of substitution of tosylate/6-deoxy-6-chloro/6-deoxy-6-amino and propylsulfonate moieties (DS_{Tosyl}, DS_{Cl}, DS_{Amine}, and $DS_{Sulfonate}$) was calculated by elemental analysis (sulphur-, chlorine-, and nitrogen content). The 1D NMR spectra (^{1}H and ^{13}C APT) and 2D NMR spectra (ASAP HSQC/HSQC DEPT) were acquired with Bruker Avance 250 (250 MHz) and Avance 400 (400 MHz) spectrometers in D_2O at 60 °C (DMSO-d_6, room temperature for cellulose tosylate) at a concentration of at least 5% (w/w) of dissolved polymer for both measurements. The scan number was 32 for ^{1}H- and 10,240 for ^{13}C NMR spectra.

2.3. Typical synthesis procedures

2.3.1. Cellulose tosylate (**2**)

Cellulose **1** (, 62 g, 0.382 mol) was slurried in 1300 mL DMA and stirred for 2 h at 120 °C under exclusion of moisture. After cooling to 100 °C, 93 g LiCl were added and stirring was continued until a clear and viscous cellulose solution was obtained. After cooling to 8 °C, triethylamine (107 mL, 0.764 mol, 2 mol/mol anhydroglucose unit, AGU) and *p*-toluenesulfonyl chloride (72.9 g, 0.382 mol, 1 mol/mol AGU) were added. The colour of the pale yellow mixture turned dark reddish brown during stirring for 24 h at 8 °C. The polymer **2** was isolated by precipitation in 8 L ice water, filtration, washing with water (five times, 1.5 L), and subsequently with ethanol (2 times, 1.5 L). It was dried under vacuum at 60 °C to constant mass.

Yield: 103.8 g (96%)

Elemental analysis: C 47.45%, H 5.11%, S 8.69%, Cl 0.55%

DS_{Tosyl}: 0.76, DS_{Cl}: 0.04.

^{13}C NMR (62.90 MHz, DMSO-d_6): δ [ppm] 21.6 (CH_3, Tosyl), 60.4 (C–6_{OH}), 69.1 (C-6_{Tosyl}), 72.2–81.5 (C-2,3,4,5), 103.1 (C-1), 128.3–145.4 (4 x CH, Tosyl)

2.3.2. 6-Deoxy-6-(N,N-dimethyl-1,3-propanediamino) cellulose ***4b***

Cellulose tosylate **2** (3.0 g, 0.0108 mol, DS_{Tosyl} 0.76) was dissolved in 30 mL DMSO and DMPDA **3b** (13.49 mL, 0.108 mol, 10 mol/mol modified AGU) was added. The temperature was increased to 100 °C under stirring. After 4 h at 100 °C, the mixture was cooled to room temperature and the polymer was isolated by precipitation in 400 mL acetone, filtration, and washing with acetone (4 × 200 mL). The wet product was dissolved in 200 mL water and treated with 50 mL ion exchange resin IRA-401 for 3 h at room temperature. After evaporating the solvent, the product DMPDA cellulose **4b** was finally lyophilized.

Yield: 2.05 g (90%)

Elemental analysis: C 46.84%, H 7.88%, N 7.52%, S 0.23%

DS_{Amine}: 0.57; DS_{Tosyl}: 0.02 (traces)

^{13}C APT NMR (100 MHz, D_2O): δ [ppm] 25.3 (CH_2 b/c′), 38.1 (CH_2 d′), 43.8 (2 x CH_3 d), 46.7 (CH_2 a), 49.4 (C–6_{NH}), 52.2 (2 x CH_3 a′), 56.8 (CH_2 c), 60.6 (C–6_{OH}), 64.8 (CH_2 b′, C–6_{N+}), 73.7–81.4 (C-2-5), 102.9 (C-1)

2.3.3. 6-Deoxy-6-(N,N,N′-trimethylethylenediamino) cellulose ***4c***

Cellulose tosylate **2** (3.0 g, 0.0108 mol, DS_{Tosyl} 0.76) was dissolved in 30 mL DMSO and TriMEDA **3c** (6.97 mL, 0.054 mol, 5 mol/mol modified AGU) was added. The temperature was increased to 100 °C under stirring. After 5 h at 100 °C, the mixture was cooled to room temperature and the polymer was isolated by precipitation in 400 mL acetone, filtration, and washing with acetone (4 × 200 mL). The wet product was dissolved in 200 mL water and treated with 50 mL ion exchange resin IRA-401 for 3 h at room temperature. After evaporating the solvent, the product TriMEDA cellulose **4c** finally lyophilized.

Yield: 1.91 g (85%)

Elemental analysis: C 47.22%, H 7.65%, N 6.66%, S 0.53%

DS_{Amine}: 0.50; DS_{Tosyl}: 0.03 (traces)

^{13}C APT NMR (100 MHz, D_2O): δ [ppm] 20.9 (CH_3 Tosyl), 35.3 (CH_3 d′), 42.2 (CH_3 a), 43.8 (CH_2 c′), 44.4 (2 x CH_3 d), 52.7 (2 x CH_3 a′), 54.2 (CH_2 b), 55.5 (CH_2 c), 58.2 (C–6_N), 60.5 (C–6_{OH}), 61.3 (CH_2 b′), 64.4 (C–6_{N+}), 72.9–81.6 (C-2,3,4,5), 102.9 (C-1)

2.3.4. 6-Deoxy-6-(N,N,N′,N′-tetramethylethylenediamino) cellulose ***4i***

Cellulose tosylate **2** (8.0 g, 0.0286 mol, DS_{Tosyl} 0.76) was dissolved in 100 mL DMSO and TetraMEDA **3d** (64.75 mL, 0.429 mol, 15 mol/mol modified AGU) was added. The temperature was increased to 100 °C under stirring. After 5 h at 100 °C, the mixture was cooled to room temperature and the polymer was isolated by precipitation in 1.3 L 2-propanol, filtration, and washing with 2-propanol (4 × 400 mL). The wet product was dissolved in 500 mL water and treated with 200 mL ion exchange resin IRA-401 for 16 h at room temperature. After evaporating the solvent, the product TetraMEDA cellulose **4i** was finally lyophilized.

Yield: 5.43 g (89%)

Elemental analysis: C 47.52%, H 7.62%, N 5.89%, S 0.66%

DS_{Amine}: 0.45; DS_{Tosyl}: 0.04 (traces)

^{13}C APT NMR (100 MHz, D_2O): δ [ppm] 21.2 (CH_3 Tosyl), 44.9 (2 x CH_3 d), 51.5 (CH_2 c), 52.6 (2 x CH_3 a), 63.0 (CH_2 b), 60.7 (C-6 OH), 65.6 (C-6 N^+), 69.7–80.8 (C-2,3,4,5), 102.8 (C-1)

2.3.5. 6-Deoxy-6-(N,N,N′,N′-tetramethylethylenediamino) propylsulfonate cellulose **5e**

TetraMEDA cellulose **4i** (0.5 g, 0.0024 mol) was dissolved in 15 mL water and 1,3-propane sultone (0.42 mL, 0.0048 mol) was added. The clear solution was stirred 2 h at room temperature. The product was isolated by precipitation in 100 mL THF, washed with THF (two times with 60 mL), dissolved in water, dialysed and treated with 60 mL ion exchange resin IRA-401 for 16 h at room temperature. After evaporating the solvent, the product **5e** was finally lyophilized.

Yield: 0.31 g (58%)

Elemental analysis: C 42.12%, H 7.43%, N 5.06%, S 2.58%

DS_{Amine}: 0.22; $DS_{Sulfonate}$: 0.18.

^{13}C NMR (62.9 MHz, D_2O): δ [ppm] 18.7 (CH_2 f), 21.3 (CH_3, Tosyl), 43.7 (2x CH_3 d^+), 44.6 (2 x CH_3 d), 47.31 (CH_2 g), 50.8 (CH_2 c), 52.5 (2 x CH_3 a), 55.8 (CH_2 c^+), 61.8 (CH_2 e), 60.5 (C–6_{OH}), 63.4 (CH_2 b), 65.8 (C–6_{N+}), 69.7–80.9 (C-2,3,4,5), 102.9 (C-1)

3. Results and discussion

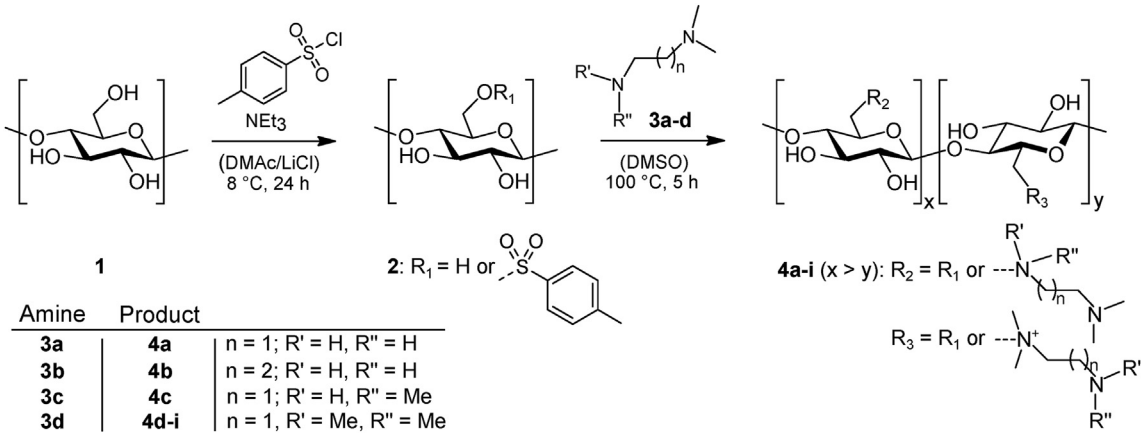
Cellulose tosylate **2** (Scheme 1), which could be easily produced by the reaction of cellulose **1** with tosyl chloride homogeneously in *N,N*-dimethyl acetamide/LiCl as solvent [27], was used as a key intermediate to design new amino celluloses and thus cellulose based polyampholytes (see Scheme 2).

3.1. Synthesis and characterization of amino cellulose

Cellulose tosylate (**2**, DS_{Tosyl}: 0.76) was allowed to react with the asymmetric diamines *N,N*-dimethylethylenediamine (DMEDA, **3a)**, *N,N*-Dimethyl-1,3-propandiamin (DMPDA, **3b**, *N,N,N′*-trimethylethylenediamine (TriMEDA, **3c**), or symmetric diamine *N,N,N′,N′*-tetraethylenediamine (TetraMEDA, **3d**) under typical reaction conditions of nucleophilic substitution reaction [28] as summarized in Scheme 1.

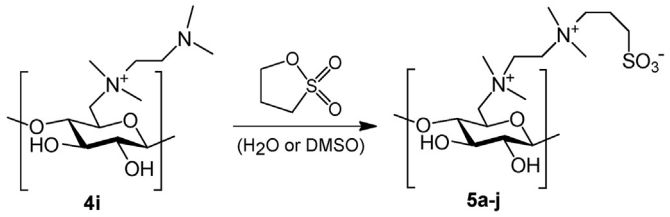
Depending on the reaction conditions, the amines **3a-c** yield the corresponding amino celluloses **4a-c** (Scheme 1) with high conversion of the tosyl moieties in the range from 78% (TriMEDA, product **4c**) to 90% (DMEDA, product **4a**). There is a small amount of remaining tosylate moieties ($DS_{Tosyl} \leq 0.03$) for all products obtained. However, it turned out – as expected – that the reaction of cellulose tosylate with the asymmetric amines **3a-c** leads to a non-selective reaction because both amino groups may react with the cellulose tosylate. It is obvious that the amines **3a-c** react with both primary/secondary and tertiary amine groups as it is concluded from the NMR spectra. The reactivity of the different amino groups depends on both the steric hindrance and the nucleophilicity. While an increasing number of methyl groups at the nitrogen atom improves the nucleophilic strength and, hence, should increase the reactivity, the steric hindrance of the tertiary amine decreases the reactivity. For instance, it turned out that the conversion occurred mainly with the primary amino group of DMEDA **3a** (87%) yielding main structural unit of **4a**. In addition, 13% of the side structural unit is formed as a result of the reaction of the tertiary amine moiety. The ratio of main structural unit to side structural unit (**x** to **y)** could be determined by ^{13}C NMR spectroscopy (inverse-gated decoupling ^{13}C NMR experiment) by setting integral c in relation to integral a'. Further, ^{13}C-APT spectra (Fig. 1A–C) were used for quantification since for 4a calculation by ^{13}C-APT spectrum (Fig. 1, A) gave similar results to calculation by inverse-gated decoupling ^{13}C NMR experiment of **4a**. Conversion of cellulose tosylate with DMPDA **3b** resulted in 82% of **4b** and 18% (Fig. 1, **B**, integral d in relation to integral a') comparable result was found for the reaction of diamine TriMEDA **3c**; a conversion of 84% of the secondary amino group and 16% of the tertiary amino group occurred yielding product **4c** as determined by ^{13}C-APT spectrum (Fig. 1, C).

To get a uniform starting material for partial betainization (Section 3.2), the amino cellulose was prepared with the symmetric diamine TetraMEDA **4d**. The products **4d-i** obtained show a lower conversion of the tosyl groups in comparison to diamines **3a-c** most likely due to the steric hindrance of the tertiary amino moieties. At a reaction temperature of 80 °C, 43% of the tosylate is converted (Table 1, **4d**). Increasing the reaction temperature to 100 °C, almost independent of the molar ratio of tosyl cellulose **2** to TetraMEDA **3d** in the range from 1/6 to 1/15 of AGU/diamine, the conversion can be optimised to about 60% (Table 1, **4e-i**). However, applying the high molar ratios of 1/10 and 1/15 and especially upscaling the reaction, a significant aminolysis of tosylate occurred additionally to the nucleophilic substitution reaction. Hence, the products **4h** and **4i** contain almost no remaining tosyl groups (Table 1). Nevertheless, as the amount of amine increase, also partial aminolysis of the tosylate groups occurs and the overall DS (DS_{Amine} + DS_{Tos}) decreases.



Amine	Product	
3a	**4a**	n = 1; R' = H, R'' = H
3b	**4b**	n = 2; R' = H, R'' = H
3c	**4c**	n = 1; R' = H, R'' = Me
3d	**4d-i**	n = 1, R' = Me, R'' = Me

Scheme 1. Overview of amino celluloses **4a-i** (x: main structural unit, y: side structural unit) obtained by reaction of cellulose tosylate **2** with amines **3a-d** in DMSO for 5 h and 100 °C.



Scheme 2. Reaction of 6-deoxy-6-(*N,N,N′,N′*-tetramethylethylendiamino) cellulose **4i** with 1,3-propane sultone to yield polyampholytic celluloe derivatives **5a-j**.

The structure of the novel type of amino cellulose, TetraMEDA cellulose **4d-i** could be characterized by means of NMR spectroscopy in detail. The ^{13}C-APT spectrum of the product **4i** with a DS of amino moieties of 0.45 and with a DS_{Tosyl} of remaining tosyl groups of 0.04 is exemplarily shown in Fig. 2, **A**. The signals of the amino substituent could be clearly assigned at 63.0 ppm for CH_2 (b) and 51.5 ppm for CH_2 (c) of the ethylene moiety. The signals arising from *N*-methyl groups can be observed at 52.8 ppm (2x CH_3, a) and 44.9 ppm (2x CH_3, d). The typical signals of the cellulose repeating unit are in the range from 102.8 ppm (C-1) to 60.6 ppm for the non-modified primary C—6_{OH}. The peak at about 65.6 ppm is assigned to C-6 of the 6-deoxy-6-amino moiety (C—6_{N+}). The ASAP-HSQC-DEPT spectra of sample **4i** clearly indicate that 6-deoxy-6-(*N,N,N′,N′*-tetramethylethylenediamino) moiety is the main repeating unit (Fig. 3, A). In addition, the residual tosyl moiety is visible at 21.2 ppm (signal for CH_3). Moreover, signals could be found for partly protonated moieties in aqueous solution. The signal of 2 x CH_3 (d) shifted after protonation from 44.8 to 44.0 ppm (d^+).

3.2. Synthesis and characterization of cellulose polyampholytes

It is known that 1,3-propane sultone may react with amino groups under ring opening. The reaction of the tertiary amino groups of 2-(dimethylamino)ethyl methacrylate was used for the selective betainization of the diblock copolymer applying THF or water as reaction medium [29]. Thus, TetraMEDA cellulose dissolved in water could be homogeneously modified under variation of the reaction parameters to prepare 6-deoxy-6-(*N,N,N′,N′*-tetramethylethylenediamino) propylsulfonate cellulose (TetraMEDA-SO_3 cellulose **5a-j**) (Table 2).

Increasing the molar ratio of AGU to amine from 1:1 to 1:2 leads to an increase of the DS value (**5a/b** and **5d/e**). By increasing reaction time (**5a-c**) and reaction temperature (**5f**, **g**), the DS of propylsulfonate could be increased from 0.08 to 0.20. However, increasing the reaction temperature does not lead to an

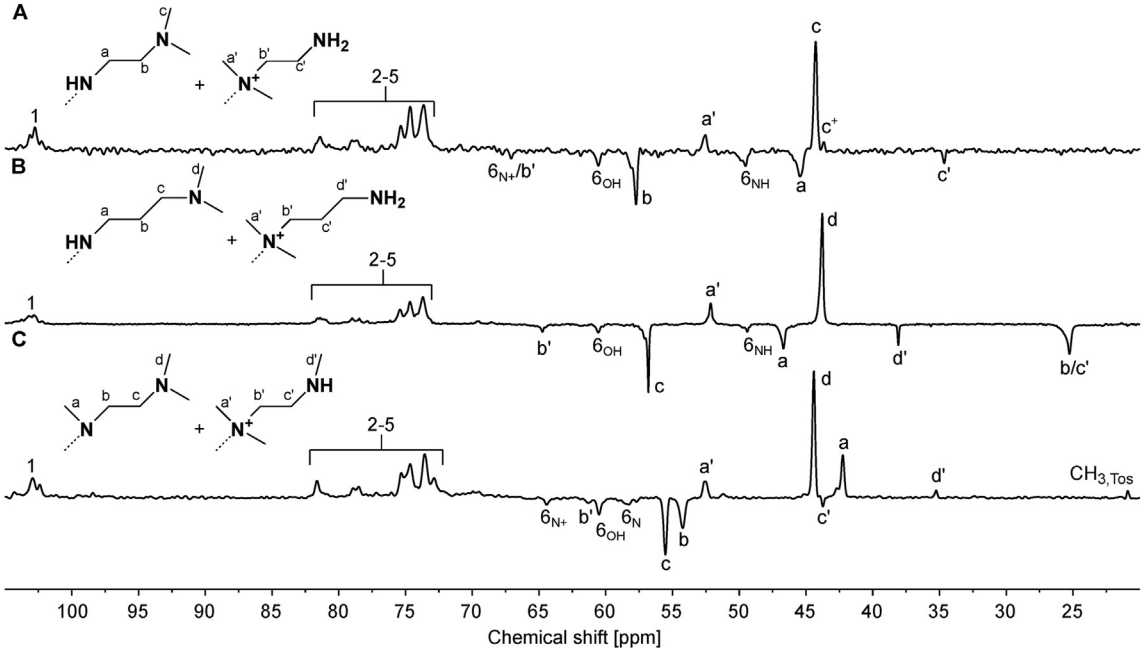


Fig. 1. ^{13}C-APT spectra (100 MHz, D_2O) of **A**) 6-deoxy-6-(*N,N*-dimethylethylenediamino) cellulose **4a** (DS_{Amine}: 0.72, DS_{Tosyl}: 0.02), **B**) 6-deoxy-6-(*N,N*-dimethyl-1,3-propandiamino) cellulose **4b** DS_{Amine}: 0.57, DS_{Tosyl}: 0.02), and **C**) 6-deoxy-6-(*N,N,N′*-trimethylethylenediamino) cellulose **4c** (DS_{Amine}: 0.50, DS_{Tosyl}: 0.03).*c^+ signal when terminal amine protonated.

Table 1
Products obtained by conversion of cellulose tosylate **2** (DS_{Tosyl}: 0.76) with *N,N,N′,N′*-tetraethylenediamine (TetraMEDA, **3d**) under different reaction conditions.

Reaction conditions		Product		
Molar ratio of AGU: Amine	Time [h]/ Temperature [°C]	No.	DS_{Amine}	DS_{Tosyl}
1 : 10	5/80	**4d**	0.34	0.29
1 : 6	5/100	**4e**	0.45	0.23
1 : 8	5/100	**4f**	0.48	0.29
1 : 10	5/100	**4g**	0.46	0.15
1 : 10	5/100	**4h**[a]	0.42	0.05
1 : 15	5/100	**4i**[a]	0.45	0.04

[a] Upscaling.

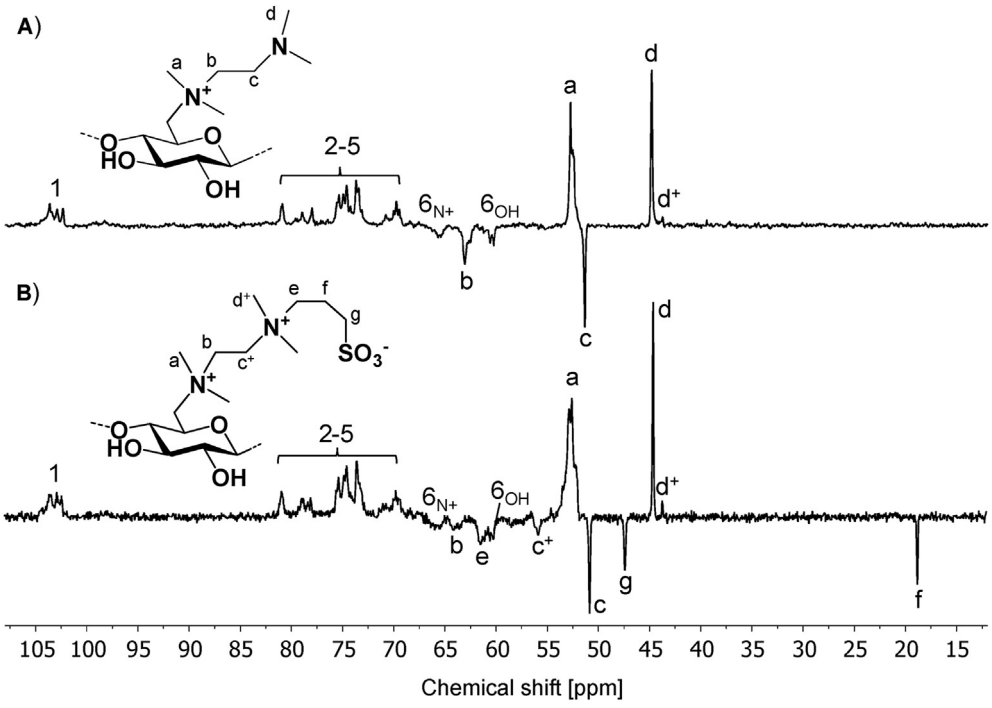


Fig. 2. ^{13}C-APT spectra (100 MHz, D_2O) of **A**) 6-deoxy-6-*N,N,N′,N′*-tetramethylethylendiamino cellulose **4i** (DS_{Amine}: 0.45, DS_{Tosyl}: 0.04). **B**) 6-deoxy-6-(*N,N,N′,N′*-tetramethylethylendiamino) propylsulfonate cellulose **5e** (DS_{Amine}: 0.22, $DS_{Sulfonate}$: 0.18).

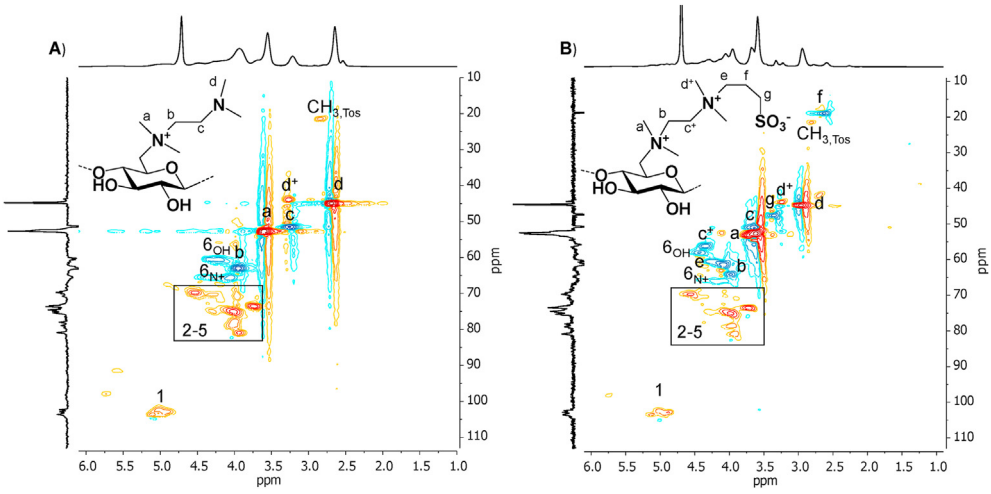


Fig. 3. ASAP-HSQC-DEPT spectra (100 MHz, D_2O) of **A**) 6-deoxy-6-(*N,N,N′,N′*-tetramethylethylendiamino) cellulose **4i** (DS_{Amine}: 0.45, DS_{Tosyl}: 0.04) and **B**) 6-deoxy-6-(*N,N,N′,N′*-tetramethylethylendiamino) propylsulfonate cellulose **5c** (DS_{Amine}: 0.18, $DS_{Sulfonate}$: 0.14).

optimization of the conversion efficiency due to fast hydrolytic decomposition of the sultone at high temperatures [30]. Reaction in DMSO at various temperatures leads to products with DS values of up to 0.26, whereas the sample obtained by reaction at 80 °C (**5j**) is heterogeneous and partially insoluble.

To characterize products **5a-j**, NMR spectroscopy was applied. At first glance, it seems that not only the terminal amino groups but also the hydroxyl groups of cellulose were involved in the reaction. In a typical NMR spectrum acquired after the reaction, there are different signals that might be assigned to the functional sulfonate groups bound to nitrogen (e, g, and f) and alternatively bound to the oxygen. However, a careful consideration of the reaction path yield to the assumption that counter ion of the ammonium moieties formed may be hydroxysulfonic acid, respectively, the corresponding sulfonate. Hence, samples **5a-j** were subjected to an ion exchange with chloride ions (IRA-401). The NMR spectra of the treated samples appear to be more simple and, more important, it may be concluded that the reaction occurred at the nitrogen only under the conditions applied. A typical ^{13}C APT spectrum of sample **5e** is shown in Fig. 2, B. The assignment of the signals was possible using ASAP-HSQC spectrum (Fig. 3, B). The spectra show all signals of the 6-deoxy-6-TetraMEDA moiety. The DS value of the sulfonate group of sample **5e** is 0.18 while the DS of remaining amino moieties is 0.22. The signals of the modified repeating unit occurred in the range from 102.8 (C-1) ppm to 60.5 ppm for the unmodified C–6_{OH}. The signals for the functional propylsulfonate group bound

Table 2
Products obtained by conversion of 6-deoxy-6-*N,N,N′,N′*-tetramethylethylenediamine cellulose **4i** (DS_{Amine} = 0.44) with 1,3-propane sultone applying different reaction conditions.

Reaction conditions				Product		
Solvent	Molar ratio of modified AGU: sultone	Time [h]	Temperature[a] [°C]	No.	$DS_{Sulfonate}$	DS_{Amine}
H_2O	1 : 1	1	RT	**5a**	0.08	0.33
H_2O	1 : 1	2	RT	**5b**	0.13	0.26
H_2O	1 : 1	20	RT	**5c**	0.14	0.18
H_2O	1 : 2	1	RT	**5d**	0.16	0.27
H_2O	1 : 2	2	RT	**5e**	0.18	0.22
H_2O	1 : 10	2	40	**5f**	0.20	0.18
H_2O	1 : 10	2	80	**5g**	0.20	0.20
DMSO	1 : 2	2	RT	**5h**	0.21	0.21
DMSO	1 : 2	6	RT	**5i**	0.21	0.16
DMSO	1 : 2	2	80	**5j**[b]	0.26	0.15

[a] RT, room temperature,
[b] Heterogeneous material.

to nitrogen appear at 61.9 ppm for CH_2 (e), 47.3 ppm for CH_2 (g) and 18.7 ppm for CH_2 (f). Additionally, the signal of CH_2 (c) of the amino moiety shifts after conversion with 1,3-propansultone from 50.8 to 55.8 ppm (c^+). Both signals are visible in sample **5e** proving the presence of both structures, TetraMEDA moiety and the sulfobetainic TetraMEDA-SO_3 residue.

In addition to 1D NMR spectrum (Fig. 2, B), the 2D NMR (ASAP-HSQC-DEPT) spectrum of **5c** is shown in Fig. 3, B. Signals in the region of 15−25 ppm can be assigned to CH_3 of tosylate moiety and more important. The distinct peak at 44.8 ppm, arising from CH_3 of terminal amino moiety of TetraMEDA cellulose, indicates that a significant amount of the starting material is not converted (**6c,** DS_{Amine}: 0.18, DS_{Betain}: 0.14). Nevertheless, CH_2 (f) of propylsulfonate proofs the partial betainization of the terminal tertiary amino group. Further CH_2 groups of propylsulfonate residue around 50−65 ppm can be assigned less clearly, because of the multitude of other signals in this region. This indicates the successful introduction of propylsulfonate moiety by nucleophilic addition to the terminal tertiary amine of TetraMEDA cellulose **4i**.

4. Conclusions

It was shown that amino cellulose can be easily prepared by nucleophilic substitution of tosyl moieties at C6 with asymmetric diamines and symmetric *N,N,N′,N′*-tetrametylethylenediamine. Amino celluloses obtained can be used as building blocks to introduce further functional groups. Thus, libraries of different functional polymers can be produced, by e.g. Michael-analogous reaction, based on the same amino cellulose. Here a subsequent conversion of the amino cellulose obtained with 1,3-propane sultone leads to polyampholytic polymers based on cellulose. The content of sulfonate moieties could be adjusted up to 55% of the terminal amino group. The amino celluloses and the polyampholytes synthesized were well soluble in water. For further studies, the upscaling of the production of polyampholytes and removal of interfering residual tosyl groups will be investigated. Moreover, other sulfonate containing agents will be used for the preparation of polysaccharide based sulfobetaines. For potential application of the derivatives obtained biocidal efficacy, suitability as antifouling agent, and exploitation as polymeric surfactant is of interest.

Declaration of competing interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcomes.

Acknowledgements

We would like to acknowledge the NMR platform at the Friedrich-Schiller University Jena for support in the NMR spectroscopy.

References

[1] L.D. Blackman, P.A. Gunatillake, P. Cass, K.E.S. Locock, An introduction to zwitterionic polymer behavior and applications in solution and at surfaces, Chem. Soc. Rev. 48 (2019) 757−770.
[2] A. Laschewsky, Structures and synthesis of Zwitterionic polymers, Polymers 6 (2014) 1544−1601.
[3] S.E. Kudaibergenov, A. Ciferri, Natural and synthetic polyampholytes, 2, macromolecular, Rapid Commun. 28 (2007) 1969−1986.
[4] E. Zhang, B. Song, Y. Shi, H. Zhu, X. Han, H. Du, et al., Fouling-resistant zwitterionic polymers for complete prevention of postoperative adhesion, Proc. Natl. Acad. Sci. Unit. States Am. 117 (2020) 32046.
[5] J. Ladd, Z. Zhang, S. Chen, J.C. Hower, S. Jiang, Zwitterionic polymers exhibiting high resistance to nonspecific protein adsorption from human serum and plasma, Biomacromolecules 9 (2008) 1357−1361.
[6] L. Zheng, H.S. Sundaram, Z. Wei, C. Li, Z. Yuan, Applications of zwitterionic polymers, React. Funct. Polym. 118 (2017) 51−61.
[7] M. Li, B. Zhuang, J. Yu, Functional Zwitterionic polymers on surface: structures and applications, Chem. Asian J. 15 (2020) 2060−2075.
[8] G.P.S. Ibrahim, A.M. Isloor, Inamuddin, A.M. Asiri, N. Ismail, A.F. Ismail, et al., Novel, one-step synthesis of zwitterionic polymer nanoparticles via distillation-precipitation polymerization and its application for dye removal membrane, Sci. Rep. 7 (2017) 15889.
[9] S. Kudaibergenov, J. Koetz, N. Nuraje, Nanostructured hydrophobic polyampholytes: self-assembly, stimuli-sensitivity, and application, Adv. Compos. Hybrid Mater. 1 (2018) 649−684.
[10] M. Casolaro, I. Casolaro, CHAPTER 20 multiple stimuli-responsive hydrogels based on α-amino acid residues for drug delivery. Smart materials for drug delivery, Royal Soc. Chem. 2 (2013) 199−227.
[11] H. Ladenheim, H. Morawetz, A new type of polyampholyte: poly(4-vinyl pyridine betaine), J. Polym. Sci. 26 (1957) 251−254.
[12] R. Hart, D. Timmerman, New polyampholytes: the polysulfobetaines, J. Polym. Sci. 28 (1958) 638−640.
[13] J. Bohrisch, U. Wendler, W. Jaeger, Controlled radical polymerization of 4-vinylpyridine, Macromol. Rapid Commun. 18 (1997) 975−982.
[14] S. Kudaibergenov, W. Jaeger, A. Laschewsky, Polymeric Betaines: Synthesis, Characterization, and Application. Supramolecular Polymers Polymeric Betains Oligomers, Springer Berlin Heidelberg, Berlin, Heidelberg, 2006, pp. 157−224.
[15] M. Casolaro, S. Bottari, A. Cappelli, R. Mendichi, Y. Ito, Vinyl polymers based on l-histidine residues. Part 1. The thermodynamics of poly(ampholyte)s in the free and in the cross-linked gel form, Biomacromolecules 5 (2004) 1325−1332.
[16] J.M. Lázaro Martínez, A.K. Chattah, R.M. Torres Sánchez, G.Y. Buldain, V. Campo Dall' Orto, Synthesis and characterization of novel polyampholyte and polyelectrolyte polymers containing imidazole, triazole or pyrazole, Polymer 53 (2012) 1288−1297.
[17] A.B. Lowe, C.L. McCormick, Synthesis and solution properties of Zwitterionic polymers, Chem. Rev. 102 (2002) 4177−4190.

[18] T. Elschner, T. Heinze, Cellulose carbonates: a platform for promising biopolymer derivatives with multifunctional capabilities, Macromol. Biosci. 15 (2015) 735–746.
[19] S. Liu, J. Liu, A.R. Esker, K.J. Edgar, An efficient, regioselective pathway to Cationic and Zwitterionic N-heterocyclic cellulose ionomers, Biomacromolecules 17 (2016) 503–513.
[20] P. Xu, G. Bajaj, T. Shugg, W.G. Van Alstine, Y. Yeo, Zwitterionic chitosan derivatives for pH-sensitive stealth coating, Biomacromolecules 11 (2010) 2352–2358.
[21] N.B. Haro-Mares, J.C. Meza-Contreras, F.A. López-Dellamary Toral, R. González-Cruz, J.A. Silva-Guzmán, R. Manríquez-González, A simplified method of synthesis to obtain Zwitterionic cellulose under mild conditions with active ionic moieties, Molecules (Basel, Switzerland) 25 (2020).
[22] C. Laureano-Anzaldo, N. Haro-Mares, J. Meza-Contreras, J. Robledo-Ortíz, R. Manríquez-González, Chemical modification of cellulose with zwitterion moieties used in the uptake of red Congo dye from aqueous media, Cellulose 26 (2019).
[23] T. Heinze, M. Siebert, P. Berlin, A. Koschella, Biofunctional materials based on amino cellulose derivatives – a nanobiotechnological concept, Macromol. Biosci. 16 (2016) 10–42.
[24] L.C. Fidale, M. Nikolajski, T. Rudolph, S. Dutz, F.H. Schacher, T. Heinze, Hybrid Fe3O4@amino cellulose nanoparticles in organic media – heterogeneous ligands for atom transfer radical polymerizations, J. Colloid Interface Sci. 390 (2013) 25–33.
[25] S. Finger, M. Zieger, C. Wiegand, T. Liebert, T. Heinze, P. Elsner, et al., Biocompatibility and antibacterial effects of 6-Deoxy-6-aminoethyleneamino cellulose, J. Biosci. Med. 6 (2018) 51–62.
[26] N.S. El-Sayed, M. El-Sakhawy, P. Hesemann, N. Brun, S. Kamel, Rational design of novel water-soluble ampholytic cellulose derivatives, Int. J. Biol. Macromol. 114 (2018) 363–372.
[27] K. Rahn, M. Diamantoglou, D. Klemm, H. Berghmans, T. Heinze, Homogeneous synthesis of cellulose p-toluenesulfonates in N,N-dimethylacetamide/LiCl solvent system, Angew. Makromol. Chem. 238 (1996) 143–163.
[28] M. Zieger, M. Wurlitzer, C. Wiegand, K. Reddersen, S. Finger, P. Elsner, et al., 6-Deoxy-6-aminoethyleneamino cellulose: synthesis and study of hemocompatibility, Journal of Biomaterials Science, Polym. Ed. 26 (2015) 931–946.
[29] V. Butun, Selective betainization of 2-(dimethylamino)ethyl methacrylate residues in tertiary amine methacrylate diblock copolymers and their aqueous solution properties, Polymer 44 (2003) 7321–7334.
[30] R.F. Fischer, Propanesultone, Industr. Eng. Chem. 56 (1964) 41–45.