Study of Sulfonic Acid Esters from 1→4-, 1→3-, and 1→6-Linked Polysaccharides

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ABSTRACT: Sulfonic acid esters of differently linked polysaccharides including cellulose, dextran, lichenan, and pullulan were synthesized homogeneously applying *N,N*-dimethylacetamide/LiCl as the solvent. The dependence of the degree of substitution (DS) on the molar ratio of repeating unit to sulfonic acid chloride and on the structure of the reagent (benzene-, *p*-toluene-, 4-chlorobenzene-, 2,4-dinitrobenzene-, 2,4,6-trimethylbenzene-, and 2,4,6-triisopropylbenzene sulfonic acid chloride), as well as on the polysaccharide, was studied. DS values in the range of 0.2–2.3 were obtained. Bulky and electron withdrawing substituents on the aromatic ring inhibited ester formation. None of the sulfonic acid chlorides applied showed distinct regioselectivity. The polysaccharide sulfonic acid esters were soluble in organic solvents depending on the type of substituent and the degree of substitution. The molecular structure of the new polymers was confirmed by elemental analysis, FTIR, and ^{13}C-NMR spectroscopy. Subsequently, nucleophilic displacement reactions were carried out, which showed that the reactivity of the primary sulfonic acid ester group was higher than that of the secondary ones. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 100: 2142–2150, 2006

Key words: biopolymers; esterification; NMR; polysaccharides; structure

INTRODUCTION

Chemical functionalization of polysaccharides directly at the C atoms of the anhydrosugar unit is possible by the nucleophilic displacement reaction (S_N). An indispensable prerequisite for S_N is the transformation of the hydroxyl moieties to a leaving group, which can be achieved by sulfonic acid ester formation. Sulfonic acid esters are well-known leaving groups in low-molecular organic chemistry and have gained attention in the field of polysaccharides as well. Various cellulose sulfonic acid esters like *p*-toluenesulfonic acid (tosylates)-, methanesulfonic-, and trifluoromethanesulfonic acid esters have been studied in this context, as recently reviewed.[1] In particular, the influence of cellulose type and reaction conditions on the degree of substitution (DS) and the functionalization pattern of cellulose tosylates have been investigated.[2,3] Moreover, subsequent functionalization both by esterification of the remaining OH groups and by S_N reactions have been described.[4–6] Cellulose tosylates are the basis for advanced materials, for example, chemical-optical sensors with proteins covalently attached to the carrier using S_N reactions.[7,8] Furthermore, aminodeoxycellulose derivatives were obtained by S_N reactions of cellulose tosylates with mono- and bifunctional amines like triethylamine and 1-phenylethylamine.[9–11]

Regioselective functionalization—even by S_N reactions—is an important prerequisite for the elucidation of structure–property relationships. It is known that under homogeneous reaction conditions the reactivity of the hydroxyl groups in the solvent *N,N*-dimethylacetamide (DMA)/LiCl depends on the polysaccharide. In cellulose the OH group at position 6 shows the highest reactivity followed by positions 2 and 3 of the repeating unit. However, there is no regiospecific functionalization of position 6. In contrast, tosylation of starch yields a polymer with a preferred functionalization at position 2, as confirmed by ^{1}H-NMR spectroscopy.[12,13] The homogeneous tosylation of chitin in DMA/LiCl is possible as well.[14] Dextran tosylates prepared in an organic solvent without any salt also have been investigated.[15] Mocanu et al. reported the reaction of methanesulfonic acid chloride with crosslinked pullulan particles.[16] Information about tosylates of lichenan and pullulan is not available.

In the present article we describe the reaction of various polysaccharides including cellulose, dextran,

lichenan, and pullulan with sulfonic acid chlorides. Although tosylation of polysaccharides and their subsequent conversions have been reported in the past few years, the selective introduction of the leaving groups has not been achieved until now. The present study investigated, on the one hand, the reaction of cellulose with differently substituted benzenesulfonic acid chlorides to get information about their structure–reactivity relationships and, on the other, the conversion of lichenan, pullulan, and dextran to novel *p*-toluenesulfonic acid esters.

EXPERIMENTAL

Materials

Cellulose (Avicel® PH 101, Fluka, Buchs, Switzerland), dextran from *Leuconostoc ssp.* (M_w 70,000 g/mol; Fluka, Buchs, Switzerland), lichenan from *Cetraria islandica* (Sigma, Taufkirchen, Germany), and pullulan (M_w 100,000 g/mol; Aldrich) were dried in vacuum over potassium hydroxide at 105°C. Lithium chloride (Fluka, Buchs, Switzerland) was dried in vacuum at 150°C. Triethylamine was distilled over calcium hydride prior to use. All other reagents were used as received.

Measurements

The ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance 400 spectrometer working at 400.2 and 100.6 MHz, respectively, in dimethyl sulfoxide-d_6 or *N,N*-dimethylformamide-d_7 at 70°C. A polymer concentration between 5% and 10% (w/v) was chosen. Standard pulse sequences (Bruker, Rheinstetten, Germany) for proton decoupled ^{13}C-NMR spectra and DEPT135 NMR spectra were applied. A Nicolet Avatar 370 (Thermo electron, Bremen, Germany) device was used for the acquisition of FTIR spectra (KBr pellets). Elemental analyses were obtained from a Vario ELIII (Elementar Analysensysteme, Hanau, Germany). The halogen content was determined by a titration method after combustion.

Synthesis of cellulose 4-chlorobenzenesulfonic acid ester (sample **7b**)

For a typical preparation, 1.0 g (6.17 mmol) of cellulose was slurried in 25 mL of *N,N*-dimethylacetamide (DMA) and stirred for 1 h at 130°C. The temperature was decreased to 100°C followed by the addition of 1 g of LiCl. While cooling down to room temperature and further stirring, the polymer dissolved completely. At a temperature of 8°C, a solution of 7.4 mL (53.09 mmol, 1.7 mol/mol 4-chlorobenzene sulfonic acid chloride) of triethylamine in 2.5 mL of DMA and subsequently 6.5 g (31.85 mol, 5 mol/mol anhydroglu-

cose unit, AGU) of 4-chlorobenzene sulfonic acid chloride in 10 mL of DMA were added dropwise. The mixture was stirred for 24 h at 8°C and poured into ice water. After filtration the precipitate was carefully washed with water and ethanol and dried in vacuum at 60°C.

> Yield: 2.24 g (97%), degree of substitution 1.23,
> ELEM. ANAL. C, 41.67; H, 3.35; S, 10.38; Cl, 13.30.
> IR (KBr): 3342 (νOH), 3066 (νCH, aromat), 2891 (νCH), 1587 (νC=C$_{aromat}$), 1449 (δCH), 1365 (ν_{as}SO$_2$), 1193 (ν_sSO$_2$), 1061 (νCOC), 815 (δCH$_{aromat}$).

Conversion of cellulose 4-chlorobenzenesulfonic acid ester with sodium iodide (sample **14**)

For this conversion, 1 g (2.5 mmol) of cellulose 4-chlorobenzenesulfonic acid ester (sample **7b**, DS 1.23) was dissolved in 35 mL of acetylacetone. After the addition of 1.67 g (11.1 mmol) of dry sodium iodide, the mixture was stirred for 2 h at 130°C. The polymer was isolated by precipitation in ethanol and filtration. For purification, it was carefully washed with water and stirred in 200 mL of ethanol overnight. Subsequently, it was stirred in a 1*M* Na$_2$S$_2$O$_3$ solution for 1 h, washed with ethanol, and dried in vacuum at 60°C.

> Yield: 0.41 g (96%).
> ELEM. ANAL. C, 31.97; H, 3.03; S, 5.01; chlorine and iodine, 49.96.
> IR (KBr): 3310 (νOH), 3093 (νC—H$_{aromat}$), 2887 (νC—H), 1583 (νC=C$_{aromat}$), 1478 (δCH), 1372 (δCH$_3$, ν_{as}SO$_2$), 1190 (ν_sSO$_2$), 1098 (νC—O—C), 825 (δC—H$_{aromat}$).

Conversion of cellulose 4-chlorobenzenesulfonic acid ester with sodium azide (sample **17**)

For this conversion, 0.56 g (1.4 mmol) of cellulose 4-chlorobenzenesulfonic acid ester (sample **7b**, DS 1.23) was slurried in 30 mL of dry *N,N*-dimethylformamide. After the addition of 0.46 g (7 mmol, 5 mol NaN$_3$/mol modified AGU) of NaN$_3$, the mixture was stirred for 24 h at 100°C. The polymer was precipitated in ice water, washed with water and ethanol, and dried in vacuum at 60°C.

> Yield: 0.29 g (89%).
> ELEM. ANAL. C, 34.19; H, 4.02; N, 11.44; S, 4.02; Cl, 1.85.
> IR (KBr): 3353 (νOH), 2900 (νC—H), 2108 (νN$_3$), 1591 (νC=C$_{aromat}$), 1373 (δCH$_3$, ν_{as}SO$_2$), 1158 (ν_sSO$_2$), 1060 (νC—O—C), 826 (δC—H$_{aromat}$).

RESULTS AND DISCUSSION

The dissolution of polysaccharides is a useful activation method under laboratory-scale conditions. Ho-
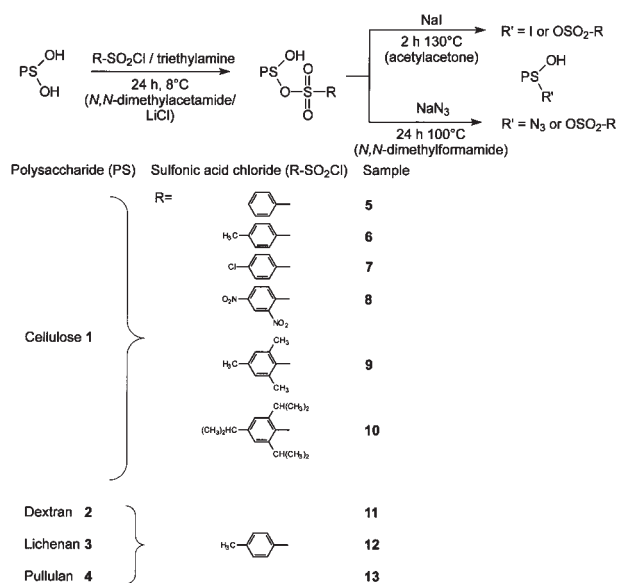
Figure 1 Reaction scheme for the conversion of polysaccharides with sulfonic acid chlorides and the subsequent nucleophilic displacement reactions.

mogeneous conversion of polysaccharides is known to yield products with an even distribution of substituents along the polymer chain. The synthesis of polysaccharide sulfonic acid esters was carried out in N,N-dimethylacetamide (DMA)/LiCl as the nonderivatizing solvent applying sulfonic acid chlorides, as summarized in Figure 1.

Influence of steric and electronic effects on the reaction of sulfonic acid chloride with cellulose

The reactivity of the various reagents may have varied because of steric and electronic effects, which also may influence the formation of cellulose sulfonic acid esters in the degree of substitution (DS) and the functionalization pattern. It is well known that regioselective derivatization can be achieved with the use of bulky reagents, which are widely used for the selective protection of primary OH groups by the formation of triphenylmethyl ethers or trialkylsilyl ethers bearing at least one bulky substituent. Therefore, it was of interest to study the regioselectivity of differently substituted sulfonic acid chlorides. The objective of this research was to achieve the exclusive derivatization of the primary OH group of a polysaccharide with sulfonic acid ester moieties, which enables subsequent nucleophilic displacement (S_N) reactions. Sulfonic acid ester groups at secondary hydroxyl functions are hard to split off and undergo S_N reactions under strong conditions only, at least in cellulose.[1] The reaction of cellulose with 5 mol p-toluenesulfonic acid (tosyl) chloride/mol anhydroglucose unit (AGU) yielded a polymer with DS 2.30 (sample **6a**), which is

the maximum DS known up to now (Table I).[2] Further alkyl substituents in the aromatic ring strongly increased the steric demand of the reagent. With 2,4,6-trimethylbenzenesulfonic acid chloride (molar ratio 1 : 5, sample **9c**), a low DS of 0.82 was realized compared to with tosylation. Lower molar ratios (1 : 0.5, sample **9a**; 1 : 1.5, sample **9b**) yielded no or a small amount of functionalized products. The more bulky reagent 2,4,6-triisopropylbenzenesulfonic acid chloride did not react with cellulose (0.72% sulfur, sample **10c**) even if excess reagent was applied (molar ratio 1 : 5). The chlorine content of samples **6a** and **9c** was low (0.43% and 0.33%) compared to 2.00% (sample **10c**). Obviously, the formation of some chlorodeoxy moieties occurred as a result of the S_N reactions.

The results clearly show the influence of the steric hindrance of the reagent on the DS. Regioselective esterification, that is, the preferred reaction at the primary OH groups from the steric effect, could not be achieved.

The mechanism of sulfonic acid ester formation was the attack of the electrophilic sulfur of the reagent on the nucleophilic oxygen of the OH group. The electrophilic property of the sulfur atom may be controlled depending on the substituent attached at the aromatic moiety. Tosyl chloride carrying a methyl group (electron-donating effect) yielded a derivative with the highest DS (DS 2.30, sample **6a**). The reactivity of the benzenesulfonic acid chloride without any substituent decreased. A cellulose benzenesulfonic acid ester with a DS of 1.43 (sample **5b**) was obtained with a molar ratio of 5 mol reagent/mol AGU. A lower molar ratio (1 : 0.5) yielded a product with a DS of only 0.21 (**5a**). Chloro- and nitro group substituted reagents showed interesting behavior. 4-Chlorobenzenesulfonic acid chloride is less reactive than benzenesulfonic acid chloride or tosyl chloride. The conversion of cellulose with 5 mol reagent/mol AGU yielded a product with a DS of 1.23 (sample **7b**). With a molar ratio of 1 : 0.5, no reaction occurred (0.06% sulfur, sample **7a**). An even more drastic influence was found for 2,4-dinitrobenzenesulfonic acid chloride. The reaction with a molar ratio of 1 : 0.5 led to a product with 0.29% sulfur (sample **8a**). By increasing the molar ratio from 1 : 0.5 to 1 : 1.5, a cellulose derivative with a slightly increased DS of 0.20 (sample **8b**) could be synthesized. However, even with 5 mol reagent/mol AGU, a comparable low DS of 0.42 was found (sample **8c**). Moreover, a high chlorine content was determined (3.49%, sample **8c**), indicating that a rather fast S_N reaction occurred compared to that with other derivatives under the conditions applied.

The influence of the steric effect on reactivity is of course superseded by the electronic effects of the alkyl moieties in the aromatic ring. However, electronic effects on the reactivity of benzenesulfonic acid chlorides with cellulose are difficult to understand. Although chloro and nitro groups increase the reactivity of acid chloride, the experimental results showed that

TABLE I
Synthesis of Sulfonic Acid Esters of Cellulose Dissolved in _N,N_-Dimethylacetamide/LiCl
in the Presence of Triethylamine (24 h at 8°C)

Conditions			Elemental analysis (%)		Degree of substitution[b]		
Reagent	Molar ratio[a]	No.	S	Cl	DS_S	DS_{Cl}	Solubility[c]
Benzenesulfonic acid chloride	1:0.5	5a	3.56	0.57	0.21	0.03	insoluble
	1:5.0	5b	12.57	1.14	1.43	0.12	DMA, DMF, DMSO
_p_-Toluenesulfonic acid chloride	1:5.0	6a	14.20	0.43	2.30	0.06	DMA, DMF, DMSO, acetone, THF, CHCl₃
4-Chlorobenzenesulfonic acid chloride	1:0.5	7a	0.06	0.56	0.003	0.03	insoluble
	1:5.0	7b	10.38	13.30	1.23	n.c.	DMA, DMF, DMSO, acetone, THF
2,4-Dinitrobenzene-sulfonic acid chloride	1:0.5	8a	0.29	0.30	0.02	0.01	insoluble
	1:1.5	8b	2.17	0.33	0.20	0.02	DMA, DMF, DMSO
	1:5.0	8c	5.11	3.49	0.42	0.26	DMA, DMF, DMSO, acetone, THF, CHCl₃
2,4,6-Trimethylbenzene-sulfonic acid chloride	1:0.5	9a	0.37	0.94	0.02	0.04	insoluble
	1:1.5	9b	4.20	0.72	0.28	0.04	DMSO
	1:5.0	9c	8.44	0.33	0.82	0.03	DMA, DMF, DMSO
2,4,6-Triisopropyl-benzenesulfonic acid chloride	1:0.5	10a	0.03	0.27	0.002	0.01	insoluble
	1:1.5	10b	0.75	1.39	0.04	0.07	insoluble
	1:5.0	10c	0.72	2.00	0.04	0.1	insoluble

[a] Anhydroglucose unit: sulfonic acid chloride, 2 mol triethylamine/mol sulfonic acid chloride.
[b] Degree of substitution (DS) of sulfonic acid ester (index S) and chlorodeoxy (index Cl) groups; n.c., not calculated.
[c] DMSO, dimethyl sulfoxide; DMF, _N,N_-dimethylformamide; DMA, _N,N_-dimethylacetamide; THF, tetrahydrofuran.

conversions of 4-chloro- and 2,4-dinitrobenzenesulfonic acid chloride yielded products with a low DS compared to reactions with tosyl chloride. It may also be possible that the stability of these compounds against hydrolysis was decreased compared with that of the _p_-toluenesulfonic acid esters of cellulose. Hence, a loss of ester functions during the standard workup procedure may have occurred, that is, high reactivity is connected to low stability.

The solubility of cellulose derivatives depends on both the type of substituent and the DS as well as on the distribution of the substituents within the AGU and along the chain. The solubility of cellulose tosylate was extensively studied.[2] Polymers with a DS > 0.4 are soluble in aprotic-dipolar solvents like DMA, _N,N_-dimethylformamide (DMF), and dimethyl sulfoxide (DMSO). Beginning at a DS of 1.4, they dissolve in less polar media like dioxan and tetrahydrofuran (THF), and they become soluble in chloroform with a DS > 1.8. Cellulose benzenesulfonic acid esters with low DS are insoluble. Sample **5b** (DS 1.43) dissolved in DMA, DMF, and DMSO. The cellulose 4-chlorobenzenesulfonic acid ester **7b,** with a DS of 1.23 also was soluble in acetone and THF. However, the 2,4-dinitrobenzenesulfonic acid ester possessed lower solubility limits than the benzenesulfonic and tosyl esters. For instance, a polymer

with a DS of 0.20 (sample **8b**) was already soluble in DMA, DMF, and DMSO. Sample **8c** was, despite the comparably low DS of 0.42, soluble in aprotic-dipolar solvents and also in acetone, THF, and chloroform.
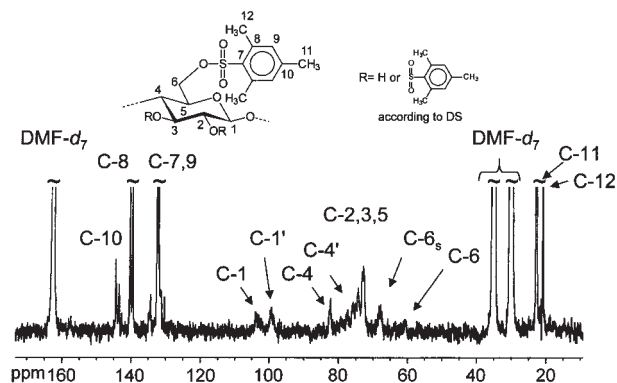
Structure characterization

Structure characterization was carried out by FTIR and ¹³C-NMR spectroscopy. In addition, S_N reactions
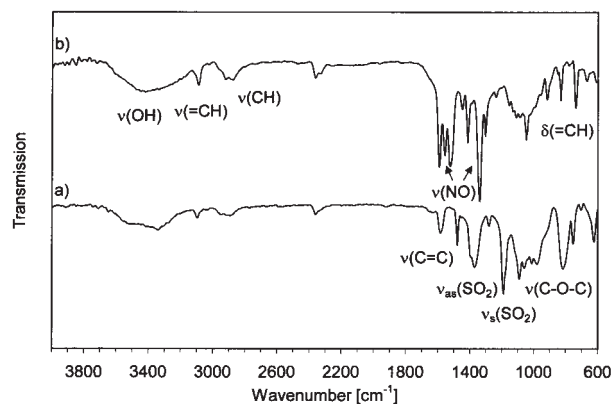
Figure 2 FTIR spectra of cellulose 4-chlorobenzenesulfonic acid ester: (a) **7b** (degree of substitution, DS 1.23) and cellulose 2,4-dinitrobenzenesulfonic acid ester (b) **8c** (DS 0.42).

Figure 3 ^{13}C-NMR spectrum of cellulose 2,4,6-trimethyl-benzenesulfonic acid ester **9c** in dimethylformamide-d_7 (degree of substitution, DS 0.82; number of scans, 13,800). Index *s* means substituted; prime (′) means influenced by substitution at a neighboring carbon atom.

with sodium iodide and sodium azide were used to estimate the functionalization pattern in the AGU.

Representative FTIR spectra of cellulose 4-chlorobenzenesulfonic acid ester **7b** and the 2,4-dinitrobenzenesulfonic acid ester **8c** (Fig. 2) showed the typical absorption bands for the cellulose backbone at 3400 ν(OH), 2900 ν(CH), 1061 cm^{-1} ν(COC). Signals of the aromatic ring appeared at 3090–3096 ν(=C—H), 1584–1592 ν(C=C), and 817–832 cm^{-1} δ(=C—H). Moreover, ν_{as}(SO$_2$) was detected at 1338–1371 cm^{-1} and ν_s(SO$_2$) at 1154–1189 cm^{-1}. The C—Cl vibration of the 4-chlorobenzene moiety (sample **7b**) could not be clearly assigned because of superposition with other signals. Sample **8c** contained nitro groups, which caused a signal at 1523 cm^{-1}. The second N—O absorption band overlapped with the signal of the sulfonyl group around 1340 cm^{-1}.

It is difficult to analyze cellulose sulfonic acid esters by NMR spectroscopy because the cellulose backbone and the aromatic substituents have very different peak intensities. This is because the behavior of the polymer chain differed from that of the comparably more mobile substituents, leading to an apparently different

signal intensity that did not reflect the real ratios of the signals corresponding to the DS. Moreover, the ^{13}C-NMR spectra were not acquired under nuclear Overhauser effect–free conditions, which also generates different signal intensities. Nevertheless, by having a long acquisition time, the weak signals of the modified AGU appeared alongside the strong peaks of the aromatic ester moieties. A representative spectrum of a cellulose 2,4,6-trimethylbenzenesulfonic acid ester with a DS of 0.82 (sample **9c**) is shown in Figure 3. The peaks at 20.9–22.9 ppm were caused by the carbon atoms of the methyl groups of the benzene ring. Signals of the AGU appeared between 60 and 102 ppm. A weak signal at 60 ppm indicated an unmodified position 6. The peak at 67 ppm was assigned to the functionalized primary hydroxyl group. Moreover, the resonances of carbon atoms 2, 3, and 5 were detected between 72 and 77 ppm. The peak at 82.2 ppm was assigned to C-4. In addition, two signals were found for position 1, indicating functionalization with an ester moiety at position 2. The chemical shifts of the aromatic carbon atoms were in the range from 129.7 to 143.5 ppm. The clearly visible splitting of the signals for C-1 and C-6 indicates that both the primary and secondary hydroxyl groups were partially esterified.

Sulfonic acid esters can be modified by S$_N$ reactions with nucleophilic reagents like azide or iodide ions. I$^-$ is considered to react preferentially with the sulfonic acid esters of the primary hydroxyl groups. Therefore, iodination was a useful tool for distinguishing between primary and secondary ester functions. Nevertheless, it has to be taken into account that this reaction does not proceed quantitatively.[17–19] In most cases, the overall DS after the S$_N$ reaction was lower than the DS of the starting material. Some selected cellulose sulfonic acid esters were treated with sodium azide and sodium iodide (Table II). The combustion analysis of the products may be doubtful because impurities of inorganic salts influenced the results as well. Therefore, FTIR spectroscopy was used to show the presence of deoxyiodo and deoxyazido groups (Fig. 4). The C-I vibration appeared at 500 cm^{-1} but

TABLE II
Nucleophilic Displacement Reaction of Cellulose Sulfonic Acid Esters with Sodium Iodide and Sodium Azide

Cellulose sulfonic acid ester				Reaction product					
	No.	Reagent	DS$_S$[a]	No.	Iodine (%)	Nitrogen (%)	Sulfur (%)	DS[b]	DS$_S$[a]
4-Chlorobenzene	7b	NaI	1.23	14	49.96[c]	—	5.01	0.56	0.53
2,4-Dinitrobenzene	8c	NaI	0.42	15	3.06	—	1.97	0.04	0.12
Benzene	5b	NaN$_3$	1.43	16	—	20.10	2.74	1.02	0.18
4-Chlorobenzene	7b	NaN$_3$	1.23	17	—	11.44	4.02	0.62	0.29
2,4-Dinitrobenzene	8c	NaN$_3$	0.42	18	—	0.32	0.00	0.01	0

[a] Degree of substitution of sulfonic acid ester groups.
[b] Degree of substitution of deoxyiodo (conversion with NaI) and deoxyazido groups (conversion with NaN$_3$), see Table I.
[c] Halogen content (Cl and I).
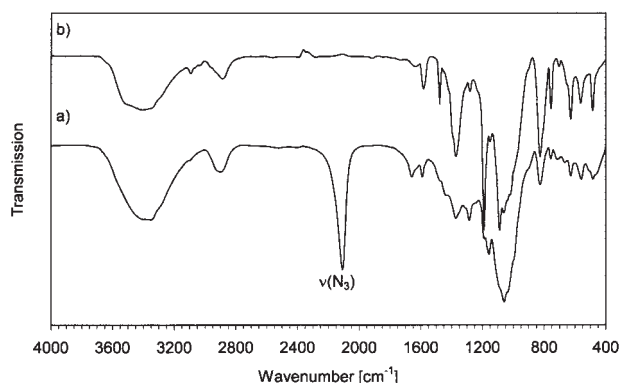
Figure 4 FTIR spectra of (a) deoxyazido cellulose **17** and (b) deoxyiodo cellulose **14** starting from the cellulose 4-chlorobenzenesulfonic acid ester **7b**.

sodium azide led to product **17,** with a DS_N of 0.62 and a DS of 0.29 of the sulfonic acid ester groups. Obviously, the reactivity of the 4-chlorobenzenesulfonic acid moiety was lower than that of the benzenesulfonic acid ester of cellulose. However, a cellulose 2,4-dinitrobenzenesulfonic acid ester (DS 0.42, sample **8c**) could not be converted to a deoxyazido derivative. The polymer obtained contained only 0.32% nitrogen and no sulfur (sample **18**). That means that the sulfonic acid ester was cleaved, and the hydroxyl groups were regenerated.

was not easy to assign, whereas the specific absorption band of the N_3 function could be clearly observed in the range from 2107 to 2110 cm^{-1}.

The iodination of 4-chlorobenzene sulfonic acid ester **7b** (DS 1.23) revealed a DS of deoxyiodo groups (DS_I) of 0.56 and a DS 0.53 of the remaining 4-chlorobenzenesulfonic acid ester groups (sample **14**). However, the reaction of cellulose 2,4-dinitrobenzenesulfonic acid ester **8c** (DS 0.42) yielded sample **15** with 3% iodine only, corresponding to a DS_I of 0.04. This result may lead to the conclusion that the partial DS at position 6 was lower than those of sample **7b**.

The conversion of cellulose benzenesulfonic acid ester (DS 1.43, sample **5b**) with azide ions yielded a product with a content of deoxyazido groups (DS_N) of 1.02% (sample **16**). The benzenesulfonic acid ester groups (DS 0.18) remained in the polymer. A similar result was found for the cellulose 4-chlorobenzenesulfonic acid ester, **7b** (DS 1.23). The conversion with

p-Toluenesulfonic acid esters of dextran, lichenan, and pullulan

Although information about the tosylation of cellulose and starch is accessible, knowledge about tosyl esters of dextran, lichenan, and pullulan is poor. Consequently, dextran **2**, lichenan **3**, and pullulan **4** were allowed to react with 0.5, 1.5, and 5 mol tosyl chloride homogeneously in a DMA/LiCl solution (see Fig. 1 and Table III).

Unlike the other polysaccharides investigated in this study, dextran contains only secondary hydroxyl functions. The treatment with 0.5 mol reagent/mol repeating units yielded a product with a DS of 0.08 (**11a**), showing the typical solubility of dextran in DMA, DMF, and DMSO. Using 1.5 mol reagent, the DS was increased to 0.75 (sample **11b**), and with 5 mol reagent/mol repeating units, even a DS of 1.39 was achieved (sample **11c**), indicating that the secondary OH$^-$ groups readily reacted under these conditions. In contrast to tosyl cellulose, the polymers dissolved in THF, acetone, and chloroform at comparable low DS values (DS 0.75: soluble in THF; DS 1.39: soluble in acetone and chloroform).

TABLE III
Conditions for and Results of Reactions of Different Polysaccharides Dissolved in *N,N*-Dimethylacetamide/LiCl with *p*-Toluenesulfonic Acid Chloride in the Presence of Triethylamine for 24 h at 8°C

| Polysaccharide | Molar ratio[a] | No. | Elemental analysis (%)[b] | | Degree of substitution[c] | | Solubility[d] |
			S	Cl	DS_S	DS_{Cl}	
Dextran	1 : 0.5	11a	1.54	0.32	0.08	0.03	DMSO, DMA, DMF
	1 : 1.5	11b	8.63	0.21	0.75	0.02	DMSO, DMA, DMF, THF
	1 : 5.0	11c	11.83	0.22	1.39	0.02	DMSO, DMA, DMF, THF, acetone, CHCl$_3$
Lichenan	1 : 0.5	12a	3.02	0.39	0.18	0.02	DMSO
	1 : 1.5	12b	10.48	0.26	1.07	0.02	DMSO, DMA, DMF
	1 : 5.0	12c	12.25	n.d.	1.51	n.c.	DMSO, DMA, DMF, THF, acetone
Pullulan	1 : 0.5	13a	3.58	0.25	0.22	0.01	DMSO, DMA, DMF
	1 : 1.5	13b	8.88	0.34	0.79	0.03	DMSO, DMA, DMF, THF
	1 : 5.0	13c	11.25	0.61	1.25	0.06	DMSO, DMA, DMF, THF, acetone

[a] Repeating unit: *p*-toluenesulfonic acid chloride, 2 mol triethylamine/mol *p*-toluenesulfonic acid chloride were used as base.
[b] n.d., not determined.
[c] Degree of substitution of *p*-toluenesulfonic acid ester (index S) and chlorodeoxy (index Cl) groups; n.c., not calculated.
[d] DMSO, dimethyl sulfoxide; DMF, *N,N*-dimethylformamide; DMA, *N,N*-dimethylacetamide; THF, tetrahydrofuran.
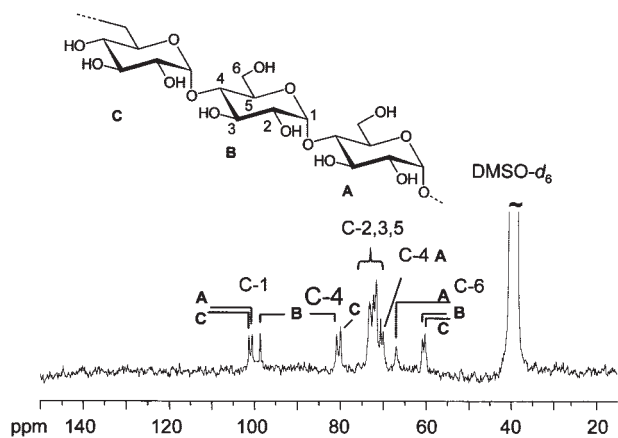
Figure 5 ^{13}C-NMR spectrum of pullulan recorded in dimethyl sulfoxide-d_6. **A**, **B**, and **C** are the three sugar rings of the pullulan repeating unit (number of scans: 10,200).

With lichenan, unlike with dextran, a DS of 0.18 was achieved by applying 0.5 mol tosyl chloride/mol repeating units (sample **12a**). The DS of sample **12c** (DS 1.51, 5 mol reagent/mol repeating units) was slightly increased compared to the dextran derivative. The reaction of pullulan with 0.5 mol reagent/mol repeating units yielded sample **13a** with a DS of 0.22. The DS could be increased to 1.25 (5 mol reagent/mol repeating units, sample **13c**). In summary, the tosylation of lichenan yielded the product with the highest DS (1.51, sample **12c**), whereas DS values of 1.39 (dextran, sample **11c**) and 1.25 (pullulan, sample **13c**) were reached by applying excess reagent (5 mol/mol AGU).

Structure characterization was carried out by ^{13}C-NMR spectroscopy. The spectrum of pullulan (Fig. 5) showed well-resolved signals, especially the peaks for C-1, C-4, and C-6 of the repeating unit. The chemical shift values are given in Table IV. Further NMR experiments were carried out in order to characterize the tosyl pullulan, sample **13c**. The spectrum was acquired by applying the DEPT135 technique in order to increase sensitivity [Fig. 6(a)]. Compared with the resolution for the spectrum of pure pullulan, the resolution of the NMR spectra of the pullulan derivatives was lower. However, the presence of all structural features could be proved. The signals of the tosyl moiety appeared at 21.5 ppm (CH$_3$) and 128–130 ppm

(aromatic carbon atoms). Note that the signals for C-7 (~130 ppm) and C-10 (~145 ppm) did not appear in the DEPT135 NMR spectrum because of their nature as quaternary carbon atoms. The peak at 60.19 ppm was attributed to position 6 of the **C** ring, which was not influenced by tosylation. A second methylene group was detected at 64.77 ppm, which might be tosylated position 6 of the **B** ring. The chemical shift of this carbon atom without a substituent was 60.8 ppm. The methylene signal at 68.4 ppm could be assigned as tosylated position 6 of the **A** ring. Further signals of the modified repeating unit were detected in the range of 70.4–80.2 ppm (positions 2–5). The peaks of the anomeric carbon atoms (position 1) were shifted about 4 ppm high field and appeared as separated signals at 96.3, 95.5, and 94.7 ppm. Moreover, two peaks of low intensity were detected between 41 and 46.7 ppm, which might have been a result of deoxychloro moieties because the tosyl pullulan contained 0.61% chlorine.

The subsequent conversions of dextran-, lichenan-, and pullulan tosylates with sodium iodide were performed (Table V). After iodination of dextran tosylate (DS 1.39, sample **11c**), a product with a DS$_I$ of 0.18 and a DS$_S$ of 1.06 (sample **19**) was obtained, indicating that only a few tosyl groups were substituted. A possible conclusion is that tosylated secondary OH groups also reacted or that a small amount of tosylated primary OH groups was in the polymer as a result of deviation from the uniform α-(1→6)-linked backbone. According to Leathers,[20] dextran also may contain branches with primary OH moieties at the end groups. As discussed above, the S$_N$ reaction does not proceed only at the tosylated primary OH groups. For cellulose tosylates, secondary tosyl groups also can react to a small extent.[17–19] For tosyl lichenan (DS 1.51, sample **12c**), iodination indicated ester moieties bound to both primary and secondary OH groups (DS$_I$ 0.45, DS$_S$ 0.26, sample **20**). Tosyl pullulan **13c** yielded a deoxyiodo derivative with a DS$_I$ of 1.05 and a DS$_{Tos}$ of 0.26 (sample **21**).

A preliminary investigation of the S$_N$ reaction of the new polysaccharide tosylates with sodium azide was carried out (Table V). The conversion of tosyl dextran **11c** (DS 1.39) with NaN$_3$ yielded a polymer with a DS$_N$ of 0.62 and a DS$_S$ of 0.66 (sample **22**). Nearly 45% of

TABLE IV
Peak Assignment of ^{13}C-NMR Spectrum of Pullulan in Dimethyl Sulfoxide-d_6

	Position					
Ring	1	2	3	4	5	6
A	101.4	70.7–73.2		69.98	70.7–73.2	67.0
B	98.7	70.7–73.2		80.84	70.7–73.2	60.8
C	100.7	70.66–73.25		79.96	70.7–73.2	60.2

According to Figure 4 (chemical shifts in ppm).
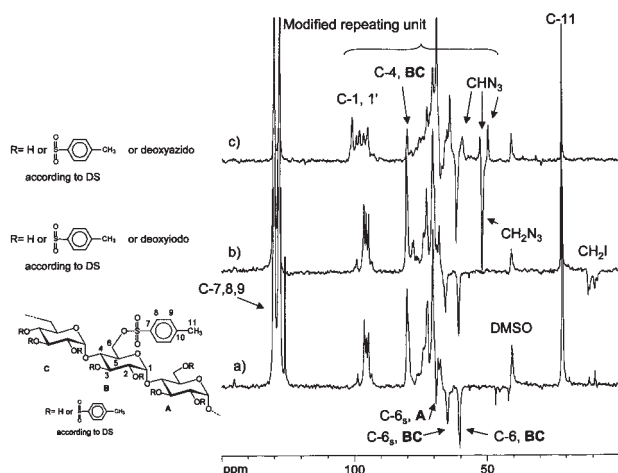
Figure 6 DEPT135-NMR spectra of (a) pullulan *p*-toluenesulfonic acid ester **13c** (degree of substitution, DS 1.25), (b) deoxyiodo pullulan **21**, and (c) deoxyazido pullulan **24** recorded in dimethyl sulfoxide-d_6. **A**, **B**, and **C** are the three sugar rings of the pullulan repeating unit (number of scans: **13c,** 6930; **21,** 69,300; **24,** 112,600).

the tosyl moieties were substituted. Almost 75% of the tosyl groups of lichenan tosylate **12c** were replaced by deoxyazido functions (DS_N 1.14, DS_S 0.26, sample **23**). A similar result was found for pullulan tosylate **13c** (DS 1.25). Compared to with lichenan, it yielded a lower DS_N (0.84, sample **24**) that corresponded to a replacement of 67% of the tosyl groups (DS_S 0.26 after conversion). The higher DS_N values of the lichenan and pullulan derivatives compared with the dextran compound may have been a result of the presence of primary tosyl functions of higher reactivity.

The structure of the deoxyiodo and deoxyazido derivatives was characterized by NMR spectroscopy. Examples of these spectra, the DEPT135 NMR spectra of deoxyiodo pullulan **21** and deoxyazido pullulan **24,** are shown in Figure 6. In the NMR spectrum of sample **21** the typical signals of the tosyl moiety appear as discussed for tosyl pullulan **13c** [Fig. 6(b)]. Moreover,

two methylene groups were detected at 8.9 and 11.5 ppm that represent the CH_2I moiety as the result of displacement of the primary tosyl groups bound to the **A** and **B** rings of the pullulan repeating unit. However, detailed assignment was not possible. Additional signals of the modified repeating unit appeared in the range from 60 to 100 ppm. The peaks of the anomeric carbon atoms showed a high-field shift of about 4 ppm, indicating the presence of functional groups at position 2. In the NMR spectrum of sample **24**, the intensive resonance of the CH_2N_3 group was detected at 51.7 ppm. The additional signals with nearly the same chemical shift might be caused by deoxyazido moieties at positions 2 and 3 of the modified repeating unit. An exact peak assignment was not possible by two-dimensional NMR spectroscopy because no sufficient resolution appeared. Nevertheless, the region of the anomeric carbon atoms was significantly different from those of pullulan and derivatives **13c** and **21**. For deoxyazido pullulan **24**, this region was broad, which might be a hint of differently modified positions 2. In addition, the typical signals of the tosyl group were clearly detected.

CONCLUSIONS

The homogeneous reaction of polysaccharides with sulfonic acid chlorides represents a useful method for the preparation of organosoluble sulfonic acid esters. In contrast to heterogeneous phase reaction, the incorporation of halogendeoxy moieties was low. A distinct influence of the type of sulfonic acid chloride, that is, its steric and electronic nature, on the degree of substitution (DS) of the cellulose sulfonic acid esters was observed. Although benzene- and *p*-toluenesulfonic acid chloride readily react with cellulose, bulky sulfonic acid chlorides showed remarkably lower reactivity. However, electron-withdrawing substituents in the aromatic ring also led to decreased reactivity. Solubility in the organic solvents depended on both ester

TABLE V
Nucleophilic Displacement Reaction of *p*-Toluenesulfonic Acid Esters of Dextran, Lichenan,
and Pullulan with Sodium Iodide and Sodium Azide

p-Toluenesulfonic acid ester				Reaction product					
Polysaccharide	No.	$DS_S{}^a$	Reagent	No.	Iodine (%)	Nitrogen (%)	Sulfur (%)	DS^a	$DS_S{}^b$
Dextran	11c	1.39	NaI	19	8.70	—	9.64	0.18	1.06
Lichenan	12c	1.51	NaI	20	28.05	—	3.05	0.45	0.26
Pullulan	13c	1.25	NaI	21	12.80	—	9.01	1.05	0.26
Dextran	11c	1.39	NaN$_3$	22	—	9.26	7.59	0.62	0.66
Lichenan	12c	1.51	NaN$_3$	23	—	20.70	3.56	1.14	0.26
Pullulan	13c	1.25	NaN$_3$	24	—	15.67	3.74	0.84	0.26

^{a} Degree of substitution of *p*-toluenesulfonic acid ester groups (see Table III).
^{b} Degree of substitution of deoxyiodo (conversion with NaI) and deoxyazido groups (conversion with NaN$_3$).

type and DS. No sulfonic acid chloride investigated yielded a regioselectively esterified polysaccharide.

In addition, it was shown that the polysaccharides dextran, lichenan, and pullulan can be converted to their corresponding tosyl esters. The DS could be controlled by adjusting the molar ratio reagent/repeating unit. Sulfonic acid esters of polysaccharides opened various paths for subsequent polymer modifications, which is an interesting route for the preparation of new functional materials by either functionalization of the remaining hydroxyl groups or nucleophilic displacement reactions of the sulfonic acid ester moieties. Conversions with sodium iodide and sodium azide led to novel deoxyiodo and deoxyazido derivatives. The structures of the modified polysaccharides were confirmed by FTIR and NMR spectroscopy.

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