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Investigations on synthesis and characterization of carboxy-groups containing cellulose sulfates

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SUMMARY

Carboxymethyl cellulose and C-6-carboxy cellulose were treated with SO_3 and HSO_3Cl in DMF yielding the corresponding watersoluble sulfate half-esters. A preferred sulfation of primary hydroxyl groups was found by ^{13}C-n.m.r. spectroscopy. The potentiometric titration of the polyelectrolytes showed significant differences in the titration behaviour which can be explained by the different acidity of the carboxy groups in the two cellulose derivatives.

INTRODUCTION

Ionic polysaccharides possess a growing interest due to their gel- and symplex-forming tendency (1,2) and their biological activity (3). The properties of such polymers are influenced not only by the nature and the degree of substitution (DS) but also by the distribution within the anhydrosugar units.

Numerous papers have been published dealing with the synthesis and characterization of cellulose derivatives with one kind of ionic groups, e.g. carboxymethyl cellulose, and cellulose sulfate (4-6). Less attention has been paid to cellulosic polymers bearing two or more different ionic groups. Dependent on the content and the ionic strength of these charged groups a significant influence on the polyelectrolyte behaviour should to be expected.

Starting from carboxymethyl cellulose (CMC) and C-6-carboxy cellulose (COC) we investigated in this connection the sulfation of these carboxy-groups containing derivatives with SO_3/DMF and HSO_3Cl/DMF. Furthermore, preliminary results on the distribution of the introduced ionic substituents and the polyelectrolyte properties obtained by ^{13}C-n.m.r. spectroscopy and potentiometric titration resp. are presented.

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EXPERIMENTAL

Materials

The carboxymethylation of cellulose (wood sulfite pulp, DP 700) with monochloroacetic acid in the presence of NaOH was performed heterogeneously in an isopropanol/water mixture (7) (samples 1 and 2; DS_{COONa}: 0.47, 0.90 resp.) and also homogeneously with N-methylmorpholine-N-oxide as solvent in analogy to (8) (3: DS_{COONa}= 0.85). C-6-carboxy cellulose (samples 4 and 5; DS_{COONa}: 0.62, 0.42 resp.) was synthesized by oxidation of linters cellulose with $NaNO_2$ in H_3PO_4 according to the literature (9). The SO_3-DMF complex was obtained by distillation of fumic sulfuric acid and careful dissolution of the developed SO_3 in ice-cooled dry DMF.

Preparation of sulfate esters

For the purpose of activation the sodium salts of the carboxy-groups containing polymers were dissolved in water and precipitated into DMF followed by distillative removal of water under reduced pressure. To a stirred suspension of 15 mmol of the activated polymer in 80 ml of dry DMF were added 30 mmol of the sulfating agent dissolved in 30 ml dry DMF at 10°C. After stirring 3 h at 20°C the sulfate ester was isolated by precipitation into acetone and washed three times with acetone. It was then suspended in ethanol and neutralized with a solution containing 2 wt-% NaOH in ethanol/water (10:1 v/v). The obtained sodium salt of the sulfate half-ester was washed with ethanol/water (80:20 v/v) and dried to constant weight in vacuo. DS-values are given in Table 1.

^{13}C-n.m.r. spectroscopic measurement

The ^{13}C-n.m.r. spectra were recorded on a Bruker MSL 400 spectrometer operating at 100.63 MHz in the pulsed Fourier-transform mode with proton decoupling. The samples were measured at 20°C as 5-10 % (w/v) solutions in D_2O using sample tubes with a diameter of 10 mm and C_6D_6 as external standard. 500-2000 scans were accumulated.

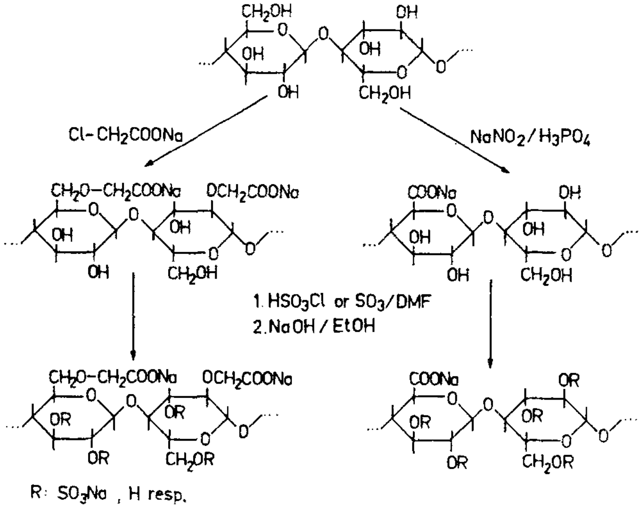
Potentiometric titration

The potentiometric titrations were carried out with a digital pH-meter (MV 870, Präcitronic, Germany) at 298±0.5 K using a combination glass electrode OP-08080 (Radelkis, Hungary). 50 ml of a 0.1 wt-% solution of the polyelectrolyte were titrated after ion-exchange with the cation-exchanger KP-2^R (Chemische Werke Wolfen, Germany) in water, 0.1 n and 1 n NaCl using 0.1 n NaOH. The dosage rate of the infudriver (infucont, Hungary) was 5-6 ml/h. The change of pH was registrated continuously by a plotter.

RESULTS AND DISCUSSION

Sulfation of carboxy-groups containing polymers

After a suitable pretreatment consisting in the precipitation of an aqueous CMC or COC solution in DMF and the removal of water from the highly swelled gel by distillation under reduced pressure the sulfation of the carboxy-groups containing polymers with SO_3 or HSO_3Cl yields the instable acidic sulfate half-esters. Subsequent neutralization leads to the watersoluble sodium salts of the corresponding esters (samples 6-10). A survey of the reaction path is given by the following scheme:



Using 2 moles of sulfating agent per mole modified anhydroglucose unit DS_S -values between 0.35 and 0.85 are received (Table 1). The sulfating power of HSO_3Cl is slightly higher compared with SO_3.

In contrast to the sulfation of COC the CMC samples go into solution after addition of the sulfating agent resulting in a homogeneous reaction and a slightly higher degree of sulfation.

Except the characteristic carboxy band at about 1615 cm^{-1} (ν COO$^-$) the IR spectra of the sulfated products show absorptions at 815 cm^{-1} (ν SO) and 1240 cm^{-1} (ν SO_2) indicating the presence of sulfate groups.

Table 1
Sulfation of CMC and COC in DMF for 3 h at 20°C

Starting polymers Sample	DS_{COONa}	Sulfating agent[a]	Yield %	Sulfate ester Sample	DS_S[b]
1 (CMC)	0.47	HSO_3Cl	78	6	0.85
2 (CMC)	0.90	SO_3	80	7	0.75
3 (CMC)	0.85	HSO_3Cl	65	8	0.83
4 (COC)	0.65	HSO_3Cl	68	9	0.35
5 (COC)	0.42	SO_3	73	10	0.45

[a] Using 2 moles per mole modified anhydroglucose unit (AGU)
[b] DS of sulfate ester groups calculated on the basis of sulfur content

^{13}C-n.m.r. spectroscopic investigations

The spectral data of the starting polymers and their sulfated products are presented in Table 2.

Table 2
^{13}C-n.m.r. chemical shifts of the starting polymers and the corresponding sulfate esters

Sample	Chemical shift (ppm)					
	C-1	C-2[a] C-2(c)[b] C-2(s)[c]	C-3[a] C-3(c)	C-4	C-5[a]	C-6 C-6(c) C-6(s)
2	103.1	73.9	75.6	78.2	74.3	60.7
	102.8	82.8	-			69.4
3	103.0	73.6	75.6	79.3	74.9	60.8
		82.8	83.8			70.9
6	102.9	74.8	73.5	78.4	73.5	-
	100.8	82.4	-			68.5
		80.3				66.9
7	102.9	75.2	74.0	78.8	74.0	60.8
	100.8	83.2	-			68.8
		81.0				67.3
8	103.2	75.0	73.5	78.2	73.5	-
	100.9	82.5	-			69.1
		80.3				66.8
4	102.9	73.6	74.9	79.2	76.0	60.8
					81.7	175.5
9	103.1	73.6	74.9	79.3	76.1	60.9
		-	-	75.7	81.6	175.4
						67.1

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[a] The unambiguous designation of the peaks C-2, C-3, and C-5 is complicated; the chemical shifts can be exchanged.
[b] c: C-atom bearing a carboxymethyl group or C-atom of a carboxy group
[c] s: C-atom bearing a sulfate ester group

Both the CMC samples (2, 3) show the signals for the unsubstituted C-6, C-2, and C-3 position at about 61 ppm, 74 ppm and 76 ppm as well as the peaks for the carboxymethylated C-6 and C-2 position in the region of 69-71 ppm and 83 ppm. A substitution of the C-3 position at about 84 ppm is detectable only to a very small extent. Recent studies (7, 10) have confirmed that in the carboxymethylation of cellulose performanced heterogeneously in aqueous media the reactivities of the hydroxyl groups at the positions C-2, C-3, and C-6 decrease in the order OH-2>OH-6>OH-3. For example, by Isogai et al. the distribution of carboxymethyl groups was determined to be in the ratio OH-2: OH-6: OH-3=1.9: 1.4:1 (11).

These outcomes are in good agreement with our own results on the CMC samples 1 and 2 prepared heterogeneously in the isopropanol/water medium. In the case of sample 3 (DS=0.85) carboxymethylated homogeneously in N-methylmorpholine-N-oxide as solvent we found a substituent distribution in the order C-6>C-2>C-3. A similar ratio of C-6:C-2:C-3= 1.4:1.0:1.0 at a total DS of 1.2 obtained in the solvent system SO_2/diethylamine/DMSO is known from the literature (11).

Fig. 1 shows the ^{13}C-n.m.r. spectrum of carboxymethyl cellulose sulfate 7 (DS_{COONa}=0.90, DS_S=0.75). In addition to the above mentioned peaks two new signals appear at 81 ppm and 67 ppm assigned to a sulfated C-2 and C-6 position, resp. Similar spectra were received from the other CMC sulfates 6 and 8 (Table 2). Generally, in the CMC sulfates a preferred sulfation of free OH-groups at the C-6 position is observed.

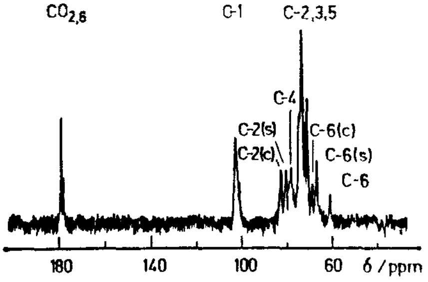

Fig. 1. ^{13}C-n.m.r. spectrum of sodium carboxymethyl cellulose sulfate 7

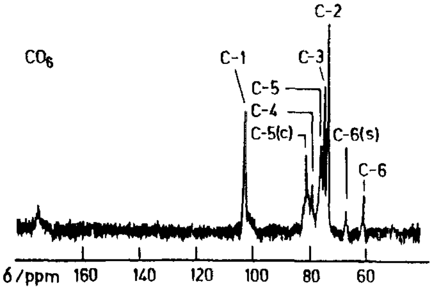

Fig. 2. ^{13}C-n.m.r. spectrum of sodium carboxy cellulose sulfate 9

As described previously, the treatment of cellulose with $NaNO_2$ in H_3PO_4 results in an exclusive oxidation of primary OH-groups at the C-6 position to carboxy groups (9). It is visible in the ^{13}C-n.m.r. spectrum by a decrease in the signal at 61 ppm and the appearence of a new peak at 175.5 ppm due to the C-6 atom of the formed carboxy group.
Fig. 2 shows the ^{13}C-n.m.r. spectrum of C-6-carboxy cellulose sulfate 9 (DS_{COONa} =0.62, DS_S =0.53). The peak at 67.0 ppm can be assigned to the carbon atom 6 bearing a sulfate ester moiety. A C-2 substitution is not unambiguously detectable because the signal indicating such a substitution overlaps with the peak of the C-5 atom. But also a splitting of the C-1 signal is not clearly visible refering to negligible substitution at this position. A preferred sulfation of OH-groups at the C-6 carbon atom may be concluded.

Results on potentiometric titrations

Fig. 3 and 4 demonstrate significant differences in the titration behaviour of a sulfated CMC in contrast to a sulfated COC in water, but not in the presence of low molecular salts (0.1 and 1 n NaCl).
Only in the case of the CMC derivative we found two distinctive inflection points. The first one can diminished by increasing the ionic strength of the system, because of the well known shielding effect of low molecular salts. The absence of a significant first inflection point in the case of the sulfated COC can be interpreted by an increase of acidity of these carboxy groups in comparison to CMC (compare also our results in (4)), resulting in a decrease of acidity-difference between COO^- and SO_3^- groups.

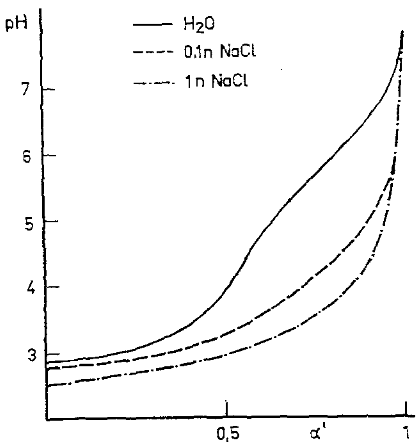

Fig. 3. Potentiometric titration curve of 7.

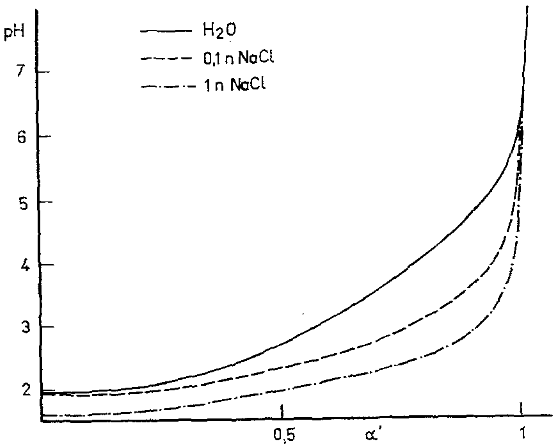

Fig. 4. Potentiometric titration curve of. 9.

CONCLUSION

The carboxy groups-containing polymers employed in the sulfation reaction differ in the number of carboxy or carboxymethyl groups situated at the C-6 position of the modified AGU. Dependent on the method of preparation in the CMC a slightly elevated or slightly diminished portion of C-6 substitution is observed compared to C-2 substitution. Contrary to this substituent distribution in the COC the carboxy groups are exclusively located at the C-6 position. Nevertheless, in all cases we found a preferred sulfation of the OH-groups at the C-6 carbon atoms. Only when the C-6 position is completely substituted a notable substitution of the secondary OH-groups takes place. This means that the carboxy groups at the C-6 position are not able to avoid a further substitution of residual primary OH-groups.

As it was shown by the results of the potentiometric titration the nature of the ionic groups has a remarkable influence on the polyelectrolyte behaviour of the cellulose derivatives. The influence of the different distribution of the two ionic groups within the anhydrosugar unit on specific properties as a heparin-like anitcoagulation activity and the gel- or simplex-formation is a further interesting aspect, which is now under investigation.

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