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Determination of the Ethylation Rate of Cellulose

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The reaction between ethyl chloride and the different hydroxyl groups in cellulose (dissolved and undissolved fibers) was studied. In both cases the substitution was much slower at C-3 than at C-2 and C-6. For the dissolved fibers the rate of reaction was proportional to the hydroxide concentration within the range 0.7 – 3 M sodium hydroxide. For the undissolved fibers the ratio of the rate constants for ethylation at C-2, C-3, and C-6 was found to be 7:1:6.5 and was virtually independent of the sodium hydroxide concentration.

In an earlier paper [1] the distribution of substituents in hydroxyethyl cellulose was determined. In this work the study has been extended to ethyl cellulose. The relative reactivities of the three hydroxyl groups in cellulose during the reaction with ethyl chloride or ethyl sulfate have been studied by several authors,[2–5] who all found that the hydroxyl group at C-3 was the least reactive. Mahoney and Purves [2] and Honeyman [3] found that the primary hydroxyl group at C-6 was the most reactive in contrast to Croon and Flamm [5] whose results indicated that the hydroxyl group at C-2 was the most reactive. The discrepancies may be explained by less satisfactory analytical methods. Considerable progress has been made in developing the analytical technique during the last ten years, and it was therefore of interest to reinvestigate the reaction between cellulose and ethyl chloride. It was also of interest to determine whether the results obtained in hydroxyethylation are valid when other substituents are introduced into cellulose.

EXPERIMENTAL

In the experiments with dissolved cellulose 3.0 g liquid ethyl chloride was added to a solution of 0.5 g hydrocellulose from rayon [1] in 35 ml aqueous sodium hydroxide (3 – 18 %). The reaction was performed at 20° in a tightly stoppered 100 ml round bottom flask with vigorous shaking so that the ethyl chloride was effectively dispersed in the sodium hydroxide solution. Since ethyl chloride has a low solubility in water and boils at 12°, an excess pressure (about 0.3 bar) was obtained in the flask. Blank experiments were performed without cellulose in order to determine the solubility of ethyl chloride in sodium hydroxide solutions and the decrease in sodium hydroxide concentration because of side reactions.

The ethylation was stopped by neutralization with hydrochloric acid after one and two weeks, respectively. After precipitation in one liter of acetone and filtration, the sodium chloride formed was removed by ultrafiltration (Diaflo Membrane) and washing with water. The derivative was dried in the air.

Purified cotton [6] was used in the experiments with undissolved fibers. The samples (2 g) were treated with aqueous sodium hydroxide (3, 10, and 18 %) at room temperature for 60 min and then pressed to a press-weight ratio of about 3.7. The finely divided cellulose was transferred to a stainless steel autoclave and liquid ethyl chloride (5 ml) was added. The autoclave was rotated in a polyglycol bath at 100° for 300 min and then cooled in ice. The reaction product was suspended in water and neutralized with hydrochloric acid. It was then washed in water and ethanol, sucked off on a Büchner funnel and dried.

The cellulose derivatives were hydrolyzed in sulfuric acid as described previously.[7] After neutralization with barium carbonate and evaporation under reduced pressure, the hydrolyzate was fractionated into four groups by partition chromatography on an anion exchanger in the sulfate form with aqueous ethanol (92.4 % w/w) as eluent.[8] A differential refractometer (Waters R401) was used to detect the chromatographic peaks. The first fraction contained tri- and disubstituted glucoses (s_{236}, s_{23}, s_{26}, and s_{36}), the second fraction glucoses monosubstituted at C-2 and C-3 (s_2 and s_3) and the two last fractions contained 6-*O*-ethylglucose (s_6) and glucose (s_0), respectively. The components of the different fractions were converted to their trimethylsilyl (TMS) derivatives [9] and determined quantitatively by gas chromatography on a QF-1 column (3 m; 3 % QF-1 on Gas Chrom Q 100/120 mesh) using a Perkin-Elmer 900 Gas Chromatograph. For s_{236} one peak was recorded and for the other derivatives two peaks were recorded. Xylitol was added as an internal standard to all fractions. The ratio, peak area/weight, of the derivatives relative to that of xylitol, was determined in calibration runs.

Reference substances of all ethylglucoses of interest were isolated from a hydrolyzate of highly substituted ethyl cellulose. After separating into four groups on the sulfate resin, the fractions were evaporated under reduced pressure and rechromatographed on a borate resin with boric acid as eluent.[10] The sugar derivatives were detected according to the orcinol method.[8] By choosing a suitable concentration and pH gradient of the eluent all ethylglucoses, except s_{236}, s_{23}, s_{26}, and s_2, could be completely separated. Almost pure substances of these derivatives were obtained by taking the fractions corresponding to the middle part of each elution band. The separation of a mixture of ethylglucoses on an analytical column is shown in Fig. 1. The boric acid in the collected fractions was removed by repeated addition of methanol and evaporation under reduced pressure.

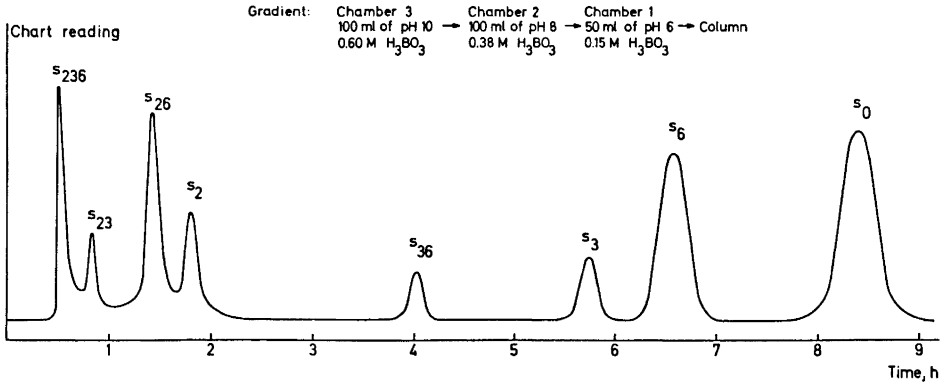

Fig. 1. Separation of a mixture of ethylglucoses as borate complexes by gradient elution at 70°. Resin bed: 2.4 × 1300 mm, Dowex 1-X8, borate form, 20 – 26 μm. Nominal linear flow: 3.9 cm min^{-1}. The Technicon gradient device (Autograd) was used. Chamber 2 was opened after 1 h and chamber 3 after 3.5 h.

The purity of the reference substances was controlled by gas chromatography of their TMS derivatives. A final confirmation of the identity of these derivatives was obtained by mass spectrometry. Since the spectra of the TMS derivatives of 2-*O*-ethylglucose and some methylglucoses are known,[11] the spectra of the other ethyl substituted glucoses could be predicted. The working conditions for mass spectrometry were the same as previously.[12]

The ethyl chloride concentration in the sodium hydroxide solutions in the blanks was determined after vigorous shaking over night. Without lowering the pressure an aliquot of the aqueous phase was taken and mixed with water containing a small amount of methanol, which was used as an internal standard. The diluted solution was directly analyzed on a Porapak N column using a Perkin-Elmer 990 Gas Chromatograph. It was necessary to clean the glass liner in the injection block often to get reproducible values. On the chromatogram traces of ethanol and diethyl ether could be seen. The solubility of ethyl chloride (S) in solutions of different sodium hydroxide concentrations ($0 < c < 5.5$ M) followed Setchenows equation, $\log (S_0/S) = kc$.

With the values $S_0 = 0.158$ and $k = 0.243$ (concentrations given as molarities) the calculated and experimental values agreed within 5 %.

RESULTS AND DISCUSSION

Chromatography on ion exchangers. Most glucose methyl ethers substituted at one or several of the hydroxyl groups at C-2, C-3, and C-6 can be easily separated by partition chromatography on an anion exchanger in the sulfate form with aqueous ethanol as eluent.[8] The corresponding ethyl ethers are not sufficiently polar to be well separated by the same technique. Even at an ethanol concentration of 95 % the two important ethers, s_2 and s_3, overlapped seriously. The method proved to be very useful for group separations of hydrolyzates of ethyl cellulose, however.

Chromatography of the sugar derivatives on the borate form of an anion exchange resin offers another way for analysis. This method has often been used for separations of unsubstituted sugars.[10] Among common sugars, glucose is held most strongly by the borate resin. This shows that favorable possibilities for complex formation must exist. In the pyranose form the hydroxyl groups of glucose are in a less favorable position for complex formation than in the furanose form.[13] This was in agreement with experiments on 4-*O*-methylglucose, which can only exist in the pyranose form. Its peak elution volume was about half of that for 2-*O*-methylglucose. The hydroxyl groups at C-1 and C-2 in α-glucofuranose are *cis* to each other and almost in the same plane, which provides excellent possibilities for borate complexes. The great importance of the C-1 – C-2 complex is demonstrated by the fact that all glucoses ethylated at C-2 are eluted much faster than the other derivatives studied. An inspection of a simple stereomodel of glucofuranose shows that borate complexes might also be formed with the following pairs of hydroxyl groups: C-5 and C-6, C-3 and C-5, C-3 and C-6. The complexes involving C-3 seem to exert a larger effect upon the retention than that with C-5 and C-6, since s_3 is eluted before s_6. These conclusions are supported by the fact that galactose is eluted before xylose.[10] Glucofuranose and galactofuranose have the same structure, except that the side chains containing C-5 and C-6 are located on opposite sides of the ring. This makes the formation of C-3 complexes impossible for galactofuranose. In xylofuranose complexes linked to C-3 and

Table 1. Relative intensity of peaks at $m/e = 191 - n44$ (J_1 series), $204 - n44$ (H_1 series) and $217 - n44$ [F_1 (G_1) series]. Only peaks greater than 1 % are included. The compounds represent one anomeric form (except for s_{236}, which only exhibited one peak on gas chromatography).

Compound	191	147	103	204	160	116	217	173	129
s_0	40	22	6	100	–	–	18	–	6
s_2	40	17	9	9	100	2	7	12	6
s_3	5	100	12	3	76	3	41	4	12
s_6	41	16	6	100	–	1	19	4	7
s_{23}	3	100	15	1	13	93	7	35	11
s_{26}	32	11	8	8	100	3	2	16	7
s_{36}	4	93	14	1	100	5	52	6	16
s_{236}	1	78	16	–	12	100	2	42	15

C-5 can exist, since xylofuranose has the same structure as glucofuranose, except that C-6 is missing.

Mass spectrometry. The identification scheme for the determination of the number and position of methoxyl substituents in TMS derivatives of methylated aldohexopyranoses given by Petersson and Samuelson [11] is also valid for the TMS derivatives of glucose ethyl ethers. The relative intensities of the peaks corresponding to the most interesting fragment ions are given in Table 1. Only small differences are observed when the intensities of these ions are compared with the corresponding ions from glucose methyl ethers.

Side reactions. During the ethylation of cellulose two side reactions compete with the main reaction:[14]

$$EtCl + OH^- \rightarrow EtOH + Cl^-$$
$$EtCl + EtOH + OH^- \rightarrow EtOEt + Cl^- + H_2O$$

In both reactions hydroxide ions are consumed. The formation of water and ethanol also contributes to a lowered hydroxide concentration. Titration of the blanks with sulfuric acid showed that under the applied conditions the decrease in alkalinity was a linear function of the time. After one week 95.3, 97.4, and 98.3 % of the sodium hydroxide was left in the solutions with the initial concentrations 3, 10, and 18 % sodium hydroxide, respectively. In Figs. 3 and 4 the mean values of the sodium hydroxide concentration during each experiment are used.

Blank experiments were also performed under the same conditions as with the reaction with undissolved fibres. Equal volumes of sodium hydroxide solutions and liquid ethyl chloride (about the same proportions as in the real experiments) were heated in autoclaves at 100° for 1, 2, and 5 h, respectively. The rapid decrease in sodium hydroxide concentration is shown in Fig. 2.

Reaction with dissolved fibers. Since ethyl chloride is only slightly soluble in sodium hydroxide solutions, the degree of ethylation was low even though the reaction times were one and two weeks for the reaction with dissolved cellulose. The D.S. values calculated from the composition of the hydrolyzate were 0.02 – 0.10. The relative rate constants for ethylation at C-2, C-3, and

C-6 (k_2:k_3:k_6) were obtained from the ratio of the amounts of the monosubstituted ethylglucoses in the hydrolyzate. The chromatographic analysis showed that disubstitution could be disregarded. The dependence of the relative reaction rates upon the sodium hydroxide concentration is given in Fig. 3. As can be seen from the figure a straight line relationship seems to exist between the relative rates and the hydroxide concentration. The broken lines represent the corresponding constants for the hydroxyethylation reaction.

The similarity between the two processes is striking. The lines representing the substitution at C-2 are parallel. The lines for the substitution at C-6 are almost parallel and exhibit a more pronounced dependence on the hydroxide concentration than those for the reaction at C-2. The difference between k_2 and k_6 is smaller for the ethylation than for the hydroxyethylation, except at low hydroxide concentration.

An attempt was made to calculate the rate constants (k_i') for the reaction between ethyl chloride and the different hydroxyl groups in cellulose using a similar method to that applied to the hydroxyethylation reaction.[15] It was assumed that at constant sodium hydroxide concentration the rate of ethylation is proportional to the ethyl chloride concentration [EtCl] and to the concentration of non-substituted hydroxyl groups. Since disubstitution could be disregarded, the rate of ethylation of a hydroxyl group at carbon atom i can be written:

$$d[s_i]/dt = k_i'[EtCl]([cell] - [s_i])$$

where [cell] is the molar concentration of glucose units (substituted or unsubstituted) and $[s_i]$ the molar concentration of glucose units with an ethyl group at carbon atom i. Only a small part of the ethyl chloride was consumed in side reactions and in the reaction with the dissolved cellulose. Most of the ethyl chloride remained undissolved. It was assumed that the ethyl chloride

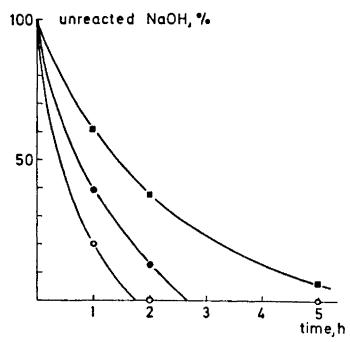

Fig. 2. Reaction between ethyl chloride and sodium hydroxide in autoclaves at 100°. ○, initial NaOH-concentration 3 %; ●, initial NaOH-concentration 10 %; ■, initial NaOH-concentration 18 %.

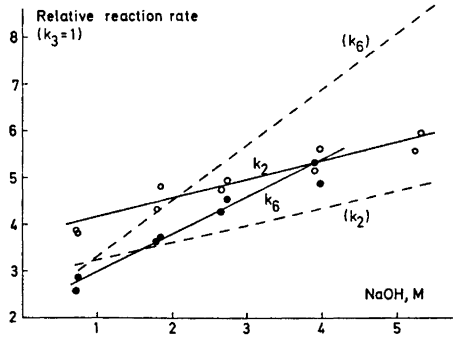

Fig. 3. Relative rate of ethylation of the different hydroxyl groups in cellulose as a function of the sodium hydroxide concentration ($k_3 = 1$). The broken lines and the constants within parenthesis refers to hydroxyethylation (1). ●, ethylation at C-6; ○, ethylation at C-2.

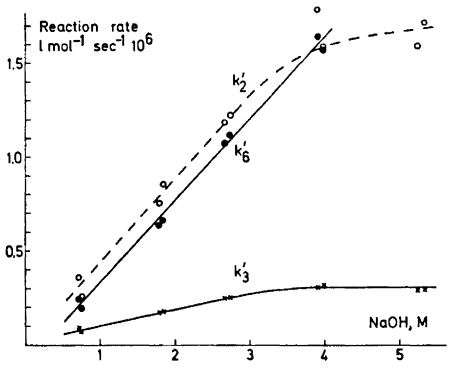

Fig. 4. Rate of ethylation of the different hydroxyl groups in cellulose as a function of the sodium hydroxide concentration.

concentration was constant in each experiment and the same as that determined in the corresponding blanks. Since $[s_i]$ is small compared to [cell], k_i' can be calculated from the following equation:

$$k_i' = [s_i]/([\mathrm{EtCl}][\mathrm{cell}]t)$$

The dependence of k_i' upon the hydroxide concentration is given in Fig. 4. From the figure it is seen that within the range 0.7 – 3 M sodium hydroxide a straight line relationship exists between the rate constants and the sodium hydroxide concentration. At concentrations greater than 4 M, k_3' is independent of the hydroxide concentration, whereas k_2' exhibits a less pronounced dependence upon the hydroxide concentration. Unfortunately, no reliable determinations of k_6' could be made at the highest concentration. The curves in Fig. 4 are similar to those in Ref. 15 for the reaction between ethylene oxide and cellulose. The hydroxyethylation was about 50 times faster than the ethylation. The similarity between the two reactions was not unexpected, since the ethylation also occurs *via* alkoxide ions. The amount of nucleophilic alkoxide ions seems to be mainly determined by the degree of dissociation, which depends upon the sodium hydroxide concentration. The ethylation is virtually determined by dissociation of the hydroxyl groups up to 3 M sodium hydroxide. The fact that k_3' is almost constant at high hydroxide concentration cannot be explained by a complete dissociation, since the hydroxyl group at C-3 is probably less acidic [16] than those at C-2 and C-6, of which the reactivities increase in this concentration range.

Reaction with undissolved fibers. The distribution of substituents after reaction with undissolved cellulose fibers is given in Table 2. Since, the gas chromatographic peaks corresponding to s_{23}, s_{36}, and s_{236} overlapped and were comparatively small, the amounts of these ethylglucoses were not determined in the hydrolyzate. The sum of the other ethylglucoses and glucose was set to 100 %, which gives rise to a negligible error in their relative amounts.

The distribution of substituents was calculated according to a statistical method suggested by Spurlin.[17] The best agreement between the observed and calculated values was obtained when the relative rate constants (k_2:k_3:k_6) were given the values 7:1:6.5. For the hydroxyethylation the corresponding

Table 2. Observed and calculated distribution of substituents (in mol %) for the reaction with undissolved fibers at different sodium hydroxide concentrations.

NaOH	3 %		10 %		18 %	
	found	calc.	found	calc.	found	calc.
s_0	95.2	95.2	72.9	72.7	43.8	43.7
s_2	2.2	2.3	11.2	12.1	21.0	21.5
s_3	0.3	0.3	1.5	1.6	2.2	2.6
s_6	2.2	2.1	10.8	11.2	18.9	19.7
s_{26}	0.1	–	3.6	1.9	14.1	9.6

relative rate constants were found to be 10:1:10.[1] The experimental and calculated amounts of all ethylglucoses investigated, except s_{26}, agreed fairly well as shown in Table 2. One of the assumptions made for the calculations was that the relative rate constants are constant throughout the reaction and that the substitution in one position does not affect the substitution in another position. The bad agreement for s_{26} indicates that this assumption could be invalid.

It was found that the relative rate constants were independent of the hydroxide concentration used in the sodium hydroxide treatment. Similar results were reported by Croon and Flamm [5] in their study of the ethylation of alkali cellulose prepared from cotton linters pulp after steeping in solutions of 16.4 and 32.2 % sodium hydroxide. In the present work experiments were made at such a high sodium hydroxide concentration (18 %) that the cellulose was completely transferred to Na-cellulose I, and at such a low concentration (3 %) that no change occurred. Evidently, the change in the supermolecular structure of cellulose has no influence upon the distribution of substituents.

It is interesting to note that in both the reaction of unbleached cotton treated with sodium hydroxide and in the reaction of the dissolved hydrocellulose with ethyl chloride the substitution was much slower at C-3 than at C-2 and C-6. The low reactivity of the hydroxyl group at C-3 can be explained by hydrogen bonding between this hydroxyl group and the ring oxygen of the adjacent glucose unit.[18]

Large differences in the relative rates during the reaction of ethylene oxide with dissolved rayon and with alkali cellulose were found previously [1] demonstrating that accessibility factors have a great influence upon the distribution of the substituents. The results obtained in the present work on ethylation lend support to this conclusion. It should therefore be expected that the relative rate constants should depend upon the source of cellulose material. This offers an explanation to the fact that the values obtained with cellulose from unbleached cotton in the present work differ more from those reported by Croon and Flamm for the reaction of bleached linters pulp than should be expected with regard to the experimental errors.

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