Determination of substituent distribution in cellulose ethers by means of a ^{13}C nuclear magnetic resonance study on their acetylated derivatives: 3. Hydroxyethylcellulose

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The distribution of substituent, i.e. oligo(ethylene oxide) groups, in hydroxyethylcelluloses having various values of molar substitution was determined by means of ^{13}C nuclear magnetic resonance after the acetylation of hydroxyl groups both at the unsubstituted position in the anhydroglucose unit and at the substituent end position of the parent hydroxyethylcellulose. The acetyl carbonyl signal of the acetylated hydroxyethylcellulose samples was found to split into a triplet in DMSO-d_6 at 100°C corresponding to the positions of acetyl groups (2, 3 or 6 overlapped with the substituent end) on the anhydroglucose unit. While in $CDCl_3$ at 40°C, the acetyl carbonyl signal for the substituent end position was observed to be separated from those on the anhydroglucose unit. By combining these results, the distribution of the substituent groups was determined for a series of hydroxyethylcellulose samples of a wide range of molar substitution values.

(Keywords: hydroxyethylcellulose; substituent distribution; ^{13}C n.m.r.; cellulose ethers; polysaccharides)

INTRODUCTION

Cellulose derivatives, produced through the reaction of hydroxyl groups in the 2, 3 and 6 position of the anhydroglucose ring unit, have been widely used in a variety of applications as indispensable polymeric materials based on a natural resource.

The control of the substituent distribution in addition to that of the total degree of substitution, *DS*, or the molar substitution, *MS*, becomes increasingly important along with the development of a variety of cellulose derivatives in the 'high-tech' and 'bio-tech' fields[1], where the precise molecular design is required to realize the desired property and function. Hence, the development of a reliable and convenient technique to provide the substituent distribution pattern of cellulose derivatives will be also of a significant importance.

We have recently proposed a new convenient analytical technique for the cellulose ethers, in which acetylated cellulose derivatives were studied using nuclear magnetic resonance (n.m.r.)[2–5]. This method has been so far applied to the structural analysis of such cellulose ethers as methyl-[2,4] and hydroxypropyl-[3,4] celluloses and was found to possess a number of advantages compared to preceding methods. The advantages are:

(1) acetylation of cellulose ethers can be easily performed and the acetylated derivatives become readily soluble in common n.m.r. solvents over a wide range of *DS*, facilitating the comparison with model polymers;

(2) the chemical shift of acetyl carbonyl carbon signals is highly sensitive to its location on the anhydroglucose ring unit to allow direct determination of the substituent distribution;

(3) the complete acetylation of hydroxyl groups can eliminate the spectral complication arising from the interaction through hydrogen bonds;

(4) the procedure can provide the analytical method for cellulose derivatives by retaining their polymeric form and avoid the troublesome hydrolysis pretreatment[6].

As an extension of our preceding studies, we describe here a structural study on hydroxyethylcellulose samples having various *MS* values using ^{13}C n.m.r. measurements of their acetylated derivatives[7].

EXPERIMENTAL

Samples

Hydroxyethylcellulose samples with a series of *MS* values were supplied from Shin-Etsu Chemical Co. Ltd. They were produced through the reaction of alkali cellulose with ethylene oxide. Acetylation of hydroxyethylcellulose samples was performed by the method described previously[2] and monitored by infra-red (i.r.) spectroscopy. Polyethylene glycol ($M_w = 2000$, Wako Pure Chemical Industry) was acetylated similarly. Cellulose triacetate (Aldrich) was used as received.

Measurements

^{13}C n.m.r. measurements were carried out at 67.8 MHz on a Jeol JNM GX270 spectrometer equipped with either

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a 5 or 10 mm i.d. C-H dual probe at 100°C in DMSO-d_6 or both at 40°C in $CDCl_3$ and in D_2O. Chemical shift values were referenced either using the solvent signal of DMSO-d_6 (43.5 ppm) and $CDCl_3$ (77.0 ppm) or the sodium salt of 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid (0.0 ppm) in D_2O. The quantitative ^{13}C n.m.r. measurements were carried out using a 10 mm i.d. C-H dual probe with a pulse repetition time of 100 s (ref. 3).

Gas–liquid chromatography (g.l.c) analyses on hydrolysate of hydroxyethylcellulose were carried out according to the method described previously in the case of hydroxypropylcellulose[3] where the distribution of anhydroglucose unit with different *MS* values was allowed to be quantitatively determined.

I.r. measurements were performed with a Jasco model IR-810 spectrophotometer, and film samples of hydroxyethylcellulose and its acetylated derivative were prepared by casting on a Teflon plate from an aqueous and acetone solutions, respectively.

Chemical analyses of hydroxyethylcellulose samples were performed according to the literature[8] after slight modification.

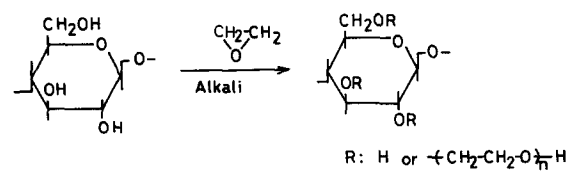
RESULTS AND DISCUSSION

As hydroxyethylcellulose is produced (*Scheme 1*) through the reaction of alkali cellulose with ethylene oxide by anionic ring opening polymerization, the substituent is comprised of a mixture of oligo(ethylene oxide) having various degrees of polymerization. Thus, the *MS* value, which refers to the number of the ethylene oxide units in an anhydroglucose unit, is commonly used for the notation of a hydroxyethylcellulose sample.

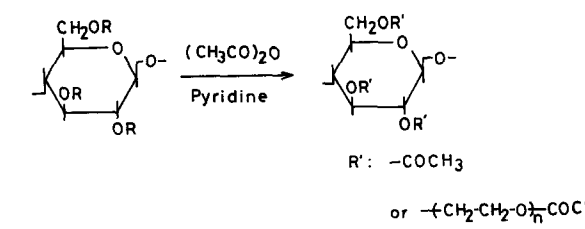
In addition to the traditional chemical analysis to provide the *MS* value, a number of chromatographic[9] or spectroscopic[10–14] techniques have been used in the structural study of hydroxyethylcellulose. The g.l.c. technique[9] was reported to provide a detailed distribution pattern of the oligo(ethylene oxide) substituent on the anhydroglucose unit of hydroxyethylcellulose samples, where careful pretreatments including methylation, hydrolysis, reduction and acetylation were required prior to g.l.c. to avoid any undesired degradation and loss of the sample.

Scheme 1

Preparation of Hydroxyethylcellulose



Acetylation of Hydroxyethylcellulose



As alternative versatile analytical techniques, ^1H (ref. 10) and ^{13}C n.m.r.[11–14] methods have also been widely applied in the structural analysis of hydroxyethylcellulose either in its intact polymeric form[11,12] or after hydrolysis[13,14]. Although the analytical method with the intact polymer is considered to be much advantageous, its practical applicability has been seriously limited due to the poor solubility of the cellulose derivative in common n.m.r. solvents over a wide range of *DS* (or *MS*). In the present study, the acetylation pretreatment of the hydroxyl groups both at the unsubstituted position on the anhydroglucose unit and at the substituent end position of the parent hydroxyethylcellulose was performed by refluxing with acetic anhydride/pyridine mixture. The complete acetylation of the hydroxyl groups was confirmed by i.r. spectroscopic analysis, where the hydroxyl absorption at 3300 cm^{-1} disappeared along with the formation of the ester absorption at 1735 cm^{-1}. The acetylated derivatives of hydroxyethylcellulose samples were found to become readily soluble in common n.m.r. solvents like $CDCl_3$ and DMSO-d_6 over the whole *MS* range examined (namely 0–3.5).

The full range spectra of an untreated hydroxyethylcellulose and of its acetylated derivative are shown in *Figure 1*. The spectrum of the acetylated hydroxyethylcellulose sample measured in DMSO-d_6 clearly exhibited resolved signals in such regions as C_1 at around 100 ppm and carbonyl at around 170 ppm, reflecting the substituent distribution pattern of the parent hydroxyethylcellulose. In contrast, the spectrum of the intact hydroxyethylcellulose obtained in D_2O showed only ill-resolved signals of the carbons in the anhydroglucose unit to provide only limited structural information.

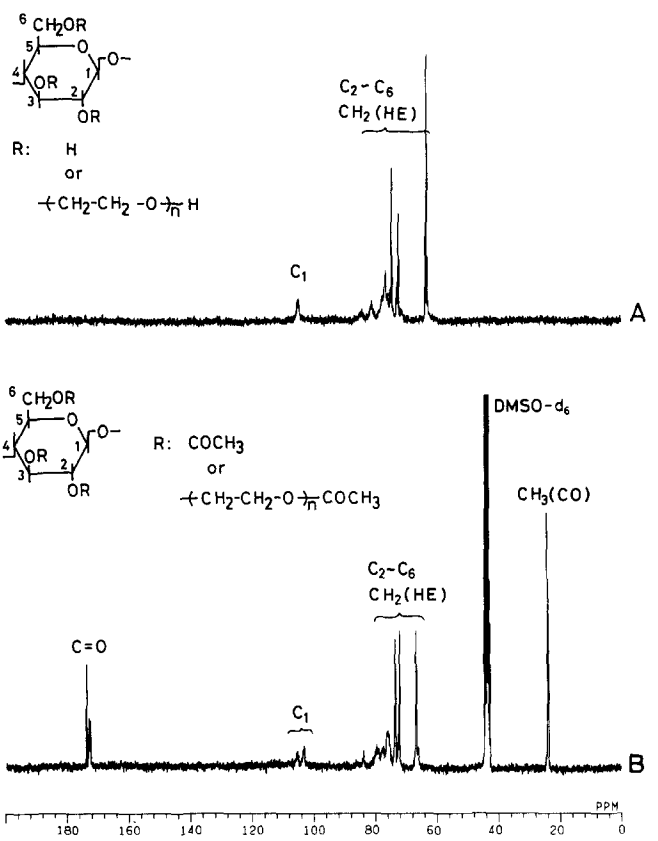


Figure 1 ^{13}C n.m.r. spectra of hydroxyethylcellulose (A) in D_2O at 40°C and its acetylated derivative (B) in DMSO-d_6 at 100°C. *MS* of the sample is 1.32

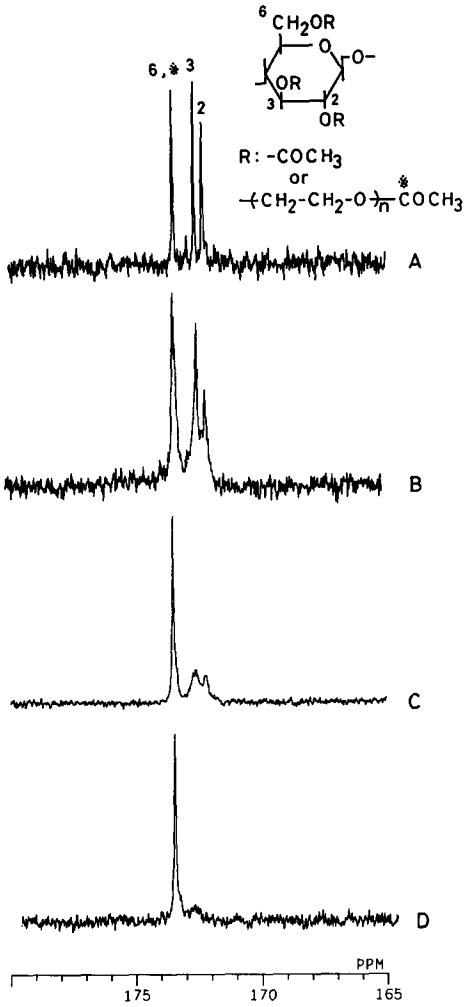


Figure 2 ^{13}C n.m.r. carbonyl region spectra of cellulose triacetate (A) and acetylated hydroxyethylcellulose (*MS* of sample: B, 0.47; C, 1.32; D, 2.88) in DMSO-d_6 at 100°C

The C_1 carbon resonance split into two peaks after acetylation; the peak at 105.4 ppm being due to the C_1 carbon with the neighbouring oligo(ethylene oxide) substituent at the C_2 position, and the peak at 102.9 ppm being due to that with the acetyl group at C_2 position.

The expanded carbonyl region spectra for a series of *MS* samples measured in DMSO-d_6 at 100°C are shown in *Figure 2*, where the spectrum of cellulose triacetate is also given for comparison. The acetyl carbonyl signal of cellulose triacetate was observed as a triplet at 172.2, 172.6 and 173.4 ppm, corresponding to C_2, C_3 and C_6 positions of the anhydroglucose unit[15–17]. The acetyl carbonyl signal of acetylated hydroxyethylcellulose samples remained to be resolved into a triplet irrespective of the *MS* value, though a notable signal broadening occurred. The signal of acetyl carbonyl carbon at the substituent end position was overlapped with that of the C_6 position at 173.4 ppm. Since all the hydroxyl groups were acetylated, the *DS* on C_2 and C_3 positions could be determined from the peak intensities at the C_2 and C_3 positions relative to the total intensity of the carbonyl region. On the other hand, the *DS* on C_6 and subsequently the total *DS* are not directly obtainable. The *DS* value on the C_2 position thus obtained was compared with that from the C_1 signal analysis and both were found to agree well (*Table 1*).

It should be noted that the spin-lattice relaxation time, T_1, is significantly longer for the acetyl carbonyl carbon at the substituent end position (ca. 10 s) compared with those directly attached on the anhydroglucose unit (2–3 s)[3]. Thus quantitative measurements for the determination of the *DS* values were carried out with the pulse repetition time of as long as 100 s using the 10 mm i.d. probe.

The total *DS* of hydroxyethylcellulose samples could be determined through the ^{13}C n.m.r. measurement of the acetylated hydroxyethylcellulose in $CDCl_3$ at 40°C.

Table 1 Structural parameters of hydroxyethylcellulose samples

Sample	*MS*[a]	Total *DS*	*DS* of individual position		
			2[b]	3	6[c]
1	0.47	0.60	0.28	0	0.32
	0.42		0.24		0.37
2	1.32	1.34	0.46	0.13	0.75
	1.37		0.42		0.73
3	2.88	2.61	1.00	0.67	0.94
	3.01		n.d.[d]		0.88

[a] By chemical (upper) and g.l.c. (lower) analyses
[b] From carbonyl (upper) and C_1 (lower) region ^{13}C n.m.r. spectra obtained in DMSO-d_6
[c] By the calculation from the equation of total $DS - DS(C_2) - DS(C_3)$ (upper) and by the subtraction of the substituent end fraction from the signal area overlapped with C_6 (lower)
[d] Not determined

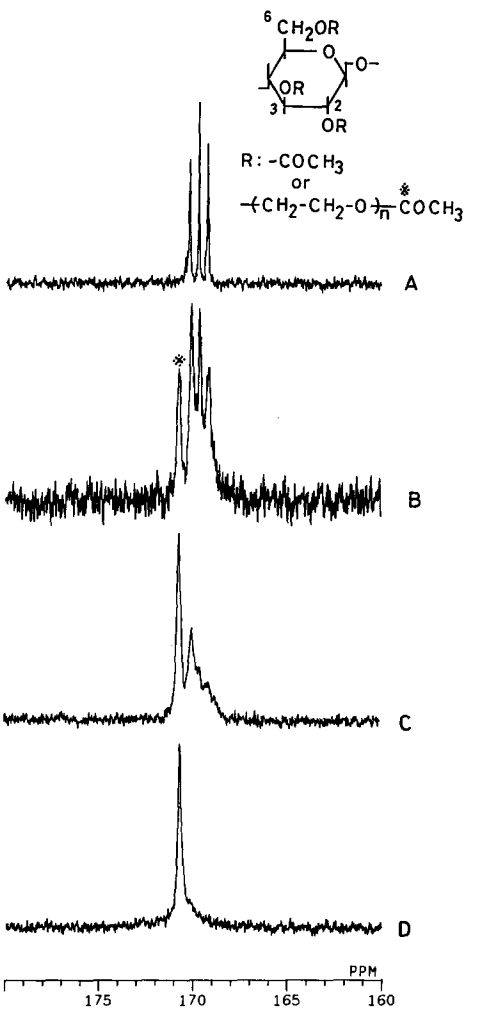


Figure 3 ^{13}C n.m.r. carbonyl region spectra of cellulose triacetate (A) and acetylated hydroxyethylcellulose (*MS* of sample: B, 0.47; C, 1.32; D, 2.88) in $CDCl_3$ at 40°C

The expanded acetyl carbonyl region spectra of a series of acetylated hydroxyethylcellulose samples together with a cellulose triacetate sample are shown in *Figure 3*. The characteristic signal at 170.8 ppm, which was assigned to the acetyl carbonyl carbon at the substituent end position by comparing its chemical shift value to that of the acetylated polyethylene glycol, increased its intensity along with the *MS* value of the sample. On the other hand, the carbonyl carbon signals of acetyl groups directly attached to the anhydroglucose unit were observed to collapse together to give an ill-resolved broad signal. This was presumably due to the interaction between the substituents on the different substituent positions on the anhydroglucose unit as was previously noticed in the case of methylcellulose[2]. The total *DS* of the hydroxyethylcellulose samples was thus estimated by dividing the signal area of the substituent-end carbonyl carbon by those directly attached to the anhydroglucose unit.

Finally, by combining the results described above, the *DS* on the C_6 position could be determined by subtracting the sum of the *DS* values on the C_2 and C_3 positions from the total *DS* value. An alternative method to give the *DS* value on the C_6 position is to subtract the signal area of the substituent end fraction from those overlapped with the signal on the C_6 position at 173.4 ppm in the spectrum measured in DMSO-d_6. These values agreed well as listed in *Table 1*.

The *DS* values of the individual substitution positions on hydroxyethylcellulose samples with a wide range of *MS* values were thus determined and are given in *Table 1*. The reactivity order of the hydroxyl groups on an anhydroglucose ring unit was found to be $C_6 > C_2 > C_3$, which coincides with previous reports[9,13]. It might appear peculiar that the *MS* values estimated by chemical analysis and by g.l.c. were lower than the total *DS* value determined by the present n.m.r. technique (particularly notable for the sample of low *DS* (or *MS*)). The possibility of an incomplete chemical conversion or hydrolysis, and of a loss of the sample during the analytical procedure in the former analytical methods might well account for the lowering of the experimental *MS* values.

In conclusion, the present n.m.r. technique using acetylated derivatives of cellulose ethers has proven to be a convenient and reliable method to determine the substituent distribution of the parent cellulose ethers. Further applications of the present technique to other cellulose derivatives[5] as well as other polysaccharides are now in progress in our laboratory.

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