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Carbon-13 NMR of Hydroxyethylcellulose: An Accurate Method for Structural Determination

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Synopsis

The high-resolution carbon-13 NMR spectrum of hydroxyethylcellulose (HEC) with about 2.5 moles of ethylene oxide (MS 2.5) average substitution per anhydroglucose ring (AHG) is presented. From models, the CMR chemical shifts for all of the different carbon atoms are assigned. Direct measurement of the relative intensities of the CMR signals for certain carbon atoms in HEC permits rapid and accurate computation of (1) the average chain length of poly(ethylene oxide); (2) the degree of substitution of ethylene oxide, and (3) the average relative degree of substitution of the alcohol groups on the AHG ring.

INTRODUCTION

Because of its complexity, the microstructure of hydroxyethylcellulose (HEC) has not been subject previously to definitive spectroscopic examination. The determination of reactivity ratios of and the degree of substitution of the alcohol groups in cellulose and HEC with ethylene oxide have been restricted to indirect wet methods which, at their best, have been approximate.[1]

Recent carbon-13 NMR (CMR) studies of polymers have demonstrated the value of this technique as a probe for polymer structure.[2] We now report the CMR-spectroscopic study of HEC with about 2.5 moles of ethylene oxide average substitution (HEC MS 2.5) per anhydroglucose (AHG) unit. The elucidation of important structural parameters of this polymer by CMR spectroscopy demonstrates the power of this tool as a probe for the structure of derivatized cellulose.

EXPERIMENTAL

The polymer samples studied were commercial samples obtained from Hercules, Inc. Low-viscosity grades for ease of sample preparation and an MS of about 2.5 for high resolution of the polyethylene oxide signals (Hercules, Inc., 250L grade) were selected (see Table II for specific lot number). Two of the three lots studied were treated with warm ethanol by Soxhlet extraction to remove poly(ethylene oxide) and other low molecular weight polymer materials.

CMR spectra were recorded on a Varian CFT-20 spectrometer at 75°C in an 8-mm tube at 10% w/v in D_2O with 3-(trimethylsilyl)-1-propanesulfonic acid

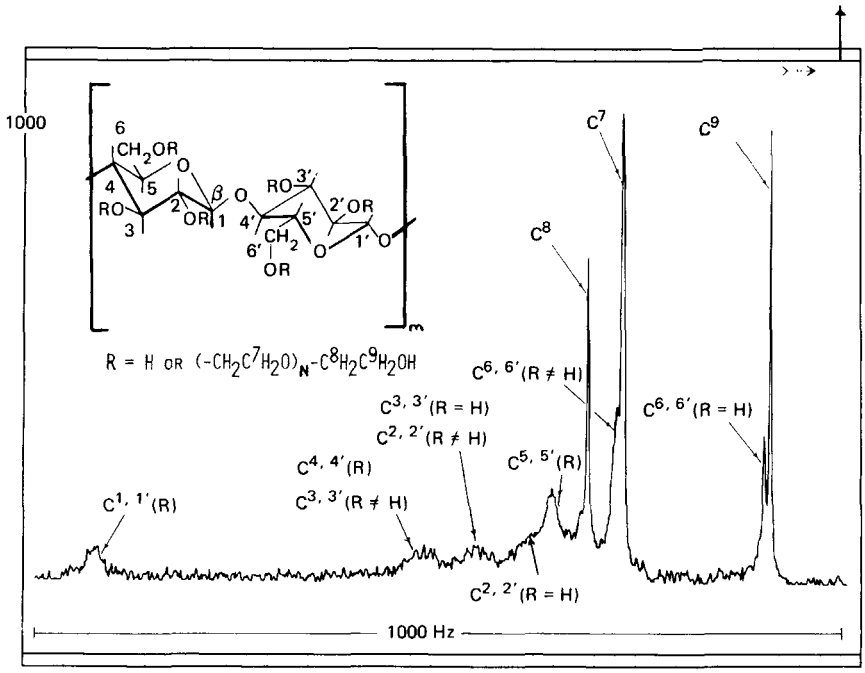

Fig. 1. CMR spectrum of HEC MS 2.5.

sodium salt (DSS) as an internal standard. Chemical shifts are reported relative to tetramethylsilane (TMS) and an RL = $\Delta\delta$ (DSS–TMS) = −33.2 Hz was used in all cases.

Solutions were prepared by adding 0.18 cc of the D_2O to an 8-mm CMR tube. The solid polymer, 200 mg, was then added to this tube and the remaining 1.6 cc D_2O was added. The tube was allowed to stand until the polymer was swollen with D_2O, and the mixture was then heated at 60°C with agitation to effect solubilization. The sample was then allowed to stand for four days to ensure a uniform solubilization and distribution of the sample in the tube. Samples prepared in this manner gave reproducible CMR spectra with a given set of spectral parameters.

The problems of differing relaxation times (RT) and Nuclear Overhauser Enhancement (NOE) and their effect on the accuracy of CMR spectral integration are well documented.[2,3,4] It has been noted for polymers, principally by Schaefer and co-workers,[3] that for carbon atoms at or near the chain backbone, the error introduced by differing NOE is substantially diminished. This is especially true for carbons with the same number of protons attached. The effect of differing RT's on polymer CMR spectra is substantially eliminated overall by very fast relaxation through segmental motion.[5]

To prevent any possible perturbation of the integration of the CMR spectra of polymers studied in this work, we have made measurements with parameters selected to eliminate the effects of RT and NOE. Relaxation times for the —$\underline{C}H_2OH$ and $C\underline{C}H_2$—O—C carbon atoms in HEC MS 2.5 were measured by the saturation recovery method with a homospoil pulse sequence (TT = 15, α = 90°, LT = 0.02, LI = 2.0 sec, AM = 30, HS = 5, ST = 4) for nondegassed 10% w/v solutions in D_2O. None of the RT's determined for HEC MS 2.5 exceeded 200 ms.

The parameters selected to acquire quantitative CMR data include an interval between pulses which substantially exceeds the maximum relaxation time of 200 ms (e.g., $AT > 10 \times RT_{max}$). This was accomplished with a spectral width of 1100 Hz, 8192 data points, $AT > 3.0$ sec, $\alpha = 90°$, and a 0.05-sec pulse delay for homospoil. It was determined also that the relative intensity data obtained from planimetry of the signals for C^7, C^9, and $C^{6,6'}$ collected from 20,000 transients were identical to those obtained with gated decoupling (suppressed NOE) for the same samples.

Planimetry of the CMR signals for C^7, C^9, and $C^{6,6'}$ was found to be a reliable method for determining the relative area of these lines. For the overlapping lines of $C^{6,6'}$ R = H with those of C^9 and C^7, respectively, (see Fig. 1) planimetry of exactly one-half of the high field half of the C^9 and C^7 signals (determined by dropping a perpendicular from peak to center baseline) eliminates any substantial error due to overlap. Three different samples, with three runs on each sample, were used to determine by average each set of data shown in Table II, and error limits represent maximum experimental deviations for each sample.

RESULTS AND DISCUSSION

As it is usual in NMR spectroscopy, the ratios of the integrated areas of two peaks can be measured with more accuracy than the absolute amount of atoms attributed to these peaks. The two ratios that can easily be measured with high accuracy in the spectrum of HEC are

$$p = [C^7]/[C^9]$$

i.e., the ratio of the average number of carbon atoms in the repeating unit of the polyethylene oxide chains to that of the carbon atoms attached to those chains bearing primary hydroxyl groups per AHG unit. The term $[C^9]$ is a measure of DS for the HEC molecule.

Another ratio easily measurable in the NMR spectrum is

$$q = [C^9]/([C^9] + [C^{6,6'}{}_{R=H}]$$

i.e., the ratio of the $[C^9]$ carbon atoms to the total number of carbon atoms bearing a primary hydroxyl group per AHG unit.

Because neither of these two ratios amenable to accurate estimation in the CMR spectrum involves a ring carbon atom, it is necessary to employ the MS value for a particular HEC sample that can be easily and accurately measured.[1] With these three parameters, MS, p, and q, the following structural features can be calculated:

1. The DS of oxyethylation:

$$DS = \frac{MS}{p/2 + 1}$$

2. The average number of repeating units of the chains (n):

$$n = p/2$$

3. The average amount of unsubstituted "ring" primary hydroxyl groups:

$$[C^{6,6'}{}_{R=H}] = \frac{DS(1 - q)}{q}$$

TABLE I
CMR Spectroscopic Data for Hydroxyethylcellulose (~ 2.5 Moles of Substitution) and Model Compounds[a]

Substance	$C^1(1')$[b]	$C^2(2')$	$C^3(3')$	$C^4(4')$	$C^5(5')$	$C^6(6')$	C^7	C^8	C^9
Cellobiose[e]	α 103.5(92.9)	74.3(72.5)	76.9(74.3)	70.7(79.9)	76.9(72.5)	61.8(61.3)			
	β[c] 103.5(96.9)	74.3(75.3)	76.9(75.8)	70.7(79.9)	76.9(75.3)	61.8(61.3)			
Poly(ethylene oxide) ($\bar{M}$ = 200)[d]							70.3 (70.4)	72.5	61.2
Maltose[e]	α 100.9(93.2)	73.8(72.6)	73.8(75.9)	70.7(76.9)	73.0(72.9)	61.9(61.9)			
	β 100.9(97.2)	73.8(75.2)	73.8(75.7)	70.7(78.6)	73.0(77.3)	61.9(61.9)			
Amylose[e] (pD 7)	100.9	73.8	72.7	82.9	73.2	61.8			
Cellulose moiety	103	~74	~77	~82	73	61.7			
HEC MS 2.5							70.4	72.6	61.4
HEC moiety	103	~79	~82	~82	73	70.8			

[a] Spectra were recorded on a Varian CFT-20 spectrometer and are reported in ppm relative to TMS; 0.5% of (DSS) was used as an internal standard and a $\Delta\delta^{TMS}$ of −33.2 Hz was used in all cases.

[b] Parenthetic value is a chemical shift for the anomeric ring in cellobiose.

[c] The 1–4 linkage in cellulose is β, hence β-cellobiose is the best model for cellulose at C^1 and C^4.

[d] Carbowax 200.

[e] See ref. 6a.

4. The average amount of unsubstituted secondary hydroxyl groups is given by

$$[C^{2,2'}] + [C^{3,3'}] = 3 - DS - [C^{6,6'}{}_{R=H}]$$

Table I shows the CMR data for HEC MS 2.5 and model compounds. The CMR spectrum of HEC MS 2.5 is shown in Figure 1.

The assignments in Table I and Figure 1 for HEC MS 2.5 are based upon analogy with the models in Table I.

$$HO—C^{9'}H_2—C^{8'}H_2(—O—C^{7'}H_2C^{7'}H_2)_n—O—C^{8'}H_2—C^{9'}H_2OH$$

poly(ethylene oxide) ($\bar{M}$ = 200)

When the secondary hydroxyl in β-cellobiose at $C^{1'}$ is methylated, a downfield shift of +5.3 ppm is observed for the CMR signal of $C^{1'6}$. Upon ethoxylation of the attached hydroxyl (i.e., $HC^nOH \rightarrow HC^nOCH_2CH_2O—)_n$, similar downfield shifts for the carbons $C^{2,2'}$ and $C^{3,3'}$ in cellulose can be expected. The CMR shifts of the unsubstituted *sec*-hydroxyl $C^{2,2'}$ and $C^{3,3'}$ carbons in HEC, as demonstrated by the maltose/amylose model,[7] should be very similar to those of β-cellobiose.[6a] The CMR assignments for $C^{2,2'}$ and $C^{3,3'}$ carbons in HEC shown in Table I and Figure 1 are based on these rationales.

The CMR assignments for $C^{1,1'}$, $C^{4,4'}$, and $C^{6,6'}$ are based upon analogy with the β-cellobiose[6a] and maltose/amylose models.[7] When the primary hydroxyl at $C^{6,6'}$ is ethoxylated, a downfield shift consistent with that observed for ($\delta^{C7'} - \delta^{C9'}$) (see poly(ethylene oxide) above) in poly(ethylene oxide) ($\bar{M}$ = 200) is expected. The assignment at 70.8 ppm for ethoxylated $C^{6,6'}$ is based on this model. $C^{1,1'}$, $C^{4,4'}$, and $C^{5,5'}$ are removed from the ethoxylation sites, and, consequently, their CMR shifts are relatively independent of R and only one major line is observed for each as shown in Figure 1.

Severe broadening of all of the CMR signals for carbons in the AHG ring (Fig. 1) is consistent with the anisotropy associated with partial ethoxylation of the alcohol groups. It is evident that the broadening is relatively diminished for the $C^{1,1'}$ and $C^{5,5'}$ carbons. This is probably related to the relatively remote position of these carbons to any reactive site. The resolution of the CMR shift of $C^{4,4'}$, which should be affected similarly, is masked by the broad CMR signal for ethoxylated $C^{3,3'}$ (Fig. 1).

The assignments for C^7, C^8, C^9 CMR shifts are based on the poly(ethylene oxide) ($\bar{M}$ = 200) model. As shown in Figure 1, these are the most intense and most highly resolved CMR signals in the spectrum of HEC MS 2.5. Table I shows that the CMR signals for these carbon atoms in HEC are virtually identical to those of poly(ethylene oxide) ($\bar{M}$ = 200). Since the accurate assignment of the signal at 61.8 to that of $C^{6,6'}$ (R = H) is critical to this work, a second means (i.e., other than models for chemical shifts) of distinguishing between $C^{6,6'}$ (R = H) carbons was employed. It was anticipated that the C^9 carbons would have a much longer relaxation time than the $C^{6,6'}$ (R = H) carbon, since it has been observed that terminal carbons at the end of flexible chains, such as poly(ethylene oxide), relax more slowly than those attached to more rigid backbones.[2,3,4] The T_1 = 80 ms for $C^{6,6'}$ (R = H) carbon and T_1 = 160 ms for the C^9 carbons, therefore, support their spectral assignments.

Table II shows data obtained for the quantitative determination of the average microstructure of HEC MS 2.5 by CMR spectroscopy. Reports on the deter-

TABLE II
Determination of the Average Microstructure of Natrosol 250L by CMR Spectroscopy[a]

MS[c] (±.15)	n (±.03)[j]	$n + 1$	DS = $[C^9]^b = [C^8]$ (±.07)[j]	$[C^{6,6'}]$ (±.2)[j]	$[C^{2,2'} + C^{3,3'}]$ (±.2)[j]	$[C^9]/[C^9] + [C^{6,6'}]$ (±.05)[j]
2.71[d]	0.88	1.88	1.44	0.7	0.9	0.67
2.68[e]	1.00	2.00	1.30	0.7	1.0	0.70
2.85[f]	0.99	1.99	1.43	0.7	0.9	0.68
2.71[g]	0.93	1.93	1.41	0.5	1.1	0.73
2.68[h]	0.91	1.91	1.40	0.6	1.0	0.71
2.70[i]	0.98	1.98	1.36	0.2	1.4	0.88
2.80[i]	1.01	2.02	1.39	0.2	1.4	0.89

[a] The samples of HEC MS 2.5 were obtained from Hercules Inc. There are two measurable parameters that provide the data to determine all of the parameters (except MS) in Table II. They are (1) the ratio of the relative area (planimetry) of the signal for C^7 to that of C^9 as shown in Fig. 1, and (2) the ratio of the relative area (planimetry) of the signal for C^7 to that of $C^{6,6'}$ as shown in Fig. 1. The relationships of these parameters to those shown in the table are shown in text.

[b] Brackets show the designation of number of subject carbon atoms per AHG unit that are present in the specific HEC MS 2.5.

[c] MS values were determined in duplicate by C. Klug at Hercules Inc. with a maximum experiment deviation ±.15.

[d] Lot #30983.

[e] Lot #301009.

[f] Lot #30988.

[g] Lot #30983.

[h] Lot #31009. Lots # 30983[g] and 31009 extracted with absolute ethanol for 24 hr. hr.

[i] Data reported by M. G. Wirick, *J. Polym. Sci.*, **6**, 1705 (1968).

[j] Error limits represent composite error of ±.15 for MS and ±.05 for P and Q values (see text).

mination of structure of HEC by Cohen and Haas[11] and Wirick were based on indirect wet chemical methods. The paper by Wirick[1c] was definitive for HEC at any MS and his data for HEC MS 2.5 are shown in Table II as superscript *i*. Wirick DS's of 1.36 and 1.39 at MS's 2.70 and 2.80, respectively, agree well with data for the three lots of HEC studied.

The data reported by Wirick also correlate well with our CMR-derived data for $n + 1$ (i.e., the average chain length of poly(ethylene oxide) units). Data shown under superscript *g* and *h* in Table II refer to HEC which was extracted with warm ethanol for 72 hr. This procedure was reported by Cohen and Haas for removal of what was presumably poly(ethylene oxide) impurity. We have analyzed these ethanol extracts and find that most of the extract material is low molecular weight HEC for the HEC lots studied in this work.

In 1950, Cohen and Haas[1b] reported data indicating that the primary hydroxyl on the AHG ring of cellulose was less reactive with ethylene oxide than expected. They also reported a correspondingly higher reactivity of the secondary hydroxyls at $C^{3,3'}$ and $C^{2,2'}$. In 1968, Wirick[1c] reported data which were not in agreement with this and suggested that a normal reactivity (i.e., rate primary $\gg$ rate secondary) is observed for the reaction of cellulose with ethylene oxide.

Presently, CMR data show a much lower consumption of the primary $C^{6,6'}$ hydroxyl of cellulose by ethylene oxide than Wirick's data suggest. CMR data

indicate that this is not accounted for by an increase in poly(ethylene oxide) chain length and correspondingly higher reactivity of C^9 primary hydroxyls. Thus, the relative concentration of $C^{2,2'}$ and $C^{3,3'}$ are lower than predicted by Wirick's data and suggests that, as Cohen and Haas found, the secondary hydroxyls on the AHG ring are more reactive than the primary hydroxyls of cellulose and HEC in the process used to prepare HEC.

We are presently studying a number of other differently substituted soluble celluloses by CMR spectroscopy and will report on these in detail in a future article.

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