Solid-State NMR Characterization of Cyclomaltoheptaose (β-cyclodextrin) Polymers Using High-Resolution Magic Angle Spinning with Gradients

G. CRINI,[1] M. BOURDONNEAU,[2] B. MARTEL,[3] M. PIOTTO,[2] M. MORCELLET,[3] T. RICHERT,[2] J. VEBREL,[1] G. TORRI,[4] AND N. MORIN[5]

[1] Centre de Spectrométrie, Université de Franche-Comté, Faculté des Sciences, 16 Route de Gray, 25000 Besançon, France

[2] UMR 7510 CNRS-Bruker, 34, rue de l'industrie 67166 Wissembourg, France

[3] Laboratoire de Chimie Macromoléculaire, UA CNRS 351, Université des Sciences de Lille, 59655 Villeneuve d'Ascq Cedex, France

[4] Istituto Scientifico di Chimica e Biochimica "G. Ronzoni", 81 Via G. Colombo, 20133 Milan, Italy

[5] Laboratoire de Chimie Physique et Minérale, Faculté de Médecine et de Pharmacie, Place St Jacques, 25030 Besançon, France

ABSTRACT: Solid-state nuclear magnetic resonance (NMR) techniques were used to characterize cyclomaltoheptaose (β-cyclodextrin, β-CD) polymers. These insoluble materials have been investigated by cross-polarization magic angle spinning with dipolar decoupling (CP/MAS), magic angle spinning without dipolar decoupling (MAS), and high-resolution magic angle spinning with gradients (HRMAS). These NMR spectra allow the assignment of the principal ^{1}H and ^{13}C signals. The presence of two distinct components (cross-linked β-CD and polymerized epichlorohydrin) in the materials was clearly demonstrated. These polymers were used as sorbents and the resulting NMR spectra are presented and discussed. © 2000 John Wiley & Sons, Inc. J Appl Polym Sci 75: 1288–1295, 2000

Key words: cyclodextrin polymer; solid-state; sorbents; HRMAS; complexation

INTRODUCTION

In the literature, there has been considerable study of the application of the insoluble cyclomaltoheptaose (β-cyclodextrin, β-CD) polymers.[1–15] These materials have been used in several fields such as analytical chemistry (chromatography, fluorescence),[1,8] thermochemistry,[7] catalysis,[2,4] pharmaceutical and food industries,[3,5,6,9] and waste water treatment.[10,11,12,14,15] In previous works,[13–15] we prepared several polymers obtaining by cross-linking β-CD with epichlorohydrin. β-CD molecule can be polymerized by reacting one or more of the 21 hydroxyl groups with epichlorohydrin. This cross-linking agent, which contains two reactive functional groups, can react with β-CD molecules (cross-linking step) and/or itself (polymerization step).[13,16] Therefore the structure of β-CD polymer is complicated. It is evident that in this material two kinds of structure could exist: β-CD cross-linked by epichlorohydrin and polymerized epichlorohydrin. These

solids contain only glucose units and hydroxyalkyls groups. Thus, it is difficult to characterize these materials using only techniques such as infrared or raman spectroscopies. So, little work has been reported on the identification and characterization of these polymers.

Previously, we have successfully used solid-state nuclear magnetic resonance (NMR) techniques (^{13}C and [29]Si cross-polarization magic angle spinning with dipolar decoupling [CP/MAS] measurements) to characterize bonded stationary phases containing β-CD for liquid chromatography and the resonances for the groups present on the surface of the silica beads have been assigned.[17] Because there is little information on the NMR characterization and structure of these insoluble polymers, we have undertaken further investigations employing solid-state NMR techniques. In a recent paper,[13] the molecular mobility of these polymers has been analyzed in terms of relaxation parameters such as ^{13}C spin lattice relaxation (T_1) and ^{1}H spin lattice relaxation in the rotating frame ($T_{1\rho}$). It was found that the T_1 values show that the β-CD trapped inside the polymers does not seem to undergo changes in its mobility whatever the amount of epichlorohydrin and the $T_{1\rho}$ values obtained reflect the homogeneous nature of the materials.

Hartmann-Hahn cross-polarization (CP)[18–20] combined with magic angle spinning (MAS) has been widely applied in high-resolution NMR studies of solids. This useful technique permit to identify, analyze, and characterize different kinds of materials.[21–26] To continue our investigations, in this work, we show for the first time high-resolution magic angle spinning (HRMAS) spectra of insoluble polymers containing β-CD. The purpose is to present some NMR spectra obtained using solid-state NMR techniques (CP/MAS, MAS, and HRMAS with gradients). These NMR techniques can give additional information and permit us to obtain well-resolved solid-state ^{1}H and ^{13}C spectra. A variable temperature study is also presented. Some preliminary NMR spectra of polymers containing pollutants are presented.

EXPERIMENTAL

General Procedure for the Cyclodextrin Polymer

The synthesis of β-CD polymers was the same described in previous works.[13–15] The materials prepared have different β-CD content (ranging from 20 to 80% w/w).

Methods

Solid-State NMR Spectroscopy

The MAS and CP/MAS spectra were recorded on a Bruker Avance-300 spectrometer equipped with a 4-mm BB CP/MAS probehead. The spinning speed of the sample was 4000 Hz. The 90° pulse width on the carbon channel was 3.2 μs at 2.5 dB. Proton high-power broad-band decoupling was achieved using an RF field of 75 kHz. The spectra were acquired on 1024 points with 64 scans, using a spectral width of 11.3 kHz; acquisition time was 45 ms and a recycle delay of 10 s was necessary to allow complete relaxation. For the CP transfer, a variable amplitude pulse with a linear ramp was used on the ^{1}H channel.[25] The duration of the spin lock was 1.5 ms.

HRMAS NMR Spectroscopy

The HRMAS NMR experiments were recorded on a Bruker Avance-400 spectrometer equipped with a 4-mm ^{13}C/^{2}H/^{1}H probehead provided with a gradient coil. The pulse lengths were 6.2 μs at −6 dB for the 90° on the proton channel and 5 μs at −6 dB for the 90° on the carbon channel. The spinning speed of the sample was 4000 Hz. The heteronuclear single quantum correlation (HSQC) spectrum of the β-CD polymer was acquired on 1024 points in F2 dimension with 128 scans and 5.2 kHz spectral width, recycle delay was 3 s. In the F1 dimension, 256 increments were used with a spectral width of 10 kHz. The nuclear Overhauser enhancement spectroscopy (NOESY) spectrum of the β-CD polymer was registered on 2048 points in F2 dimension with 96 scans and 4.4 kHz spectral width, recycle delay was 1 s and a mixing time of 200 ms. Two hundred and fifty-six experiments were done in the F1 dimension using the same spectral width as in F2. The homonuclear Hartmann–Hahn (HOHAHA) spectrum of the β-CD polymer containing the textile dye acid blue 25 was recorded on 2048 points in the F2 dimension with 32 scans and 4 kHz spectral width, recycle delay was 1 s and spin-lock duration 80 ms. In the F1 dimension, 256 increments were done on a 4-kHz spectral width.

RESULTS AND DISCUSSION

The CP/MAS spectrum of an insoluble polymer containing about 80% (w/w) of the cross-linking agent at 30°C is presented in Figure 1. We obtained the same kind of spectrum with a polymer
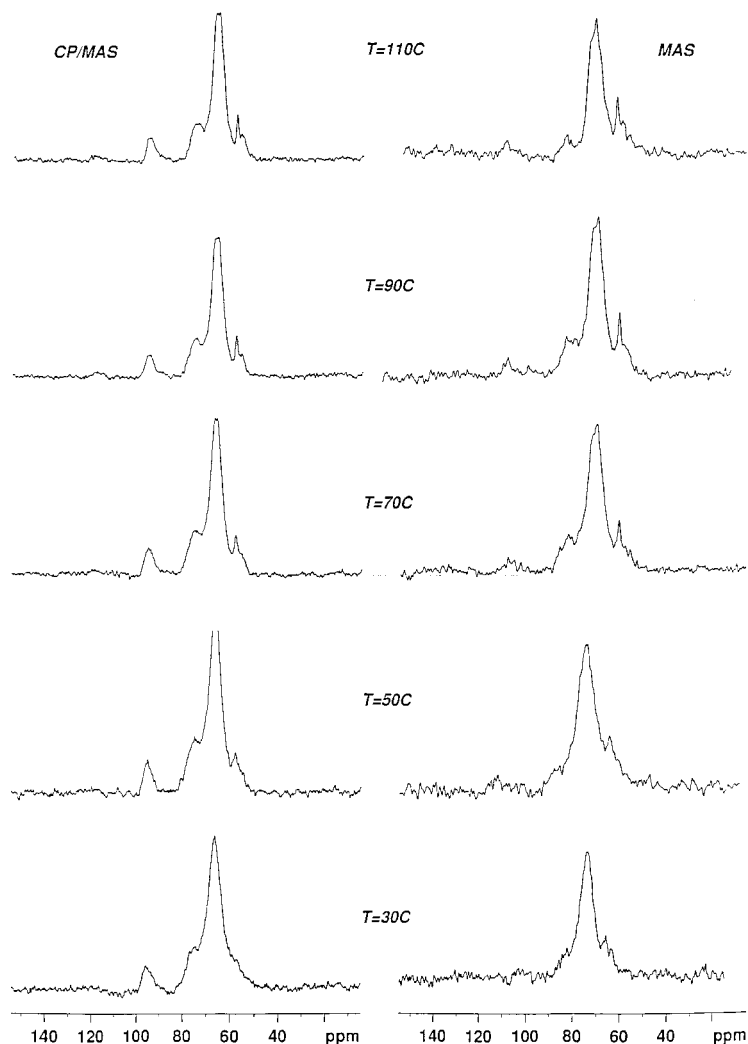
Figure 1 CP/MAS (left) and MAS (right) spectra of insoluble β-CD polymer using different temperatures.

containing 20% of epichlorohydrin. This spectrum resembles to a classical β-CD spectrum[27–30] in which we observe three broad signals at 98, 77, and 69 ppm. This spectrum permits only one signal (the resonance at 98 ppm is a well-defined peak and is due to the anomeric C-1) to be assigned because there is a large degree of signal overlap in the range 50–90 ppm.

We suppose that the signals of polymerized epichlorohydrin are completely hidden by C-2,3,4 and 5 β-CD peaks. The next step in the investigation is to confirm this hypothesis. To overcome this overlap problem, a variable temperature study was made. The sample temperature was raised from room temperature (30°C) to a temperature of 110°C by 20°C increments. For each temperature, the CP/MAS and MAS spectra were recorded (Fig. 1). After reaching this temperature

(110°C), the sample was cooled and the CP/MAS and MAS spectra were recorded. The resulting spectra were identical to those recorded during the heating cycle. The sample is stable over the temperature range studied and the nature of the gel is homogeneous.[13] When the samples were heated, two signals appeared in the CP/MAS spectra. At 110°C, these two sharp resonance (at 59 and 61 ppm) are evident and appeared high field to the main signal located at 69 ppm. These two resonances are due to a significant increase in the mobility of the terminal CH_2OH groups. These results are in agreement with data published.[13] However, this temperature is not sufficient for a better resolution. In the CP/MAS and MAS spectra presented in Figure 1, the change in resolution at higher temperature are due to a temperature dependence of the chemical shifts

and the spectra obtained also reflect the increase of the molecular mobility. These variable temperature CP/MAS spectra confirm the presence, in the broad signal at 69 ppm, of several peaks which could be attributed to both β-CD and polymerized epichlorohydrin. Using these first results, we can suppose that the two signals are attributable to the CH_2OH at position C-6 in the glucose unit of β-CD and/or to the CH_2OH group of epichlorohydrin terminal residue.

With the CP/MAS technique it is possible to observe both the rigid and mobile components in solid polymers, whereas the MAS method principally shows signals arising from the mobile component.[31,32] This can be seen in Figure 1, where the MAS spectrum of the polymer at 30°C presents different ratio of the signals as the CP/MAS spectrum at the same temperature. So, the signals of β-CD C-1 carbon (98 ppm) becomes very weak whereas resolution occurred in the high field part of the spectrum. The two signals at 59 and 61 ppm are already present at room temperature and can be assigned either to the CH_2OH at position C-6 in the glucose unit of β-CD or to the CH_2OH group of epichlorohydrin terminal residue. It is difficult to choose between these two hypothesis according only to these results. However this observation confirms the presence of two components with different molecular motions in the polymer.

A possible method for obtaining information about the structure and dynamic behavior of molecules such as β-CD is the employment of proton NMR spectroscopy.[33] However, in the solids strong dipole-dipole interactions are predominant. This dipolar interaction causes a line broadening of up to some tens of kHz. Generally, it is difficult to obtain proton spectra of materials.[31,32,34,35] A possible method is the use of combined rotation and multiple pulse spectroscopy (CRAMPS).[32,33] However, in our case, the results obtained are difficult to achieve using this technique with a CP/MAS probehead. HRMAS spectroscopy is an exciting recent technique in NMR analysis applicable to a wide range of samples with restricted motion, including membranes, polymers, gels, lipids, plant and food samples, swollen resins (used in combinatorial chemistry) and molecules attached to organic beads.[36–44] In static NMR the limited mobility of these samples associated with their large heterogeneity and the presence of some interactions such as dipole-dipole interaction and chemical shift anisotropy leads to broad proton NMR spectra which are unexploitable. By spinning the sample at the
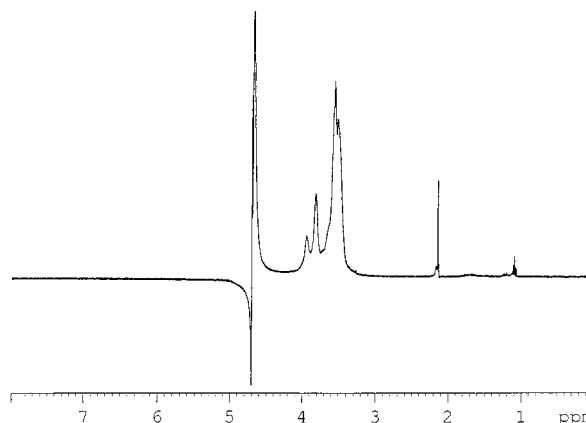

Figure 2 ^{1}H spectrum of β-CD polymer.

magic angle $(54.7°)$[45,46] and using a HRMAS probehead, the classical 2D liquid experiments (DQF-COSY (double quantum filtered homonuclear correlation), TOCSY (total correlation spectroscopy), HSQC ^{1}H/^{13}C, HMBC (heteronuclear multiple bond correlation) ^{1}H/^{13}C) can be applied with or without gradients. Thus, MAS NMR combined with multidimensional techniques can give information about structure.

In order to introduce some degree of mobility into the sample and to lock the spectrometer during the experiment, it is necessary to choose a deuterated solvent that has the property of swelling the polymer. In our case D_2O was added to the polymer directly inside the rotor. The 1D proton spectrum of the insoluble polymer sample swollen in D_2O obtained using a HRMAS probehead and a CPMG sequence with presaturation is show in Figure 2. We note the presence of at least four resonances. Running the same experiment with a liquid probehead, we observe only a broad peak, including the water signal.

NOESY, TOCSY, and HSQC ^{1}H/^{13}C experiment have been also performed. The last experiment shows the presence of two signals at 61 and 59 ppm in the ^{13}C frequency corresponding to two CH_2OH groups (with the intensities 1/3). The most important signal at 61 ppm is attributed to the CH_2OH group of the epichlorohydrin terminal residue and the signal at 59 ppm has been assigned to C-6 of β-CD. We note also the presence of four signals between 69 and 72 ppm corresponding to several CHOH and CH_2OH groups (Fig. 3).

In the NOESY (Fig. 4) spectrum, recorded with a mixing time of 200 ms, we observe a correlation between the anomeric protons at 5.2 ppm corresponding to H-1 and the signals around 3.6 ppm
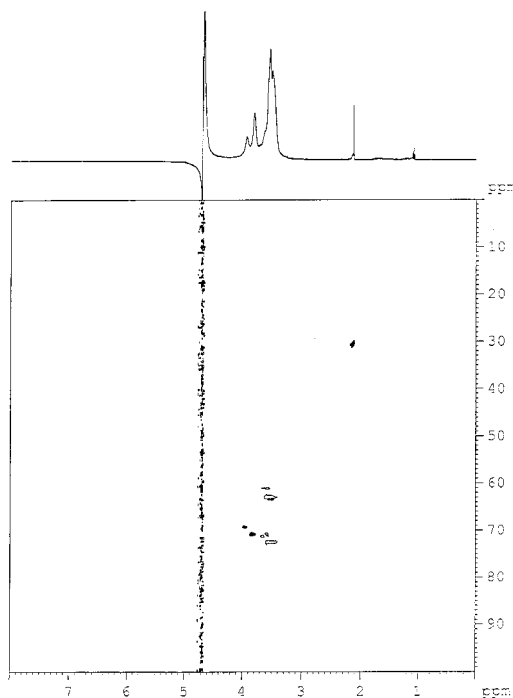
Figure 3 HSQC spectrum of β-CD polymer.

corresponding to the H-2, H-3, and H-5 protons of the glucose unit of β-CD.

These copolymers were then used as sorbents for the recovery of various organic pollutants from aqueous solutions. It is well known that the structure of β-CD and its polymers give rise to a remarkable ability to form inclusion complexes with organic molecules, especially aromatics compounds, through host-guest interactions. It was found that these prepared sorbents exhibit high sorption capacities.[14,15] The proposed sorption mechanism involves several kinds of interactions: hydrogen bonding, inclusion complex due to the presence of β-CD, and guest-guest hydrophobic interactions. We recorded also some HRMAS NMR spectra of polymers containing organic compounds, after they have been used in sorption experiments.[14,15] In a first step, we ran the 1D proton spectrum of the insoluble polymer containing β-naphtol and swollen in D_2O using a CPMG sequence with presaturation (Fig. 5). The peaks in the range 7–8 ppm are attributed to the protons of β-naphtol but unfortunately the low quantity of the organic compound in the complex limited the study to the 1D proton experiment.

In a second step, we started the analysis of the complex made of the same polymer and a textile dye[15] (acid blue 15). The solvent used to swell the sample was dimethylformamide (DMF) instead of D_2O. Figure 6 shows the 1D proton spectrum of the textile dye (a) and the 1D proton spectrum of the complex (b), the large peaks in the spectrum b are attributed to the aromatic protons of the dye.
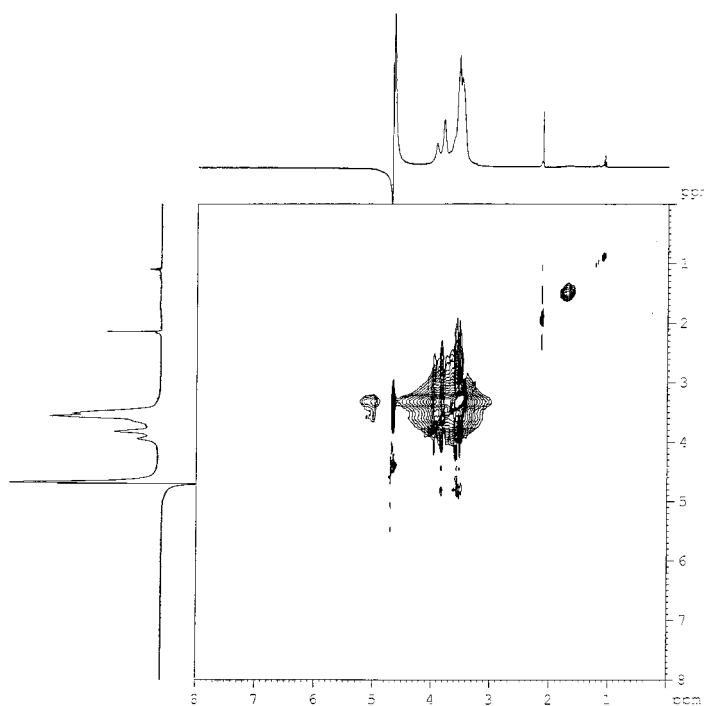
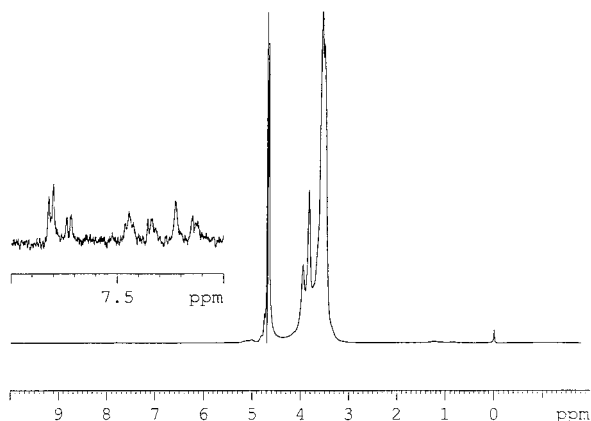

Figure 4 NOESY spectrum of the β-CD polymer.

Figure 5 ^{1}H spectrum of β-CD polymer containing β-naphtol.

To confirm the presence of an inclusion complex between the textile dye (acid blue 15) and the polymer, a small quantity of dye was added to the complex. As we can see in Figure 7, the 1D proton spectrum is then the sum of the 1D proton spectrum of the noncomplexed dye and the 1D proton spectrum of the complex, in which the signals corresponding to the protons of the dye are very large. Unfortunately the difficulties of observing
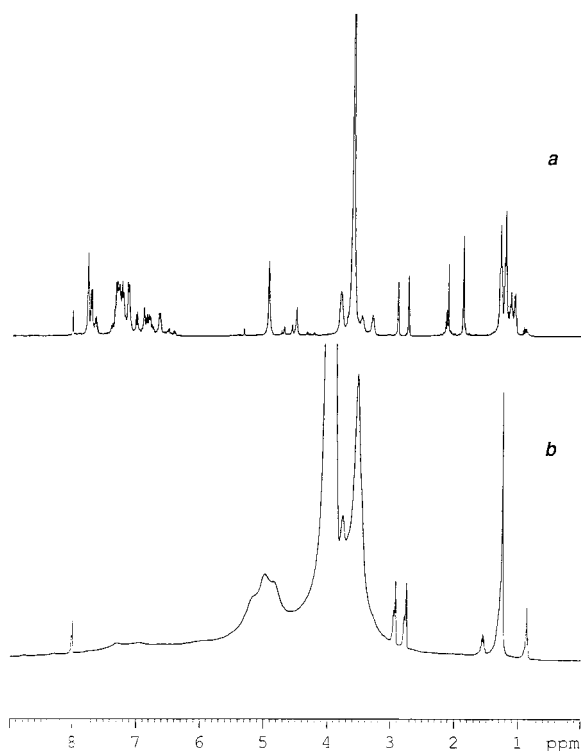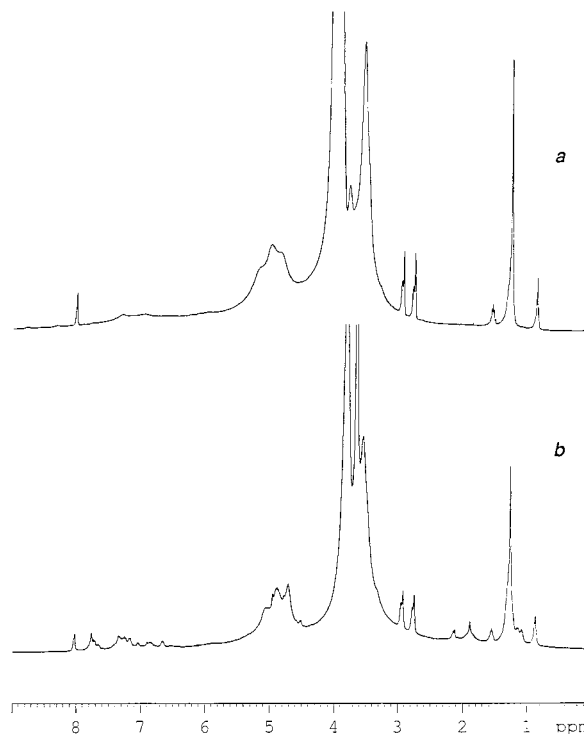

Figure 7 ^{1}H spectrum of the β-CD polymer containing the textile dye acid blue 15 (a) and the ^{1}H spectrum after adding a small quantity of dye (b).

the signal of the dye prevented us from running 2D NOESY experiment to analyze the interactions between the polymer and the organic compound (acid blue 15).

Others results are presented in Figure 8 using acid blue 25 as solute. The 1D proton spectra of the noncomplexed dye (Fig. 8a) and the complexed dye (Fig. 8b) in the gel are completely different in the proton aromatic region. In Figure 8b, we note the presence of three new signals, two in the region aromatic at 7.7 and 6.9 ppm and one at 4.5 ppm in the broad signal (the signals in this region have been assigned to the gel).[13] These changes are due to the formation of an inclusion complex. An important contribution was achieved by using an HOHAHA experiment (Fig. 9). In this spectrum, we observe a correlation between the protons at 1.1 ppm (corresponding to the textile dye) and the signals around 3.6–3.7 ppm corresponding to the protons of the glucose units of β-CD.

Figure 6 ^{1}H spectrum of the textile dye acid blue 15 (a) and ^{1}H spectrum of the β-CD polymer containing the textile dye (b).

CONCLUSION

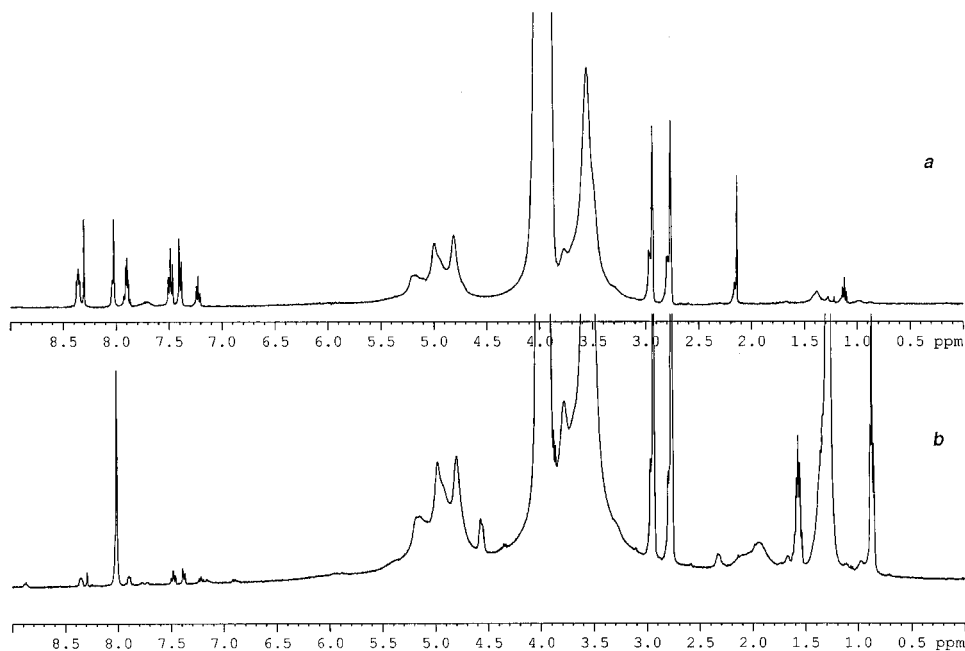This study was carried out in order to present for the first time, NMR spectra of insoluble β-CD

Figure 8 ¹H spectrum of the β-CD polymer containing the textile dye acid blue 25 (a) and the ¹H spectrum after adding a small quantity of dye (b).

polymers using HRMAS spectroscopy. The spectra obtained show that it is possible, using this new NMR technique to characterize cross-linked materials having a limited mobility. There is evidence of two kinds of structures, cross-linked β-CD and polymerized epichlorohydrin, that can interact with a organic compound complexed in the sorbent. Until now, the study was mainly limited to 1D NMR experiments for the analysis of complexes because of the small concentration of the organic compound in the complex. All the results presented here show that HRMAS spec-
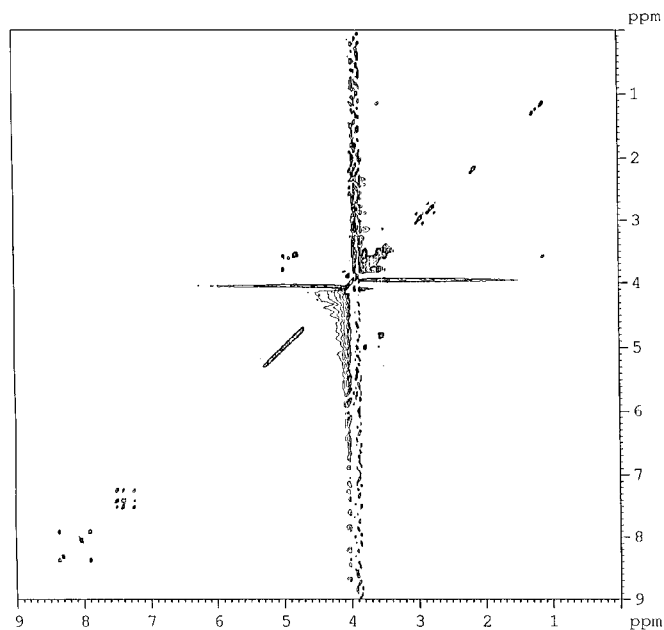

Figure 9 HOHAHA spectrum of a β-CD polymer containing the textile dye acid blue 25.

troscopy proved to be a useful technique to clearly identify the polymeric structures. Our next objective will be to test others examples on which we will run 2D experiment to analyze the interactions in the complex, to find the relationship between their retention behavior and molecular structure in order to analyze the molecular mobilities of the β-CD.

REFERENCES

1. Hoffman, J. L. J Macromol Sci Chem 1973, A7, 1147.
2. Komiyama, M.; Sugiura, I.; Hirai, H. Polym J 1985, 17, 1225.
3. Fenyvesy, E. J Incl Phenom 1988, 6, 537.
4. Sugiura, I.; Komiyama, M.; Toshima, N.; Hirai, H. Bull Chem Soc Jpn 1989, 62, 1643.
5. Rouseff, R. L. In Developments in Food Science; Elsevier: New-York, 1990; p 309.
6. Su, C. S.; Yang, C. P. J Sci Food Agric 1991, 54, 635.
7. Irwin, P. L.; King, G.; Hicks, K. B. Carbohydr Res 1996, 282, 65.
8. Werner, T. C.; Colwell, K.; Agbaria, R. A.; Warner, I. M. Appl Spectrosc 1996, 50, 511.
9. Zhu, X. X.; Brizard, F.; Wen, C. C.; Brown, G. R. J Macromol Sci, Pure Appl Chem 1997, A34, 335.
10. Murai, S.; Imajo, S.; Inumaru, H.; Takahashi, K.; Hattori, K. J Colloid Interface Sci 1997, 190, 488.
11. Murai, S.; Imajo, S.; Maki, Y.; Takahashi, K.; Hattori, K. J Colloid Interface Sci 1996, 183, 118.
12. Murai, S.; Imajo, S.; Takasu, Y.; Takahashi, K.; Hattori, K. Environ Sci Technol 1998, 32, 782.
13. Crini, G.; Cosentino, C.; Bertini, S.; Naggi, A.; Torri, G.; Vecchi, C.; Janus, L.; Morcellet, M. Carbohydr Res 1998, 308, 37.
14. Crini, G.; Bertini, S.; Naggi, A.; Torri, G.; Vecchi, C.; Janus, L.; Morcellet, M. J Appl Polym Sci 1998, 68, 1973.
15. Shao, Y.; Martel, B.; Morcellet, M.; Weltrowski, M.; Crini, G. J Incl Phenom 1996, 25, 209.
16. Renard, E.; Deratani, A.; Volet, G.; Sebille, B. Eur Polym J 1997, 1, 49.
17. Crini, G.; Torri, G.; Morcellet, M. J Chromatogr Sci 1996, 34, 477.
18. Hartmann, S. R.; Hahn, E. L. Phys Rev 1962, 128, 2042.
19. Pines, A.; Gibby, M. G.; Waugh, J. S. J Chem Phys 1971, 56, 1776.
20. Pines, A.; Gibby, M. G.; Waugh, J. S. J Chem Phys 1973, 59, 569.
21. Morgan, K. R.; Hemmingson, J. A.; Furneaux, R. H.; Stanley, R. A. Carbohydr Res 1994, 262, 185.
22. Brindle, R.; Albert, K. Solid State Nuclear Magn Reson 1996, 6, 251.
23. Larsson, P. T.; Wickholm, K.; Iversen, T. Carbohydr Res 1997, 302, 19.
24. Derouet, D.; Forgeard, S.; Brosse, J. C.; Emery, J.; Buzare, J. Y. J Polym Sci 1998, 36, 437.
25. Metz, G.; Wu, X.; Smith, S. O. J Magn Reson 1994, Series A, 110, 219.
26. DeAngelis, A.; Capitani, D.; Crescenzi, V. Macromolecules 1998, 31, 1595.
27. Inoue, Y.; Okuda, T.; Chujo, R. Carbohydr Res 1983, 116, C5.
28. Inoue, Y.; Okuda, T.; Chujo, R. Carbohydr Res 1985, 141, 179.
29. Heyes, S. J.; Clayden, N. J.; Dobson, C. M. Carbohydr Res 1992, 233, 1.
30. Sfihi, H.; Legrand, A. P.; Doussot, J.; Guy, A. Colloids Surf 1996, 115, 115.
31. Schaefer, J.; Stejskal, E. O. Topics in carbon-13 NMR of solid polymers, Wiley-Interscience, New-York, 1978, p. 283.
32. Bovey, F. A., Ed. In Nuclear Magnetic Resonance Spectroscopy; 2nd ed.; Academic Press: New York, 1988; p. 399.
33. Brindle, R.; Albert, K.; Harris, S. J.; Tröltzsch, C.; Horne, E.; Glennon, J. D.; J Chromatogr 1996, 731, 41.
34. McBrierty, V. J. Polym 1974, 15, 503.
35. Silvestri, R. L.; Koenig, J. L. Anal Chim Acta 1993, 283, 997.
36. Filtch, W. L.; Dettre, G.; Holmes, C. P.; Scoolery, J.; Keiffer, P. A. J Org Chem 1994, 59, 7995.
37. Anderson, R. C.; Jarema, M. A.; Shapiro, M. J.; Stokes, J. P.; Zilliox, M. J Org Chem 1995, 60, 2650.
38. R. C.; Anderson, J. P.; Stokes, and M. J. Shapiro, Tetrahedron Lett 1995, 36, 5311.
39. Manzi, A.; Salimath, P. V.; Spiros, R. C.; Keiffer, P. A.; Freeze, H. H. J Biol Chem 1995, 270, 9154.
40. Keiffer, P. A. J Org Chem 1996, 61, 1558.
41. Pop, I. E.; Dhalluin, C. F.; Déprez, B. P.; Melnyk, P. C.; Lippens, G. M.; Tartar, A. L. Tetrahedron Lett 1996, 52, 37.
42. Dhalluin, C.; Boutillon, C.; Tartar, A.; Lippens, G. J Am Chem Soc 1997, 119, 10494.
43. Jelinek, R.; Valente, A. P.; Valentine, K. G.; Opella, S. J. J Magn Reson 1997, 125, 185.
44. Gross, J. D.; Costa, P. R.; Dubacq, J. B.; Warschawski, D. E.; Lirsca, P. N.; Desvaux, P. F.; Griffin, R. G. J Magn Reson Series B 1995, 106, 187.
45. Andrew, E. R.; Bradbury, A.; Eades, R. G. Nature 1959, 183, 1802.
46. Lowe, I. J. Phy Rev Lett 1959, 2, 285.