Carbohydrate Research, 197 (1990) 41–52
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

TOWARDS UNDERSTANDING ^{13}C-N.M.R. CHEMICAL SHIFTS OF CARBOHYDRATES IN THE SOLID STATE. THE SPECTRA OF D-MANNITOL POLYMORPHS AND OF DL-MANNITOL

T. BRUCE GRINDLEY, MICHAEL S. MCKINNON, AND RODERICK E. WASYLISHEN
Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, B3H 4J3 (Canada)
(Received February 7th, 1989; accepted for publication, June 8th, 1989)

ABSTRACT

The cross-polarization, magic-angle spinning ^{13}C-n.m.r. spectra of solid DL-mannitol and of three polymorphs of D-mannitol have been recorded and assigned. Recrystallization of D-mannitol from several solvents under different conditions gave either one of the three known pure polymorphs or mixtures containing two or more of these polymorphs. The ^{13}C-chemical shifts from the four species in the solid state were all less than the solution values. Conformations in deuterium oxide and di($^2H_3$)methyl sulfoxide solutions were obtained from the vicinal proton coupling constants that resulted from analysis of the ^{1}H-n.m.r. spectra. The major cause of the differences between solid-state and solution chemical shifts is that there are significant populations of one of the *gauche* rotamers and the *anti* O–C–C–C rotamer about the terminal C–C bonds in solution. Other effects on solid-state ^{13}C-chemical shifts are discussed.

INTRODUCTION

The ^{13}C-n.m.r. spectra of solids obtained under conditions of cross-polarization and magic-angle spinning (c.p.–m.a.s. spectra) have resolutions approaching that obtained from spectra of solutions. The isotropic chemical shifts which result are very close to those from solution spectra for most organic compounds, particularly those for which conformations are fixed[1] (often ±1 p.p.m.). However, this generalization does not appear to apply to carbohydrates, where considerable differences between solid-state and solution chemical shifts are often observed[2–5]. A number of factors have been considered to explain the differences[2,6–9]. We considered that the study of smaller molecules, particularly those that existed as one or more polymorphs for which solid-state structures from X-ray or neutron diffraction are available, would be informative.

There has been considerable recent interest in studying polymorphs in order to gain insight into structural effects on ^{13}C-n.m.r. chemical shifts[10]. Mannitol is a particularly interesting compound in the solid state because it crystallizes in several polymorphic forms. Seven different Greek letters have been used in the literature

0008-6215/90/$ 03.50

to describe the polymorphic forms of solid D-mannitol. Berman *et al.*[11] re-examined the earlier literature and suggested that only three different polymorphs exist. This group has reported complete X-ray structural studies on two of these and a partial study of the third[11,12]. Levy and Strauss[13] also prepared three polymorphs but under quite different conditions. Unit-cell dimensions and point groups[13] indicated that two of these were the same as those of Jeffrey and co-workers[11,12]. In addition, an X-ray structural study of DL-mannitol has been reported[14]. The heavy carbon and oxygen atoms have essentially the same relative locations in all four structures[11–14]. However, there are subtle differences in the hydrogen-bonding arrangements for each polymorph.

We demonstrate herein that cross-polarization, magic-angle spinning ^{13}C-n.m.r. spectra can be used to unambiguously identify the D-mannitol polymorphs. We also evaluate a number of potential explanations of the differences in chemical shifts between solution and solid-state spectra of mannitol.

EXPERIMENTAL

Methods. — C.p.-m.a.s. ^{13}C-n.m.r. spectra were recorded at 50.32 MHz with a Bruker MSL-200 n.m.r. spectrometer. Spectra were acquired under conditions of the Hartmann–Hahn match using 90° pulses of 4 μs, contact times of 1 ms, and 20-s recycle delays. Samples (~400 mg each) were examined as powders in spinners constructed of Al_2O_3 and spun at about 3 kHz at the magic angle in a double-bearing spinner assembly using air as the drive gas. Chemical shifts (δ) were referenced to the signal of external adamantane and are reproducible to ±0.3 p.p.m.

Simulations of ^1H-n.m.r. spectra of D-mannitol solutions were performed by use of the program LAME[16]. The spectra of D-mannitol in aqueous (D_2O) solutions were simulated as an AA'BB'CC'DD' system for the H-1a, H-6a, H-1b, H-6b, H-2, H-5, H-3, and H-4 signals, respectively. The line widths observed for the H-1a, H-6a, H-1b, and H-6b signals were ~0.4 Hz, and those for H-2–H-5 ~1.2 Hz. Simulation indicated that the broadening of the latter group of signals resulted from the additional splitting which arises because the spectrum is an eight-spin system and not two identical, isolated four-spin patterns. Thus, $J_{3,4}$ must have a non-zero value. Because the lines were broadened but not split, the uncertainty for this J value is considerably higher, estimated to be ±0.3 Hz. The r.m.s. deviation between observed and calculated transitions was 0.19 Hz on assigning 825 transitions. The di($^2H_3$)methyl sulfoxide spectrum was an AA'BB'CC'DD'XX'YY'ZZ' pattern where the last six signals arise from OH groups. Because the spin system was too large to simulate in total, segments of the overall pattern were simulated separately. The n.m.r. parameters for H-1a, H-1b, and OH-1 were obtained by simulating the H-1a, H-1b, OH-1, and H-2 segment; those for H-2 and OH-2 were obtained from the H-1a, H-1b, H-2, OH-2, and H-3 segment; and those for H-3, H-4, OH-3, and OH-4 were obtained from the H-2, H-3, H-4, OH-3, and OH-4 segment.

Materials. — D-Mannitol was recrystallized under a variety of conditions from water, ethanol–water, and ethanol. Under these conditions, only three polymorphs or mixtures of the three basic polymorphs were ever obtained (as assessed by c.p.-m.a.s. ^{13}C-n.m.r. spectroscopy, *vide infra*). A variety of Greek letters have been used to name polymorphs that are most likely identical. We have decided to use the nomenclature of Berman *et al.*[11], except that we have called the α' form simply α. The α' polymorph of Berman *et al.*[11] and of Mak[15] was obtained by recrystallization from 100% ethanol solutions. It was shown to belong to the $C222_1$ point group. The δ form of Levy and Strauss[13], obtained by recrystallization from dilute aqueous solutions at low temperatures, was assigned to the $P2_1$ point group. The unit-cell dimensions and β value reported[13] can be shown to be equivalent to those of a unit cell with $C222_1$ symmetry and cell dimensions almost identical to those reported for crystals obtained from 100% ethanol[11,15]. The crystals which gave a c.p.-m.a.s. spectrum of the α polymorph had an X-ray powder diffraction pattern identical to that reported by Levy and Strauss[13] for their δ form. We concluded that the α' and δ forms are identical. D-Mannitol obtained from ICN was present in this polymorphic form, termed the α form here.

The β form of Levy and Strauss[13], Berman *et al.*[11], and earlier workers is obtained by recrystallization from aqueous ethanol[11] or from water at room temperature[13]. Samples obtained from Sigma and Fluka were present in this polymorphic form. The last polymorph, termed κ here, is the κ form of Kim *et al.*[12], the γ form of Rye and Sorum[17], and the α form of Levy and Strauss[13]. The κ polymorph was reported as being obtained from methanol and boric acid, 1:1 water–ethanol solutions, or aqueous solutions at 100°, respectively. The identity of these preparations was established through the similarity of the reported unit-cell dimensions and assigned-point groups. Levy and Strauss[13] also reported that this form was obtained by fusion of D-mannitol, and this technique was found to be the most convenient method of preparation for our purposes. The samples of the β and κ forms used here gave X-ray powder-diffraction patterns very similar to those reported by Levy and Strauss[13] for the corresponding polymorphs.

DL-Mannitol was obtained by combining D-mannitol with a sample of L-mannitol obtained by reduction of L-mannono-1,4-lactone.

RESULTS AND DISCUSSION

Fig. 1 shows the c.p.-m.a.s. ^{13}C-n.m.r. spectra of the three polymorphs of D-mannitol and DL-mannitol; chemical shifts are reported in Table I. Note that each polymorph gave rise to six ^{13}C-resonances instead of three as observed for solutions. Each polymorph gave distinctly different chemical shifts that were used for characterization. As described in the experimental section, it was possible to demonstrate that only three polymorphs of D-mannitol were obtained under the wide range of conditions for recrystallization employed here. During the many recrystallizations, mixed polymorphs were often obtained. C.p.-m.a.s. spectra of

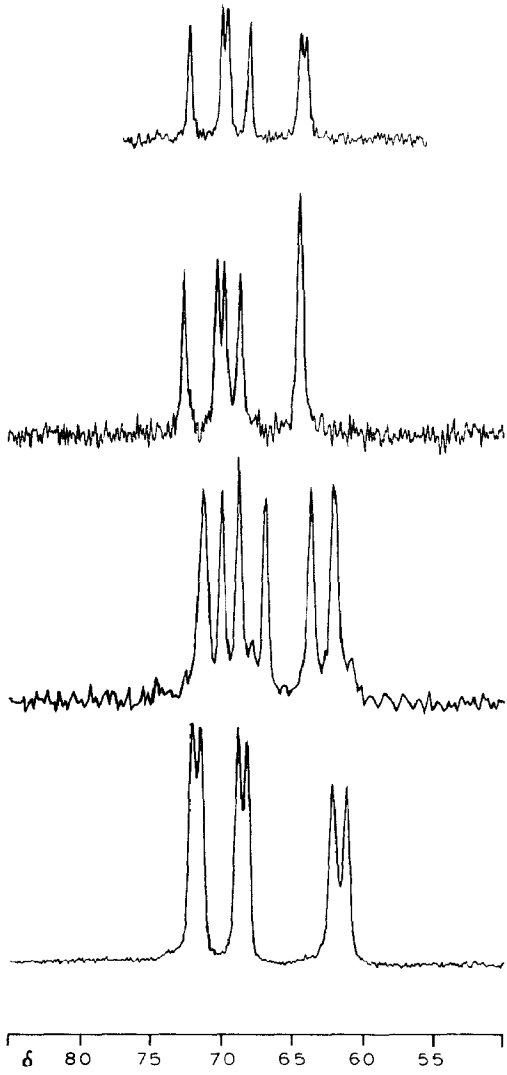


Fig. 1. The 50.32 MHz c.p.-m.a.s. solid-state ^{13}C-n.m.r. spectra of D-mannitol polymorphs and of DL-mannitol. The spectra from the top down are those of DL-mannitol, and the α, β, and κ polymorphs of D-mannitol.

these mixtures could be analyzed as arising from various combinations of the three different polymorphs, and indicated how the compositions of the mixtures changed as the recrystallization conditions were altered. X-Ray powder diffraction patterns were used to relate the present three polymorphs to those of Levy and Strauss[13]. Point groups and unit-cell dimensions were used to relate the polymorphic forms of Levy and Strauss[13] to those reported by other groups[11,12,15,16].

Also listed in Table I are the chemical shifts previously recorded for deuterium oxide[14] and di($^2H_3$)methyl sulfoxide[15] solutions, and differences between

TABLE I

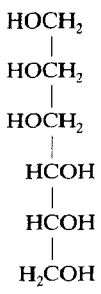
^{13}C-N.M.R. CHEMICAL SHIFTS (δ) OF D-MANNITOL POLYMORPHS AND DL-MANNITOL IN SOLUTION AND IN THE SOLID STATE

D-Mannitol in solution *Solvent*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
D_2O[a]	64.6	72.2	70.7	70.7	72.2	64.6
Di($^2H_3$)methyl sulfoxide[b]	63.7	71.3	69.6	69.6	71.3	63.7
In the solid state						
D-Mannitol α	64.4	72.5	69.7	68.5	70.2	64.4
β	64.3	71.7	69.3	67.4	70.5	62.8
λ	62.1	71.9	68.7	68.1	71.4	61.1
DL-Mannitol	63.9	71.8	69.1	67.5	69.5	63.5
Difference between values for a D_2O solution and for solid state						
D-Mannitol α	0.2	−0.3	1.0	2.2	2.2	0.2
β	0.3	0.5	1.4	3.3	1.7	1.8
κ	2.5	0.3	2.0	2.0	0.8	3.5
DL-*Mannitol*	0.7	0.4	1.6	3.2	2.7	1.1

[a]From ref. 18. [b]From ref. 19.

the solution and solid-state spectra. Chemical-shift assignments for c.p.-m.a.s. ^{13}C-n.m.r. spectra were based on the solution values. For a solution, the signals of the primary carbon atoms occurred at positions that were approximately 6 to 8 p.p.m. to low frequency of the secondary carbon atoms. The spectra of all polymorphs contained two signals with chemical shifts at least 3.1 p.p.m. smaller than the others. The chemical shifts observed for these two signals were also slightly smaller than those for the primary carbon atoms in solution. In the solution spectra, the signals of C-3 and C-4 were observed at lower frequencies than those of C-2 and C-5 by 1.5 and 1.7 p.p.m. for deuterium oxide and di($^2H_3$)methyl sulfoxide solutions, respectively, and the solid-state signals were assigned on the assumption that this relationship is also valid for spectra from this phase. We will later show that the solid-state chemical shifts of C-3 and C-4 should occur at lower frequencies with respect to those of C-2 and C-5 than they are in spectra obtained from solution; the differences were observed to increase in agreement with this expectation. Representations of D-mannitol (**1**) such as the Fischer diagram indicate the four chiral centers can be divided into two pairs related by a C_2 axis. For ^{13}C-n.m.r. spectra of solutions, where the mixtures of conformations present for the two halves of the molecule must have the same composition, three signals are observed. This apparent C_2 symmetry is lost in the solid state and it is not possible to assign the pairs of signals which arise from the loss of this averaged symmetry.

The differences between the solid-state and solution ^{13}C-n.m.r. spectra will be discussed first. Chemical shift effects in the solid state can be affected by solid-state phenomena including specific intermolecular hydrogen bonds, hydration, or unusual structural features. However, in most cases, it is conformational effects



1

that cause differences between solid-state and solution chemical shifts[1,2]. The conformations of the β and κ polymorphs of D-mannitol and of DL-mannitol have been established by X-ray crystallography[11,12,14] and some information is available on the α polymorph[11]. All forms exist in extended conformations with the carbon atoms in one plane. The oxygen atoms in all four crystals adopt the same relative orientation. The terminal oxygen atoms are in the same *gauche* orientation with respect to the carbon chain in all four forms. The only major differences between the reported structures lie in how the hydrogen-bonding networks are arranged. Inevitably, there are numerous, very minor differences in the structural details of the four structures.

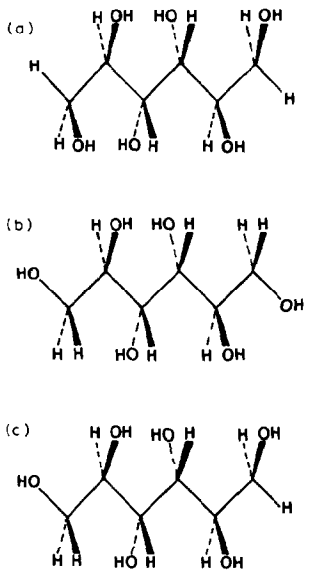
^{13}C- (refs. 18, 19) and ^{1}H-n.m.r.[20] spectral studies have been used to establish conformations in deuterium oxide[18,20] and di($^{2}H_3$)methyl sulfoxide[19] solutions. It is agreed[18–20] that, in solution, the predominant conformations have the carbon backbone in the same extended planar conformation that is present in the solid-state forms. In a previous ^{1}H-n.m.r. study of D-mannitol in aqueous solution, the vicinal coupling constants were obtained by simulation of the signals of H-1a, H-1b, H-2, and H-3 as an ABCD system with the assumption that the $J_{3,4}$ value was zero[20]. Because the signals actually form an AA'BB'CC'DD' pattern, we decided to repeat the simulation here. The coupling constants obtained (Table II) were very similar to those originally calculated, except that $J_{3,4}$ is now 1.1 ±0.3 Hz. The signals of six hydroxyl groups are present in the spectra of di($^{2}H_3$)methyl sulfoxide

TABLE II

^{1}H-N.M.R. COUPLING CONSTANTS FOR D-MANNITOL (Hz)[a]

Solvent	$J_{1a,1b}$	$J_{1a,2}$	$J_{1b,2}$	$J_{2,3}$	$J_{3,4}$	$J_{1a,OH} = J_{1b,OH}$	$J_{2,OH}$	$J_{3,OH}$
D_2O[b]	−11.75	3.0	6.25	8.95	0.0			
D_2O	−11.87 (±0.02)	2.88 (±0.02)	6.35 (±0.02)	8.57 (±0.02)	1.1 (±0.03)			
Di($^{2}H_3$)methyl sulfoxide	−11.0 (±0.05)	3.4 (±0.06)	5.7 (±0.07)	8.6 (±0.07)	[c]	5.7 (±0.04)	5.7 (±0.05)	7.1 (±0.07)

[a]Uncertainties from LAME output in parentheses. [b]From ref. 20. [c]Not obtained, see text.



Scheme 1. Conformations of D-mannitol: (a) The conformation partially present in solution and favored in the solid state with *gauche* arrangements about the two terminal carbon atoms at both ends of the chain; (b) another conformation present in solution, the one with both terminal oxygen atoms *anti* to the carbon atoms in the chain; and (c) the mixed *gauche* and *anti* conformation.

solutions, yielding a 14-spin system, too large for simulation as a whole. Good agreement between simulated and experimental spectra was obtained by simulation in segments. The larger linewidths observed for spectra from di($^2H_3$)methyl sulfoxide solutions precluded estimation of $J_{3,4}$. All coupling constants from the di($^2H_3$)methyl sulfoxide solution differed from the corresponding values measured from an aqueous (D_2O) solution by <1.0 Hz. Thus, the conclusions previously drawn for deuterium oxide solutions apply[20]. In both solutions, the carbon backbone is essentially planar. It was demonstrated, by comparison of observed $J_{1a,2}$ and $J_{1b,2}$ values with those calculated for model staggered conformations by means of a Karplus equation modified to incorporate electronegativity effects[21], that the conformational mixture arising from rotation about the C-1–C-2 bond contains about equal amounts of the two staggered rotamers with O-1 *gauche* to O-2. Of these two rotamers, the extended conformation with O-1- *anti* to C-3 was calculated to be present to a slightly greater extent in D_2O [54% (ref. 20), 56% from the *J*-values obtained here) than the conformation present in all solid-state polymorphs[11,12,14] that has O-1 *gauche* to both O-2 and C-3 (Scheme 1)[20]. If the same assumptions are made for the $J_{1,2}$ value of 5.7 Hz observed in the spectra obtained from di($^2H_3$)methyl sulfoxide solutions, the proportion of the former rotamer is reduced to about 49%. However, the observed value of $J_{1b,2}$ in this solvent is 3.4 Hz, larger than either of the values calculated for this *J* value in the two rotamers. Possible explanations for the larger value include (a) the third rotamer contributes

to a slight extent; (b) the coupling constants calculated for the individual rotamers are different than the real values because the equilibrium geometries of the individual rotamers deviate from the assumed exactly staggered arrangements; and (c) the bond angles in these acyclic systems are different from those in the cyclic systems used to determine the parameters for the modified Karplus equation[21] resulting in incorrect model values. Clearly, the populations of the individual rotamers obtained from this treatment must be regarded as being approximate with uncertainties being as large as ±10%.

Coupling constants to OH protons for solutions in di($^2H_3$)methyl sulfoxide were 5.7 Hz for H-1a, H-1b, H-6a, H-6b, H-2, and H-5; and 7.1 Hz for H-3 and H-4. Karplus-type relationship have been proposed for OH protons[22]. *Anti* H–O–C–H relationships yield a value of ~12 Hz, and *gauche* relationships gave values of ~3 Hz. Thus, a J value obtained from a rotameric mixture containing equal amounts of the two *gauche* and the single *anti* contributers would have a coupling constant of ~6 Hz, very similar to the values observed here. If *anti* and *gauche* conformations contribute equally, a J value of ~7.5 Hz is predicted. The value of the $J_{H,OH}$ for H-3 and H-4, 7.1 Hz, indicates that *anti* conformers about these C–O bonds contribute more to the conformational mixture present, perhaps to the same extent as in the solid state, where 50% of the six relationships studied are *anti*[11,12,14].

X-Ray diffraction studies indicated that all four solid-state structures contain only *gauche* C–C–C–O conformers about the terminal C–C bonds. In comparison with the solution conformers present in approximately half of the populated C–C–C–O rotamers with *anti*-conformations have been removed and chemical-shift consequences should ensue. Because *gauche* O–C–C–C conformations cause larger upfield shifts than do *anti* conformations[23,24], the chemical shifts for C-3 and C-4 in the solids should be smaller than for those in solution. This expectation was confirmed by observation; differences ranged from 1.0 to 3.5 p.p.m. (Table I) and averaged 2.1 p.p.m. Thus, one cause for the differences between the solution and solid-state spectra is the mixture of rotamers present for the terminal hydroxymethyl groups in solution. Increased amounts of *gauche* rotamers in an C–C–C–O unit would also be expected to result in slightly decreased shifts for the two central carbon atoms[18,19,24]. The average upfield-shift observed for C-2 and C-5 was 1.0 p.p.m., and 1.3 p.p.m. for C-1 and C-6.

Whitesell *et al.*[24] have successfully calculated the ^{13}C-n.m.r. chemical shifts of acyclic alcohols by combining chemical-shift effects from decalins with conformational populations derived from MM2 calculations. An upfield shift effect of 2.7 p.p.m. for an *anti* H–H pair was derived to obtain the observed upfield-shift for the middle carbon atoms when a propanol *anti* conformation is changed to *gauche*[24]. If the *gauche* population about the terminal carbon atoms of mannitol in aqueous solution is 45%, upfield shifts for C-1, C-2, C-5, and C-6 of 1.5 p.p.m. were calculated, similar to the observed average values. For C-3 and C-4, the *gauche* conformation about the terminal carbon atoms contains one extra C–O *gauche*

interaction. Combination of the upfield-shift effect[24] with the conformational population gave a value of 4.1 p.p.m., considerably larger than the observed, average upfield-shift of 2.1 p.p.m.

One factor influencing solid-state ^{13}C-chemical shifts of carbonyl carbon atoms in molecules containing hydroxyl, amino, or ammonium groups is the length of any hydrogen bonds formed[25,26]. Differences between solution and solid-state, carbonyl group chemical shifts were found to be inversely related to this distance in cases where the hydrogen-bond donor is the hydroxyl or amino group, but directly related when it is an ammonium group[25,26]. Quantum mechanical calculations at the FPT INDO level do not explain these trends, although it was suggested that the contribution of excitation terms to the paramagnetic part of the shielding tensor could explain the change in direction of the trend for the ammonium groups[26]. A simple explanation of most of the trends is that stronger hydrogen-bond acceptance by a carbonyl oxygen atom results in a more positive charge on the oxygen and hence on the carbon atom. This would be expected to produce a downfield shift if changes in electron density dominate. The situation for the polyols considered here is more complicated since each hydroxyl group acts as both a donor and acceptor of hydrogen bonds. Table III lists hydrogen-bonded O–O distances for the B and C polymorphs of D-mannitol[11,12] and for DL-mannitol[14] calculated here from the atomic positions reported[11,12,14]. In the following discussion, we will use the term hydrogen-bond accepting distance as the distance from the oxygen on the carbon atom being discussed to the oxygen bonded to the hydrogen atom to which the first oxygen atom is hydrogen-bonded, and the hydrogen-bond donating distance as the distance from the oxygen atom of the hydroxyl group on the carbon atom being discussed to the oxygen atom it is related to by a hydrogen bond. Here, the polymorph having the longest hydrogen-bond accepting distances, κ, had the largest shifts to low frequency when solution and solid-state values were compared for its primary carbon atoms. In contrast, the polymorph having the shortest hydrogen-bond accepting distances, β, had much smaller shifts to low frequency on moving from solution to solid state. The two polymorphs have similar hydrogen-bond donating distances. In DL-mannitol, the hydrogen-bond donating and accepting distances are almost identical so this effect should be small. This factor is in the direction that is consistent with the observed changes and may be partially responsible for differences between polymorphs but is clearly not dominant.

The ^{13}C-n.m.r. spectra from solution reflect mannitol's pseudo-C_2 axis of symmetry. The differences in the solid-state ^{13}C-chemical shifts of the two ends of each polymorphic form must be related to structural deviations from C_2 symmetry. Changes in solid-state ^{13}C-chemical shifts have been tentatively linked[27] to differences in the sizes of torsional angles over ranges of 80 to 130°, and it is possible to evaluate the importance of this effect here. Table 6 in ref. 14 summarizes all of the torsional angles involving only C and O atoms in the β and κ polymorphs of D-mannitol and in DL-mannitol. Chemical-shift differences between the signals from

TABLE III

THE RELATIONSHIP BETWEEN HYDROGEN-BONDING DISTANCES AND CHEMICAL SHIFTS FOR PRIMARY CARBON ATOMS

Compound	*O–O Distances (Å)*[a]					*Differences in chemical shifts (p.p.m.)*[b]
	O–H · · · O–C			*C–O–H · · · O*		
D-Mannitol β	O-2–H · · · O-1	2.692		O-1–H · · · O-2	2.755	0.3, 1.8
	O-5–H · · · O-6a	2.721		O-6a–H · · · O-3	2.765	
κ	O-2–H · · · O-1	2.802		O-1–H · · · O-2	2.756	2.5, 3.5
	O-3–H · · · O-6a	2.835		O-6a–H · · · O-5	2.737	
DL-Mannitol	O-6a–H · · · O-1	2.711		O-1–H · · · O-2	2.714	0.7, 1.1
	O-5–H · · · O-6b	2.704		O-6a–H · · · O-1	2.711	

[a]Calculated from atomic parameters and unit-cell dimensions in refs. 11, 12, and 14. [b]Differences between chemical shift value for solutions in D_2O and solid-state value.

TABLE IV

INTERNAL CHEMICAL-SHIFT DIFFERENCES FOR D-MANNITOL POLYMORPHS IN THE SOLID STATE AND RELATED TORSIONAL-ANGLE DIFFERENCES[14]

Carbon atoms	*Chemical-shift differences (p.p.m.)*			
	α	β	κ	DL
C-1–C-6	0.0	1.5	1.0	0.4
C-2–C-5	2.3	1.2	0.5	2.3
C-3–C-4	1.2	1.9	0.6	1.6
Average	1.2	1.3	0.7	1.4
Absolute values of torsional angle differences (degrees) *Torsion angles*				
O-1–C-1–C-2–O-2 – C-4–C-5–C-6–O-6		0.7	2.5	8.6
O-1–C-1–C-2–O-2 – O-5–C-5–C-6–O-6		0.4	4.5	3.9
C-1–C-2–C-3–C-4 – C-3–C-4–C-5–C-6[a]		4.5	1.7	1.2
C-1–C-2–C-3–O-3 – O-4–C-4–C-5–C-6		5.8	1.5	12.2
O-2–C-2–C-3–O-3 – O-4–C-4–C-5–O-5[a]		0.5	1.5	0.8
O-3–C-3–C-4–C-5 – C-2–C-3–C-4–O-4		0.4	3.7	5.5
Average differences		2.1	2.6	5.4

[a]*Anti* torsional angle. The differences given are those between the differences from 180°.

carbon atoms at the two ends of the mannitol chain in the four crystalline forms, and the related torsional angle differences derived from the data from ref. 14 are listed in Table IV. Any correlations between the changes in torsional angles and chemical shifts in the mannitol polymorphs is, at best, slight. For instance, the torsional angle differences in DL-mannitol are consistently large, and yet the chemical shift differences are, on average, about the same as those from the β polymorph. In addition, we were unable to relate any observed chemical-shift differences to differences in values of individual torsional angles.

In conclusion, we have demonstrated that c.p.–m.a.s. ^{13}C-n.m.r. spectra are useful for the characterization of polymorphs. The major effect causing the isotropic, solid-state ^{13}C-n.m.r. chemical shifts to be different from those obtained from solutions are the differences in conformations about the terminal C–C bonds. Although the gross features of the four crystal structures are identical, there are a sufficient number of subtle differences in the geometric details that distinctly different chemical shifts result.

ACKNOWLEDGMENTS

The authors thank the Natural Sciences and Engineering Research Council of Canada for support in the form of grants and a Post-doctoral Fellowship (M.S.M.). They also thank Dr. James Britten for help with interpretation of crystallographic data and Mr. G. Owen for recording the powder diffraction patterns. They are grateful to Professor G. A. Jeffrey for a sample of DL-mannitol.

REFERENCES

1 G. H. Penner and R. E. Wasylishen, *Can. J. Chem.*, 67 (1989) 525–534.
2 For reviews, see H. Saito, *Magn. Reson. Chem.*, 24 (1986) 835–852; P. E. Pfeffer, *J. Carbohydr. Chem.*, 3 (1984) 613–639.
3 C. F. Brewer, J. S. Blanchard, S. Englard, G. Jacob, and G. Avigard, *Carbohydr. Res.*, 102 (1982) 294–297; P. E. Pfeffer, K. B. Hicks, and W. L. Earl, *Carbohydr. Res.*, 11 (1983) 181–194.
4 F. Horii, A. Hirai, and R. Kitamura, *Polym. Bull.*, 8 (1982) 163–170.
5 P. E. Pfeffer, K. B. Hicks, M. H. Frey, S. J. Opella, and W. L. Earl, *J. Carbohydr. Chem.*, 3 (1984) 197–217.
6 H. Saito, R. Tabeta, T. Sasaki, and Y. Yoshioka, *Bull. Chem. Soc. Jpn.*, 59 (1986) 2093–2101.
7 J. Hewitt, M. Linder, S. Perez, and A. Buleon, *Carbohydr. Res.*, 154 (1986) 1–13.
8 C. A. Fyfe, P. J. Stephenson, M. G. Taylor, T. L. Bluhm, Y. Deslandes, and R. H. Marchessault, *Macromolecules*, 17 (1984) 501–505; R. L. Dudley, C. A. Fyfe, P. J. Stephenson, Y. Deslandes, G. K. Hamer, and R. H. Marchessault, *J. Am. Chem. Soc.*, 105 (1983) 2469–2472.
9 M. J. Gidley and S. M. Bociek, *J. Am. Chem. Soc.*, 107 (1985) 7040–7044.
10 S. R. Byrn, P. A. Sutton, B. Tobias, J. Frye, and P. Main, *J. Am. Chem. Soc.*, 110 (1988) 1609–1614; R. A. Fletton, R. K. Harris, A. M. Kenwright, R. W. Lancaster, K. J. Packer, and N. Sheppard, *Spect. Acta*, 43A (1987) 1111–1120; and references cited therein.
11 H. M. Berman, G. A. Jeffrey, and R. D. Rosenstein, *Acta Crystallogr., Sect. B*, 24 (1968) 442–449.
12 H. S. Kim, G. A. Jeffrey, and R. D. Rosenstein, *Acta Crystallogr., Sect. B*, 24 (1968) 1449–1455.
13 L. W. Levy and R. Straus, *Hydrobiologia*, 40 (1972) 423–446.
14 J. A. Kanters, G. Roelofson, and D. Smits, *Acta Crystallogr., Sect. B*, 33 (1977) 3635–3640.
15 T. C. W. Mak, private communication in ref. 6.
16 C. W. Haigh, *Annu. Rep. NMR Spectrosc.*, 4 (1971) 311.
17 A. Rye and H. Sorum, *Acta Chem. Scand.*, 6 (1952) 1128–1129.
18 S. J. Angyal and R. Lefur, *Carbohydr. Res.*, 84 (1980) 201–209.
19 G. W. Schnarr, D. M. Vyas, and W. A. Szarek, *J. Chem. Soc., Perkin Trans. 1*, (1979) 496–503.
20 G. E. Hawkes and D. Lewis, *J. Chem. Soc., Perkin Trans. 2*, (1984) 2073–2078.
21 C. A. Haasnoot, F. A. A. M. de Leeuw, and C. Altona, *Tetrahedron*, 36 (1980) 2783–2792.
22 C. P. Rader, *J. Am. Chem. Soc.*, 91 (1969) 3248–3256; R. R. Fraser, M. Kaufman, P. Morand, and G. Govil, *Can. J. Chem.*, 47 (1969) 403–409.
23 D. K. Dalling and D. M. Grant, *J. Am. Chem. Soc.*, 89 (1967) 6612–6622; J. D. Roberts, F. J. Weigert, J. I. Froschivitz, and H. J. Reich, *ibid.*, 921 (1970) 1338–1347.

24 J. K. WHITESELL, T. LACOUR, R. L. LOVELL, J. POJMAN, P. RYAN, AND A. YAMADA-NOSAKA, *J. Am. Chem. Soc.*, 110 (1988) 991–998.
25 F. IMASHIRO, S. MAEDA, K. TAKEGOSHI, AND A. SAIKA, *Chem. Phys. Lett.*, 99 (1983) 189–192.
26 S. ANDO, I. ANDO, A. SHOJI, AND T. OZAKI, *J. Am. Chem. Soc.*, 110 (1988) 3380–3386.
27 R. P. VEREGIN, C. A. FYFE, R. H. MARCHESSAULT, AND M. G. TAYLOR, *Carbohydr. Res.*, 160 (1987) 41–56; R. HORII, A. HIRAI, AND R. KITAMARU, *ACS Symp. Ser.*, 260 (1984) 27–42.