IV. Conclusions

We examined the signs and magnitudes of the primary and secondary isotope effects on one- and two-bond spin–spin coupling constants observed in high-resolution NMR spectra. The usual negative sign of the primary isotope effect on one-bond couplings and the primary and secondary isotope effects on the two-bond coupling in $HC\equiv CH$ are interpreted by a simple model and a dynamical calculation on $HC\equiv CH$ isotopomers. The interpretation involves mass-independent electronic factors (derivatives of spin–spin coupling) and mass-dependent dynamic factors (mean bond displacements $\langle \Delta r \rangle$, etc.). The positive sign of the primary isotope effect on ^1J(PH) in 3-coordinate phosphorus compounds and its negative sign in 4-coordinate phosphorus are reproduced by calculations of ^1J(PH) as a function of bond length in PH_3 and $H_2P(O)OH$. With these theoretical calculations and physical models, the observed general trends in primary and secondary isotope effects on one- and two-bond couplings can be understood.

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Studies of Cyclodextrin Inclusion Complexes in the Solid State by the ^{13}C CP/MAS and ^{2}H Solid Echo NMR Methods[1]

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Abstract: Solid complexes have been formed from a variety of organic molecules encaged in the α- and β-cyclodextrins, in heptakis(2,6-di-*O*-methyl)-β-cyclodextrin, and in β-cyclodextrin peracetate. The ^{13}C cross polarization magic angle spinning spectra of these inclusion complexes in the solid state have been assigned by comparison with the corresponding solution spectra and suggest that the guest molecules undergo anisotropic motion, which can be detected by use of the dipolar dephasing technique. The deuterium quadrupole echo method has been used to study the molecular reorientation of the guest molecules, and it is shown that the motion of the smaller guests is least affected by the cavity size of the host.

Cyclodextrins (CDs) were first isolated as degradation products of starch in the last century by Villiers[2] and were subsequently characterized as cyclic oligosaccharides in 1904 by Schardinger.[3,4] They are cyclic, nonreducing sugars containing between 6 and 12 α(1 -- > 4)-linked glucopyranose units in the form of torus-like macrorings with a 6–10-Å diameter cavity which is capable of forming inclusion complexes with small "guest" molecules. Selective chemical modification[5] of the CDs provides an array of opportunities to tailor both the equilibrium thermodynamics and the molecular motion of these complexes. Thus, methylated CDs have been shown[6] to be versatile complexing agents, in both aqueous and organic solvents; the stability of their crystalline complexes depends on the shape and size of the encaged molecule.[7] Fully O-acetylated β-CD may also serve as host for smaller size organic molecules.

Although ^{1}H and ^{13}C NMR methods have been used extensively to study soluble complexes of unsubstituted CDs in solution, equivalent studies in the solid state have only been reported recently.[8,9] A preliminary report[9] gave an evaluation of the ^{13}C CP/MAS[10] and ^{2}H quadrupole echo[11] methods for studying inclusion complexes of both unsubstituted- and substituted-CD inclusion complexes, and we now describe a more detailed analysis of the relationships between motion, structure, and mobility for several related series of guest molecules.[12]

As will be seen, the resonances observed by the ^{13}C CP/MAS method reflect not only chemical distinctions and stoichiometry but also magnetic inequivalences present in those complexes,[13]

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which depend on the extent of the host–guest interactions. For smaller aromatic molecules in heptakis(2,6-di-*O*-methyl)-β-cyclodextrin (2,6-di-*O*-Me-β-CD) the isotropic chemical shift values of the neat liquids and the solid complexes are essentially identical, whereas the chemical shift differences for complexes of β-cyclodextrin peracetate (2,3,6-tri-*O*-Ac-β-CD) are greater than 1.0 ppm. In the solid state, the mobility of the guest molecules is affected by the cavity size of the hosts. Supporting evidence which is indicative of differential motion of individual segments of the guest stems from the ^{13}C CP/MAS, dipolar dephasing measurements.[14] However, ^{2}H quadrupole echo method provides a better insight to the motion of the guest molecules within the annulus of the CD ring.

Experimental Section

All commercial materials were purified by standard methods. However, the α- and β-CDs obtained from the Sigma Chemical Co. were used without further purification. 2,6-di-*O*-Me-β-CD and 2,3,6-tri-*O*-Ac-β-CD were prepared according to the procedures of Szejtli et al.[15] and Stoffyn and Jeanloz,[16] respectively. Microanalyses and ^{13}C-{^{1}H} spectra of these compounds indicated that they were pure. The solid inclusion complexes were obtained by slow (overnight) cooling of a hot methanolic solution containing a 1:1 molar ratio of the modified CDs and the respective guest compound. ^{1}H NMR and UV methods were then used to study the crystalline complexes in solution[17] to confirm that the guest molecule had been included and to estimate the stoichiometry of the resultant complex.

The CD inclusion complexes of dimethyl-d_6 sulfoxide or acetone-d_6 were obtained from an aqueous or methanolic/aqueous solution by gradual cooling. The monosubstituted benzenes, toluene-α-d_1 and ethylbenzene-β-d_1 were prepared following the method of Brown and Russell.[18]

All NMR spectra were determined in the Fourier mode by using a Bruker CXP-200 spectrometer, operating at 200 MHz for ^{1}H, 50.3 MHz for ^{13}C, and 30.7 MHz for ^{2}H. ^{13}C CP/MAS spectra were obtained at room temperature by using a doubly tuned, single-coil probe. Spin-locked cross polarization was established by the single contact Hartmann–Hahn procedure,[10] by using applied ^{1}H and ^{13}C radio frequency fields of 15 and 60 G, respectively. Contact times were optimized by measuring the magnetization response to variable spin-locking times (2–5 ms) when integration of the carbon resonances was desired. Delrin and deuterated plexiglas spinners were used, and the spinning frequency, estimated from the spinning sidebands, was 4.2 ± 0.3 kHz. The ^{13}C NMR signal of liquid benzene was used as the external reference to determine the chemical shifts, which were subsequently expressed as ppm downfield from Me_4Si (benzene is 128.5 ppm downfield from this reference).

^{2}H NMR spectra were recorded on the same instrument by using a 10-mm o.d. sample tube and a quadrupole echo pulse sequence.[11] The radio frequency pulse width varied between 2.5 and 6.0 μs, depending on the size of the spectral width; pulse spacing of 100–240 μs and recycle times of 0.5–1.0 s were used. All data were acquired in quadrature with a 2.5-MHz-digitization rate. The temperature at the sample was controlled with a flow of compressed air or nitrogen gas and stabilized with a Bruker temperature control unit (Model BVT 1000). All ultraviolet measurements were determined by using a Gilford Instrument (Model 2530).

Results and Discussion

X-ray. Prior to analyzing the NMR data, a brief review on a number of pertinent X-ray studies relevant to our discussion is included. Reported X-ray data[19] of hexakis(2,3,6-tri-*O*-methyl)-α-cyclodextrin and its inclusion complexes show that the six O(2)–C(7) bonds are directed outside the CD ring, with the six O(3)–C(8) bonds turned inside the ring. Nevertheless, as compared to the β-CD derivatives we would expect a wider opening for the O(2),O(3) side of the cavity of 2,6-di-*O*-Me-β-CD but probably not in the case of 2,3,6-tri-*O*-Ac-β-CD. It is also known[19,20] that the molecular dispositions of the substituted benzenes may differ from one host to another, and their 1:1 complexes may crystallize in "cage"- or "channel"-type structures, depending on the nature and size of the guest molecule. For larger elongated guest molecules, their 1:1 complexes may well crystallize in "channel"- or discontinuous "channel"-type structures.[20] Here, one guest molecule is included within the cylinder of two CD units, while the other is located outside the CD ring to afford a molar ratio of 1:1. Alternatively, one guest molecule is assigned to a ring, thereby disrupting the channel-type structure of the host. Examples of such molecules used in the present studies are biphenyl, 4,4′-dimethylbiphenyl, and *p*-di-*tert*-butylbenzene.

Table I. Crystalline Complexes Formed by Cyclodextrins

complex no.	substrate	host	molar ratio[a]
	With Apolar Compounds		
3	benzene	**1**	1:1
4	toluene	**1**	1:1
5	ethylbenzene	**1**	1:1
6	*p*-xylene	**1**	1:1
7	chlorobenzene	**1**	1:1
8	bromobenzene	**1**	1:1
9	cyclohexane	**1**	1:1
10	methylcyclohexane	**1**	1:1
11	biphenyl	**1**	2:1
12	4,4′-dimethylbiphenyl	**1**	1:1
13	*p*-di-*tert*-butylbenzene	**1**	1:1
14	*p*-bromotoluene	**1**	1:0.2
15	durene	**1**	1:0.1
16	naphthalene	**1**	1:0.2
	With Polar Compounds		
17	pyridine	**1**	1:0.2
18	*p*-hydroxytoluene	**1**	1:0.2
19	*p*-toluidine	**1**	1:0.1
20	benzoic acid	**1**	1:0.1
	With Apolar Compounds		
21	benzene	**2**	1:1
22	toluene	**2**	1:1
23	*p*-xylene	**2**	1:1

[a] Molar ratio of cyclodextrin:substrate.

Biphenyl crystals are known[21] to be monoclinic, with two molecules in the unit cell of space group $P2_1/a$. The single, symmetry-independent molecule, which is situated on a center of symmetry, has a completely planar structure for the carbon skeleton. Albeit that the hydrogen atoms are situated in the plane defined by the carbon atoms of biphenyl, there are small in-plane displacements of the ortho hydrogen atoms from idealized positions that reduce the steric strain. The gain in stabilization energy from attainment of planarity is probably of the same order as that required to compress the C and H atoms slightly;[22] thus, it is reasonable to suppose that planar or nonplanar arrangements could occur in the crystal, depending on the packing.

4,4′-Dimethylbiphenyl crystals are monoclinic,[22] with eight molecules in the unit cell of space group $P2_1/c$. There are two molecules in the asymmetric unit, with dihedral angles of 36 and 40°, respectively. Reported X-ray crystal structure of *p*-di-*tert*-butylbenzene[23] indicates no inequivalent molecules in the unit cell of space group $P2_1/n$.

^{13}C NMR. 2,6-di-*O*-Me-β-CD (**1**) was found to afford crystalline 1:1 complexes with many guest molecules and, therefore, provided a good series of complexes for our studies. In contrast, 2,3,6-tri-*O*-Ac-β-CD (**2**) was found to be less suitable as a host, probably due to space restriction at both ends of its cavity. A list of the complexes studied is given in Table I.

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Table II. Chemical Shifts (ppm) for the Liquid Guest Molecules[a]

substrate	host	(unsub)	C_1	ortho	meta	para	CH_2	CH_3
benzene		128.5						
	1	128.7						
	2	129.7						
toluene			137.7	129.2	128.6	125.6		
	1		138.0	(128.7)		126.2		
	2		140.5	(130.0)		126.6		
p-xylene			134.5	(129.1)				20.8
	1		135.0	(128.7)				21.6
	2		(137.5, 136.5)	(130.3, 129.1)				(obscured)
ethylbenzene			144.1	128.4	127.9	125.8	29.1	15.7
	1		144.5	128.8	127.7	(obscured)	29.5	17.1
chlorobenzene			134.7	128.9	130.1	126.8		
	1		134.3	128.6	130.0	(obscured)		
bromobenzene			123.0	131.9	130.5	127.3		
	1		122.0	131.5	130.3	128.5		

[a] Chemical shifts are expressed as ppm downfield from Me_4Si.

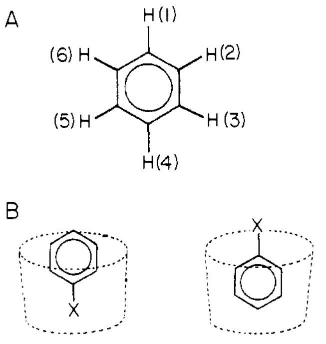

Figure 1. Schematic drawings of the inclusion possibilities for monosubstituted benzene molecules.

According to Van Hooidonk and Breebaart-Hansen,[24] the diameter of the β-CD cavity is 7.5 Å, and the size of the benzene ring is about 6.8 Å, that is the distance measured between H(2) and H(6) (Figure 1A). One would expect a monosubstituted benzene ring to orient along its long axis in the cavity, rather than in a "crosswise" manner. However, the "upright" position allocated to the benzene ring could be either "head-first" or "head-last". It may not be possible to distinguish the correct orientation solely by the ^{13}C CP/MAS method in this complicated system. Such uncertainties will not seriously limit our discussion on other interesting static and motional aspects of the "guest–host" structure in the solid state.

Figure 2 shows the ^{13}C NMR spectra obtained for several related inclusion complexes of 2,6-di-*O*-Me-β-CD. The gradual change in the line shape patterns of the sugar resonances, from complex **3** to **10**, suggests the same "upright" orientation inside the host cavity for the benzene ring as has been found for other aromatic molecules.[25] Presumably, the long axis of the aromatic molecule lies almost parallel to the channel (cavity) axis of the CD.

The splittings of the ^{13}C resonances of the host may be discussed in terms of the parameters which are known[26] to contribute to changes in the chemical shifts on complex formation in solution. If the π-cloud deshielding effect was of significance in perturbing the carbon resonances, this perturbation should be slightly different for a given set of carbons due to restricted mobility of the guest molecules. As in solution, such an effect is unlikely because similar splitting patterns were observed for the host with smaller aromatic and nonaromatic guest molecules. Hence, the major contributions may well come from the steric interactions and conformational changes of the cavity on substrate complexation. It is seen from the set of spectra that the splittings become more complex with increasing size of the substituent groups in monosubstituted benzenes and more so in the disubstituted benzenes. Here, the participation of conformational change may be considered large since the macrocyclic conformation of this host is relatively free of steric hindrance at the C-2,C-3 side of the cavity. This would provide a good fit between the guest and the host. On the other hand, the bulky acetyl groups of compound **2** may impose severe restriction on bond distortions and also constriction for the opening at both ends of the truncated cone. Figure 3 reveals the complexity of the ^{13}C resonances of the host, even with benzene as the guest molecule. Again, a similar trend was observed in the splitting patterns; the effect is most pronounced for the complex with the largest substrate, *p*-xylene, that can be accommodated inside the cavity.

Depending on the extent of the host–guest interactions, noticeable changes in the chemical shifts of the guest molecules can be anticipated. Table II lists the chemical shift values of the ^{13}C resonances of the aromatic molecules as neat liquids and as encaged aromatic "solids". The isotropic chemical shift values of these molecules remain practically the same, on going from the free to the complexed forms with host molecule **1**. This indicates that the guest molecules have very weak van der Waals contacts with the interior surface of the cavity and that they are essentially "free". In the case of 2,3,6-tri-*O*-Ac-β-CD complexes, the isotropic chemical shift differences are greater than 1.0 ppm; the maximum experimental drift in chemical shift for this NMR instrument is estimated to be ±0.5 ppm. Hence, the downfield shift of the guest resonances could be attributed to the small cavity of the host molecule, in which the acetyl groups bestow a strong deshielding effect on the guest molecule. An interesting observation is the splittings of the aromatic carbon resonances of *p*-xylene into doublets in complex **23**. We suggest that this may be caused by incomplete penetration of the rigid guest molecule into the cavity.

In the solid state, the aromatic ring of the guest molecules is not freely rotating about its twofold axis within the annulus of the host. However, it can undergo librational flip motion with a very small amplitude.[27] Large angle rotation by the aromatic ring about its long axis may be restricted in the cavity of compounds **1** and **2**; this is particularly true in the latter because of severe steric hindrance imposed by the acetyl groups. The perturbation from the rigid crystalline field may ultimately determine the differences in the time scale and mode of motion of the aromatic rings in solution and in the solid complexes.

The ^{13}C resonances of host molecule **1** show no strong multiplicity changes[28] in going from its free state to its complexed state with smaller guest molecules. Hence, only a slight departure from cylindrical symmetry is expected for this host in which the guest molecules are undergoing motion within the annular space.

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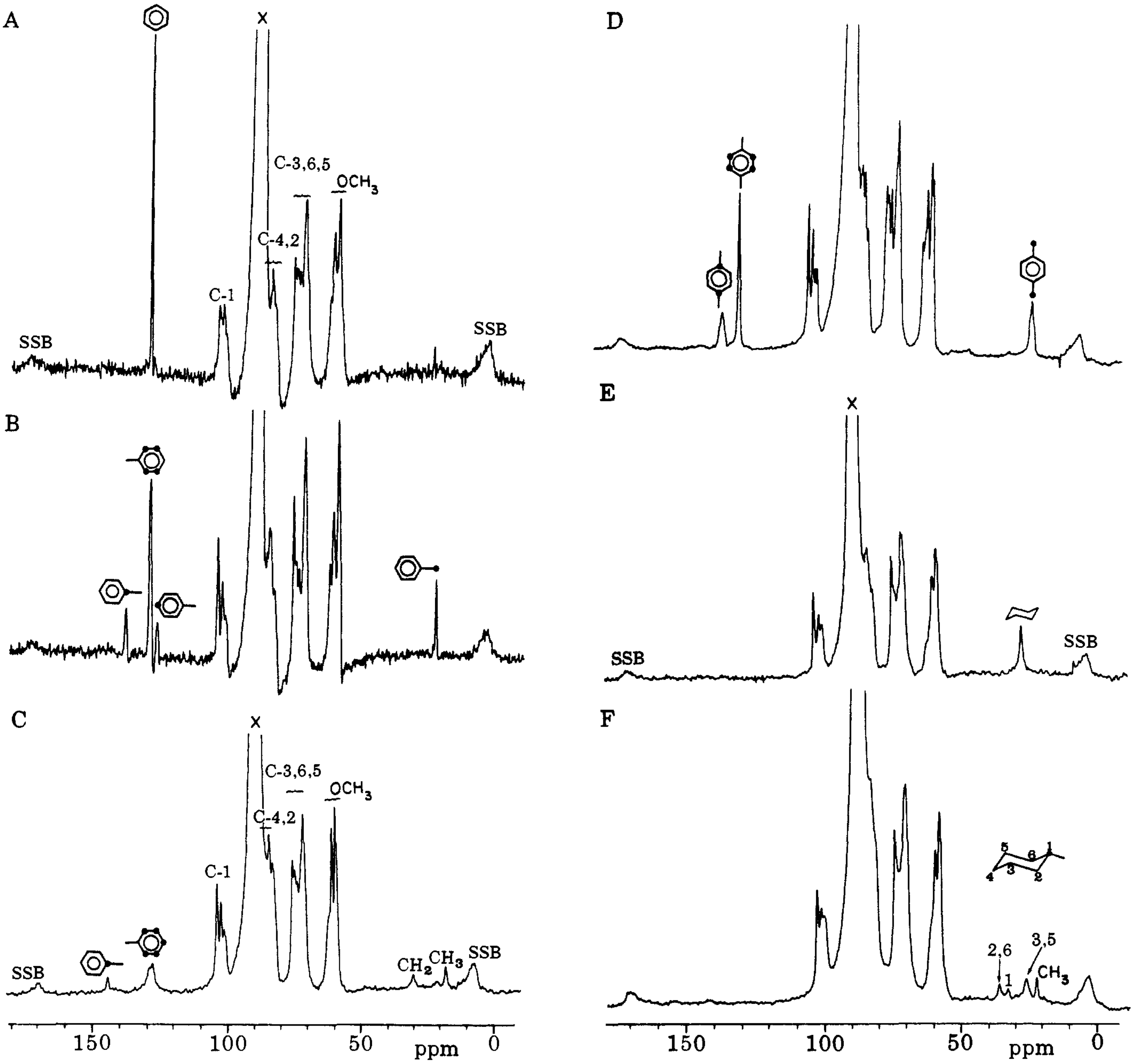

Figure 2. ^{13}C NMR spectra of 2,6-di-*O*-Me-β-CD inclusion complexes (A) **3**; (B) **4**; (C) **5**; (D) **6**; (E) **9**; and (F) **10**. The Delrin signal and spinning sidebands are indicated as X and SSB, respectively.

Supporting evidence for differential motion of individual segments of the guest stems from the ^{13}C CP/MAS measurements used to differentiate between the resonances of protonated and nonprotonated carbons. The dipolar dephasing technique[14] can be used to eliminate spectral signals from carbons strongly coupled to protons, leaving signals from both nonprotonated carbons and weakly coupled carbons because of averaging of dipolar interactions by extensive molecular reorientation. In this way, the signals from pendant substituents attached to the CDs, such as methoxyl and acetoxyl moieties, are retained. Substantial signals were obtained for all the resonances of the guest molecules within the crystalline matrix of compound **1**. However, the resonances of the aromatic carbons of complexes **22** and **23** are essentially suppressed because residual, or no, motion is allowed for the ring that is intimately associated with the cavity (Figure 4). Only the methyl groups give substantial signals that reflect the various additional degrees of freedom available to all these carbon atoms.

It was found that variations in crystalline field can alter the chemical shift dispersions of solid substrates between their values in the free state and those when complexed with the host molecule **1**. This occurs when relatively large guest molecules are involved in the complexation; i.e., biphenyl, 4,4′-dimethylbiphenyl, and *p*-di-*tert*-butylbenzene. One would expect their combining ratios of the guest:host to be 1:2; this is only true for biphenyl, whereas the others yield 1:1 complexes.

The ^{13}C NMR spectra of solid biphenyl and its complex with compound **1** are shown in Figure 5. The line widths and chemical shifts of the carbon resonances belonging to the guest molecule are affected by the change in its environments. Carbon atoms C-1,C-1′ or C-4,C-4′ probably have equivalent molecular and crystal environment since a single ^{13}C resonance was observed in the solid state for the C-1,C-1′ pair of carbons. It should be noted that crystal symmetry does not require that the ortho or meta carbon pairs to be equivalent.[29] In this case, the difference is not sufficiently large for spectral resolution, and, hence, only broad resonances were observed for the ortho and meta carbons. The in-plane displacements of the hydrogen atoms may not cause any broadening of the carbon resonances because the overall symmetry of the molecule is still retained. The encaged biphenyl molecule

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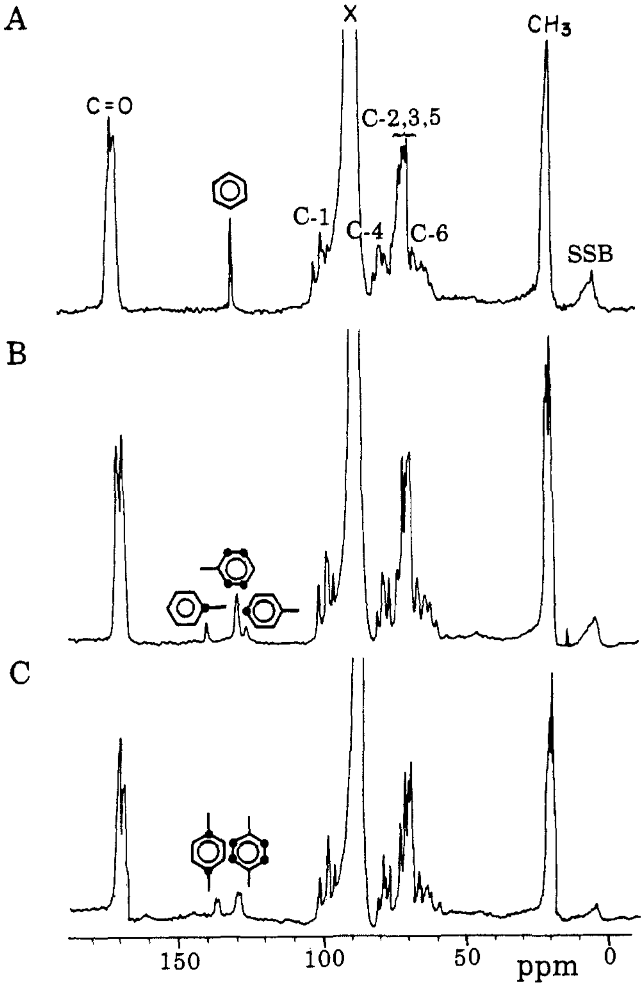

Figure 3. ^{13}C NMR spectra of 2,3,6-tri-*O*-Ac-β-CD inclusion complexes (A) **21**; (B) **22**; and (C) **23**. The Delrin signal and spinning sidebands are indicated as X and SSB, respectively.

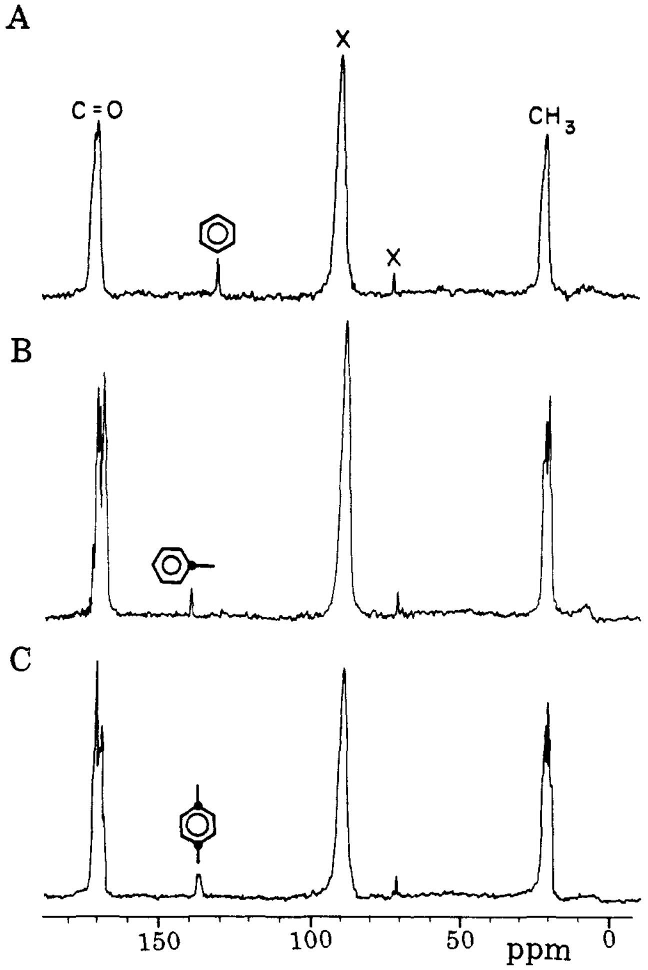

Figure 4. Dipolar dephasing ^{13}C NMR spectra of 2,3,6-tri-*O*-Ac-β-CD inclusion complexes (A) **21**; (B) **22**; and (C) **23** (obtained by setting a 40-μs period without proton decoupling prior to ^{13}C data acquisition). The Delrin signals are indicated as X.

would probably adopt a coplanar structure within the annulus of the ring. This is evident from the narrower and well-resolved line widths, and any slight magnetic inequivalence in the pairs of carbon atoms is now removed because the molecule is experiencing a "solution-like" environment. At the same time, the steric compressions[30] are relieved as indicated by the downfield shifts of the C-1 and ortho carbons, which are close to those values measured in solution. Librational motion of the molecule, about its long axis, is suggested from the dipolar dephasing spectrum.

The crystal structure of 4,4′-dimethylbiphenyl indicates the presence of two molecules in the asymmetric unit and, therefore, its solid-state spectrum should be more complicated than that of biphenyl. Each carbon resonance is expected to split at least into a doubleted doublet; instead, broad signals with fewer splittings were observed (Figure 6). The intramolecular and intermolecular effects may not be large enough to give resolvable splittings due to the small difference in the dihedral angles, yet considerable shifts are induced by the latter. The splittings and shifts in the carbon resonances can be removed by encaging the molecule inside the cavity of compound **1**. If this 1:1 complex crystallizes in a channel-type structure, the chemical shifts of the guest molecule situated inside and outside the long column should differ. But sharp signals with isotropic chemical shifts close to those data obtained in solution were observed. Therefore, the molecule is probably planar and undergoing molecular reorientation within the discontinuous channel-type structure of the host.

The ^{13}C NMR spectrum of *p*-di-*tert*-butylbenzene shows two peaks for the ortho carbons due to inequivalent molecular and crystal environments (as discussed earlier for the biphenyl molecule); the other carbon resonances appear as singlets. Similarly, molecular reorientation of the guest molecule within the cavity of the host affords sharp signals (Figure 7); a singlet for the ortho carbons and, surprisingly, a doublet of equal intensity for the methyl carbons. We conclude that the two *tert*-butyl moieties probably experience different local environments and that these differences are largest for the methyl groups.

^2H NMR. Attention was next directed to the evaluation of molecular reorientation of the various guest molecules within the annular space of the various cyclodextrins. For two reasons, it was convenient to start by studying the complexes formed from dimethyl sulfoxide (Me_2SO) and both α- and β-CDs, prepared from solutions in Me_2SO-d_6/H_2O or Me_2SO-d_6/MeOH/H_2O. Thus, an X-ray study[31] of the complex of Me_2SO with α-CD showed the Me_2SO to be located in the host cavity nearest to the secondary hydroxyl groups and with two hydrogen bonds to the adjacent α-CD molecules. Furthermore, the quadrupole coupling constant, e^2qQ/h, of $(CD_3)_2SO$, was known[32] to be 162 kHz which could be used to estimate the magnitude of the quadrupole splitting for a rigid lattice to be 121.5 kHz. Thus, fast C_3 rotation of the methyl group provides an average over all directions of the C–D axis giving the spectrum with a reduction factor[32,33] of $(3\cos^2 109°28' - 1)/2$; for sp^3 bonds, the asymmetry parameter is assumed to be zero. The splitting of 38.8 kHz observed experimentally at −23 °C for β-CD–Me_2SO-d_6–H_2O complex **24** is sufficiently close to the expected value[32] (40.5 kHz) to lend credence to the method. However, it is interesting to note that

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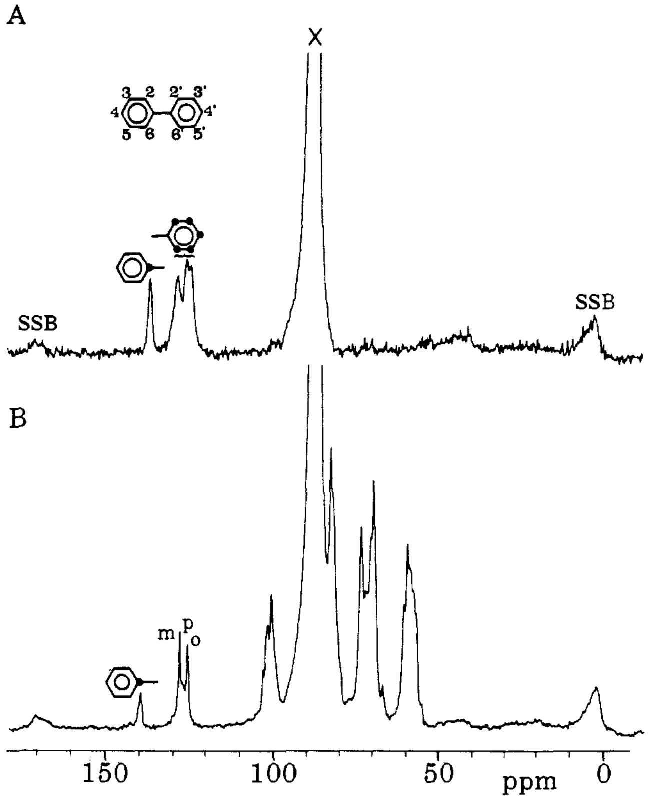

Figure 5. ^{13}C NMR spectra of (A) biphenyl and (B) 2,6-di-*O*-Me-β-CD-biphenyl inclusion complex, **11**. The Delrin signal and spinning sidebands are indicated as X and SSB, respectively.

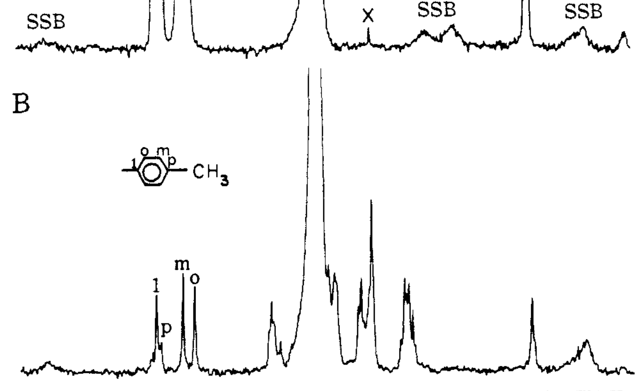

Figure 6. ^{13}C NMR spectra of (A) 4,4'-dimethylbiphenyl and (B) 2,6-di-*O*-Me-β-CD-4,4'-dimethylbiphenyl inclusion complex, **12**. The Delrin signals and spinning sidebands are indicated as X and SSB, respectively.

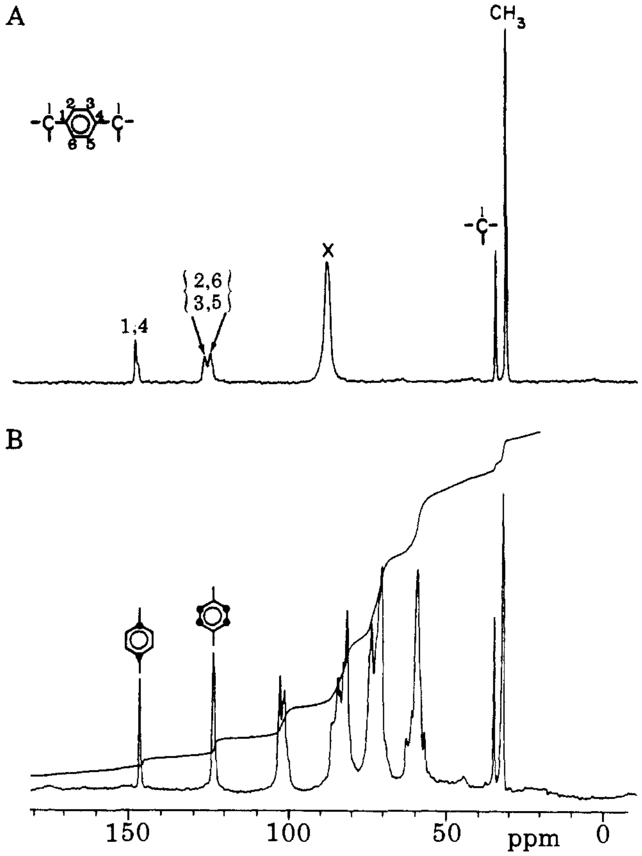

Figure 7. ^{13}C NMR spectra of (A) *p*-di-*tert*-butylbenzene and (B) 2,6-di-*O*-Me-β-CD-*p*-di-*tert*-butylbenzene inclusion complex, **13**. The latter was obtained by using a deuterated, plexiglas spinner.

at higher temperatures the splitting decreases to ca. 10 kHz (Figure 8A). This must be due to additional anisotropic motion which is fast on the NMR time scale. If that motional averaging involved rotation of the molecule about the axis through the sulfur and oxygen atoms, then the splitting would be further reduced from its motional value of 40.5 kHz by a factor of (3 cos^2 123° − 1)/2 to afford a 13.8 kHz splitting in not unreasonable agreement with the experimental value.

The success of this simple model, prompted us to examine the complex **25** of acetone-d_6 with β-CD. The observed splitting at 20 °C is <5 kHz. Although the acetone molecule is of planar symmetry, rotation about the carbonyl bond would reduce the motional splitting by (3 cos^2 123° − 1)/2 to give a separation of 4.6 kHz. Fast rotation about an axis perpendicular to the plane of the acetone molecule seems unlikely since it would lead to a substantially larger splitting (20 kHz) than that observed experimentally. Thus, these results suggest that both guest molecules behave similarly within the annulus of β-CD.

Comparison with the analogous α-CD complexes enables an evaluation to be made of the effects of ring size. The quadrupole splitting for $(CD_3)_2SO$ in the α-CD complex **26** at 20 °C is larger (40 kHz) than that of the β-CD complex (10 kHz), which suggests a substantially tighter fit within the smaller annular space of the former. A further important difference is the presence of a small, sharp isotropic peak, which is indicative of "free" $(CD_3)_2SO$ molecules. Heating the sample to higher temperatures increased the intensity of the isotropic peak and, concomitantly, decreased the breadth of the large splitting (see Figure 8B). Furthermore, the former could not be removed even by careful washing of the crystals with cold methanol. The α-CD complex of acetone **27** also reveals two kinds of guest molecules within the crystal lattice, although in this case the isotropic peak was more intense than that of complex **26**. It is of interest to note that when these complexes were crystallized from methanol/water solution, no significant changes of their line shapes were observed. Presumably, the methanol and/or water molecules present in the crystal lattice have no substantial influence on the molecular reorientation of the guest molecules.

The ^{2}H quadrupole splittings of benzene-d_6 sequestered in the host molecules **1** and **2** clearly illustrate the influence of cavity size on its mobility. The values measured at 20 °C for complexes **3** and **21** are 48 and 68.5 kHz, respectively (Figure 9). For a rigidly bound benzene molecule, a splitting of 141 kHz would be

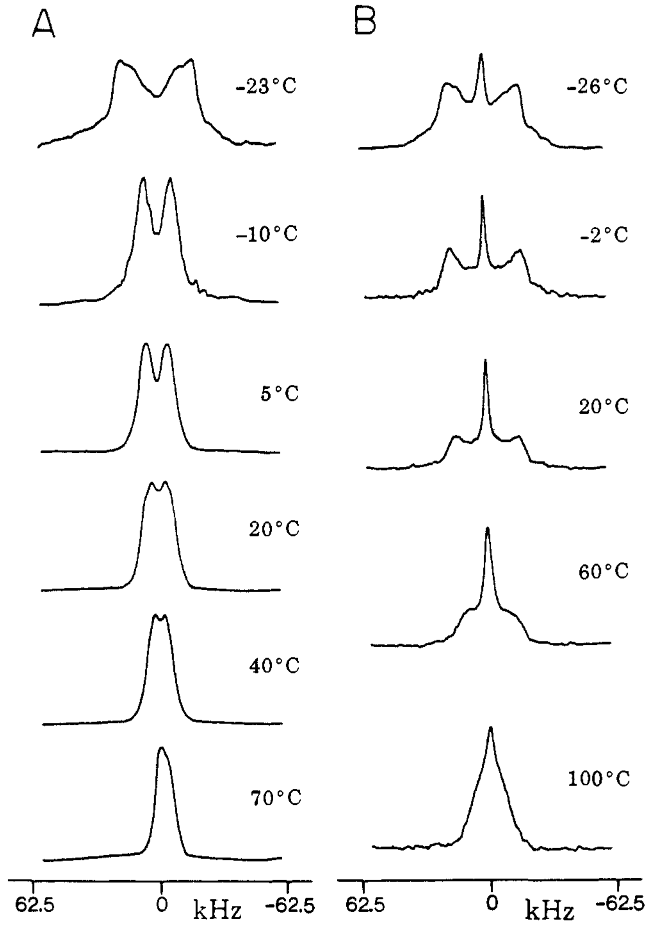

Figure 8. ^2H NMR spectra of $(CD_3)_2SO$ (A) in the β-CD complex **24** and (B) in the α-CD complex **26**, recorded at the temperatures indicated.

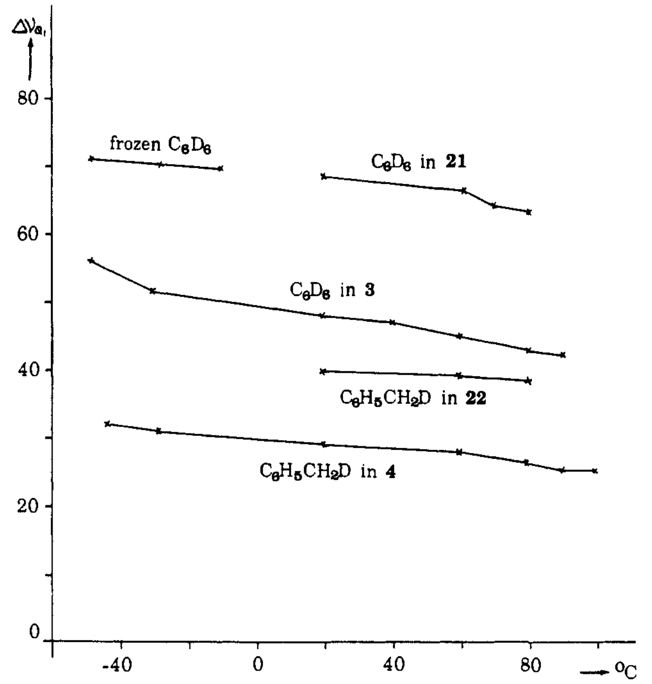

Figure 9. Variation of the quadrupole splitting, $\Delta\nu_{Q_1}$, with temperature for C_6D_6 in complexes **3** and **21** and $C_6D_5CH_2D$ in complexes **4** and **22**.

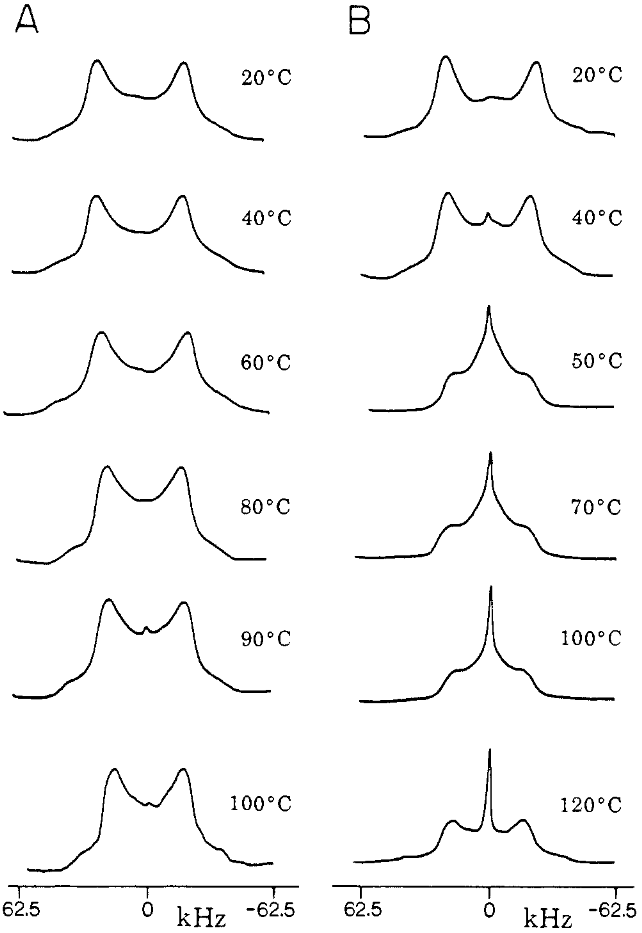

Figure 10. ^2H NMR spectra of C_6D_6 in the 2,6-di-*O*-Me-β-CD complex **3** (A) in unsealed and (B) in sealed tubes, recorded at the temperatures indicated.

expected;[34] rapid rotation of the benzene about its C_6 axis ($>10^8$ s^{-1}) within the cavity would give an observed splitting of 70 kHz and about a C_2 axis a 15 kHz splitting. From these values, it is clear that rapid rotation occurs principally about the C_6 axis; an additional angular fluctuation of the axis (root mean square angle ca. 20°) would account for the smaller value observed experimentally for complex **3**. Interestingly, it is possible to freeze out this angular fluctuation by decreasing the temperature of sample **3**, as indicated by the larger quadrupole splitting values obtained at lower temperatures (Figure 10). Furthermore, the molecular motion can also be perturbed further by raising the temperature up to a limit of 90 °C. Above this temperature, steady "distillation" of benzene from the annulus makes it difficult to obtain a spectrum. When the experiment is performed in a sealed tube, the free benzene appears as a single peak centered at the Larmor frequency, and a thermal equilibrium exists between the guest and the host. It should be noted that interpreting of ^2H line shapes of this guest molecule in some intermediate state of the host/guest environments may, in general, be quite difficult.

The axially symmetric powder spectra[35] observed suggest, at least for higher temperatures, that the benzene molecule may also reorient about a second diffusion axis perpendicular to the rapidly rotating C_6 axis. Since the benzene ring assumes an upright position within the inclusion channel, both the channel and the second diffusion axes are likely to be collinear. As a consequence of motional averaging along this axis, the quadrupole splitting observed for the pure C_6 rotation would be further reduced by a geometric factor of $(3\cos^2 90° - 1)/2$ to afford a value of 35.1 kHz. In the case of 2,3,6-tri-*O*-Ac-β-CD complex **21**, the mobility of the benzene molecule is restricted by the cavity size to rotation about the C_6 axis, even at higher temperatures.

A similar differential was found for toluene-α-d_1 $C_6H_5CH_2D$, sequestered in the same two host molecules **1** and **2**. The observed splittings measured at 20 °C (see Figure 9) are 29 and 40 kHz,

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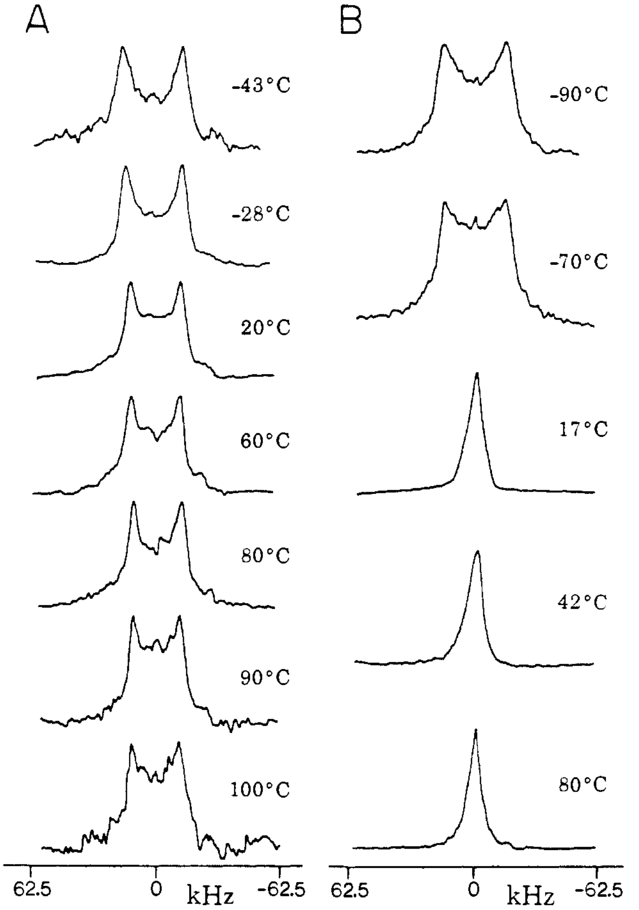

Figure 11. ^2H NMR spectra of (A) $C_6H_5CH_2D$ in complex **4** and (B) $C_6H_5CH_2CH_2D$ in complex **5**, recorded at the temperatures indicated.

respectively. The latter value is close to that (45 kHz) expected[36] for the fast rotation of a methyl group about its C_3 axis. Additional fast motion about the long molecular axis in which the aromatic ring undergoes molecular reorientation may be the source of the small additional reduction observed. That same motion would also explain the results described earlier from the dipolar dephasing ^{13}C spectrum of **4**. It should be noted[37] that reorientation of toluene precisely about its long axis would not further alter the powder pattern of the methyl group because the reduction factor corresponding to $(3 \cos^2 0° - 1)/2$ is unity. Presumably, the fast motion occurs about an axis which is tilted slightly away from the long molecular axis. On heating the sample above ambient temperature, the toluene gradually distilled off and this was accompanied by a decreased quadrupole splitting (Figure 11A); a reduction in splitting was not obvious for 2,3,6-tri-*O*-Ac-β-CD complex **22**.

Intuitively, it seemed reasonable to expect an increase in motion with increase in distance of the pendant group from the annulus, due to decreased energy barriers to aliphatic conformational changes. This is nicely illustrated by the decrease in the magnitude of the quadrupole splitting at 20 °C in going from the 2,6-di-*O*-Me-β-CD complex of $C_5H_5CH_2D$ (29 kHz) to that of $C_6H_5CH_2CH_2D$ (<5 kHz). For fast motion about the long molecular axis, the quadrupole splitting of the methyl group would be reduced by a further factor of $(3 \cos 109.5° - 1)/2$ to give a value of about 15 kHz. The sharp, isotropic-like peak observed at ambient temperature for complex **5** suggests that the aromatic ring of ethylbenzene also reorients about a similar axis as for toluene. On cooling the sample to −90 °C, the observed splitting of complex **5** increased to 37 kHz (see Figure 11B). This observation indicates that the molecular motion is almost completely confined to the methyl group, with some additional motion of the aliphatic chain being responsible for the slight reduction of the quadrupole splitting from the 44 kHz value expected for a pure methyl rotation.[36]

Conclusions

Since crystal structures are not available for neither of the two host molecules **1** and **2** nor for their inclusion complexes, the studies reported here provide new information for these systems. However, the interpretations given here have been facilitated by comparison with the ^1H and ^{13}C NMR studies of these complexes in solution and with the X-ray data of the guest molecules themselves and of related guest–host complexes.

We have found that the sugar resonances of CDs are relatively broad and are often complicated by the substantial splittings induced by the presence of the guest molecules. Reciprocal shifts are induced for the guests; those of the smaller guest molecules were found to be least affected by the cavity size of the host molecule **1**, and their isotropic chemical shift values are similar to those measured for solutions. Those molecules which undergo anisotropic motion within the cavity[8,38] could be detected by the dipolar dephasing technique. Deuterium quadrupole echo spectroscopy provided direct evidence concerning the molecular motion of the guest molecules and could be interpreted by comparison with results reported in the literature for other systems. Indeed, the present study supports previous reports[34,35] that the deuterium quadrupole method can provide very detailed insight concerning molecular motion of complex organic systems; this potential is further enhanced by the ease and low cost with which specific deuteration can be achieved.

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Registry No. 3, 88946-27-4; **4**, 100939-42-2; **5**, 100939-43-3; **6**, 100946-35-8; **7**, 100939-44-4; **8**, 100939-45-5; **9**, 100939-46-6; **10**, 100939-47-7; **11**, 100939-48-8; **12**, 100939-49-9; **13**, 100939-50-2; **14**, 100939-51-3; **15**, 100939-52-4; **16**, 100946-33-6; **17**, 100939-53-5; **18**, 100939-54-6; **19**, 100939-55-7; **20**, 100946-36-9; **21**, 100946-34-7; **22**, 88946-28-5; **23**, 100939-56-8; **24**, 100993-29-1; **26**, 100939-57-9.

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