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Inclusion Compounds of Cyclodextrin and Azo Dyes. III.[1] ^{13}C Nuclear Magnetic Resonance Spectra of Cyclodextrin and Azo Dyes with a Naphthalene Nucleus[2]

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Inclusion compounds of azo dyes which have a naphthalene nucleus were examined by ^{13}C nuclear magnetic resonance (NMR). The azo dyes used form 1: 1 complexes with cyclodextrin. The guest molecule is uniformly affected by the cavity, as if it were dissolved in a hydrophobic solvent. $C\text{-}SO_3^-$ at the end of the molecule shows the largest shift and can be used as an index of inclusion.

Almost all carbons of the guest molecule show low field shifts on inclusion, which are consistent with the ^1H NMR behavior. Thus, the shift mechanism may be due not to a simple steric polarization effect, but to hydrophobic interaction with the host molecule.

The host molecule is deformed at the glycosidic linkage rather than at the small diameter side of the cavity by the bulky naphthalene nucleus.

Keywords——inclusion compound; cyclodextrin; azo dye; ^{13}C NMR; inclusion shift; complex formation ratio; localization; deformation

Introduction

The cavity of cyclodextrin (cdx) can include many organic molecules to form inclusion compounds. Recently, studies by nuclear magnetic resonance (NMR) have become practical[4-10]; the chemical shift and the relaxation time can indicate the orientation of inclusion and the freedom of movement. Tabushi *et al.*[4] examined the ^1H NMR of 1-anilino-8-naphthalenesulfonate-β-cdx complex and concluded that the phenyl part is at the periphery of β-cdx. From the orientational specificity of the inclusion shift value, signal broadening, nuclear Overhauser effect (NOE) and the positions of the substituents, Bergeron *et al.*[8] reported that sodium *p*-nitrophenolate enters from the uncharged, hydrophobic NO_2 group site and is partially included. Moreover, the guest molecule is fixed firmly into the cavity and cannot move. Saenger *et al.*[5] concluded from the results of both X-ray and NMR that α-cdx includes *p*-iodoaniline from the hydrophobic iodine site and the amino group remains at the periphery of the cavity. Behr *et al.*[9] examined the relaxation time of α-cdx and cinnamic acid derivatives and concluded that upon inclusion the orientation times of the guest molecule increase by a factor of *ca.* 4, and that the guest-host molecules have different molecular motions and are weakly coupled from the dynamic point of view. Information for several analogs was reported. Uekama *et al.*[10] also examined the relaxation time of β-cdx and sulfa-

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1) Part II: M. Suzuki and Y. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **27**, 1343 (1979).
2) A part of this work was presented at the 97th Annual Meeting of the Pharmaceutical Society of Japan at Tokyo, April, 1978 and the 27th Annual Meeting of the Kinki Branch at Kobe, Nov. 1977.
3) Location: *a) 133-1, Yamada-Kami, Suita, Osaka, 565, Japan*; *b) Motoyama Kita-machi, Higashinada-ku, Kobe.*
4) I. Tabushi and T. Nishitani, *Kagaku* (Kyoto), **32**, 768 (1977).
5) D.J. Wood, F.E. Hruska, and W. Saenger, *J. Am. Chem. Soc.*, **99**, 1735 (1977).
6) K. Takeo, K. Hirose, and T. Kuge, *Chem. Lett.*, **1973**, 1233.
7) P. Demarco and A.L. Thakkar, *Chem. Commun.*, **1970**, 2.
8) *a)* R. Bergeron and R. Rowan, *Bioorg. Chem.*, **5**, 425 (1976); *b)* R. Bergeron and M.A. Channing, *ibid.*, **5**, 437 (1976); *c) Idem*, *ibid.*, **99**, 5146 (1977).
9) J.P. Behr and J.M. Lehn, *J. Am. Chem. Soc.*, **98**, 1473 (1976).

thiazole. They concluded that when sulfathiazole is included, its molecular movement is decreased, especially at the phenyl residue, and both the interior and exterior of the cavity of β-cdx interact with it.

In the previous paper,1) inclusion compounds of azo dyes which have a naphthalene nucleus were examined by ^1H NMR, circular dichroism (CD) and ultraviolet spectroscopy. The following results were obtained. Azo dyes used form a 1:1 complex with cdx. The nature of the substituent, the bulkiness of the molecule, the changes of the spectral pattern of cdx in ^1H NMR and the signs of the maximum in the CD spectra can indicate the specific orientation and freedom of motion of the guest molecules in the cavity after inclusion. For example, in the orange II-β-cdx complex, the ^1H NMR spectrum of cdx rules out inclusion from the benzenesulfonate side of orange II. The CD spectrum suggests inclusion from the short molecular axis side and firm fitting with β-cdx. The azo dyes used have a length corresponding to about one and a half times the depth of the cavity of cdx. Nevertheless, the inclusion shifts of the guest molecules are not localized at one side of the molecule.

In the present work, the inclusion compounds of azo dyes which have a naphthalene nucleus were examined by ^{13}C NMR. Special emphasis was placed on the following points.

1) Whether or not C–SO_3^- (which is situated at the end of the guest molecule) shows an inclusion shift; this could not be determined by ^1H NMR due to the absence of a hydrogen.

2) Whether or not the inclusion shifts of the guest molecule are localized at one side of the molecule.

3) Whether or not the complex formation ratio is consistent with the ^1H NMR data.

4) Whether or not the sugar carbons for which the attached protons could not be differentiated by ^1H NMR can give information concerning individual regions of the host molecule.

Experimental

The materials used were as described previously.1) Host molecules from 0 to 0.10 M were added to ~0.05 M guest molecules.

Pulsed Fourier transform ^{13}C NMR spectra were recorded on a Hitachi R-22 CFT type spectrometer operating at 22.6 MHz. Parameters (unless otherwise stated) were set in the following ranges; maximum frequency 200 ppm, sampling points 8 k, pulse angle 30°, band-pass filter 4 kHz, pulse interval 5 sec, wide band decoupling ±500 Hz, decoupling power 9W. Resolution was ±0.06 ppm.

^{13}C NMR spectra (unless otherwise stated) were proton-decoupled and were obtained at a temperature of 34±0.5° in 8 mm tubes.

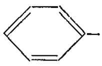
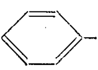
Chemical shifts were measured in ppm downfield from external tetramethylsilane (TMS). A positive sign in tables indicates a low field shift.

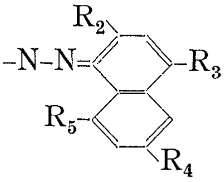
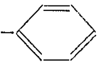
Assignment

Guest molecules and their chemical shifts are shown in Tables I and II.

Coupling constants, peak heights, additivity of substituent chemical shifts, comparison with the spectral data of related compounds, off-resonance and no ^1H decoupling have all been used for assignment of the chemical shifts.

In Table II, calculated values indicate the results obtained by assuming additivity of substituent chemical shifts, and the following approximations were used where data were unavailable;

-N=N- was used in place of SO_3^---N=N-,

 and -N=N--NMe$_2$.11)

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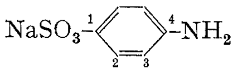
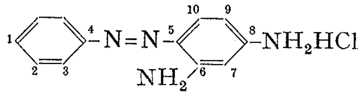
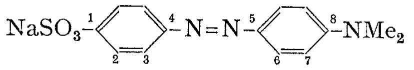
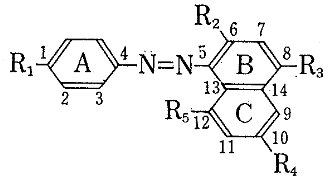
10) K. Uekama, F. Hirayama, and H. Koinuma, *Chem. Lett.*, **1977**, 1393.
11) M. Mishima, Ph. D. Thesis, Osaka University (1976), p. 63.

TABLE I. Guest Molecules Used

I	Sodium sulfanilate	
II	Crysoizine	
III	Methyl orange	



		R_1	R_2	R_3	R_4	R_5
IV	Orange II	$NaSO_3$	OH	H	H	H
V	Yellow V	$NaSO_3$	OH	H	SO_3Na	H
VI	Orange I	$NaSO_3$	H	OH	H	H
VII	Croceine orange	H	OH	H	SO_3Na	H
VIII	Orange G	H	OH	H	SO_3Na	$NaSO_3$

TABLE II. Observed and Calculated ^{13}C Chemical Shifts of Azo Dyes and Related Compounds (ppm from TMS)

Compound		1	2	3	4	5	6	7	8
I	Observd.	142.5	123.0	127.8	135.7				
	Calcd.	132.1	126.7	115.2	152.4				
II	Observd.	126.3	130.0	116.6	161.2	141.9	157.7	93.4	127.0
	Calcd.	131.6	129.6	122.8	152.4	140.9	143.4	108.6	130.8
III	Observd.	143.1	127.1	122.4	154.3	142.6	126.0	112.4	153.9
	Calcd.	145.8	126.8	123.6	155.8	140.4	123.3	113.7	153.8
IV	Observd.	139.5	127.0	116.4	143.1	132.4	179.1	121.4	143.9
	Calcd.	145.8	126.8	123.6	155.9	133.2	147.2	118.5	132.7
V	Observd.	140.7	127.6	117.6	143.8	134.8	178.4	122.5	142.9
	Calcd.	145.8	126.8	123.6	155.9	133.4	149.7	120.5	134.2
VI	Observd.	145.0	126.9	114.8	136.9	135.5	132.4	123.0	186.3
	Calcd.	145.8	126.8	123.6	155.8	144.5	119.9	109.7	154.1
VII	Observd.	127.9	129.8	117.8	141.7	134.6	175.7	121.9	141.5
	Calcd.	131.6	129.6	122.8	152.4	133.4	149.7	120.5	134.2
VIII	Observd.	128.7	130.0	119.7	142.0	132.6	177.3	127.6	141.8
	Calcd.	131.6	129.6	122.8	152.4	133.4	149.7	120.5	134.2

Compound		9	10	11	12	13	14	Me
I	Observd.							
	Calcd.							
II	Observd.	119.3	121.6					
	Calcd.	110.5	123.7					
III	Observd.							40.0
	Calcd.							
IV	Observd.	(127.0	125.0	129.2	129.3)	127.7	129.7	
	Calcd.	127.7	123.5	126.4	126.3	128.6	129.8	
V	Observd.	126.6	141.0	126.6	126.6	127.5	129.6	
	Calcd.	125.9	137.5	122.8	127.8	130.0	128.3	
VI	Observd.					131.6	128.5	
	Calcd.					134.8	124.4	
VII	Observd.	126.1	140.1	125.6	126.3	126.9	128.6	
	Calcd.	125.9	137.5	122.8	127.8	130.0	128.3	
VIII	Observd.	130.0	139.1	128.2	139.1	130.2	130.2	
	Calcd.	129.5	138.5	120.2	142.2	127.4	129.3	

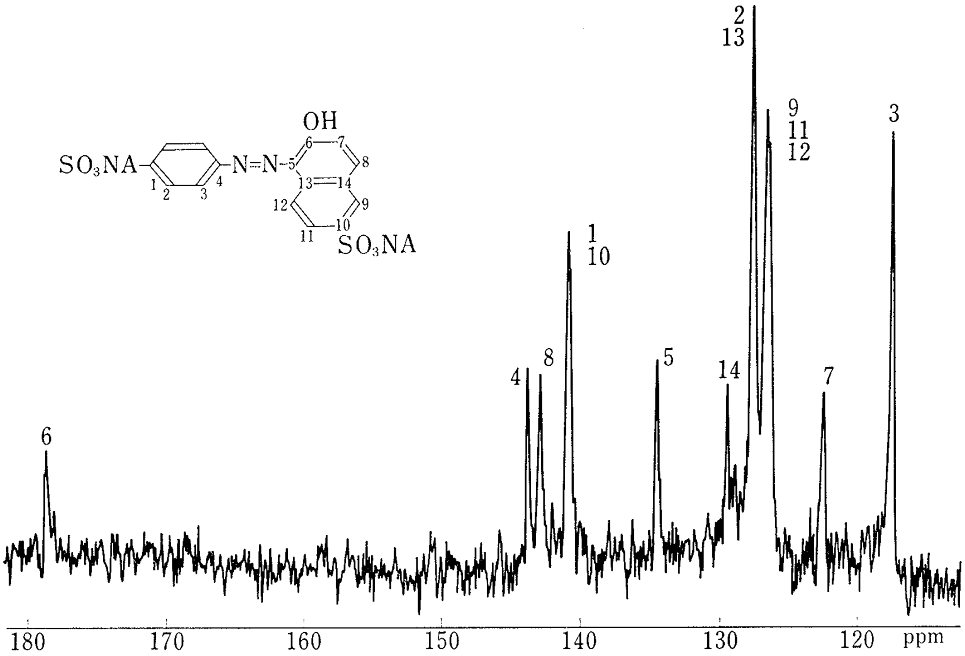


Fig. 1a. Wide-band ^{1}H Decoupled ^{13}C NMR Spectrum of V (0.05 M)

Maximum frequency 100 ppm, pulse angle 30°, pulse interval 5 sec, wide band decoupling ± 500 Hz, decoupling power 9 W, band-pass filter 2 kHz, sampling points 4 k.

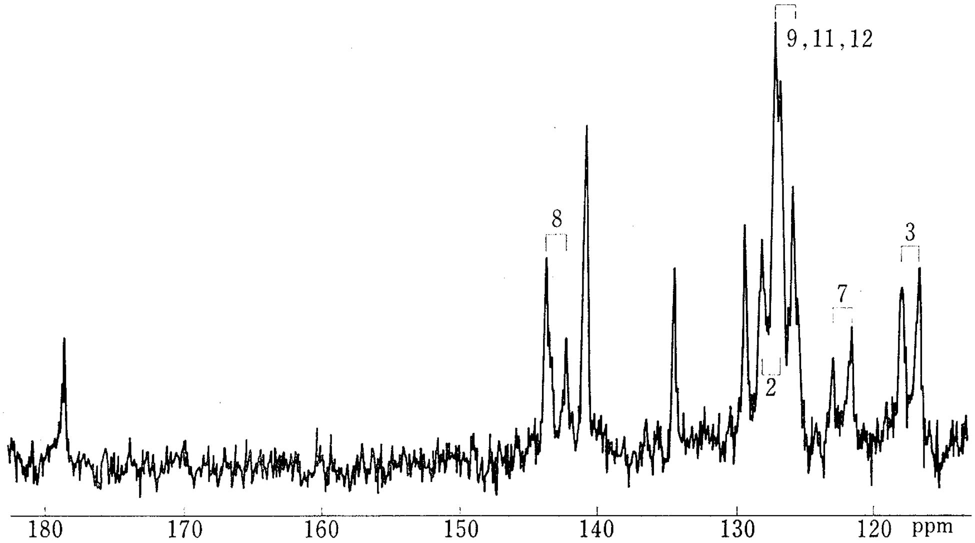


Fig. 1b. Off-resonance ^{1}H Decoupled ^{13}C NMR Spectrum of V

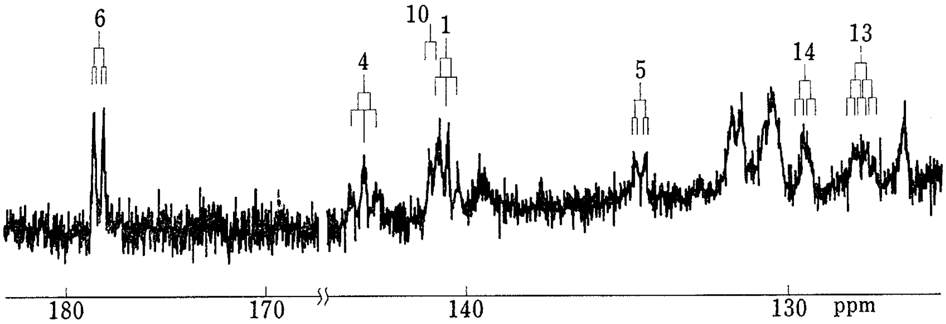
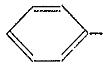
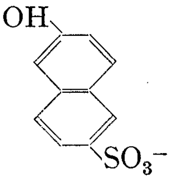
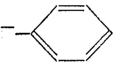
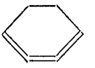


Fig. 1c. ^{13}C NMR Spectrum of V (saturated solution) without ^{1}H Decoupling

Maximum frequency 55 ppm (70 ppm for 170—180 ppm), sampling points 16 k, pulse interval 7.7 sec.

For example, V was calculated using the substituent parameters -N=N- +  at the naphthalene side and SO_3^-- + -N=N- at the benzene side. However, the substituent effect of the *p*-sulfobenzeneazo group was neglected at the C ring. The coincidence of calculated and observed values is good, confirming the correctness of the assignment.

V is taken as the example (*cf.* Fig. 1). First, V was divided to tertiary and quaternary carbons by the off-resonance technique. The assignment of quaternary carbons was decided using the coupling constant obtained by the no ^1H decoupling technique and assuming additivity. The C-6 signal is lowest due to the effect of the OH oxygen. The C-6 signals in IV, V, VII and VIII, which have similar structures, appear between 175.7 ppm and 178.7 ppm (within 3 ppm). The C-8 signal in VI, which has OH at the 8 position appears at 186.3 ppm, which is about 9 ppm lower than the 6 position. In Fig. 1c, the C-6 signal shows a doublet due to meta coupling with the 8 position (8.6 Hz in naphthalene)[12] and ortho coupling with the 7 position (0.3 Hz in naphthalene).[12] VIII, which has two SO_3^- groups in the naphthalene nucleus, shows a sharp singlet at 139.1 ppm in the off-resonance technique. Thus, in V, the signals at 140.7 ppm and 141.0 ppm are assigned to carbons which carry SO_3^-. In Fig. 1c, the 141.0 ppm signal shows a doublet due to meta coupling with H-12. The 140.7 ppm signal shows a triplet due to meta coupling with (H-3)×2. Thus, the latter is C-1 and the former is C-10. The C-14 signal shows a quartet-like pattern due to meta coupling with H-7 and H-12. In III, there is no quaternary carbon situated at such a high field. Thus, it is natural to assign the 129.6 ppm signal to C-14 of the naphthalene nucleus, surrounded by other carbons. The C-13 signal shows a multiplet in Fig. 1c. The band width is wide (20.6 Hz in 2,6-acetoxynaphthalene),[12] because the C-13 signal is split by three meta couplings with H-8, H-9 and H-11. The C-4 signal shows a triplet due to meta coupling with (H-2)×2 and the C-5 signal shows a quartet with coupling constants of 8 and 2 Hz. The latter singal ought to show a triplet meta coupled with H-7 (4.3 Hz in 2,6-acetoxynaphthalene)[12] and H-12 (4.6 Hz in 2,6-acetoxynaphthalene).[12] Specular substituent effect by the *p*-sulfobenzeneazo group may occur at the 5 position. The C-4 and C-5 signals are difficult to differentiate clearly, C-5 is situated at the ortho position with respect to OH, so should be at higher field than C-4. Moreover, the 143.8 ppm signal shows nearly the same pattern as the C-1 signal, and can therefore be identified as the C-4 signal.

The assignment of the tertiary carbons was decided from the peak heights and the additivity rule. The peak heights of the C-2 and C-3 signals are twice those of the other carbons, or more. The signal at 127.6 ppm was assigned to C-2 on the basis of the calculated value and by comparison with that of III. The C-9, C-11, C-12 signals show nearly the same chemical shift value. The height is almost the same as that of the C-3 signal, but the former signal is split by the solvent effect. 122.5 ppm is the C-7 signal and 142.9 ppm is the C-8 signal. Comparison with the calculated value and the absence of such a tertiary carbon in VI confirm the assignment of C-8.

^{13}C NMR spectra of α- and β-cdx were assigned by Takeo *et al.*[6]

Results and Discussion

In the previous paper,[1] we reported the following conclusions for the IV-β-cdx complex.

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[12] P. Granger and M. Maugral, *J. Mag. Reson.*, **22**, 405 (1976).

Table III. α- and β-Cyclodextrin-induced ^{13}C Chemical Shifts of Azo Dyes and Related Compounds (ppm)

Compound	add[a]	1	2	3	4	5	6	7	8
I	β	0.2	−0.3	0.0	0.3				
II	β	−0.2	−0.2	0.1	−0.2	0.4	−0.1	0.2	0.7
III	α	0.9	−0.2	0.4	0.4	0.5	0.2	−0.1	0.2
	β	1.1	0.4	0.0	0.1	0.9	−0.5	−0.6	−1.0
IV	α	0.2	0.2	0.4	0.2	0.3	0.3	0.3	0.2
	β	2.0	0.2	0.7	0.6	0.4	0.1	1.1	−0.1
V	α	0.1	0.1	0.1	0.1	0.1	−0.1	0.1	−0.1
	β	0.7	0.2	0.1	0.5	0.4	−0.8	0.1	0.0
VI	α	0.2	0.2	0.2	0.2	0.2	0.2	0.1	−0.3
	β	1.5	0.2	1.1	1.5	0.1	0.9	0.3	
VII	α		0.4	0.5					0.4
	β	−0.1	0.1	0.2	1.0	0.2	−0.2	0.4	0.1
VIII	β			−0.1	0.6	0.0	0.2	0.2	0.3

Compound	add[a]	9	10	11	12	13	14	Me
I	β							
II	β	0.2	0.4					
III	α							0.4
	β							0.1
IV	α					0.3	0.3	
	β	(1.0, 0.3, −0.3, 0.9)				0.4	0.6	
V	α	(0.1, 0.1, 0.1)				0.1	0.2	
	β	(0.5, 0.5, 0.1, 0.1)				0.0	0.7	
VI	α					0.2	0.2	
	β					0.9	0.1	
VII	α		0.2					
	β	(0.7, 0.8, 0.0, 0.3)				0.4	−0.5	
VIII	β	−0.1	0.1	−0.1	0.1	0.1	0.1	

a) add indicates addition of: α, α-cyclodextrin; β, β-cyclodextrin. A positive sign indicates a low field shift.

1) In ^{1}H NMR, the signals H-2 and H-8 (which are at a distance from N=N) showed low field shifts of about half compared with those of H-3 and H-7 (which are situated in the neighborhood of N=N); the inclusion shifts were not localized at one side of the molecule. Thus, ambiguity remains concerning inclusion of the end position of IV.

2) ^{1}H NMR and CD spectra suggested inclusion not from the benzenesulfonate side, but from the short molecular axis side of IV. IV may be situated at the rim of β-cdx. ^{13}C NMR data may now offer further information.

In Fig. 2, plots of molar ratios of β-cdx/IV *vs.* changes in the chemical shifts of IV suggest that a 1:1 complex is formed. Above a molar ratio of one β-cdx molecule per IV, no further substantial change of the chemical shifts occurs. The values are shown in Table III. Almost all the signals shift to lower field. In particular, the C-1, C-7 and some of the C-ring carbons situated in different aromatic rings show large shifts.

On the basis of X-ray data for 1-*p*-nitrobenzeneazo-2-naphthol, which is an analog of the azo dyes used in the present work, the length along the long molecular axis of IV corresponds to about one and a half times the depth of the cavity of cdx.[13] It is interesting to examine in what manner IV forms the complex with β-cdx. It is perceived that the inclusion

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[13] C.T. Grainger and J.F. McConnell, *Acta Cryst.*, **B25**, 1962 (1969).

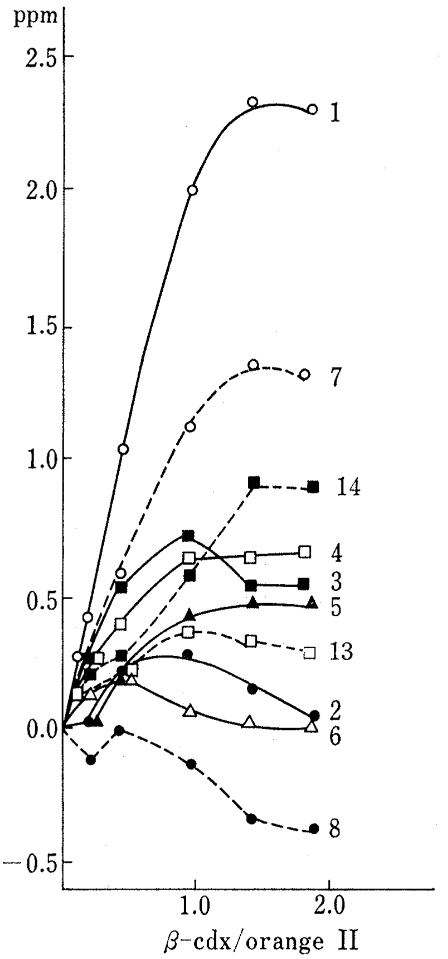

Fig. 2. β-Cyclodextrin-induced Shifts of Orange II

—○—; C-1, —●—; C-2, —■—; C-3, —□—; C-4, —▲—; C-5, —△—; C-6, ···○···; C-7, ···●···; C-8, ···□···; C-13, ···■···; C-14.

A positive sign indicates a low field shift.

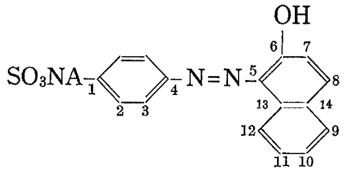

Table IV. Solvent Effect and Induced Shifts of Orange II (ppm)

Position	MeOH : H_2O 1:1	Induced shift
1	1.9	2.0
2	0.7	0.2
3	0.6	0.7
4	1.0	0.6
5	0.7	0.4
6	−0.4	0.1
7	0.4	1.1
8	−0.2	−0.1
9	3.1	1.0
10	1.8	0.3
11	−0.5	−0.3
12	−0.4	0.9
13	0.7	0.4
14	−0.1	0.6

effect of the guest molecule is mainly due to hydrophobic interaction with the host molecule.[1,14]

So, the solvent effect of a hydrophobic solvent was examined. The ^{13}C NMR spectrum of a solution composed of IV/β-cdx=1/2 in D_2O, was compared with that of IV in MeOH. The former clearly resembles the NMR spectrum of IV in the hydrophobic solvent. In ^1H NMR, similar behavior was observed.[1] Thus the ^1H and ^{13}C NMR spectra both indicate that IV is affected by the hydrophobic cavity over the whole molecule, as if IV were dissolved in a hydrophobic solvent. In particular, the latter spectrum indicates that the C–SO_3^- signal shows the largest shift and is a good index of the hydrophobic interaction with β-cdx.

Table III shows that the inclusion effect on the chemical shift is not large, namely$<2.0 \pm 0.06$ ppm, but the reproducibility is satisfactory. The inclusion effect is in the order β-cdx>α-cdx, except in the case of III.

Judging from the bulkiness of the benzene nucleus and the behavior of the III-β-cdx complex, which includes the benzenesulfonate side,[15] partial inclusion of the benzene nucleus side in IV—VII should occur, even if the naphthalene nucleus side (which is too large to be included by α-cdx) could not be included. In both α- and β-cdx complexes, the shift values of the benzene side of the molecule are not large compared with those of the naphthalene side.

Compared with I, carbons which carry SO_3^- in azo dyes show large inclusion shifts with β-cdx. When one SO_3^- is situated at either the 1 or the 10 position in the molecule (IV and

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14) *a*) Y. Shibusawa, T. Hamaycri, and R. Sasaki, *Nihon Kagaku Kaishi*, 2121 (1975); *b*) T. Shibusawa and Y. Hirose, *Sen-i Gakkaishi*, **29**, 1 (1973).

15) M. Suzuki and Y. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **27**, 609 (1979).

VII), the ring carbons show nearly the same shift values. When the number of SO_3^- groups increases (V and VIII), the shift values are decreased, and VIII, which has SO_3^- at the 12 position, shows scarcely any inclusion shift. The values obviously reflect the bulkiness of guest molecules and hence their suitability for inclusion. CD spectra indicated that azo dyes, except for IV, are included from the long axis side of the molecule.[1] The C–SO_3^- signal can now be used as an index of inclusion, but it was impossible to obtain any information about the orientation of inclusion.

Most of the carbons show low field shifts which are consistent with the ^1H NMR behavior. The above behavior cannot be explained on the basis of a simple polarization mechanism, which requires a shift of the ^{13}C signal in the opposite direction to the ^1H signal,[16] and has been demonstrated in a large number of systems.[17]

From the ^1H NMR of the guest molecule, the following alternations may be considered.[1]

1) When azo dye is included in the cavity, breakdown of the whole H_2O structure around the azo dye molecule may occur and the whole molecule may be affected by the hydrophobic cavity.

2) When an azo dye group which is situated at the center of the molecule is introduced to the cavity, it produces different substituent shifts at *ortho*-, *meta*- and *para*-H's, so even protons which are not included may experience low field shifts.[8]

The following results support the first possibility: the elimination of the steric polarization mechanism; the similarity of the solvent effect and the inclusion shift in ^{13}C NMR; and the fact that in NOE[8] and T_1,[9] the guest molecule shows the inclusion effect over distances greater than the depth of cdx. In addition, the large inclusion shift of the signal of C–SO_3^-, which is situated at the end of the molecule, obviously rules out the second possibility.

In the host molecule, the sugar carbons for which the attached protons could not be

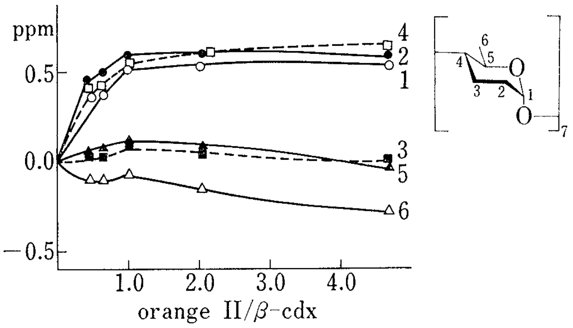
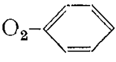


Fig. 3. Orange II-induced Shifts of β-Cyclodextrin

—○—; C-1, —●—; C-2, ---■---; C-3, ---□---; C-4, —▲—; C-5, —△—; C-6.

TABLE V. Azo Dye-induced ^{13}C Chemical Shifts of α- and β-Cyclodextrin (ppm)

Compound	Cyclodextrin	1	2	3	4	5	6
III	α	0.6	0.2	0.1	−0.2	−0.1	−0.5
	β	1.0	0.3	0.1	−0.1	0.3	−0.4
IV	α	0.1	0.0	0.1	0.2	0.1	0.1
	β	0.5	0.6	0.1	0.5	0.1	−0.1
V	α	0.2	0.0	0.1	0.0	0.0	0.1
	β	0.1	0.2	0.1	−0.1	0.1	−0.2
VI	α	0.1	0.0	0.1	0.1	0.1	0.1
	β	0.2	0.3	0.1	0.2	0.0	0.0
VII	α	0.0	0.0	0.1	0.0	−0.1	−0.1
	β	0.2	0.3	0.1	0.3	0.1	−0.1
VIII	β	−0.1	0.1	−0.1	−0.2	0.1	−0.1
NO_2--OH[8b]	α	0.4	0.3	0.0	0.0	−0.2	−0.6

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16) S.H. Grover, J.P. Guthrie, J.B. Sthothers, and C.T. Tan, *J. Mag. Reson.*, **10**, 227 (1973).
17) D.M. Grant and B.V. Cheney, *J. Am. Chem. Soc.*, **89**, 5135 (1967).

differentiated in ^{1}H NMR give distinct bands in ^{13}C NMR, so detailed information could be obtained.

When the IV-induced shifts are plotted as a function of the molar ratio of IV per *β*-cdx, inflexions appear at a ratio of 1: 1 (Fig. 3). Their values are shown in Table V. The C-1 and C-4 positions show low field shifts, which may be due to changes of the bond angle of the glycosidic linkage loop arrangement. C-5 and C-6 show only marginal shifts. Such behavior is common to *β*-cdx complexes of guest molecules which have a naphthalene nucleus. On the other hand, in the III- and *p*-nitrophenol-*α*-cdx complexes, only the C-1 signal shows a low field shift and the C-4, C-5 and C-6 signals show high field shifts.$^{8)}$ Thus the bulky naphthalene nucleus may cause deformation of the glycosidic linkage rather than conformational change of the small diameter side of the cavity. In the previous paper,$^{1)}$ the H-6 signal of *β*-cdx in ^{1}H NMR rules out inclusion from the benzenesulfonate side of IV. The ^{13}C NMR is also consistent with this. C-2 is the only carbon carrying OH in the cavity, and shows a large low field shift in most complexes. It may be that C-2 is fully affected by the change of environment in the cavity on inclusion. The 3 position, which experiences high field shift due to the ring current effect in ^{1}H NMR, shows only a marginal low field shift in ^{13}C NMR. Thus, the ring current effect appears not to have a major role in ^{13}C NMR.

Based on X-ray$^{18)}$ and ORD$^{19)}$ data, it has been suggested that changes of cdx on inclusion are mainly due to conformational changes about the C–O bonds joining each glucose unit. The ^{13}C NMR data obtained here add detailed information regarding the behavior of the interior of the cavity.

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