

Structural Studies of DM β CD/Dihalogenated Norcarane Inclusion Complexes¹

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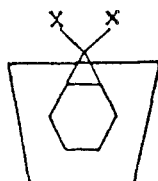
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Abstract. Inclusion complexes of 7,7-dibromonorcarane (**1**) and 7,7-dichloronorcarane (**2**) with 2,6-dimethyl- β -cyclodextrin (DM β CD) have been synthesized. Their structures have been studied by chemical analysis, thermal behavior, IR spectra, UV absorptions and ¹³C NMR spectra in DMSO solutions. The studies show that the orientation of (**1**) is different from that of (**2**) in the DM β CD cavity.

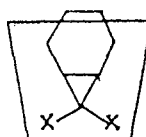
Key words. dihalogenated norcarane, DM β CD, inclusion complex, orientation, complexation effects.

1. Introduction

Cyclodextrins and their derivatives provide very good models to study complex formation, and the structure of the inclusion complex can be studied by many methods [1], especially ¹³C NMR spectroscopy. ¹³C NMR spectroscopy is one of the most useful tools which can provide direct elucidation of the spatial effects on the inclusion complexation [2]. The present study deals with the structural elucidation of the inclusion complexes of DM β CD with dihalogenated norcarane. The orientation of the guests in the DM β CD cavity may be of type (**I**) or type (**II**):



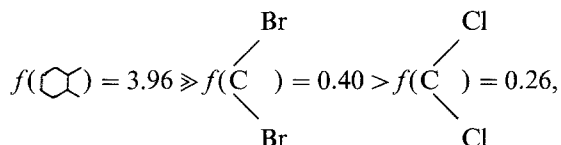
(I)



(II)

There are two main factors which will affect the complexation:

(i) *Hydrophobic Interaction*. According to the hydrophobic fragmental constants [3],



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the cyclohexylene moiety will enter the hydrophobic cavity of DM β CD, while the halogen atoms will be exposed to the solution of higher dielectric constant. So the orientations of both guests in the DM β CD cavity would be of type (I).

(ii) *Spatial Match*. According to the literature [4] and CPK models, the geometric parameters of dihalogenated norcarane were calculated. The maximum size of the cyclohexylene moiety, the dibromocyclopropylene, and the dichlorocyclopropylene moiety is 5.2Å, 5.6Å and 4.9Å, respectively. Comparison of the data with the size of DM β CD [5] suggests that both orientations are possible. But based on a consideration of van der Waals' radii, it is more possible that the orientation of (I) in the DM β CD cavity would be of type (I); while that of (2) be of type (II).

The techniques of thermal analysis, IR, UV, and especially ¹³C NMR spectroscopy are used to investigate the orientations of the guests in the DM β CD cavity in this work.

2. Experimental

2.1. MATERIALS

DM β CD is a product of Chinoin Pharmaceutical and Chemical Works Ltd., Budapest. Dihalogenated norcaranes were prepared according to the procedure described in the literature [6]. Deionized distilled water was used throughout the study.

2.2. PREPARATION OF THE INCLUSION COMPLEXES

An aqueous DM β CD solution (60°C) was prepared. The ether solution of the guest substance was added dropwise to this stirred, nitrogen-atmosphere system. The host:guest ratio was maintained at 1:2. The reaction mixture was heated for 4 h at 60°C and then cooled to room temperature slowly. The white precipitate formed was removed by filtration, washed successively with water and a few mL of acetone, ether, and dried *in vacuo* at ambient temperature (Yield: 50%).

2.3. PHYSICAL MEASUREMENTS

DSC curves were obtained on a Du Pont model 1090 DSC-TGA system at a heating rate of 10°C min⁻¹ under a nitrogen atmosphere.

Infrared spectra of samples were recorded in the 4000–400 cm⁻¹ region on a NICOLET 5DX-FT-IR spectrometer.

UV spectra were recorded on a Shimadzu UV 260 spectrometer (solvent and reference: DMSO).

¹³C NMR spectra were obtained on a Bruker-MSL 300 NMR spectrometer operating at 75.468 MHz. DMSO was used as external reference.

3. Results and Discussion

The elemental analysis shows that the isolated solid has a DM β CD: dihalogenated norcarane molar ratio of 1:1, which suggests the stoichiometry of the inclusion complexes are 1:1.

The elemental analysis data for the inclusion compounds are: DM β CD·0.95(1)·0.5 H₂O (*Calc.* C: 47.58 H: 6.92. *Found* C: 48.33 H: 7.01) DM β CD·0.95(2)·0.5 H₂O (*Calc.* C: 50.27 H: 7.31. *Found* C: 50.41 H: 7.41)

3.1. THERMAL ANALYSIS

Differential Scanning Calorimetry (DSC) curves for DM β CD and the complexes of DM β CD/dihalogenated norcarane are shown in Figure 1. There are two new endothermic peaks for the release of guests in the curves of the inclusion complexes: at 208.8°C for dibromonorcarane; at 180.7°C for dichloronorcarane.

3.2. IR SPECTRA

Generally IR techniques are not suitable for the detection of inclusion compounds because the characteristic bands of cyclodextrin representing the overwhelming part

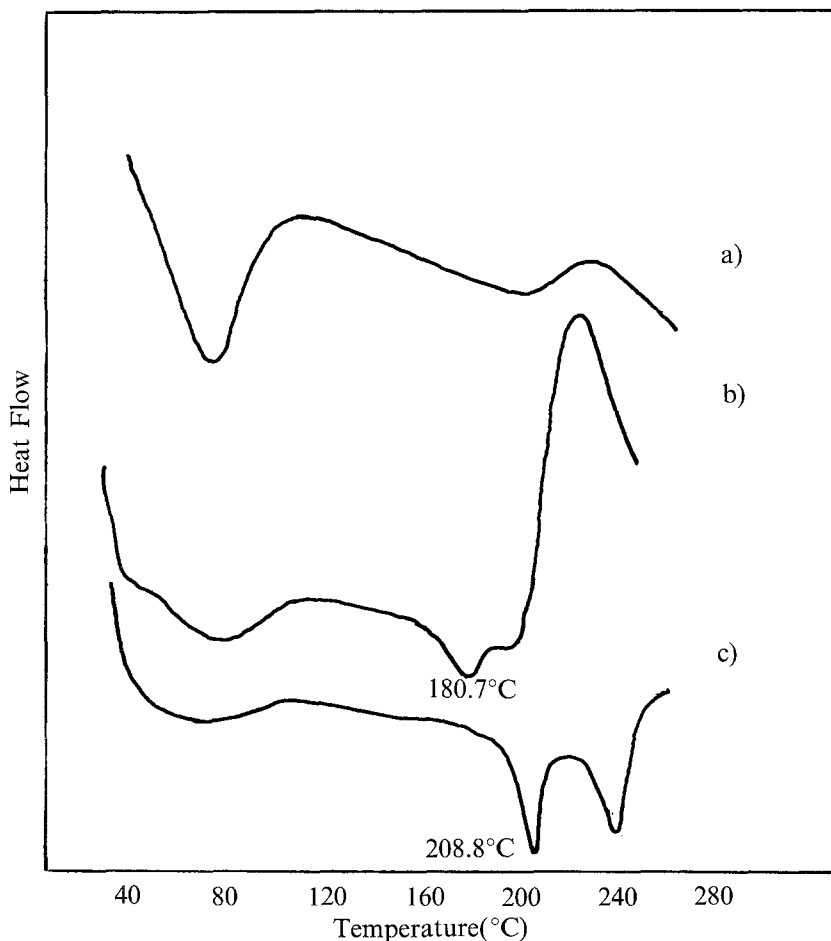


Fig. 1. DSC curve of a) DM β CD b) DM β CD-(2) c) DM β CD-(1).

of the complex are hardly influenced by complexation. Fortunately, in this work, the useful information indicating the formation of the inclusion complexes have been provided by IR spectroscopy.

Some IR spectral data are listed in Table I. DM β CD has no absorptions at 731 cm^{-1} and 793 cm^{-1} , while DM β CD-(1) has an absorption at 731.2 cm^{-1} which corresponds to the absorption at 731.2 cm^{-1} of (1), and DM β CD-(2) has an absorption at 793.8 cm^{-1} which corresponds to the absorption at 796.9 cm^{-1} of (2). Though these changes indicate complex formation, they do not provide information about the orientations of the guests in the DM β CD cavity.

3.3. UV SPECTRA

If a guest molecule enters the DM β CD cavity, changes in its UV absorption will be observed [7]. As for the dihalogenated norcaranes, their UV absorptions are mostly generated from the transition of unshared electrons on the halogen atoms. It follows that if the halogen atoms enter the cavity of the host, the maximum absorption frequencies of the guest will change somewhat.

The maximum absorption frequencies of the samples are listed in Table II.

It can be observed that after complexation, the maximum UV absorption of (1) at 268 nm shifts to 259 nm ('blue shift') while that of (2) at 260 nm shifts to 264 nm ('red shift'). This result indicates that the different orientation of the two guests in the host cavity makes the unshared electrons on the halogen atoms have different environments and changes the maximum absorption frequency in different ways.

3.4. ^{13}C NMR

^{13}C NMR is very useful in the structural study of inclusion complexes. The ^{13}C NMR spectra of the samples were recorded in DMSO solutions. After complexation the chemical shift of DM β CD, the host, was found to change little, while that of the guests changed significantly, especially C-7. If the halogen atoms enter the

Table I. IR Spectra data of the samples

Sample	Absorption frequency	(cm^{-1})
DM β CD	–	–
DM β CD-(1)		731.2
DM β CD-(2)	793.8	
(1)		731.2
(2)	796.9	

Table II. UV data of the samples

	(1)	DM β CD-(1)	(2)	DM β CD-(2)
λ_{max} (nm)	268	259	260	264
ϵ ($\text{L mol}^{-1} \text{cm}^{-1}$)	114	108	97	88

DM β CD cavity, C-7 will be deshielded and its chemical shift will move to lower field. Otherwise, if the cyclohexylene moiety enters the DM β CD cavity, C-7 will be near the oxygen atoms of 3-OH of DM β CD according to CPK models and it will be shielded and its chemical shift will move to higher field [8, 9].

^{13}C NMR spectra of the samples are shown in Figure 2. Chemical shift changes of the guests are illustrated in Table III.

It can be observed that the C-7 peak of (1) shifts 0.20 ppm to higher field; while that of (2) shifts 0.13 ppm to lower field. The result suggests that the orientations of the two guests in the DM β CD cavity are different: (1) is of type (I) while (2) is of type (II).

4. Conclusion

Through the study of thermal analysis, IR, UV, and especially ^{13}C NMR, it is considered that the orientations of dibromonorcarane and dichloronorcarane in the cavity of DM β CD may be different. The result demonstrates that the hydrophobic interaction and spatial match are the two main factors which simultaneously affect the interaction of cyclodextrin and guest molecules. It is also apparent from the

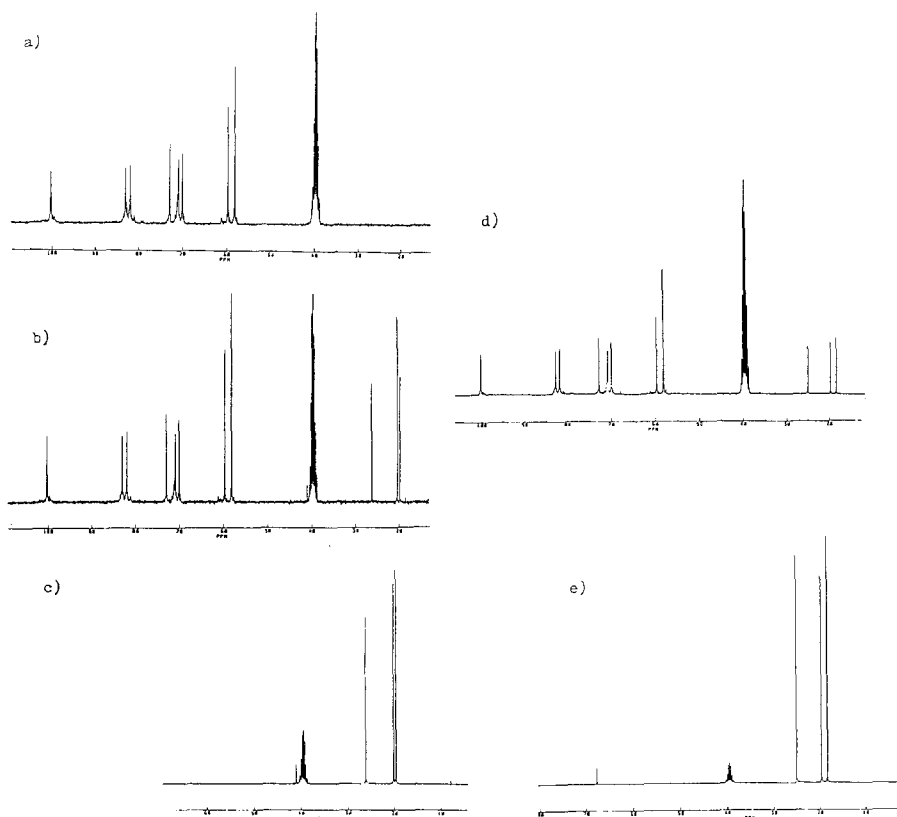
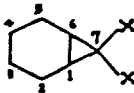


Fig. 2. ^{13}C NMR Spectra of a) DM β CD b) DM β CD-(1) c) (1) d) DM β CD-(2) e) (2).

Table III. Chemical shift changes of guests (ppm)

	dibromonorcarane			dichloronorcarane		
	Free	Complexed	Change	Free	Complexed	Change
C-2,5	19.626	19.616	-0.01	18.306	18.339	+0.03
C-3,4	20.150	20.181	+0.03	19.663	19.656	-0.01
C-1,6	26.136	26.080	-0.06	25.085	25.049	-0.04
C-7	41.074	40.877	-0.20	67.678	67.806	+0.13

study that the specific spatial relationship can help set up all kinds of intermolecular interactions between two or more molecules, therefore reaching a low energy, stable inclusion complexation state. This is the process from molecular recognition to the formation of inclusion complex.

Acknowledgements

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