Separation of 2-Methylquinoline from 8-Methylquinoline through Inclusion Complexation with α -Cyclodextrin

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Inclusion complexation with α -cyclodextrin (α -CD) was found to be effective for separating 2-methylquinoline (2-MQ) from 8-MQ. Examination of the α -CD-MQ stoichiometric ratios in the complex solids indicated that 1 : 1 α -CD-MQ complex was formed when the molar ratios of MQ to α -CD were 4 and 2, and that 2 : 1 α -CD-MQ complex solid was formed when the molar ratio of MQ to α -CD was 0.25. The inclusion selectivity for 2-MQ was higher in the 2 : 1 complex than in the 1 : 1 complex. The results were explained on the basis of the Corey-Pauling-Koltun molecular model.

1. Introduction

The inclusion complex formation between cyclodextrin (CD) and guest species is said to depend chiefly on the size and shape of the guest¹⁾. This is the reason that CDs can be used as selective separating agents for disubstituted benzene derivatives etc.

In a previous paper²⁾, we showed that the inclusion complexation with α -CD was successfully applied to the selective concentration of indole in coal tar. We noticed in the study that quinaldine, *i.e.*, 2-methylquinoline (2-MQ), formed a stable inclusion complex with α -CD. Therefore, we presumed that inclusion with α -CD might be effective for the separation of 2-MQ from its isomers, especially from 8-MQ.

2-MQ is a material for producing quinophthalone dyes. It occurs in the crude quinoline fraction obtained from coal tar. 2-MQ is obtained by distilling the crude quinoline. The purity of 2-MQ is, at best, about 85% because of the presence of 8-MQ whose boiling point (247.8°C) lies very close to that of 2-MQ (247.6°C). Therefore, ways for separating them are in demand by the industries. Two ways related to the use of inclusion complexation to raise the purity of 2-MQ are presented. One is to use urea which forms an adduct with 2-MQ³⁾. The other is to use diol like benzopinacol which forms an inclusion complex solid with 2-MQ⁴⁾.

In this study we have found that α -CD is a useful agent for including and separating 2-MQ. It has also been found that the selectivity for including 2-

MQs is correlated with the stoichiometric ratio of α -CD to MQs in the complex.

2. Experimental

α -CD, β -CD, 2-MQ, 8-MQ, and 7-MQ were obtained from Tokyo Kasei Kogyo Co., Ltd. Quinoline was purchased from Nakarai Chemicals Ltd. The water used was distilled and deionized.

2.1 Inclusion Reaction between CD and 1:1 Mixture of 2-MQ and 8-MQ (MQs)

A 1:1 mixture of 2-MQ and 8-MQ was prepared. Four kinds of experiments were carried out by changing the quantities of the MQs mixture added. The molar ratios of total MQs to α -CD were 4, 2, 1, and 0.5 (see Table 1.).

α -CD was used always as a 10 wt% aqueous solution. The MQs mixture was added to it and stirred in a thermostated bath at 25°C for 1 h. White solids of α -CD inclusion complexes were deposited. They were filtered with a membrane filter (pore size: 0.4 μ m), washed with acetone and dried in a desiccator at room temperature for 1 h under reduced pressure (0.5 Torr). Then some of the dried product was weighed and suspended in

Table 1 Inclusion Selectivity and Composition of Complex Solids

Source (in molar ratio)	Inclusion complex solid		
α -CD : 2-MQ : 8-MQ	2-MQ	8-MQ	α -CD:TMQ*
1 : 2 : 2	70.4%	29.6%	2 : 2.14
1 : 1 : 1	75.4%	24.6%	2 : 1.62
1 : 0.5 : 0.5	78.0%	22.0%	2 : 1.37
1 : 0.25 : 0.25	86.9%	13.1%	2 : 1.09
α -CD : 2-MQ : 8-MQ	2-MQ	8-MQ	β -CD:TMQ
1 : 2 : 2	42.1%	57.9%	2 : 2.24

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*TMQ means total methylquinoline.

Table 2 Composition of Inclusion Complex Solid

Source (in molar ratio)	Inclusion complex solid
α -CD : 2-MQ	α -CD : 2-MQ
1 : 4	2 : 1.87
1 : 2	2 : 1.89
1 : 1.5	2 : 1.57
1 : 1	2 : 1.54
1 : 0.75	2 : 1.27
1 : 0.25	2 : 0.989
α -CD : 8-MQ	α -CD : 8-MQ
1 : 5	*
1 : 2	*
1 : 0.5	*

*No solid was deposited.

Table 3 Composition Change Accompanied by Inclusion Complexation

	Crude oil of 2-MQ	Inclusion complex
2-Methylquinoline	85.8%	93.1%
8-Methylquinoline	12.3%	5.1%
Isoquinoline	0.1%	0.7%
Others	1.8%	1.1%

water. Quinoline was added to the suspension as the internal standard for chromatographic analysis. The mixture was shaken with diethyl ether. Then the inclusion complex was dissociated; the aqueous layer then became a homogeneous and transparent solution of α -CD. The MQs and quinoline were transferred to the ether layer. The ether solution was subjected to chromatographic measurements.

For comparison, a similar experiment using β -CD instead of α -CD was carried out. Since the solubility of β -CD is about 1.8 g/100 ml water at 25°C, a 1.5 wt% aqueous solution of β -CD was used.

2.2 Inclusion Reaction of α -CD with 2-MQ or 8-MQ

Several kinds of experiments were carried out by changing the quantity of 2-MQ or 8-MQ added. The molar ratios of 2-MQ to α -CD were from 0.25 to 4 and those of 8-MQ to α -CD were 0.5, 2, and 5 (see Table 2). The experimental procedure was almost the same as that in 2.1.

2.3 Inclusion Complexation between α -CD and Crude Oil of 2-MQ

Crude oil of 2-MQ was provided by Sumikin Chemical Co., Ltd.; its composition is shown in Table 3. 0.5 g of the crude oil was added to 25 ml of a 10 wt% aqueous solution of α -CD. The mixture was vigorously stirred in a thermostated bath at 30°C for 1 h. White solids of α -CD inclusion complexes were deposited. They were filtered with a membrane filter (pore size: 0.4 μ m), washed with acetone and dried. Then they were suspended in water, and diethyl ether was then

Table 4 Composition Change Accompanied by Inclusion Complexation

	Sample oil	Inclusion complex
7-Methylquinoline	74.6%	99.0%
5-Methylquinoline	24.9%	1.0%
Others	0.5%	0%

added. After shaking the mixture for a while, the guest species included were extracted into the ether layer. Evaporation of ether gave an oil in which 2-MQ was selectively concentrated.

2.4 Inclusion Concentration of 7-MQ

The 7-MQ reagent used here consisted of about 75% of 7-MQ and 25% of 5-MQ as shown in Table 4.

0.30 g of the reagent was added to 5 ml of a 10 wt% aqueous solution of α -CD. The subsequent procedure was the same as described in 2.1.

2.5 Chromatographic Measurement of Organic Components

The composition of organic compounds was determined with a GC-9A gas chromatograph (Shimadzu Corporation) with a fused-silica wall-coated capillary column (50 m $\times$ 0.25 mm I.D.) using OV-1 as the liquid phase under the conditions as follows: carrier gas, He; flow rate 0.6 ml/min; injection port temperature, 300°C; sample size, 0.4–5 μ l; splitting ratio, 1:50; flame ionization detector; column temperature, 130°C for 23 min then increased to 200°C at a rate of 5°/min. Under such conditions, the retention times were 14.6 min for quinoline, 18.9 min for 2-MQ, 20.2 min for 8-MQ, 22.7 min for 7-MQ, and 24.1 min for 5-MQ.

In the experiments of 2.1 and 2.2, the compositions were calculated reducing the peak area to the mass of each compound using quinoline as the internal standard. In the experiments of 2.3 and 2.4, the compositions were simply calculated from the chromatographic peak area of each compound.

3. Results and Discussion

Table 1 shows that 1:1 α -CD-MQ complex solids were formed when the molar ratio of total MQs, meaning 2-MQ and 8-MQ, to α -CD was 4 and that 2:1 α -CD-MQ complex solid was formed when the molar ratio of total MQs to α -CD was 0.5. When the molar ratios were 2 and 1, the complex solids seem to be the mixtures of 1:1 and 2:1 CD-MQ complexes. Furthermore, Table 1 shows that inclusion selectivity for guest species is correlated with the stoichiometric ratio of α -CD to MQ in the complex solids, *i.e.*, the inclusion selectivity for 2-MQ was higher in the 2:1 complex than in the 1:1 complex.

Compared with α -CD, β -CD did not show any remarkable selectivity for including 2-MQ or 8-

MQ. The analysis of the stoichiometric ratio indicates that β -CD forms 1:1 complex with MQs.

Table 2 indicates that 1:1 α -CD-2-MQ complex solid was formed when the molar ratios of 2-MQ to α -CD were 2 and 4 and that 2:1 complex solid was formed when the molar ratio of 2-MQ to α -CD was 0.25. When the molar ratios of 2-MQ to α -CD were 0.75, 1, and 1.5, the complex solids seem to be the mixtures of 1:1 and 2:1 complex solids. The results are similar to those shown in **Table 1**.

Solid of α -CD-8-MQ complex was not obtained regardless of the amount of 8-MQ used for α -CD complexation. When a mixture of α -CD aqueous solution and 8-MQ was stirred vigorously, the mixture became emulsified and opaque. When the resulted emulsion was left standing for half an hour, it became a transparent liquid containing some drops of 8-MQ, and no solid was deposited.

This result seems to be inconsistent with the fact that solid α -CD-8-MQ complex was produced by the reaction of α -CD with a 2-MQ and 8-MQ mixture. A similar phenomenon was observed in the complexation with 1-methylnaphthalene (1-MN) and 2-MN in which a complex solid of 1-MN was produced by the reaction of α -CD with a 1-MN and 2-MN mixture, while it was not obtained by the reaction of α -CD with pure 1-MN. Causes for such phenomena have not yet been clarified.

Although we still have not examined the reaction of α -CD-MQs in dilute solution systems, 1:1 and 2:1 complexes must be present in the solution phase. It is natural that such complexes exist in the solution since the presence of both 1:1 and 2:1 complexes of α -CD with quinoline or isoquinoline has been reported⁵⁾.

The results of inclusion selectivity can be well explained by the result of above-mentioned stoichiometric ratio analysis and by the Corey-Pauling-Koltun (CPK) molecular model. According to the CPK model, the heterocyclic part of methylquinoline (see **Fig. 1**) can be included completely in the pore of α -CD. Since the methyl group at 2-position does not cause much steric hindrance and that at 8-position hinders a deep inclusion, 2-MQ can be included by α -CD more firmly than 8-MQ. One 2-MQ molecule can be included more firmly by two α -CD molecules than 8-MQ since the methyl group at 8-position causes

Fig. 1 Monomethylquinoline Isomer

great steric hindrance to the inclusion by second α -CD molecule. The steric effect seems to be more obvious in the 2:1 complex than in the 1:1 complex. This is consistent with the experimental result that the inclusion selectivity for 2-MQ was higher in the 2:1 complex than in the 1:1 complex (see **Table 1**).

As for β -CD, its pore is about 2 Å greater in diameter than that of α -CD, and both 2-MQ and 8-MQ can be included without steric hindrance. Therefore, no remarkable selectivity for including 2-MQ or 8-MQ was observed as shown in **Table 1**.

As can be seen in **Table 3**, the use of α -CD as a separating agent was effective for crude oil of 2-MQ.

From the viewpoint of molecular size and shape, 7-MQ and 5-MQ appear to correspond to 2-MQ and 8-MQ, respectively (see **Fig. 1**). Therefore, we have attempted to separate 7-MQ and 5-MQ. **Table 4** shows that 7-MQ was concentrated very selectively in the α -CD complexes⁶⁾. This result supports our explanations above-mentioned based upon the CPK model.

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- 6) This seems very useful for obtaining 7-MQ of high purity. To our knowledge, the commercially available reagent of 7-MQ usually includes about 20–25% of 5-MQ except the reagent of Aldrich Chemical Co.

要 旨

**α -シクロデキストリンの包接錯体生成を用いる
2-メチルキノリンと 8-メチルキノリンの分離**

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α -シクロデキストリン (CD) による包接錯体生成を利用して, 2-メチルキノリン (MQ) と 8-MQ の分離が有効に行えることがわかった。錯体固体の α -CD-MQ 量論比を検討したところ, ゲスト種が α -CD に対し 4 倍モル, 2 倍モルあるとき

は 1:1 α -CD-MQ 錯体が生成し, ゲスト種が α -CD の 0.25 倍モルのときは 2:1 錯体が生成した。2-MQ に対する包接選択性は, 2:1 錯体の方が 1:1 錯体の場合よりも高かった。Corey-Pauling-Koltun 分子模型に基づき, 結果を説明した。

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Keywords

α -Cyclodextrin, Monoethylquinoline isomer, Inclusion complex, Separation, Inclusion selectivity