

# Precipitation Behavior of 1,1-Di-(*p*-hydroxyphenyl)-cyclohexane Clathrate Crystals from Acetone Solutions Containing *d*-Limonene

MITSUTAKA KITAMURA, AKIO KURODA

Department of Chemical Engineering, Hiroshima University, Saijo-cho, Higashihiroshima, 724 Japan

and

FUMIO TODA

Department of Industrial Chemistry, Ehime University, Bunkyo-cho, Matsuyama, 790 Japan

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**Abstract.** The precipitation behavior of 1,1-di(*p*-hydroxyphenyl)cyclohexane (DHC) from acetone solutions containing *d*-limonene (1-methyl-4-(1-methylethenyl)cyclohexene) was studied. From the pure acetone solution or the solutions containing a small amount of *d*-limonene crystals (B) precipitated, which clathrate only acetone with a guest/host (G/H) molar ratio of 1.0. However, when the *d*-limonene concentration is increased to more than ca. 2 mol/L, crystals (A) precipitated which had a different habit from the B crystals. In the A crystals *d*-limonene is clathrated together with a large amount of acetone and the G/H value of *d*-limonene increases with the concentration in the solution up to the maximum value of 0.2. As the diffraction patterns of the A and B crystals are similar, it is assumed that a part of the acetone molecules in the B crystals are replaced by *d*-limonene molecules. The acetone in the A crystals escapes rapidly, but the *d*-limonene remains for a long time. This may indicate that the large molecule of *d*-limonene cannot diffuse rapidly within the host lattice owing to three-dimensional hindrance. It was clear that the solubility of the A crystals is higher than that of the B crystals and the transformation from the metastable A to the stable B crystals proceeds during the crystallization of A crystals.

**Key words.** Crystallization, adductive crystallization, nucleation, crystal growth, polymorph, transformation, release rate, perfume.

## 1. Introduction

The practical application of clathrate compounds has recently been developing, especially in the fine chemical industries, e.g. for the separation of organic isomers, the stabilization of chemically unstable substances, and improvement of the bioavailability of medicines. These clathrate crystals are generally formed by crystallization (adductive crystallization) from solutions. In the adductive crystallization process both kinetic and thermodynamic approaches are important [1–3]. Primarily the thermodynamic stabilities of the host structures in solutions influence not only the selectivity of the guest molecule but also the precipitation behavior of the polymorphs of the clathrate crystals. Secondly, such a precipitation process comprises three processes, viz. nucleation, crystal growth and transformation.

On the other hand, Toda [4] and Goldberg *et al.* [5] have indicated that 1,1-di(*p*-hydroxyphenyl)cyclohexane (DHC) can clathrate many kinds of guest

molecules with good selectivity and the host is practically useful for the separation of various compounds.

In this paper the precipitation process of the host (DHC) in the presence of *d*-limonene (1-methyl-4-(1-methylethenyl)cyclohexene in acetone solutions is investigated and the release characteristics of *d*-limonene (a perfume) are investigated.

## 2. Experimental

### 2.1. MATERIALS

1,1-Di(*p*-hydroxyphenyl)cyclohexane (DHC) from Sumitomokagaku Co. Ltd. was recrystallized from methanol twice and used as the host. Acetone and *d*-limonene (Katayamakagaku special grade) were used as received.

### 2.2. CRYSTALLIZATION

The clathrate crystals were formed by cooling the solution from 333 K to the crystallization temperature of 293 K in a stirred tank equipped with a glass impeller. The molar ratios of acetone and *d*-limonene to the host in the precipitated solids (G/H) were periodically analyzed by liquid chromatography (Shimadzu LC-6AD) after filtration. The precipitated solids were also analyzed by X-ray diffraction.

The solubility of the host was measured by analyzing the host concentration with liquid chromatography. The acetone and *d*-limonene enclathrated in the crystals were distinguished from the same materials adhering to the crystal surface by a specially devised test: potassium sulphate crystals, which are inert to both acetone and *d*-limonene, were dipped in the same solution as that used in the crystallization, and the evaporating behavior in the atmosphere after filtration was compared with that of the precipitated crystals.

## 3. Results and Discussion

### 3.1. PRECIPITATION BEHAVIOR AND THE CRYSTAL COMPOSITIONS

The solubility of the host, which was recrystallized from methanol, was measured first. The solubility increases with temperature and decreases with *d*-limonene concentration. In Figure 1 the dependence of the solubility of the host in acetone solutions containing *d*-limonene on the *d*-limonene volume fraction (VOL) in the mixture of *d*-limonene and acetone at 293 K is shown.

Initially, crystallization was performed from a pure acetone solution at an initial host concentration ( $C_H$ ) of 0.852 mol/L. A microscopic photograph of the crystals precipitated (B) is shown in Figure 2. The amounts of acetone in the crystals were analyzed periodically after filtration in the atmosphere (see Figure 3). The results indicate that the quantities of acetone in the crystals decrease rapidly with time. On the other hand, it was observed that the acetone adhering to the potassium sulphate, which was filtrated after being dipped in the same solution, evaporated very quickly and diminished completely within 10 min. This suggests that the acetone in Figure 3 is clathrated rather than adhered and the decrease of the

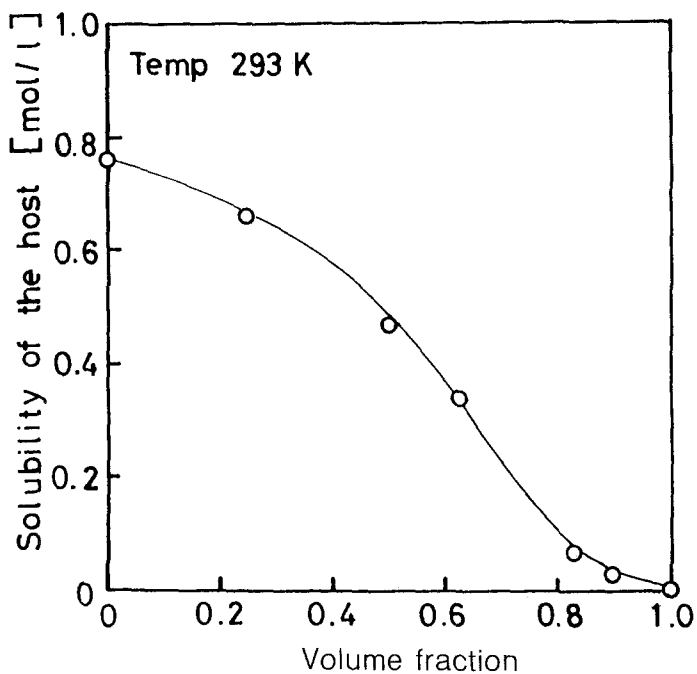
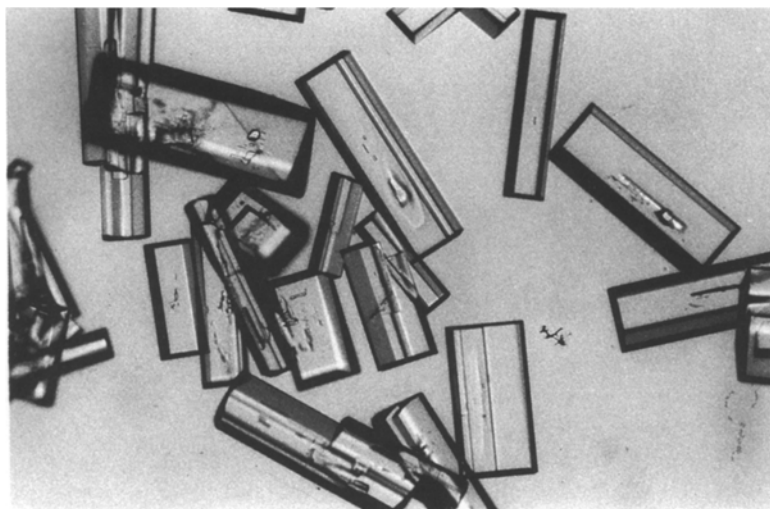


Fig. 1. Dependence of the host solubility on the *d*-limonene volume fraction in the mixture of *d*-limonene and acetone at 293 K.



200  $\mu\text{m}$

Fig. 2. Microscopic photograph of the crystals precipitated from a pure acetone solution.

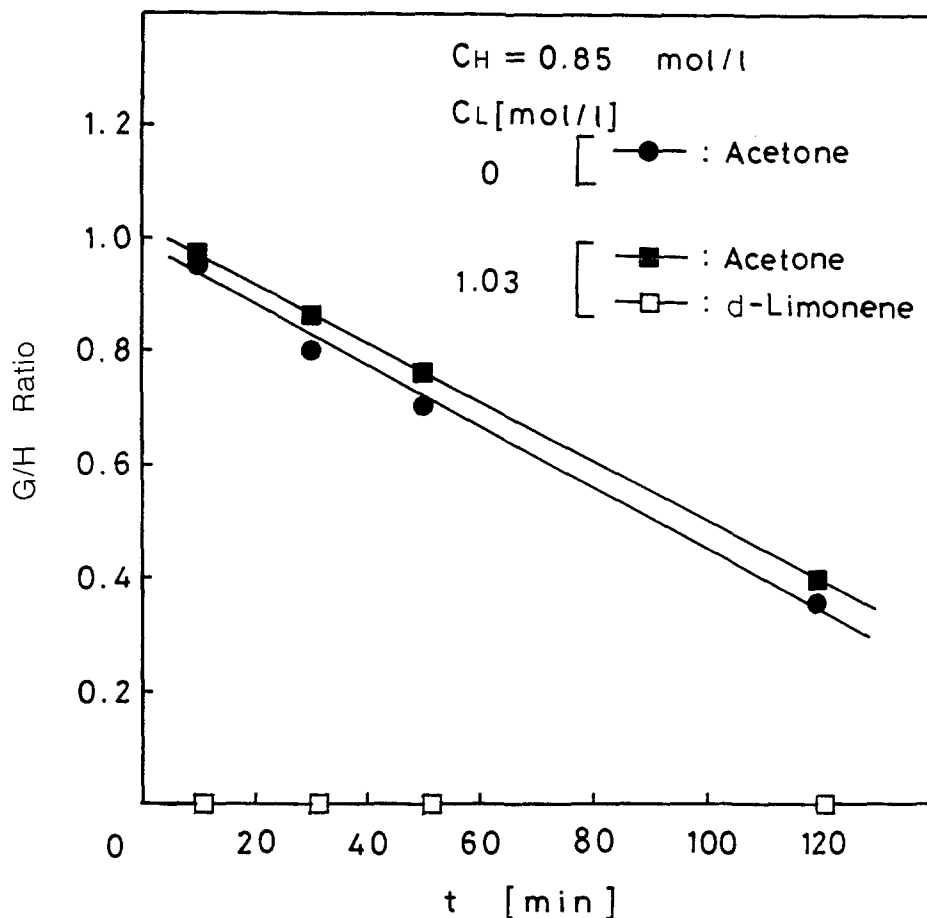


Fig. 3. Time dependence of the molar ratio of acetone to the host in the crystals ( $G/H$ ) after filtration (crystals B).

acetone is due to the escape from the lattice structure. Furthermore, Figure 3 indicates that the molar ratio of acetone to the host ( $G/H$ ) just after the filtration is 1.0, a value which agrees well with the result reported by Toda [4].

From a solution of low concentrations of *d*-limonene the same crystals precipitated as were obtained from pure acetone. However, when the concentration of *d*-limonene ( $C_L$ ) was increased above ca. 2 mol/L (VOL is 0.38), crystals (A) were obtained, having a different habit from crystals B in Figure 2 (Figure 4). Figure 5 shows typical results of the time dependence of the amounts of acetone and *d*-limonene in the crystals after the filtration. (The crystallization was carried out at a *d*-limonene concentration of 5.14 mol/L (VOL is 0.83).) It can be seen that both amounts decrease and the acetone disappeared within about three hours. The *d*-limonene, however, attained a constant value ( $G/H$ ) of about 0.2 and remained for a long time. From the evaporation test using potassium sulphate it was observed that adherent *d*-limonene and acetone evaporated completely in about 60 min and within 10 min, respectively. Accordingly it is considered that the part of the declining

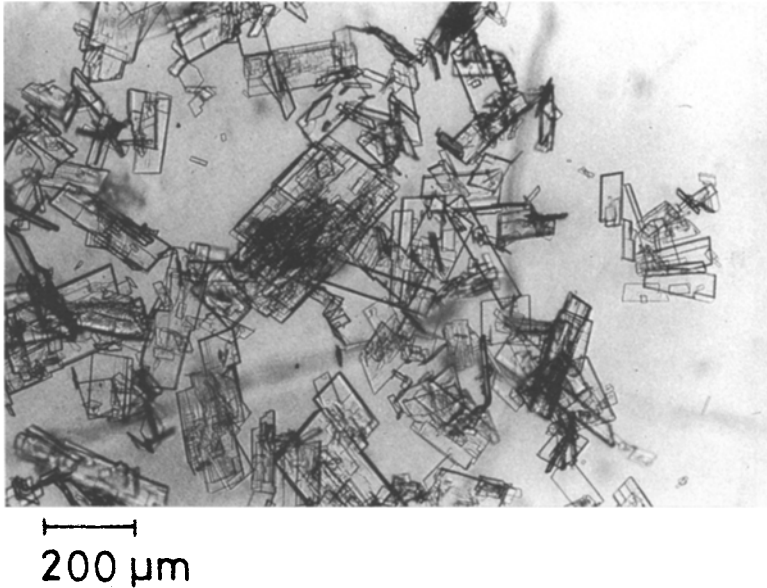


Fig. 4. Microscopic photograph of the crystals precipitated from acetone solutions containing *d*-limonene.

curve of *d*-limonene in Figure 5 is adherent, and the residual *d*-limonene and the acetone are clathrated. As the X-ray diffraction pattern of the A crystal (Figure 6(a)) is similar to that of the B crystal (Figure 6(b)), it is assumed that a portion of the acetone molecules in the B crystals are replaced by *d*-limonene and the small amount of *d*-limonene induces the change in the morphology of the B crystals. The G/H value of clathrated *d*-limonene tends to increase with the concentration in the solution; however, 0.2 seems to be the maximum since no increase was observed even if the *d*-limonene concentration in the solution was much higher.

Goldberg *et al.* [5] showed that the cresol clathrate crystal of DHC (triclinic, space group  $\bar{P}$ , G/H = 1) is composed of 'layers' of hydrogen-bonded species containing a host-host-host pattern along the *b* axis and a guest-(host-host)-guest-(host-host) pattern along the *a* axis. The small acetone molecule may be clathrated in the same manner as the cresol guest (G/H are the same), whereas the bulky molecule of *d*-limonene may be clathrated with a low packing efficiency. The results in Figure 5 may also mean that the interaction between the host and acetone is weak and the small acetone molecule can rapidly escape from the lattice structure. The clathrated *d*-limonene molecules, on the other hand, cannot diffuse smoothly within the host lattice because of the three-dimensional hindrance. Furthermore, the X-ray diffraction patterns of Figures 5(a) and (b) did not change, even after all the acetone had evaporated, indicating that the host structures remained intact.

The test of the release characteristics of *d*-limonene from the A crystals over a long time span showed that only about 30% of the *d*-limonene is lost during the course of one month.

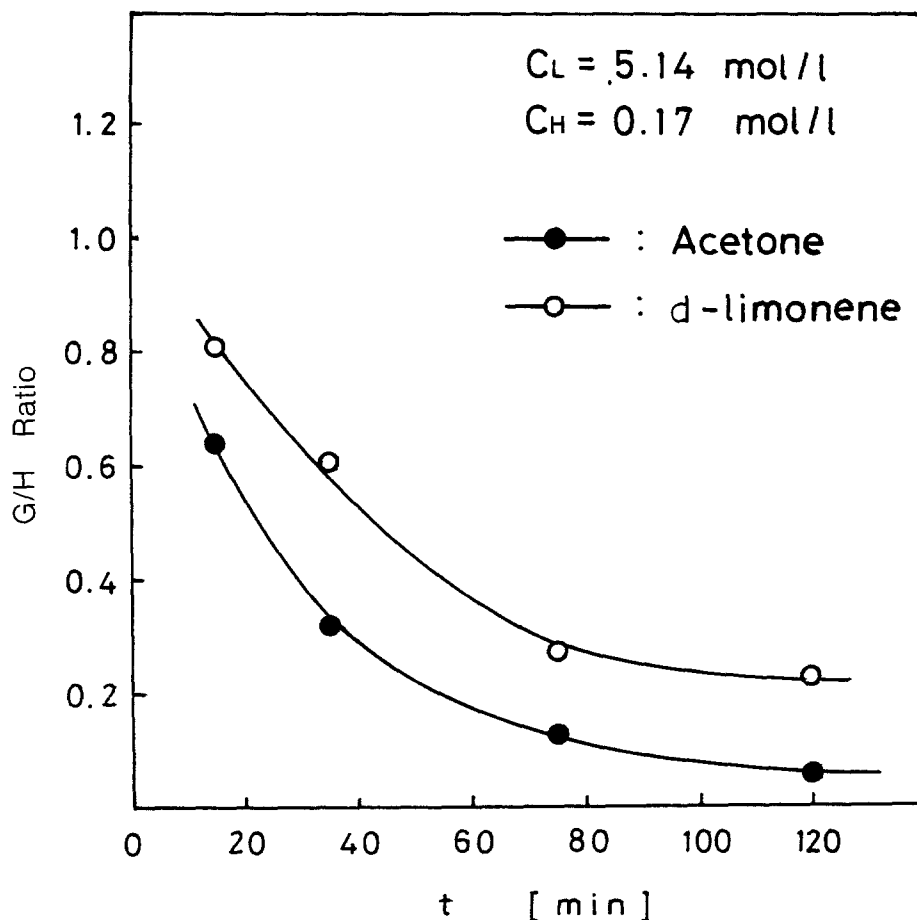


Fig. 5. Time dependence of G/H in respect to acetone and *d*-limonene after filtration (crystals A).

### 3.2. TRANSFORMATION OF THE CLATHRATE CRYSTALS IN SOLUTIONS

It was observed that in the crystallization of the A crystals, the crystals initially precipitated (Figure 4), dissolved, and B crystals (Figure 2) nucleated and grew with the passage of time and the clathrated *d*-limonene was released into the solution. This means that the solubility of the A crystals is higher than that of the B crystals (the free energies are different), and the transformation from the metastable A to the stable B crystals proceeds due to the difference in the solubilities. Such a transformation was also observed in the crystallization of nickel-complex clathrate crystals [1, 3] i.e. the transformation mechanism is 'solution-mediated'.

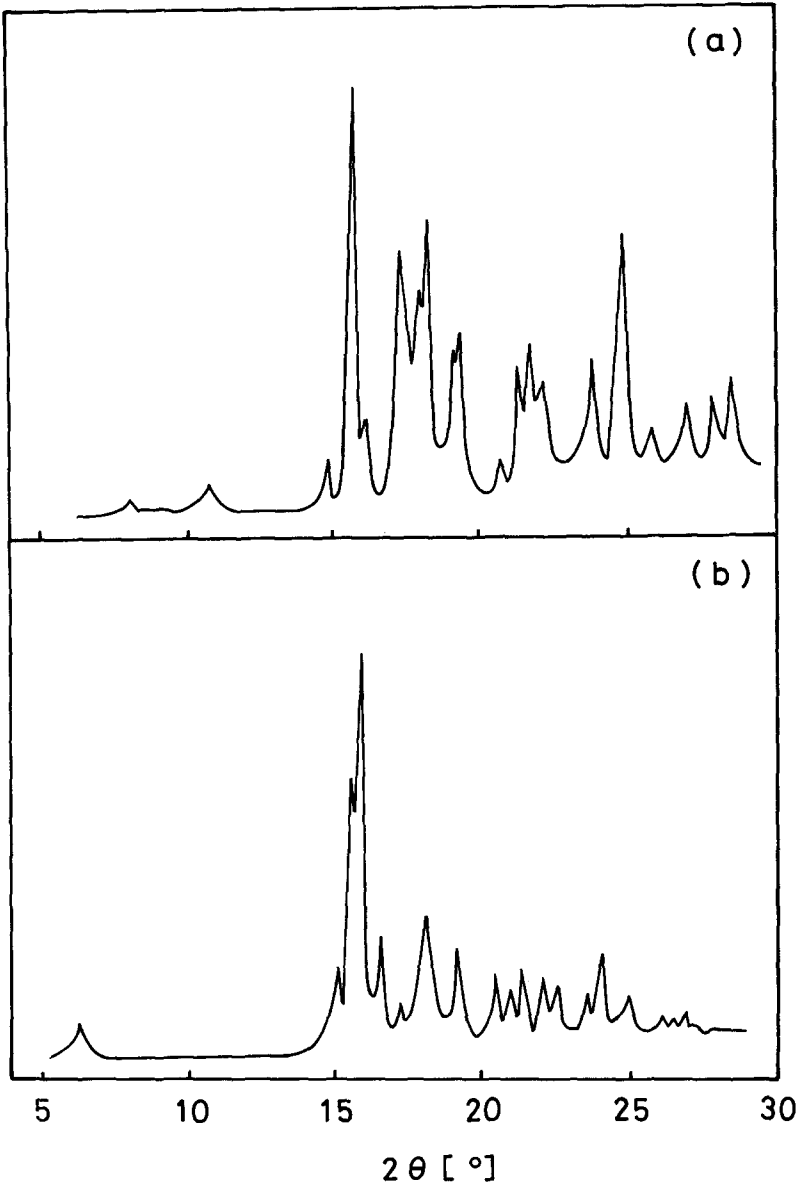


Fig. 6. X-ray diffraction patterns of crystals A (a), and B (b).

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