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Seeded Batch Cooling Crystallization of Tetrahydroxybenzophenone from Acetone Solution

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Abstract:

Granular particles of acetone solvate tetetrahydroxybenzophenone (THBP) were crystallized by cooling from acetone solution in a jacketed vessel of 2 L. Cooling was made simply by circulating water of a constant temperature through the jacket with no control so that the temperature of the content fell in an exponential manner. Crystals, obtained from a previous batch, were conveniently used as seeds after being ground and sieved. The product crystals obtained at seed-loading ratios (the mass ratio of the seeds to the theoretical crystal yield) lower than or equal to 5.07×10^{-3} consisted of grown seeds and grown nuclei with bimodal size distribution. On increasing the seed loading, the fraction of grown nuclei was decreased and, at a highest seed-loading ratio of 5.07×10^{-2} it became virtually zero (no grown nuclei). Solvated acetone was completely removed from the product on drying at 60 °C, and the granular shape remained unchanged. Dried product exhibited better flow characteristics with less tendency of powder scattering. An additional experiment using a pilot-scale crystallizer gave the product of the same quality as that of laboratory experiments. The technique proposed can be used in an actual purification process.

1. Introduction

Tetrahydroxybenzophenone (THBP: molecular weight = 246.2) is a raw chemical compound of light-sensitive materials used in industries for photolithography and photoengraving. The chemical structure of THBP is shown in Figure 1. It is purified in industry by cooling crystallization from a mixed solvent of acetone, water and other organic solvents. It crystallizes as thin needle crystals. Because of this, the downstream processes such as centrifuging and drying need a long time. Breakage of particles into fragments, low flowability and variations in the product quality and the crystal yield from batch to batch are other problems.

According to a previous study[1] on the solubility of THBP in acetone, there are two types of crystals: granular crystals and thin needle crystals. The former is an acetone solvate or a pseudopolymorph, and the latter is a nonsolvate. The solubility of the granular crystals is lower than that of the needle crystals at temperatures lower than 41.7 °C, while at temperatures higher than 41.7 °C, it is higher than that of the needle crystals. Thus, the solubility of the granular crystals exhibits a higher temperature dependency. Therefore, the high yield is expected if the granular crystals are crystallized by cooling. THBP acetone solution is very stable according to our preliminary experiments. Neither the thin needle crystals nor the granular crystals precipitate on cooling unless seeding is made.

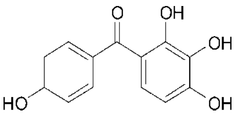

Figure 1. **Chemical structure of tetrahydroxybenzophenone.**

In practice, crystallization of solvate or hydrate is not suitable for the purpose of purification, because solvent or water is inevitably included as impurity into the solvate or hydrate. In this paper, however, we propose a technique using solvate crystallization for the purification of THBP. It will be shown that this technique can be satisfactorily applied to purification because solvated acetone can be removed completely without any special caution on drying and the dried powder shows a better flow characteristic with less scattering tendency.

2. Results and Discussion

2.1. Seeding Effect on Crystal Size Distribution. The amount of seeds in batch cooling crystallization is known to have a large effect on product crystal size distribution; the product is a mixture of grown secondary nuclei and grown seeds at low seed-loadings; therefore, the size distribution is bimodal, while at high seed-loadings, the product consists of grown seeds and the size distribution becomes unimodal.[2–11] The same tendency in seeding effect was observed in this study for the crystallization of THBP from acetone solution. The crystal size distributions of THBP are shown in Figure 2.

The size distributions are bimodal when the seed-loading ratio was less than or equal to $\mathrm{Cs} = 5.06 \times 10^{-4}$. The peak

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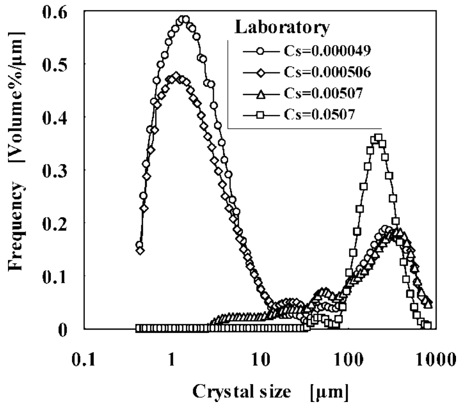

Figure 2. **Size distribution of product crystals obtained for different seed-loading ratios.**

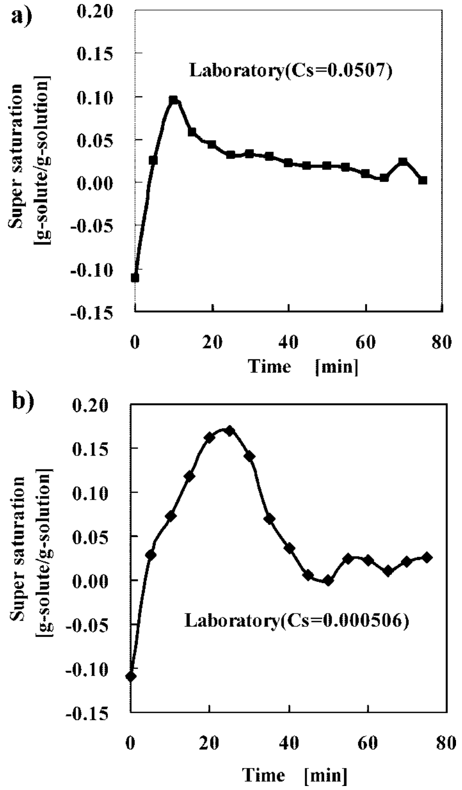

Figure 3. **(a) Supersaturation transient in case of Cs = 5.07 × 10^{-2}. (b) Supersaturation transient in case of Cs = 5.06 × 10^{-4}.**

height in small size range (corresponding to the grown secondary nuclei) becomes lower as the seed-loading ratio is increased and it finally disappears at the highest seed-loading ratio of Cs = 5.07 × 10^{-2}. The disappearance of secondary nuclei at the highest seed-loading will be explained as follows. The transient supersaturation was suppressed as shown in Figure 3a, which can be explained in this way: supersaturation created by cooling was consumed by the high rate of the growth of seed crystals with large total surface area. On the other hand, the secondary nucleation rate B is known[11] to be written as a function of the number density n_s of seed crystals present, supersaturation ΔC and size L_s of seed crystals as

$$B \propto n_s(\Delta C)^n L_s^m \qquad (1)$$

where n and m are constants. Therefore, the secondary nucleation rate at Cs = 5.07 × 10^{-2} is considered to be suppressed virtually.

Contrary to this, the peak of supersaturation was high at Cs = 5.06 × 10^{-4} as seen in Figure 3b. In this case, the small amount of seeds continued to grow for a while at relatively high supersaturations so that the size of the seeds became large enough for secondary nucleation to occur and the supersaturation finally began to decrease with the growth of seeds and secondary nuclei.

Figure 4 shows transient temperatures at Cs = 5.07 × 10^{-2} and Cs = 5.06 × 10^{-4} obtained simultaneously with the measurements of the above supersaturation transients. A transient temperature in case of no seeding is also plotted in this figure. The temperature, when no seeds were added, falls simply in an exponential manner, while when the seeds are loaded, it falls nearly in the same way but accompanied with a small temperature rise. The temperature rise for the case of Cs = 5.07 × 10^{-2} can be said to be an indication of crystallization heat liberation by the growth of seeds, because no secondary nucleation occurred due to suppressed supersaturation (see eq 1). On the other hand, the temperature rise in case of Cs = 5.06 × 10^{-4} can be attributed to the growth of seed crystals and secondary nuclei, where the sizes of the seeds are large enough at relatively high supersaturations to generate secondary nuclei as mentioned above. In Figure 5, temperature profiles of the other runs are shown. The position of the temperature rise moves to the later stage as the seed-loading ratio is decreased. This can be explained as follows. When the seed-loading ratio is low, the number density of the seed is low. Therefore, the seed grows larger (with small heat liberation), but longer time is needed for secondary nucleation to occur. Therefore, the temperature rise will be delayed. At the same time, the supersaturation decrease by the growth of the seeds is not large because of the small amount of seeds, and the large amount of supersaturation remains for the generation of secondary nucleation. This is the reason why the amount of secondary nuclei is increased with a decrease in seed loading.

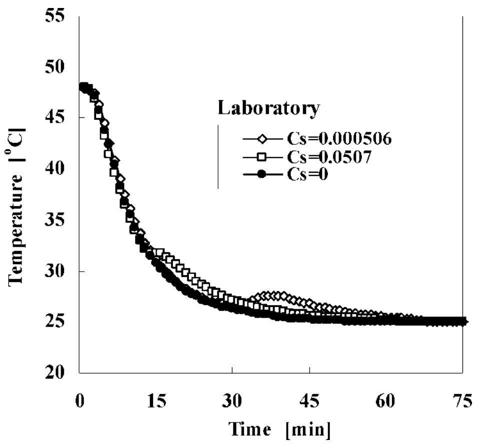

Figure 4. **Transient temperatures in cases of Cs = 5.07 × 10^{-2} and Cs = 5.06 × 10^{-4}.**

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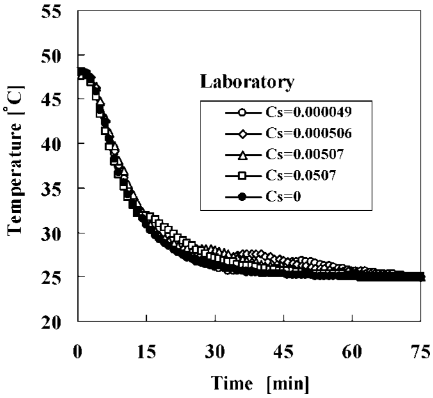

Figure 5. **Transient temperatures for different seed-loading ratios.**

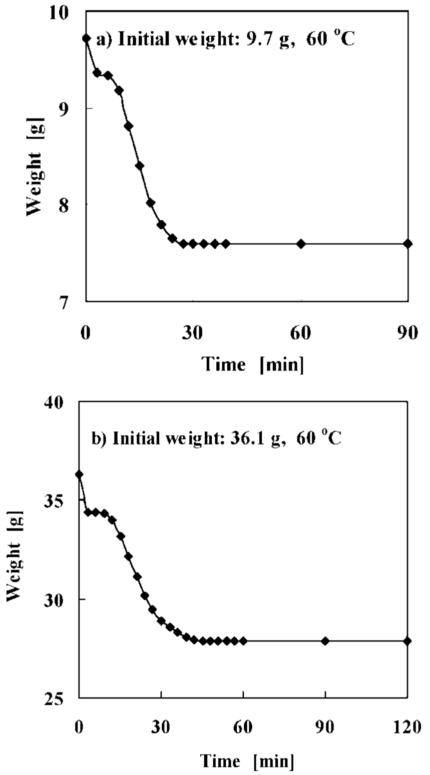

Figure 6. **Drying curves of the granular solvate THBP crystals (a) initial weight: 9.7 g, (b) initial weight: 36.3 g.**

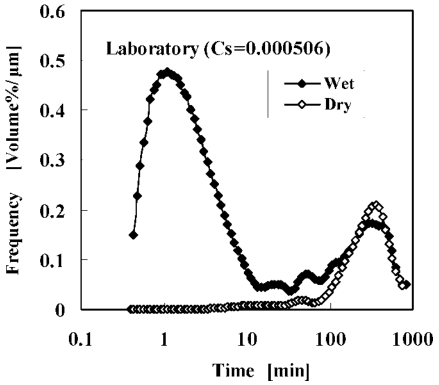

Figure 7. **Effect of drying on crystal size distributions.**

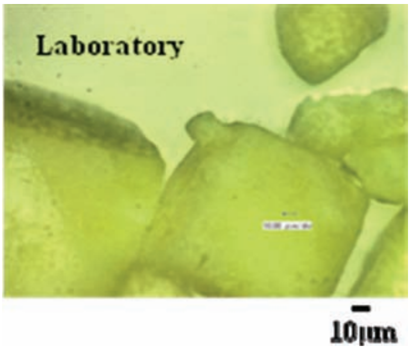

Figure 8. **A photograph of dried THBP crystals. A small particle is seen adhering to a larger one.**

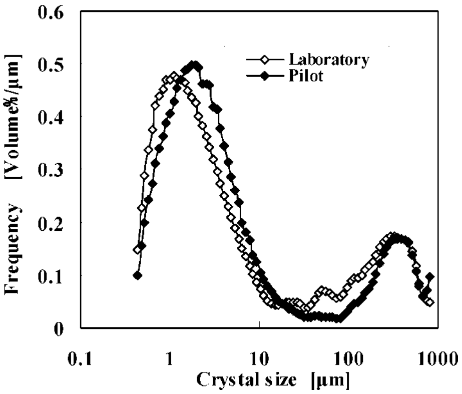

Figure 9. **Crystal size distribution of the product obtained from the pilot-scale crystallizer compared with that from the laboratory-scale crystallizer.**

2.2. Drying Characteristics of Acetone Solvate Crystals. Solvated acetone should be removed from the product without any difficulties by drying. Otherwise, crystallization of the solvated THBP cannot be applied to an actual process as a separation or purification technique. As shown in Figure 6, the wet cake could be dried in about 30 min at 60 °C under the condition of gentle air flow. After acetone on the surface of crystals is lost in about 1 min, the weight continues to decrease and finally reaches dryness in about 30 min. The second loss of weight exactly corresponds to that of solvated acetone. No acetone was detected in the dried THBP by HPLC (high performance liquid chromatography). The shape of the crystals did not change on drying. The size distribution of the dried THBP crystals is shown in Figure 7. As seen in the figure, the size distribution changes on drying, and the peak in the small size range disappears. This is considered to be due to sticking of small particles to larger ones during the drying process, as shown in Figure 8, where a small particle is seen adhering to a large one. Acetone liberated from inside of the acetone solvate THBP crystals may act as a binder by partially dissolving the surface of THBP crystals. This phenomenon is advantageous in industry, because the dried granular THBP crystals exhibit less tendency to scatter with better flowability.

2.3. Result of the Pilot-Scale Experiment. In Figure 9, the size distribution of the product crystals obtained from the pilot-scale crystallizer is compared with that obtained from the laboratory-scale crystallizer. The seed-loading ratio Cs was 5.06 $\times 10^{-4}$. The size distributions are almost the same. Scale-up did not have a significant effect of the crystal size distribution. It can be concluded, therefore, that the seeding technique developed in this study is safely applied to an actual industrial

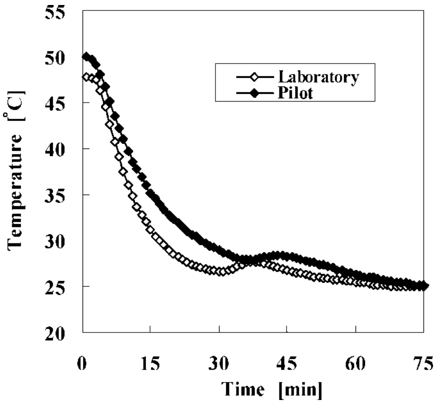

Figure 10. **Transient temperature in the pilot-scale experiment compared with that of the laboratory-scale experiment.**

crystallizer. The actual amount of the added seeds was only 2 g for the pilot-scale crystallizer of 50 L. This small amount of seeds is acceptable for industrial operation. Figure 10 shows that the transient temperature in the pilot scale experiment, which is compared with that of the laboratory scale crystallizer. The temperature of the pilot scale crystallizer falls in an exponential manner and a small temperature rise is accompanied. But it changes more slowly and the temperature rise is delayed. This is because the heat transfer resistance of the glass-lined wall is larger and the surface to volume ratio is smaller in the pilot scale crystallizer.

3. Conclusions

(1) Neither thin needle crystals of nonsolvate nor granular solvate of THBP crystallized by simple cooling from acetone solution. Seeding is crucial to induce crystallization.

(2) Granular acetone solvate crystals were safely crystallized by seeding ground solvate crystals even if the seed-loading ratio was as low as $Cs = 4.90 \times 10^{-5}$. This small amount of seeds is advantageous for industrial operation.

(3) Ground, sieved granular acetone solvate crystals were able to be used as seeds.

(4) At lower seed-loading ratios of $Cs = 4.90 \times 10^{-5}$, 5.06×10^{-4}, and 5.07×10^{-3}, particles smaller than about about 10 μm (grown secondary nuclei) were generated and included in the products, while at the highest seed-loading of $Cs = 5.07 \times 10^{-2}$, virtually no small crystals were generated.

(5) These small particles fortunately disappeared during the subsequent drying process at 60 °C at atmospheric pressure. This was considered to be attributed to the sticking of the small particles to larger ones. For this, the product particles exhibited less scattering tendencies with good flow characteristics.

(6) Solvated acetone was completely removed from crystals during the same drying process. Therefore, crystallization of the granular acetone solvate can be used as a separation or purification process.

(7) A pilot-scale experiment using a 50 L crystallizer gave product of the same quality as those of laboratory experiments.

4. Experimental Section

4.1. Laboratory-Scale Experiment. The crystallizer used in the laboratory (see Figure 11) is a jacketed nonbaffled glass vessel with a working volume of 2 L. It is equipped with a

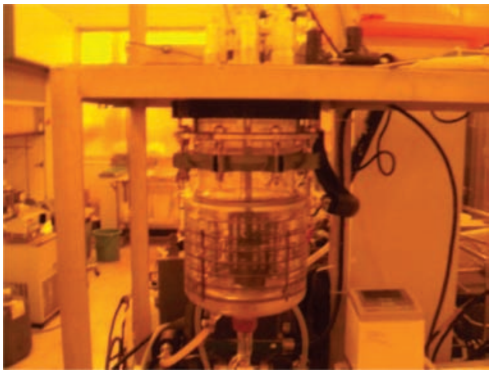

Figure 11. **Photograph of the laboratory scale crystallizer.**

Maxblend stirrer and a temperature sensor. Accurately weighed THBP thin needle crystals and acetone solvent were introduced into the crystallizer to make the solution, of which the saturation temperature with respect to the granular crystals was 42.1 °C. The solution was heated up to 48.0 °C and maintained at this temperature for about 20 min to ensure that crystals dissolved completely, and then the solution was cooled to 25.0 °C for crystallization. Cooling was made by circulating the cooling water with a constant temperature of 25.0 °C through the jacket. No temperature control was made so that it fell in an exponential manner, although a small temperature rise due to the heat of crystallization was observed. Seeding was made at 35.0 °C about five minutes later after the solution became supersaturated. The solution was agitated at 250 rpm throughout the run. Batch time was fixed at 75 min from the start of cooling. The temperature was recorded in 1-min intervals. In two runs, however, it was recorded in 5-min intervals, and a solution sample of about 5 mL was taken through a syringe fitted with a filter to know the transient solution concentration (and supersaturation). The concentration of the sampled solution was determined gravimetrically as in the previous solubility study.[1] The product crystals were separated by filtration from the final slurry, and a sample was taken from the wet cake for the measurement of crystal size distribution.

The THBP used were nonsolvate needle crystals obtained from an actual production unit. The organic purity, determined by HPLC, was 99.9% or more. The acetone used was purchased from Kyowa Hakko Kogyo Co. Ltd. in Japan. According to the manufacturer, the purity was 99.8 mass fraction % with a moisture of 0.2 mass fraction %. THBP and acetone were used without further purification. The size distributions of the product crystals and the seed crystals were measured with the laser scattering method using a Coulter LS series 100 with water as a dispersion medium.

The original granular (acetone solvate) seed crystals were prepared in the same way as in the previous solubility study,[1] by natural evaporation at room temperature, and then the product crystals of a previous batch were used as seeds for a subsequent experiment. Ground crystals were used as seeds after adjusting the size by sieving with two successive sieves of aperture sizes of 38 and 75 μm. The average of the sieve apertures was 56 μm, but the size distribution, as shown in Figure 12, is widely down to the range of a few micrometers. This suggests that the ground seeds, which were agglomerated in the air when sieving, were dispersed in the dispersion medium water. The reason for

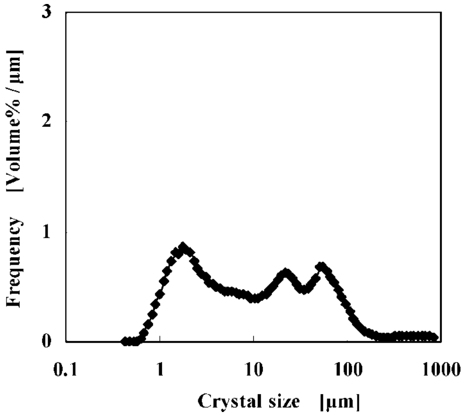

Figure 12. **Size distribution of the ground and sieved seed crystals.**

using ground crystals as seeds was that their preparation was easy. The ease of seed preparation is significantly important in industry. The seed-loading ratios examined were 4.90×10^{-5}, 5.06×10^{-4}, 5.07×10^{-3} and 5.07×10^{-2} where it is defined by the mass ratio of the added seeds to the theoretical crystal yield. The theoretical crystal yield calculated from the solubility of THBP[1] and the difference between the saturation temperature and the final temperature was 284.1 g.

Solvated acetone should be removed with no difficulties from the product crystals. Otherwise, crystallization of the granular THBP cannot be used as a purification process. The wet cake of the product crystals was dried at 60 °C in an oven with gentle air flow. The drying experiment was performed twice with different samples. The first sample was 9.7 g and the second 36.3 g. The sample weight was measured in intervals to obtain the drying curve.

4.2. Pilot-Scale Experiment. A batch experiment using a pilot-scale crystallizer of a working volume of 50 L, which was equipped with an Anchor stirrer, was performed to confirm the seeding effect observed for the laboratory crystallizer of 2 L. The inside of the crystallizer was glass-lined. The scale-up ratio in volume was 25. The stirrer speed was 100 rpm so that the tip speed was nearly the same as that of laboratory experiments. The experimental condition was almost the same as that of the above laboratory crystallization. A THBP solution of the same concentration as that of the laboratory experiments was used. It was cooled to 25 °C by circulating cooling water through the jacket with no temperature control. The temperature was measured with a sensor. It fell in an exponential matter with a small temperature rise caused by the heat of crystallization. The seed crystals used were also ground-sieved granular acetone solvate crystals. The seed-loading ratio was 5.06×10^{-4}. A sample for the measurement of the product size distribution was taken from the wet cake separated from the final slurry.

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