Journal of Crystal Growth 394 (2014) 106–111

Contents lists available at ScienceDirect

Journal of Crystal Growth

journal homepage: www.elsevier.com/locate/jcrysgro

Solubility measurement of a metastable achiral crystal of sodium chlorate in solution growth

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ARTICLE INFO

Article history:
Received 9 January 2014
Received in revised form
14 February 2014
Accepted 18 February 2014
Communicated by: S.R. Qiu
Available online 26 February 2014

Keywords:
A1. Optical microscopy
A1. Solubility
A2. Growth from solutions
A2. Industrial crytsallization
A2. Seed crystal
B1. Inorganic compounds

ABSTRACT

The solubility of the metastable achiral monoclinic phase in $NaClO_3$ crystallization from an aqueous solution, which appears prior to the nucleation of chiral crystals, was successfully measured in the range from 10 °C to 23 °C. Antisolvent crystallization method was used to obtain metastable crystals for the measurement. The solubility was determined to be about 1.6 times higher than that of the chiral stable cubic phase by observing growth or dissolution of the crystal in aqueous solution at the temperature and concentration of which is predetermined.

1. Introduction

Chiral symmetry breaking in sodium chlorate ($NaClO_3$) crystallization from an aqueous solution has been of great interest because it is closely related to understanding of homochirality, chiral resolution, spontaneous emergence of chirality. The system of $NaClO_3$ is a typical example of chiral crystallization, and achiral solution yields chiral enantiopure crystals having cubic $P2_13$ symmetry [1]. Crystallization of $NaClO_3$ from a *static* solution results in equal population of two enantiomorphs [2]: chirally symmetric state. However, it has been reported that perturbations on solution during crystallization causes deviation from the chirally symmetric state [3–17]. Various experiments of crystallization with the perturbations have indicated that the chiral symmetry breaking is accomplished during the early stages of $NaClO_3$ crystallization. As the cause of amplification of one-single chirality, for instance, secondary nucleation [3–13], chiral recognition of subcritical chiral cluster [14–16] have been proposed. However, the processes that lead to the chiral symmetry breaking still remain ambiguous because the most of crystallization experiments of chiral symmetry breaking has exclusively focused on the crystals that are not growing. Namely, attention has solely been paid to outcome of the process.

Recently, Niinomi et al. have performed *in-situ* microscopic observation of $NaClO_3$ crystallization from an aqueous solution to investigate the process. The observations revealed that unstable achiral crystals having monoclinic $P2_1/a$ symmetry appear prior to the formation of the chiral crystals in the early stage of crystallization, and that the achiral crystals transform to chiral crystal [18]. Previously, in $NaClO_3$ melt growth, an achiral metastable phase has been reported, and the chiral phase and the achiral phase are designated as Phase I and Phase III, respectively [19]. Ward et al. have reported chiral symmetry breaking in crystallization from $NaClO_3$ melt, and have figured out the importance of nucleation of the Phase III [20]. Niinomi et al. have pointed out that the achiral phase in solution growth is identical to the Phase III on the basis of X-ray diffraction experiment (thus, we refer the achiral phase as Phase III). Because the pathway for emergence of

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http://dx.doi.org/10.1016/j.jcrysgro.2014.02.034

chirality in solution growth has been conventionally considered to be direct nucleation of the chiral crystals, the pathway for emergence of chirality through the polymorphic transformation from the Phase III to Phase I has a potential to provide a new sight for understanding of chiral symmetry breaking in solution growth. The polymorphic transformation is easily expected to be the consequence of Ostwald's rule of stages. If it is the case, the solubility difference should exist between the chiral phase and the achiral phase. To clarify the achiral–chiral polymorphism, thus, the quantitative assessment on the solubility of the achiral phase is essential.

Numerous methods to measure solubility of crystals, such as ATR-FTIR spectroscopy [21], Raman spectroscopy [22], have been reported. However, these methods require a substantial amount of the target crystal, being not suitable for the $NaClO_3$ crystal of Phase III because of its instability. Although the method using interferometer has been developed for the crystals available only in small amount [23], even this method requires to make a sample crystal of the target material and to manipulate the sample crystal. However, owing to its instability, no method to control the $NaClO_3$ Phase III has been established. Therefore, it is also necessary to establish the method controlling the crystal of Phase III for the solubility measurement.

The purpose of this study is to develop a method to produce a sample crystal usable for the solubility measurement of the achiral crystal of $NaClO_3$ Phase III in solution growth (The state of “usable for the measurement” in this context means that the achiral crystal is isolated from the mother liquor) and to measure the solubility. Here, we report that antisolvent crystallization [24–26] can be utilized to produce a usable sample crystal of Phase III while overcoming the instability, and that the solubility of the Phase III was roughly determined by observing growth or dissolution of the sample crystal immersed in aqueous solution with various condition using a polarized-light microscope.

2. Experimental

2.1. Sample preparation

Sample crystals of $NaClO_3$ Phase III were prepared by antisolvent crystallization method using acetone. The saturated solution made by the method in the literature [18] (6 μL) was dropped on a glass slide covered with a layer of polymer film using a micropipette and then, acetone (Analytical Grade, Wako Pure Chemical Industries Ltd., Osaka, Japan), which is an antisolvent for $NaClO_3$, was vigorously injected to the droplet on the glass slide using a micropipette (about 500 μL). After the injection of the acetone, tiny crystals (about 50 μm or less) of the Phase III immediately appeared in the droplets of the mixture of aqueous solution and acetone. The crystals of Phase III were identified by detecting birefringence using a polarized-light microscope ($NaClO_3$ Phase I crystals do not exhibit birefringence because of optically isotropic cubic symmetry.). In the case of the typical crystallization such as evaporation-driven crystallization, even if the crystals of Phase III appear in the mother solution, the crystals transform to crystals of Phase I by a phase transition before the mother solution completely is dried by the evaporation. By contrast, in this method, most of the crystals remained as Phase III without phase transitions even after the mother liquor dried. Subsequently, we cut the polymer film under a crystal of Phase III using a cutter in the size of 500 μm × 100 μm while observing using the microscope and then, the crystal was transferred to the flow cell shown in another section by capturing the film using tweezers in order to avoid the phase transition. These procedures allowed us to prepare sample crystals of the achiral Phase III successfully.

Table 1
Solution conditions used for solubility measurements.

Solution No.	Temperature T_a (°C)	Concentration C_a (g/100gH_2O)	Saturation temperature with respect to Phase I T_e (°C)	Supersaturation with respect to Phase I (%)
1	10	166	80	89
2	10	150	70	71
3	10	137	60	56
4	10	125	50	43
5	23	166	80	69
6	23	150	70	52

2.2. Preparation of the solutions for the solubility measurements

We prepared six aqueous solutions of $NaClO_3$. The conditions are summarized in Table 1. All the conditions are supersaturated with respect to the Phase I. The procedure to prepare the solution at the temperature and concentration of which are T_a (°C) and C_a (g/100gH_2O) is described below [In the case of the solution No. 1, for instance, $T_a=10$ (°C) and $C_a=166$ (g/100gH_2O)]. $0.2C_a$ g of the $NaClO_3$ powder of Phase I (Analytical Grade, Wako Pure Chemical Industries Ltd., Osaka, Japan), 20 mL of distilled water and a magnetic stirrer were put in a glass container that can be hermetically closed with a screw cap. The container was heated in the hot water at T_e+10 (°C), where T_e is the saturation temperature with respect to the concentration C_a [In the case of the solution No. 1, the $T_e=80$ (°C)], and the mixture in the container was stirred using a hot-plate stirrer. After complete dissolution of the powder, the stirrer bar was removed from the container. The glass container was set in an isothermal bath, and then it was gently cooled to T_a with care not to occur any nucleation of crystal (cooling rate ~0.3 °C/min). The resulting solutions were used for the solubility measurement. Whole procedures described above were carried out in a clean room.

2.3. Experimental setup

The solubility measurement was performed on the basis of *in-situ* observations using a polarized-light microscope. We evaluated whether each solution is undersaturated or supersaturated with respect to Phase III by observing the dissolution and growth of a sample crystal immersed in the solutions. Observational procedure is described below. A flow cell was prepared as shown in Fig. 1. The flow cell contains a sample crystal, and is connected to solution in an isothermal bath and to a syringe using silicone tubes. Thus, it is possible to flow the solution into the cell by pulling the syringe (Fig. 1 (a)). The temperature of the cell was controlled at the same as that of the solution by using a Peltier stage (Fig. 1(b)). When the solution was flowed into the cell and soak the sample crystal, we observed the crystal with attention to the change in the size and the interference color of the crystal. If the size becomes larger or the interference color changed to higher-order color, we can distinguish the crystal as growing, *i.e.*, the solution condition is supersaturated with respect to Phase III and *vice versa*. During the observation, the solution continued to be flowed in order to avoid the change in the concentration of the solution due to generation of Phase I crystals.