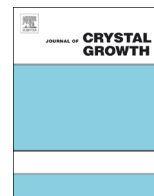




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Journal of Crystal Growth

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

Face-selective crystal growth behavior of L-aspartic acid in the presence of L-asparagine



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ARTICLE INFO

Article history:

Received 17 March 2015

Received in revised form

25 November 2015

Accepted 8 December 2015

Communicated by M. Uwaha

Available online 17 December 2015

Keywords:

A1. Crystal morphology

A1. Crystal structure

A1. Growth models

A1. Impurities

A1. Optical microscopy

B1. Organic compounds

ABSTRACT

The kinetic mechanism of L-asparagine (L-Asn) action on L-aspartic acid (L-Asp) crystal growth, namely the face-selective effect of L-Asn on the L-Asp crystal growth rate in each direction, was examined. In the *a*-axis direction, the effect of L-Asn on the L-Asp crystal growth rate was small. Enhancement and inhibition of L-Asp crystal growth, and interestingly the dissolution of the L-Asp crystal face, were observed in the *b*-axis direction, depending on the amount of L-Asn added. In the *c*-axis direction, the L-Asp crystal growth rate decreased with the increase in the amount of L-Asn added, and the experimental results were well fitted with a Langmuir adsorption isotherm. The study showed that there were crystal growth conditions where enhancement and inhibition, as well as inhibition and dissolution, coexisted in the presence of an additive with a structure similar to the growing crystal.

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1. Introduction

Crystallization is a very important technique used in a wide range of industrial areas, such as the pharmaceutical industry, the food industry, and the agricultural industry, because it is simple and productive. Impurities dissolved in the crystallization mother liquor can affect the nucleation rate and crystal growth rate. Weissbuch et al. have reviewed the effect of impurities on nucleation [1]. The inhibition of crystal growth can be explained mostly by the adsorption of impurities onto terraces on the crystal surfaces and pin step movement during crystal growth [2]. However, the impurities often adsorb onto a specific crystal face selectively, depending on their molecular structures. Accordingly, the crystal habit, which is an important factor in determining the powder characteristics, can change dramatically. The change in crystal habit often has an effect on various properties, such as filterability and slurry viscosity, and can cause problems in manufacturing. Impurities are sometimes deliberately added to control crystallization behavior and crystal habit through a chemical mechanism, via molecular structural interactions between the substrates and the impurities. These impurities are called

tailor-made additives [3]. When the impurities have molecular structures similar to the crystal and can change the functional group present on the crystal surface by replacing the crystal molecules, the crystal growth on a specific crystal face can be inhibited. However, the kinetic mechanism of the effect of impurities on crystal growth has not been well studied.

Most amino acids are produced by fermentation, and crude solutions contain diverse impurities, such as microbial enzymes, media components, and microbial metabolites, as well as the desired amino acid. The desired amino acid is commonly isolated by crystallization, and the impurities that have molecular structures similar to the desired amino acid affect crystallization behavior because of their strong interactions. Therefore, the effect of such impurities must be understood to control the crystallization process and crystal habit. Addadi et al. [4] and Sano et al. [5] examined the effect of tailor-made additives on the crystal habit of amino acids. They demonstrated that other amino acids acted as tailor-made additives and changed the crystal habit of the crystallized amino acids. Thus, other amino acids are useful for designing the crystal habit of substrate amino acids. For this purpose, it is important to discuss the kinetic mechanism, which involves relationships among various factors, such as the crystal growth behavior of the specific crystal face, the additives, their concentration, and the degree of supersaturation. However, although some studies of the kinetic mechanism of the effect of additives have been reported [6–8], no versatile model has been proposed to date.

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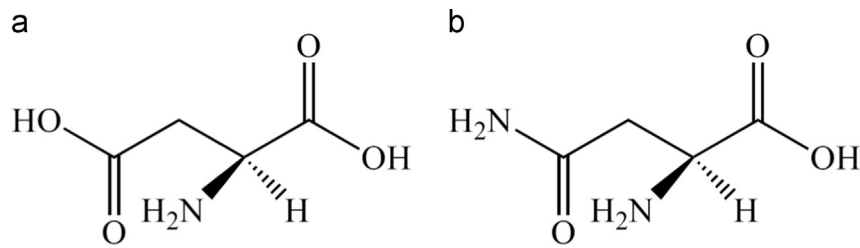


Fig. 1. Molecular structures. (a) L-Asp and (b) L-Asn.

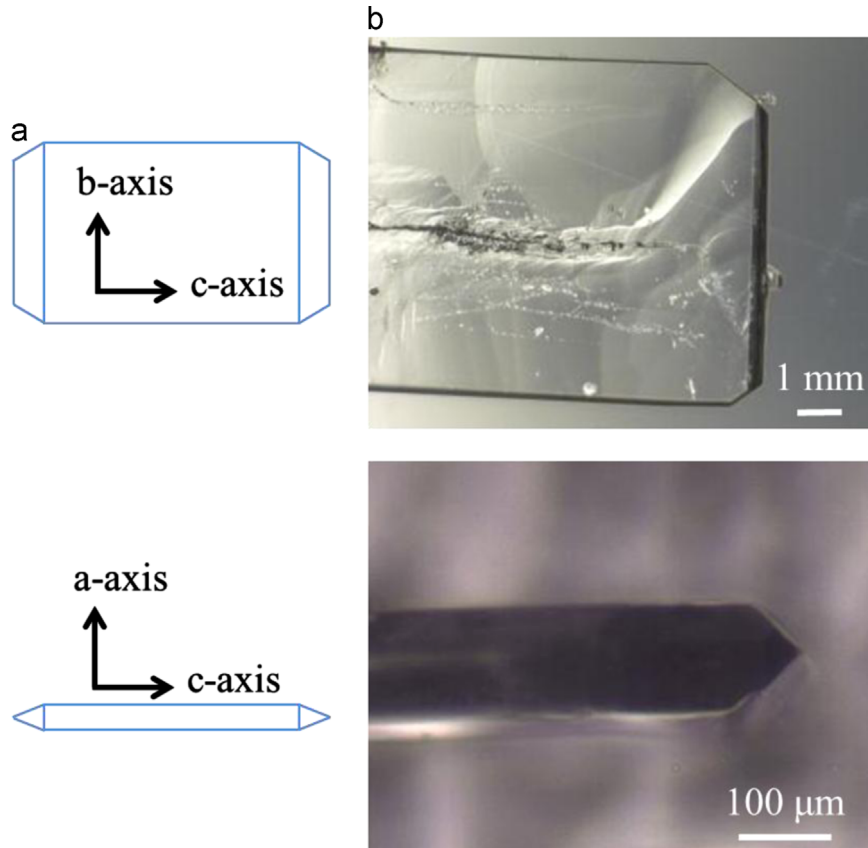


Fig. 2. Crystal of L-Asp. (a) Axis directions and (b) optical micrographs.

In this article, we examined the crystal growth behavior of L-aspartic acid (L-Asp) in the presence of L-asparagine (L-Asn) as a tailor-made additive. L-Asn has a molecular structure similar to L-Asp (Fig. 1) and can adsorb onto L-Asp through the amino acid group. We examined the kinetic mechanism of L-Asn action on L-Asp crystal growth, namely the face-selective effect of L-Asn on L-Asp crystal growth rate, for controlling the crystal habit.

2. Materials and methods

2.1. Theories of crystal growth rate in the presence of additives

Kubota and Mullin [9] proposed the crystal face growth rate (G) in the presence of additives as presented in Eq. (1),

$$\frac{G}{G_0} = 1 - \alpha\theta_{eq} \quad (1)$$

where G_0 is the crystal face growth rate in the absence of additives, α is the effectiveness factor of the additives, θ_{eq} is the equilibrium value of the coverage factor of the adsorption activity point on the crystal surface occupied by additives. According to Eq. (1), when

$\alpha > 1$, the crystal growth rate decreases sufficiently even if the amount of adsorbed additives is small. In contrast, when $\alpha < 1$, the crystal growth rate decreases but does not stop, even if the amount of adsorbed additives is at a maximum ($\theta_{eq} = 1$). Eq. (1) applies only when $\alpha\theta_{eq} \leq 1$. When $\alpha\theta_{eq} > 1$, $G/G_0 = 0$ constantly, irrespective of the value of $\alpha\theta_{eq}$.

Moreover, α is determined by Eq. (2)

$$\alpha = \frac{\gamma a}{kT\sigma L} \quad (2)$$

Here, γ is the edge energy, a is the surface area of the growth unit, k is the Boltzmann constant, T is the growth temperature, σ is the degree of relative supersaturation, and L is the distance of adsorption activity points. Thus, α is determined by the crystal properties (γ and a), the environment of the crystal growth (T and σ), and the interaction between crystals and additives (L). In addition, θ_{eq} is related to the concentration of additives (c) by Langmuir equation of adsorption isotherm presented in Eq. (3)

$$\theta_{eq} = \frac{Kc}{1 + Kc} \quad (3)$$

where K is Langmuir constant. Thus, Eq. (1) can be rewritten as

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