# Polymorphic Phase Transformation in the 3-Bromo-*trans*-cinnamic Acid System

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**3-Bromo-*trans*-cinnamic acid (3-BrCA) exists as two crystalline polymorphic forms (designated as β and γ phases). A polymorphic phase transformation from the γ phase to the β phase has been investigated using *ex situ* powder X-ray diffraction, *in situ* high-temperature optical microscopy, and differential scanning calorimetry. The transformation occurs at an observable rate at temperatures above about 100°C. A reverse transformation on subsequently cooling the β phase is not observed. Thermodynamic aspects of the polymorphic 3-BrCA system are discussed, together with kinetic aspects of the transformation from the γ phase to the β phase. The structural properties of the β phase (reported previously) and the γ phase (determined in this work from single-crystal X-ray diffraction data) are in accord with the α/β/γ structural classification of *trans*-cinnamic acid derivatives.** © 2001 Academic Press

## 1. INTRODUCTION

A polymorphic system comprises a set of crystalline materials with the same chemical composition but different crystal structures. Thus, in the case of molecular solids, polymorphism arises when a given type of molecule can form different crystal structures. The phenomenon of polymorphism (1–3) is of considerable interest in the field of organic solid state chemistry, in part because comparison of the properties of different polymorphs provides an ideal basis for understanding relationships between solid state properties and crystal structure.

By applying Gibbs' Phase Rule (4) in the case of a set of polymorphs (5), it follows that, under arbitrary conditions of temperature and pressure, only one polymorph can be thermodynamically stable and the other polymorphs must be metastable. Although there is a thermodynamic driving force for the metastable polymorphs to transform to the thermodynamically stable polymorph, such polymorphic phase transformations require that a suitable pathway for

structural reorganization is accessible to the system. If such pathways are not accessible (for example, if the temperature is not sufficiently high), the metastable polymorphs may be able to exist indefinitely (i.e., kinetic stability). Clearly, studies of phase transformations between polymorphs provide a basis for understanding the thermodynamic properties of polymorphic systems and allow an assessment of the structural and kinetic factors that govern structural interconversions between the different polymorphs.

Many examples of polymorphism in molecular crystals are known, and one widely studied family comprises derivatives of *trans*-cinnamic acid (6–8). To our knowledge, phase transformations between polymorphs of *trans*-cinnamic acid derivatives have not been reported previously. Here we focus on 3-bromo-*trans*-cinnamic acid (BrC$_6$H$_4$CH=CH CO$_2$H, abbreviated 3-BrCA; Scheme 1), which is known to exist in two polymorphic forms designated as the β and γ phases (the nomenclature is explained in Section 3.2). These polymorphs are obtained by crystal growth from different solvents. In this paper, we investigate phase transformations between the polymorphs of 3-BrCA using powder X-ray diffraction, optical microscopy, and differential scanning calorimetry. With regard to structural properties, the lattice parameters and space groups of both polymorphs have been reported previously (6, 9) and the crystal structure of the β phase has been determined previously (9). However, the crystal structure of the γ phase has not been determined previously, and is reported in this paper.

As discussed in Section 3.2, the photochemical properties of different polymorphs of *trans*-cinnamic acid derivatives in the solid state have been investigated in detail, and have led to the elucidation of clear correlations between structural properties and photochemical properties.

## 2. EXPERIMENTAL

The γ phase of 3-BrCA was prepared by slow evaporation of solvent from a solution of 3-BrCA (Aldrich; *trans*

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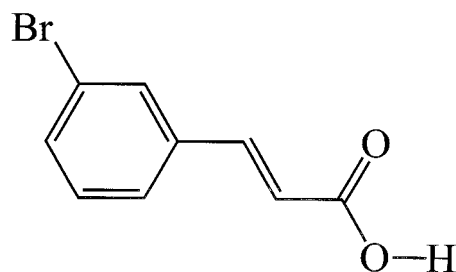
**SCHEME 1**

predominant) in ethanol at ambient temperature over a period of 4 days. The crystals were prismatic in shape and pale yellow in color. The $\beta$ phase of 3-BrCA was prepared by slow evaporation of solvent from a solution of 3-BrCA in acetic acid at ambient temperature over a period of 10 days. The crystals were needle shaped and colorless. In both cases, monophasic samples were obtained, as characterized by powder X-ray diffraction (Fig. 1).

Powder X-ray diffraction data were recorded at ambient temperature on a Siemens D5000 diffractometer (operating in transmission mode using Ge-monochromated $CuK\alpha_1$ radiation). High-temperature optical microscopy was carried out using an Olympus BX40 microscope, fitted with a Linkam LTS 350 hot-stage and crossed polarizers. Differential scanning calorimetry (DSC) was performed using a Perkin–Elmer Pyris 1 differential scanning calorimeter (calibrated for temperature and enthalpy using indium as a reference material). For the DSC experiments, the samples were placed in crimped aluminum crucibles (sample mass 2–7 mg) and subjected to cycles of heating and cooling under a flow of dry nitrogen purge gas (flow rate 20 ml min$^{-1}$). The DSC experiments were carried out for a variety of different heating/cooling rates in the range 2 to 30 K min$^{-1}$.

Single-crystal X-ray diffraction data were measured for the $\gamma$ phase of 3-BrCA at ambient temperature (293 K) using graphite-monochromated $MoK\alpha$ radiation ($\lambda = 0.71073$ Å) on a Rigaku R-Axis II rotating anode/image plate diffractometer. The data collection comprised 40 frames, each recorded over an oscillation range of 4.5°, with crystal-to-detector distance 80 mm. Selected crystal data are as follows: crystal size $0.15 \times 0.2 \times 0.1$ mm$^3$; monoclinic, $P2_1/a$; $a = 12.389(2)$ Å, $b = 4.9330(5)$ Å, $c = 14.411(2)$ Å, $\beta = 95.426(5)°$; $V = 876.8(2)$ Å$^3$; $Z = 4$; $R = 0.0529$, $R_w = 0.1267$. The structure was solved by direct methods using the SIR92 program (10) and refined by full-matrix least-squares refinement and difference Fourier techniques using the SHELXL program (11). The positions of all atoms (including hydrogen) were refined freely. Isotropic displacement parameters were refined for hydrogen atoms and anisotropic displacement parameters were refined for nonhydrogen atoms. All
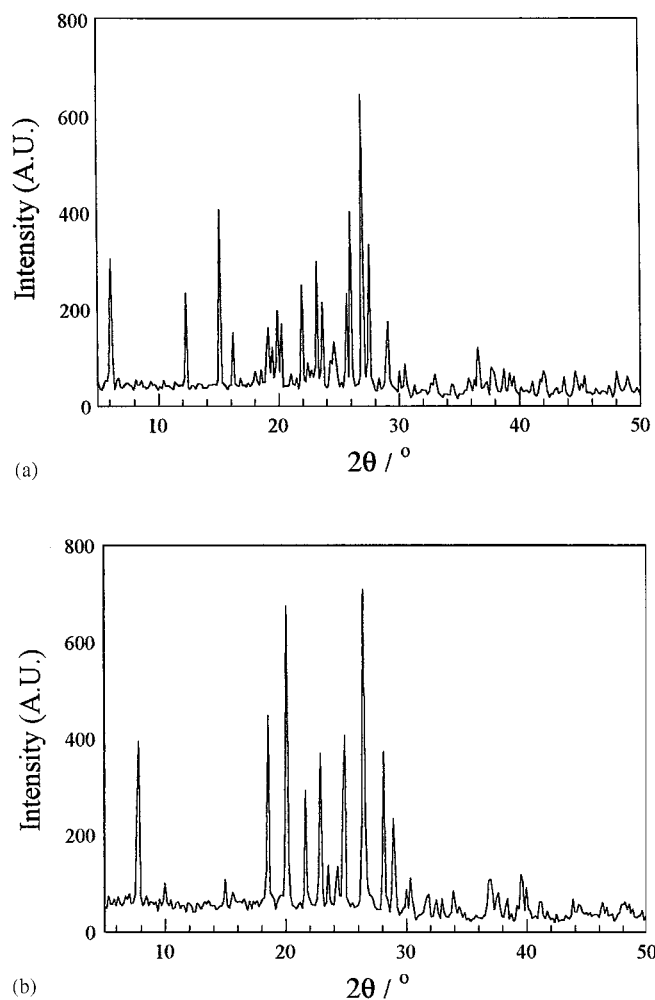


**FIG. 1.** Powder X-ray diffraction patterns ($CuK\alpha_1$ radiation) for (a) the $\gamma$ phase of 3-BrCA and (b) the $\beta$ phase of 3-BrCA.

calculations were carried out using the TEXSAN crystallographic software package (12).

## 3. RESULTS AND DISCUSSION

### 3.1. Polymorphic Phase Transformation

The possible occurrence of phase transformations between the polymorphs of 3-BrCA was investigated *ex situ* by heating samples of each polymorph to high temperature (100, 110, 115, 125, and 150°C) in a furnace and examining the products, after quenching to ambient temperature, by powder X-ray diffraction (Fig. 2). Single crystals and ground powders were studied separately (it has been observed for other materials (13) that single crystals and ground powders can behave differently with respect to solid state phase transformations). As shown in Fig. 2, these experiments provide clear evidence (both for single-crystal samples and ground powder samples) that the $\gamma$ phase transforms to the
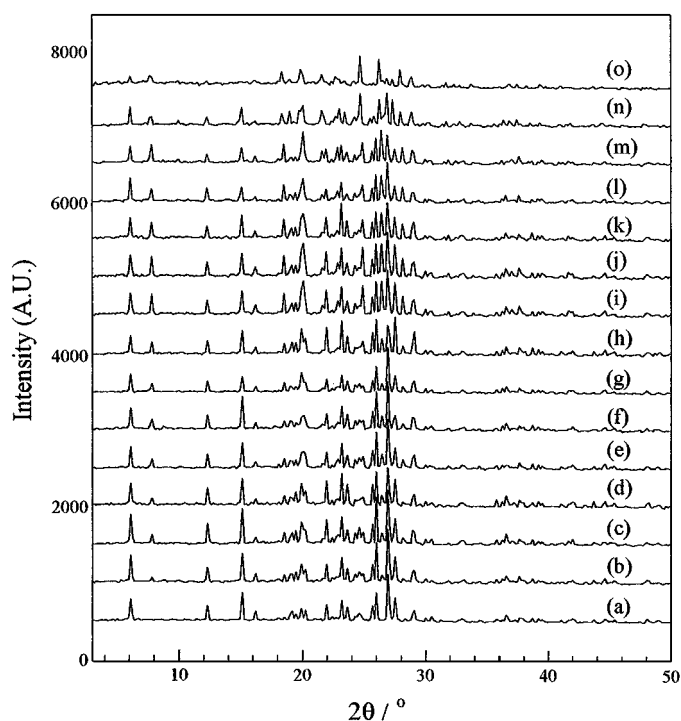
**FIG. 2.** Powder X-ray diffraction patterns (CuKα₁ radiation) recorded at ambient temperature for the γ phase of 3-BrCA: (a) before heating, and after heating *ex situ* at 110°C for the following periods of time (b) 1 h, (c) 2 h, (d) 6 h, (e) 8 h, (f) 22 h, (g) 32 h, (h) 46 h, (i) 56 h, (j) 70 h, (k) 80 h, (l) 120 h, (m) 192 h, (n) 264 h, and (o) 14 days.

Polarizing optical micrographs were recorded on heating a single crystal of the γ phase of 3-BrCA at 10 K min⁻¹. Over the range 131–136°C, the sample changed from a transparent single crystal to an opaque polycrystalline material, presumably as a consequence of the γ phase → β phase transformation. A similar change was observed at about 134°C for a single crystal of the γ phase heated at 2 K min⁻¹. The samples were observed to melt at 171°C.

Representative DSC data for the β and γ phases of 3-BrCA are shown in Fig. 3. For the γ phase, an endotherm is observed at 126°C (onset temperature) followed by a melting endotherm at 170°C. In contrast, the β phase shows only a melting endotherm at 170°C. The endotherm observed at 126°C for the γ phase may be ascribed to the polymorphic transformation. The enthalpy change associated with the transformation at 126°C is 11.5 J g⁻¹, and the enthalpy change associated with the melting transition is 136.8 J g⁻¹.

As DSC results can be sensitive to the experimental conditions (14–17), further experiments were carried out at different heating rates. For different heating rates, the temperature of the endotherm assigned as the γ phase → β phase transformation shifts slightly within the range 122–126°C, but the temperature of the melting endotherm is not significantly affected. There are no significant differences between the DSC results for single crystal and powder samples.

On cooling the samples after melting, a sharp exotherm due to recrystallization is observed around 148–152°C (the actual temperature depends on the cooling rate). No other endotherms or exotherms are observed on cooling. When the sample is reheated after returning to ambient temperature, a single melting endotherm is observed at 170°C with no evidence for an endotherm in the region of 122–126°C. These observations suggest that recrystallization of the melt gives the β phase, which does not undergo a transformation to the γ phase on further cooling.

In summary, our DSC results support the view that the β phase of 3-BrCA is thermodynamically stable with respect to the γ phase over the temperature range investigated. At ambient temperature, the γ phase can exist as a metastable phase (kinetic stability) but at high temperature the rate of transformation to the β phase is sufficiently rapid (with respect to the timescales of the techniques used) to allow the transformation to be observed.

β phase at temperatures higher than 100°C (note that at 100°C, no amount of the β phase is evident after 72 h). At 110°C, the time required for essentially complete transformation from the γ phase to the β phase is about 14 days, with only residual amounts of the γ phase evident from powder X-ray diffraction after this period of time. At 125°C and higher temperatures, the transformation is essentially complete within the first powder X-ray diffraction measurement. After formation of the β phase, no further changes are observed with time. Our *ex situ* powder X-ray diffraction results show no evidence for the presence of any intermediate crystalline phases at any stage during the transformation. Furthermore, while caution must be observed in reaching conclusions on kinetic aspects of the transformation from *ex situ* investigations, we nevertheless note that the rate of loss of the γ phase and the rate of production of the β phase are comparable, which is again consistent with the transformation occurring in a single step with no intermediate phases involved.

On heating samples of the β phase under the same conditions as those described above for the γ phase, no detectable changes are observed, and the powder X-ray diffraction pattern remains characteristic of a monophasic sample of the β phase.

### 3.2. Structural Properties

Although the lattice parameters and space group of the γ phase of 3-BrCA were reported previously (6), the crystal structure was not actually determined. In the present work, the crystal structure of the γ phase of 3-BrCA has been determined from single-crystal X-ray diffraction data recorded at ambient temperature. The crystal structure of the β phase of 3-BrCA has been determined previously (9).
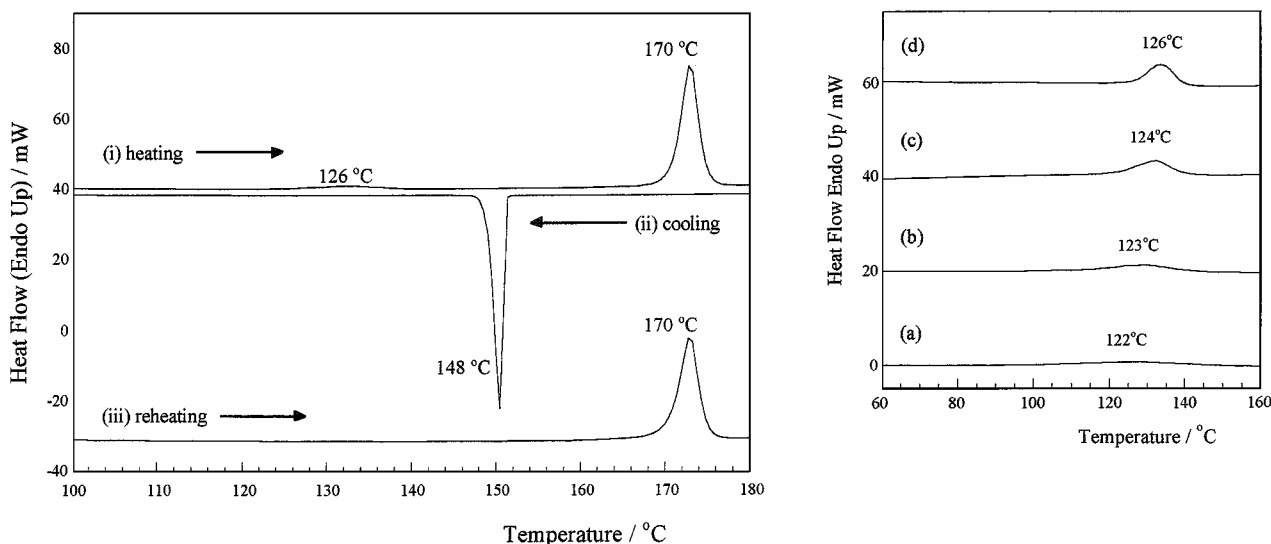
**FIG. 3.** DSC data for the $\gamma$ phase of 3-BrCA recorded for heating/cooling rates of 30 K min$^{-1}$. The melting temperature of the $\beta$ phase of 3-BrCA is approx. 170°C. The inset (right-hand side) shows an expanded plot in the region of the endotherm ascribed to the transition from the $\gamma$ phase to the $\beta$ phase, recorded for different heating rates: (a) 5 K min$^{-1}$, (b) 10 K min$^{-1}$, (c) 20 K min$^{-1}$, and (d) 30 K min$^{-1}$. The dependence of the endotherm in the region of 122–126°C on the heating rate is noteworthy.

Relevant crystal data for the $\beta$ and $\gamma$ phases are compared in Table 1 and fractional coordinates in the final refined crystal structure of the $\gamma$ phase are given in Table 2.

For both the $\beta$ and $\gamma$ phases, the molecules of 3-BrCA are planar and the molecular geometry is the same within experimental errors in both structures. As shown in Fig. 4, both polymorphs contain centrosymmetric dimers of 3-BrCA molecules linked by the common hydrogen-bonded carboxylic acid dimer motif [O(1) $\cdots$ O(2) distance: 2.61 Å ($\gamma$ phase), 2.63 Å ($\beta$ phase)]. In both polymorphs, the 3-BrCA molecules form stacks parallel to the $b$ axis (the shortest unit cell axis). The angle between this stacking axis and the normal to the molecular planes is smaller for the $\beta$ phase, giving a larger interfacial contact area of the $\pi$ systems of

adjacent molecules along the stacks in the $\beta$ phase. The distance between the centers of the C=C bonds of adjacent molecules along the stacks is 3.99 Å for the $\beta$ phase and 4.93 Å for the $\gamma$ phase.

**TABLE 2**

**Fractional Atomic Coordinates and Equivalent Isotropic Displacement Parameters for the $\gamma$ phase of 3-BrCA at Ambient Temperature**

|  | $x$ | $y$ | $z$ | $U_{eq}$ (Å$^2$) |
|---|---|---|---|---|
| Br(1) | 0.3875(1) | 0.1767(1) | 0.5401(1) | 0.070(1) |
| O(1) | 0.5099(3) | 1.2665(7) | 0.9124(2) | 0.053(1) |
| O(2) | 0.3788(3) | 1.3382(7) | 1.0045(2) | 0.054(1) |
| C(1) | 0.3251(4) | 0.6456(9) | 0.7669(3) | 0.043(1) |
| C(2) | 0.3731(4) | 0.5320(10) | 0.6926(3) | 0.047(1) |
| C(3) | 0.3196(4) | 0.3307(10) | 0.6400(3) | 0.049(1) |
| C(4) | 0.2183(4) | 0.2430(11) | 0.6576(3) | 0.054(1) |
| C(5) | 0.1698(4) | 0.3537(11) | 0.7319(4) | 0.054(1) |
| C(6) | 0.2238(4) | 0.5529(11) | 0.7866(3) | 0.051(1) |
| C(7) | 0.3840(4) | 0.8596(9) | 0.8210(3) | 0.045(1) |
| C(8) | 0.3523(3) | 0.9937(9) | 0.8930(3) | 0.044(1) |
| C(9) | 0.4172(4) | 1.2139(9) | 0.9393(3) | 0.043(1) |
| H(1) | 0.444(4) | 0.592(11) | 0.678(4) | 0.05(1) |
| H(2) | 0.185(4) | 0.100(12) | 0.624(4) | 0.05(1) |
| H(3) | 0.096(5) | 0.272(12) | 0.744(4) | 0.06(2) |
| H(4) | 0.186(5) | 0.622(12) | 0.834(4) | 0.06(2) |
| H(5) | 0.454(5) | 0.906(13) | 0.802(4) | 0.06(2) |
| H(6) | 0.289(5) | 0.954(13) | 0.920(4) | 0.06(2) |
| H(7) | 0.422(7) | 1.491(23) | 1.039(6) | 0.13(3) |

*Note.* $U_{eq}$ is defined as one-third of the trace of the orthogonalized $U_{ij}$ tensor. Estimated standard deviations are given in parentheses.

**TABLE 1**

**Comparison of Crystal Data for the $\beta$ phase of 3-BrCA (from Ref. (9)) and the $\gamma$ Phase of 3-BrCA (determined here)**

|  | $\beta$ phase | $\gamma$ phase |
|---|---|---|
| Crystal system | Monoclinic | Monoclinic |
| Lattice parameters | $a = 19.191(6)$ Å | $a = 12.389(2)$ Å |
|  | $b = 3.9879(2)$ Å | $b = 4.9330(5)$ Å |
|  | $c = 24.798(7)$ Å | $c = 14.411(2)$ Å |
|  | $\beta = 113.05(2)°$ | $\beta = 95.426(5)°$ |
| Space group | $C2/c$ | $P2_1/a$ |
| Unit cell volume | 1746.3(8) Å$^3$ | 876.8(2) Å$^3$ |
| Z | 8 | 4 |
| Calculated density | 1.728 g cm$^{-3}$ | 1.720 g cm$^{-3}$ |

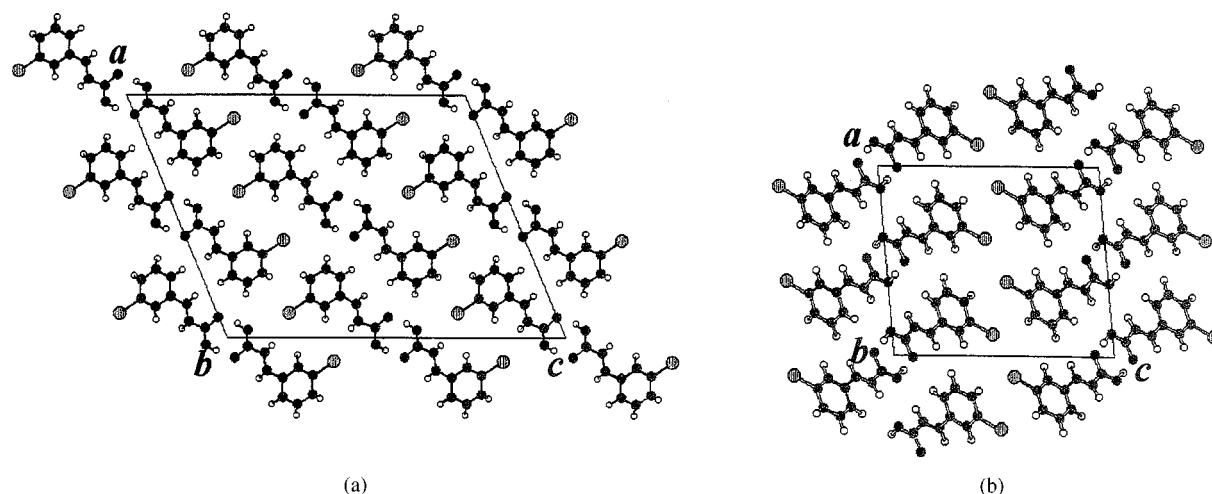*Note.* Estimated standard deviations are given in parentheses.

(a)

(b)

**FIG. 4.** Crystal structures of (a) the β phase of 3-BrCA (data from Ref. (9)) and (b) the γ phase of 3-BrCA (structure determined in this paper).

Previously, the crystal structures of derivatives of *trans*-cinnamic acid have been shown to fall into three different classes, denoted α, β, and γ-type crystals (6–8). Many of these compounds can adopt two (or all three) of the different structure types, thus representing examples of polymorphism. The structural properties of the β and γ phases of 3-BrCA discussed above are in accord with the structural properties of other β- and γ-type *trans*-cinnamic acids. It is well established that each structure type behaves in a characteristic manner on exposure to ultraviolet radiation (7, 18, 19). Thus, α- and β-type crystals undergo [2 + 2] photodimerization reactions, but lead to different reaction products, whereas γ-type crystals are photostable. Indeed, these reactions in crystals of *trans*-cinnamic acids are prototypical examples of solid state reactions that conform to the topochemical principle (8, 20–26). On this basis, for the β phase of 3-BrCA, the distance between the C=C bonds of adjacent molecules and their relative orientations are appropriate for a topochemical [2 + 2] photodimerization reaction (27). For the γ phase, the distance between adjacent C=C bonds is longer than that normally found for photoreactive *trans*-cinnamic acid crystals, and a photodimerization reaction is not expected to occur in this case. Our studies (28) of the photoreactivities of the β and γ phases of 3-BrCA upon ultraviolet irradiation confirm that the β phase produces 3,3'-dibromo-β-truxinic acid and that the γ phase is photostable, in line with the behavior of other β- and γ-type *trans*-cinnamic acids.

## 4. CONCLUDING REMARKS

As discussed above, 3-BrCA exists in two polymorphic forms, denoted as β and γ phases, which may be prepared as monophasic samples by different crystallization procedures. Both phases can coexist indefinitely at ambient temperature and pressure. Our results from *in situ* optical microscopy, differential scanning calorimetry, and *ex situ* powder X-ray diffraction suggest that the γ phase transforms to the β phase at sufficiently high temperature and that the β phase is thermodynamically stable with respect to the γ phase throughout the temperature range from ambient temperature to the melting temperature. Thus, the γ phase is metastable with respect to the β phase and can presumably exist at ambient temperature and pressure as a consequence of kinetic stability. The density (calculated from the crystal structures) at ambient temperature is slightly higher for the β phase ($1.728 \, \text{g cm}^{-3}$) than for the γ phase ($1.720 \, \text{g cm}^{-3}$), consistent with the general tendency for the stable phase among a set of polymorphs to have the highest density (29–31). However, more detailed computational studies are required to provide a more rigorous justification of this assignment.

Our results point toward the importance of kinetic aspects of the transformation from the γ phase to the β phase, and indicate that the reverse transformation (β phase to γ phase) does not occur on subsequent cooling to ambient temperature. Thus, the apparent "transition temperature" (approx. 122–126°C) defined by the endotherm in the DSC data for the γ phase reflects the temperature at which the rate of transformation is appropriate, with respect to the timescale of the DSC measurement and the heating rate used, to give a detectable response in the DSC thermogram. The transformation may also occur at lower temperatures (as observed in our *ex situ* powder X-ray diffraction studies) at a substantially lower rate. The irreversibility of the transformation is consistent with our assignment of the γ phase as metastable with respect to the β phase throughout the temperature range investigated.

It is interesting to note that our preliminary studies of 3-chloro-*trans*-cinnamic acid (which also exhibits polymorphism as $\beta$ and $\gamma$ phases) suggest that there is no corresponding transformation from the $\gamma$ phase to the $\beta$ phase at high temperature, despite the strong structural similarities between the $\beta$ and $\gamma$ phases of 3-chloro-*trans*-cinnamic acid and the $\beta$ and $\gamma$ phases of 3-BrCA. Further research is required to understand the contrasting behavior of these systems.

## ACKNOWLEDGMENTS

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