Multifarious Polymorphism of a Multiblock Amphiphilic Macrocycle Bearing Thermally Responsive Polyether Segment

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Supporting Information

ABSTRACT: Formation of multiple crystalline phases of a multiblock amphiphilic macrocycle AT2B is demonstrated. AT2B forms a single crystal (Cr-α) by vapor diffusion and shows reversible single-crystal-to-single-crystal transition between two crystalline phases (Cr-α and Cr-β) by a temperature change, and crystalline AT2B (Cr-β) melts at 422 K, and the cooling rate from the melt influences the phase of the solid formed. By cooling at 1.0 K min⁻¹, AT2B forms crystalline phases (Cr-γ and Cr-δ), which are different from both Cr-α and Cr-β. On the other hand, cooling at 2.0 K min⁻¹ results in the formation of an amorphous phase, and a mechanical stress also triggers a crystal-to-amorphous solid transition. Interestingly, the amorphous solid crystallizes to give the fifth crystalline phase (Cr-γ) upon heating before melting. It is suggested that these multiple phase transitions are driven by thermal conformational changes at the tetraethylene glycol chains of AT2B.

INTRODUCTION

Polymorphism is a ubiquitous phenomenon among crystals of organic, inorganic, and organometallic molecules and polymers. Control of the polymorphs is an important subject for pharmaceutical and materials chemistry because polymorphs influence physical and chemical properties of the crystal. For example, chloramphenicol palmitate is known to form two types of polymorphs, where the bioavailability of each polymorph is different from one another. The luminescent property of organic dyes is also dependent on polymorphs. As for the control of polymorphs, many physical and chemical factors including solvent, temperature, additives, and mechanical forces can influence the crystallization process so as to afford different polymorphs. Meanwhile, some molecular crystals exhibit a polymorphic transition by external stimuli, which are applicable for developing dynamic and switchable materials.

In recent years, thermosalient crystals, which undergo physical motions triggered by thermal phase transition between the polymorphs, are also drawing increasing attention. In this research area, we recently reported a single-crystal-to-single-crystal thermal polymorphic transition of a multiblock amphiphilic macrocycle AT2B (Figure 1), which is accompanied by a macroscopic bending motion of the needlelike crystal without breakdown of single crystallinity. X-ray crystallographic analyses indicated that the temperature elevation and reduction induces conformational changes at the tetraethylene glycol (TEG) chains of AT2B, which leads to alteration of the molecular alignment to trigger the phase transition. The single crystal has elasticity to allow for the macroscopic bending motion without collapsing, which is likely due to rather weak intermolecular interactions without the presence of directional hydrogen-bonding or ionic groups as well as the flexible conformation of AT2B in the solid state.

Here, as one of the unique features of AT2B in the solid state, we report that this compound affords totally five polymorphic phases. Among them, four of those were formed by careful control of the heating and cooling processes including thermal phase transitions. In addition, these thermal phase transitions are likely caused by thermal conformational changes of the TEG chains of AT2B. In addition to these multiple crystalline phases, an amorphous phase also appeared.
by rapid cooling from the molten state or applying a mechanical stress to the crystalline phase.

### RESULTS AND DISCUSSION

As reported in our previous paper,\(^{11}\) upon crystallization under a liquid−liquid diffusion condition between tetrahydrofuran (THF) and \(n\)-hexane at 298 K, \(\text{AT2B}\) afforded a single crystal, whose phase is denoted as \(\text{Cr-}\alpha\). A thermal phase transition occurs at 333 K (Figure 2a, black solid line; \(T_m = 422\) K, \(\Delta H = 2.4\) kJ mol\(^{-1}\), endothermic) upon heating \(\text{Cr-}\alpha\) to form \(\text{Cr-}\beta\). This phase transition is reversible if the crystal is kept under its melting point, where \(\text{Cr-}\beta\) returns to \(\text{Cr-}\alpha\) at 329 K (\(\Delta H = -3.1\) kJ mol\(^{-1}\), exothermic) in the cooling process.

Meanwhile, cooling the melt of \(\text{AT2B}\) at the rate of 1.0 K min\(^{-1}\) shows an exothermic transition at 353 K (Figure 2a, blue solid line; \(\Delta H = -34.0\) kJ mol\(^{-1}\)) in differential scanning calorimetry (DSC) analysis, which is assigned to be the freezing point.\(^{11}\) Below the freezing point, a broad exothermic transition peak was observed at 314 K (\(\Delta H = -3.2\) kJ mol\(^{-1}\)). In the subsequent heating process, an endothermic transition was observed at 328 K (Figure 2a, red solid line; \(\Delta H = 2.7\) kJ mol\(^{-1}\)), and these transitions were reversibly observed in the temperature range between 270 and 360 K (Figure 2, broken lines). Small-angle and wide-angle X-ray scattering (SAXS and WAXS) measurements of \(\text{AT2B}\) at 330 and 300 K in the cooling process from 433 K displayed sharp signals with different patterns from each other (Figure 3a,b). Both of these

![Figure 2](image.png)

**Figure 2.** (a) Solid lines: DSC profiles of \(\text{AT2B}\) in the single crystalline state in the heating process from 270 to 440 K (black line, ref 11) and in the subsequent cooling (blue line) and heating processes (red line). Broken lines: DSC profiles of \(\text{AT2B}\) after cooling from 440 K in the heating (red line) and cooling processes (blue line) between 270 and 360 K. Five times enlarged profiles are shown in the dashed-line square. Scan rate: 1.0 K min\(^{-1}\). (b) DSC profiles of \(\text{AT2B}\) in the cooling process (blue) from 440 K followed by the heating process (red). Scan rate: 2.0 K min\(^{-1}\).

X-ray scattering profiles are also different from those of \(\text{Cr-}\alpha\) or \(\text{Cr-}\beta\), suggesting the emergence of new polymorphs, \(\text{Cr-}\gamma\) (\(T < 314\) K) and \(\text{Cr-}\delta\) (\(T = 314−353\) K), in the cooling process. The phase transition between \(\text{Cr-}\gamma\) (\(T < 328\) K) and \(\text{Cr-}\delta\) (\(T = 328−420\) K) is reversible, where the transition in the heating process is endothermic. Polarized optical microscopy (POM) exhibited a streaky pattern at 330 K in the cooling process from the melt (Figure 4a) and further cooling to 300 K caused cracking (Figure 4b).

By sharp contrast, when the cooling rate from the melt was increased to 2.0 K min\(^{-1}\), no clear transition was observed in the DSC measurement (Figure 2b, blue line) until 250 K. X-ray scattering measurements displayed only a halo without any clear signals at 323 K in the cooling process from the melt at 2.0 K min\(^{-1}\) followed by heating to 373 K.

![Figure 3](image.png)

**Figure 3.** (Left) SAXS and (right) WAXS profiles of \(\text{AT2B}\) at (a) 330 and (b) 300 K in the cooling process from 430 K (melt) at 1.0 K min\(^{-1}\) and (c) 323 K in the cooling process from the melt at 2.0 K min\(^{-1}\) followed by heating to (d) 373 K.
likely a glassy solid, without crystallization. The glassy solid showed an exothermic transition at 368 K ($\Delta H = -38.2$ kJ mol$^{-1}$) below $T_m$ upon temperature elevation (Figure 2b, red line). POM exhibited a radially oriented pattern at 373 K (Figure 4d), where X-ray scattering showed sharp signals with different profiles from those of Cr-$\alpha$, Cr-$\beta$, Cr-$\gamma$, or Cr-$\delta$ (Figure 3d), thereby suggesting an emergence of a new crystalline phase (Cr-$\epsilon$) by crystallization from the glassy state. As suggested by X-ray scattering measurements (Figure S1 in the Supporting Information), the crystalline phase of AT2B also changes to amorphous by a mechanical stress such as grinding in a mortar, which would cause defects and increase disorder in crystals.

It is known that rapid cooling of a polymer in a mobile state provides its amorphous or glass state because of the kinetic factors such as entanglement and restricted motions of macromolecular chains inhibiting the ordered alignment of the molecules. Once the frozen macromolecular chains in the glass state acquire the thermal energy for mobility, they organize into crystals as an exothermic process. The characteristic “polymer-like” phase transition of AT2B observed in the rapid cooling and subsequent heating processes is likely due to the restricted yet variable conformation of the TEG chains in the macromolecular structure.

In the thermal phase transition between Cr-$\alpha$ and Cr-$\beta$, the TEG chains of AT2B change the conformations. The conformational changes at the C–C and C–O bonds in poly(ethylene glycol) can be visualized by Fourier transform infrared (FT-IR) spectroscopy. Figure 5 shows FT-IR spectra of AT2B in Cr-$\gamma$, Cr-$\delta$, Cr-$\epsilon$, and glassy solid phases, where the vibrational absorption bands corresponding to CH$_2$ twist of gauche C–C and trans C–O (1250 cm$^{-1}$), CH$_2$ twist of trans C–O (1282 cm$^{-1}$), CH$_2$ twist of gauche C–O (1300 cm$^{-1}$ shoulder), and CH$_3$ wag of gauche C–C (1350 cm$^{-1}$) are displayed in all cases. In the case of the phase transition between Cr-$\gamma$ and Cr-$\delta$, these vibrational bands showed changes in the intensities, indicating that the conformation around the C–C and C–O single bonds in the TEG chains changes into those with different rotational C–C and C–O angles. Likewise, FT-IR spectra of AT2B in Cr-$\epsilon$ and glassy solid phases showed the changes at these bands during the phase transition. In this case, the spectra showed a larger change than the case of Cr-$\gamma$/Cr-$\delta$ transition, suggesting larger conformational changes at the TEG chains upon crystallization from the glassy solid. Thus, FT-IR spectroscopic studies suggest that the conformational changes of the TEG chains occur during these polymorphic transitions. In other words, the conformational thermo-responsiveness at the TEG chains likely contributes to the diversity of polymorphs and prompts the polymorphic thermal phase transitions. The UV–vis absorption spectroscopic measurements of AT2B also showed differences in the spectral profiles between Cr-$\gamma$ and Cr-$\delta$ and Cr-$\epsilon$ and glassy solid phases. This suggests that the geometry of the packing of the aromatic units as well as their conformation is also different among these polymorphic phases (Figure 6).

The solid-state phases and their phase transition processes of AT2B are summarized in Table 1. Recrystallization by vapor diffusion from a THF and n-hexane mixture affords Cr-$\alpha$, which undergoes transition to Cr-$\beta$ at 333 K. This thermal phase transition is reversible, and the single crystal retains the crystallinity during the heating/cooling processes. Furthermore, heating above 422 K results in a phase transition to give a melt. Here, cooling rate from the melt influences the phase formed in the solid state. Namely, by cooling at 1.0 K min$^{-1}$, AT2B crystallizes into Cr-$\delta$, which changes into Cr-$\gamma$ upon further cooling. The thermal phase transition between Cr-$\delta$ and Cr-$\gamma$.
phases is reversible. Meanwhile, cooling at 2.0 K min$^{-1}$ results in the formation of the glassy solid phase. Upon heating, AT2B in the glassy solid phase crystallizes in the Cr-$\gamma$ phase at 368 K and melts at 416 K.

### CONCLUSIONS

Formation of multiple polymorphs of cyclic multiblock amphiphile AT2B was demonstrated. In addition to the already found two phases which could be formed by crystallization from solution followed by heating, four additional solid phases including a glassy solid phase were found. By controlling the cooling rate from the melt, AT2B affords different solid phases. Cooling with a slow rate (1.0 K min$^{-1}$) allows for the formation of crystalline phases (Cr-$\gamma$ and Cr-$\delta$), whereas cooling with a fast rate (2.0 K min$^{-1}$) results in the formation of a glassy solid phase. The glassy solid phase changes into Cr-$\gamma$ by heating before melting. Spectroscopic studies suggest that the conformational changes at the TEG chains in AT2B trigger the polymorphic transition. It is also suggested that the geometry and/or packing of the aromatic units of AT2B alters in the thermal phase transitions. Hence, the molecular design including oligo(ethylene glycol) chains in a macrocycle is an effective approach to develop thermoresponsive polymorphic crystalline materials, which exhibit characteristic phase-transition behaviors including amorphous solid or glassy solid and crystalline phases. This would be advantageous for fabrication of dynamic materials with switchable and memorizable functions.

### METHODS

AT2B was synthesized according to our previous paper.$^{11}$ SAXS and WAXS measurements were carried out using a Rigaku NANO-Viewer system equipped with a PILATUS detector (Cu K$\alpha$: 1.54 Å). The temperature of the material was controlled with a Mettler Toledo FP82 hot stage. FT-IR spectra were recorded on a JASCO FT/IR-4100 spectrometer equipped with JASCO ATR PRO 670H-S. DSC was performed with TA Instruments MDSC Q-100 equipped with a liquid N$_2$ cooling system. Optical microscopic observation was carried out with an Olympus BX51 optical polarizing microscope or KEYENCE VH-Z100UR with a Mettler Toledo FP82 HT hot stage and an AGC Techno Glass UV sharp cut filter Y-43. UV--vis absorption spectroscopic measurements were carried out with a JASCO V-670 spectrometer equipped with a TOYO Corporation HCS402-AP10 hot stage.

### ASSOCIATED CONTENT

$^*$ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.7b01737.

- X-ray diffraction pattern of AT2B after mechanical grinding (PDF)

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**Notes**

The authors declare no competing financial interest.

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