

Heat Capacity Signature Resembling the Glass Transition in Crystalline Solids: Challenging the Classical View of Melting

Marek Pyda,^{*,†} Anna Czerniecka-Kubicka, Peggy Cebe, and Marcin Skotnicki^{*}



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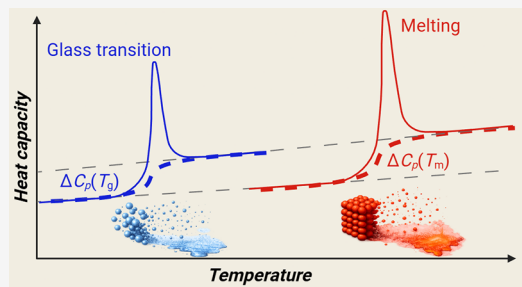


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ABSTRACT: Melting and glass transitions are classically viewed as distinct phenomena, the former in crystalline materials and the latter in amorphous systems. Here we show that fully crystalline, low-molecular-weight solids can display heat-capacity changes during melting that closely mimic those seen at the glass transition. Using temperature-modulated differential scanning calorimetry, we detect continuous, reversible steps in heat capacity in crystalline roxithromycin and glucose that mirror those of their amorphous counterparts. Similar behavior is observed during the crystallization of semicrystalline poly(3-hydroxybutyrate). These findings provide direct experimental evidence for a transition exhibiting a C_p signature similar in shape and magnitude to that observed at the glass transition, a transition-like thermodynamic signature in the melting of crystalline materials. This discovery expands the conceptual boundary of glass transitions and suggests that large-amplitude molecular motions underlie both melting and vitrification.



The occurrence of the glass transition during the solid-to-liquid transformation being a property of a crystal was initially proposed by Bridgman.¹ Similarities between the glass transition and melting were later captured within a unified conceptual framework by Stillinger, who introduced the potential energy landscape approach to describe phase transitions as movements between basins in configuration space.² Wunderlich provided evidence for the glass transition in macromolecules during the melting process, i.e., in polymeric semicrystals.^{3–5} While Wunderlich pioneered the study of glass transitions in semicrystalline polymers, such behavior has not been previously observed in fully crystalline low-molecular-weight compounds nor has a similar heat capacity change been observed upon melting and glass transition, implying a shared molecular mechanism, been demonstrated experimentally for the same small molecule, as reported herein. Although the glass transition has long been considered a hallmark of disordered, amorphous materials, our findings challenge this paradigm by demonstrating that fully crystalline low-molecular-weight compounds can exhibit thermodynamic features, such as a heat capacity jump under the melting peak, that closely resemble those observed at the glass transition. Related glass-like behavior has been observed in orientationally disordered crystals (glassy crystals), where partial freezing of molecular motions occurs despite long-range lattice order.^{6,7}

Expanding on these observations, Havránek and Marvan proposed a broader classification of glass transitions, encompassing polymers, inorganic glasses, plastic crystals, and relaxor ferroelectrics, where different types of degrees of freedom may undergo glass-like freezing, sometimes over-

lapping with phase transitions such as ferroelectric transitions.⁸ This diversity highlights that glass-like phenomena are not limited to amorphous phases but may arise from constrained molecular motions in various ordered systems.

Angell has emphasized that excess heat capacity changes observed in a variety of glass-forming systems—supercooled liquids or orientationally disordered crystals—reflect the progressive activation of configurational degrees of freedom as thermal energy allows previously constrained motions to become accessible.⁹ In particular, the activation of large-amplitude molecular motions, such as rotations or conformational rearrangements, plays a central role.¹⁰

Furthermore, recent theoretical work by Krzakala and Zdeborová demonstrated that bulk melting of an ordered phase following a first-order phase transition exhibits several dynamic features traditionally associated with glass-forming liquids, such as two-step relaxation, diverging relaxation times, growing correlation lengths, and dynamic heterogeneities.^{11,12} Although these predictions stem from statistical models, direct experimental evidence confirming such glass-like features during the melting of fully crystalline low-molecular weight system is unreported. Complementing these findings, Zaccone and Samwer recently proposed a thermodynamic framework

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unifying melting and glass-transition phenomena, demonstrating that both transition temperatures scale with the ratio of liquid fragility to thermal expansion. This relation, while macroscopic, suggests a common underlying sensitivity to cooperative molecular dynamics in both crystalline and amorphous materials.¹³

Solid materials can exist in several structural forms, i.e., crystalline, semicrystalline, amorphous solid (glass), and mesophase, which differ in the degree of molecular ordering and mobility.^{5,14,15} The phase type strongly affects the kinetic and mechanical properties. Besides structural order, molecular mobility plays a key role in defining phase behavior.^{3–5} Molecular motions are typically classified into small- and large-amplitude types. Small-amplitude motions are represented by vibrations, while large-amplitude motions include translation, rotation, internal rotations (conformational motions), and anharmonic motions (external motions). Transitions between phases often involve the progressive activation of large-amplitude motions, which underlie both glass-transition and melting behaviors. Advanced thermal analysis, such as temperature-modulated differential scanning calorimetry (TMDSC), provides insight into molecular dynamics by separating the in-phase and out-of-phase components of the modulated heat-flow response, which represent the real (storage) and imaginary (loss) parts of the complex heat capacity, with the latter capturing dissipative, time-dependent processes.^{16–18} Ultimately, the degree of order and molecular mobility determine the physicochemical properties critical for material design and processing.^{14,19–21}

Amorphous materials exhibit a glass transition characterized by the glass-transition temperature (T_g), an associated step in heat capacity (ΔC_p) at T_g , and the glass-transition transformation interval (ΔT) that reflects the kinetics of molecular relaxation.^{22–24} In contrast, during melting the C_p change occurs within a much narrower temperature range determined by melting kinetics.^{25,26} The C_p change during melting exhibits a step-like profile reminiscent of the glass transition, yet it arises from melting kinetics rather than structural relaxation. The origin of the changes in the heat capacity at T_g or during the solid-to-liquid transition on heating or on vitrification can be explained based on molecular motions.^{22,27–29}

The glass-transition parameters primarily depend on the chemical structure, molecular configuration, and dynamics of molecular motions within the material.^{18,22,30,31} The glass transition is a dynamic process characterized by an average relaxation time that reflects the time-dependent molecular rearrangements.^{22,32} Calorimetric experiments characterize this transition by determining the glass-transition temperature (T_g) and the change in heat capacity (ΔC_p), both of which depend on the applied cooling and heating rates as well as on the frequency of modulation during temperature-modulated measurements.^{33–35} The origin of the changes in heat capacity at T_g during heating or vitrification is associated with molecular motions, particularly large-amplitude segmental motions. Along with the heat capacity changes at T_g , also the mechanical, dielectric, viscous, and volumetric responses change during heating, all reflecting increased molecular mobility.^{18,22}

Melting is a first-order phase transition characterized by an enthalpy of fusion ($\Delta_f H$; latent heat) and, depending on the material, by either a well-defined melting temperature (T_m) for pure crystalline compounds or by a melting range between the

solidus and liquidus temperatures, as in polymers and partially ordered solids.^{18,26}

The apparent heat capacity represents the total heat flow normalized by the heating rate and therefore includes both the continuous heat capacity and any latent heat effects that occur on the experimental time scale. Temperature-modulated differential scanning calorimetry allows the separation of irreversible latent heat and reversible heat capacity contributions during the melting process.^{35–42} This approach has been applied to characterize polymeric systems such as poly(oxyethylene) and poly(oxytetramethylene).^{3,43–46}

Quantitative thermal analysis of glass and melting requires the definition of equilibrium heat capacity baselines for the solid and liquid states. The baseline represents the equilibrium C_p of each phase extrapolated into the transition region, serving as a reference to determine the excess heat capacity and latent heat contributions. In the solid state, C_p mainly reflects vibrational motions, while in the liquid state additional large-amplitude molecular motions (rotational, conformational, and external/anharmonic) contribute.^{5,27,28,47,48} Thus, both the glass transition in amorphous materials and the melting in crystals involve similar large-amplitude molecular motions that manifest as heat capacity changes.

Here, we investigate heat-capacity changes (ΔC_p) during both the melting of fully crystalline materials (roxithromycin, RXM; glucose, GLC) and the crystallization of semicrystalline poly(3-hydroxybutyrate) (P3HB), using standard and temperature-modulated DSC, revealing C_p features similar in form to those observed at the glass transition. Reversing heat capacity changes observed during melting closely resemble those seen at T_g in the corresponding amorphous phases, indicating similar molecular motion mechanisms. Analogous C_p changes also appear during crystallization upon cooling in semicrystalline P3HB. Although melting is classically treated as distinct from the glass transition, we propose that large-amplitude molecular motions activated during melting produce heat capacity changes similar in shape to those observed at the glass transition in the amorphous material.

The thermal behavior of crystalline and amorphous roxithromycin measured on heating by standard DSC is presented in Figure 1a. The heat-flow rate versus temperature on the first heating at 10 K·min^{−1} shows a very broad endotherm from approximately room temperature to about 373 K related to the evaporation of solvent, followed by the melting process at a temperature of $T_m(\text{onset}) = 434.3$ K and $T_m(\text{peak}) = 398.2$ K with the heat of fusion $\Delta_f H = 38.56$ kJ·mol^{−1}. After cooling from the melt and reheating, the second run shows only a glass transition at around $T_g = 357.2$ K with a change in heat capacity $\Delta C_p = 322.27$ J·mol^{−1}·K^{−1} and a small enthalpy relaxation peak. These results suggest that roxithromycin is 100% crystalline and the sample is made fully amorphous after cooling at 10 K·min^{−1} from the melt.

Temperature-modulated differential scanning calorimetry allows the separation of kinetic (latent-heat-related) and thermodynamic (heat-capacity-related) contributions to the apparent heat capacity, thus enabling the distinction between reversing and nonreversing components in the melting region of crystalline roxithromycin. Figure 1b shows the total, reversing, and nonreversing heat flow rates of roxithromycin as a function of temperature on the first heating run.

The total and nonreversing heat flow rate curves show an endothermic event corresponding to solvent evaporation and a second endothermic event corresponding to melting. The

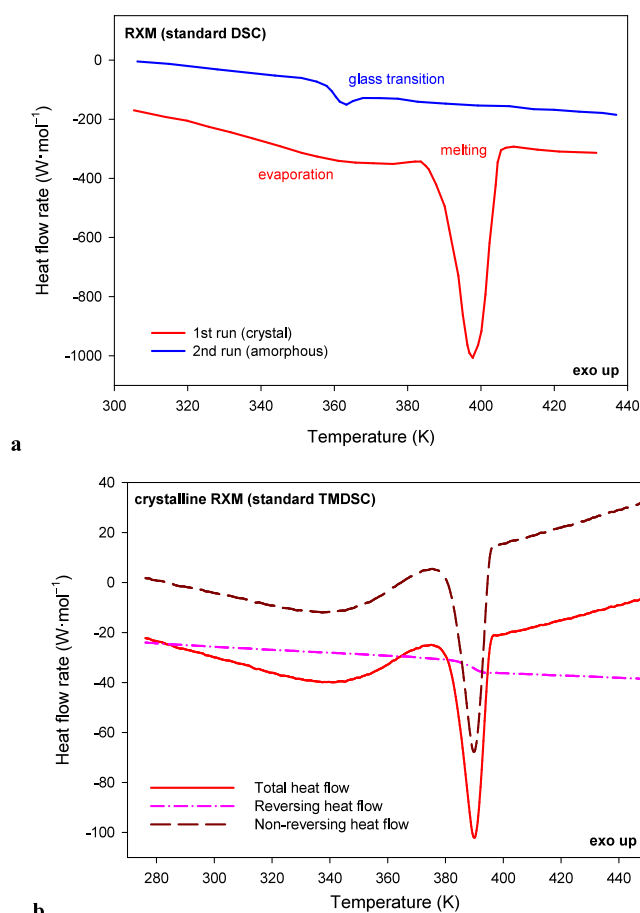


Figure 1. (a) Heat-flow curves of roxithromycin obtained by standard DSC ($q = 10 \text{ K} \cdot \text{min}^{-1}$), showing the first heating run (solvent evaporation and melting of crystalline material) and second heating run after cooling with $q = 10 \text{ K} \cdot \text{min}^{-1}$ (glass transition with enthalpy relaxation of amorphous material). The curves have been vertically offset for clarity. (b) The total, reversing, and nonreversing heat flow rates of roxithromycin by standard TMDSC during the first heating run. The scan parameters are the underlying heating rate $q = 1 \text{ K} \cdot \text{min}^{-1}$; amplitude of modulation $A_{Ts} = 0.5 \text{ K}$; and period of modulation $p = 60 \text{ s}$.

reversing heat-flow-rate curve presents a jump in the melting region related to a change in the heat capacity (ΔC_p) at T_m . It should be noted that on the reversing heat-flow-rate curve no changes in the glass-transition area of the amorphous material are observed, confirming the total crystallinity of the RXM.

Figure 2a compares the reversing heat flow rates from the first and second heating cycles of crystalline and amorphous RXM. The change in heat capacity at melting, $T_m = 388.3 \text{ K}$, was estimated as $\Delta C_p = 302.18 \text{ J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$ for the crystal, and in the glass-transition region, with glass-transition temperature $T_g = 358.5 \text{ K}$, the change in heat capacity is $\Delta C_p = 303 \text{ J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$ for the amorphous material. The reversing change in heat capacity at the glass transition is similar to that in the melting regions. This result indicates that the changes in the heat capacity originate from the same molecular large-amplitude motions. Accordingly, the C_p step observed during the melting of crystalline RXM can be described as a change exhibiting a C_p signature similar in shape and magnitude to that observed at the glass transition.

Figure 2b shows the reversing heat capacity of crystalline and amorphous RXM obtained by standard and quasi-

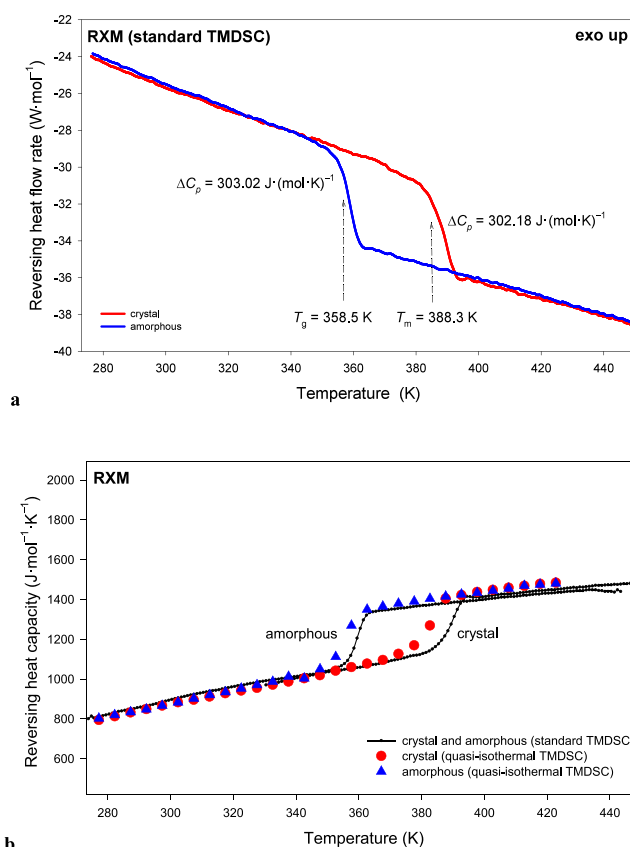


Figure 2. (a) Reversing heat-flow rate as a function of temperature in the glass-transition region of amorphous roxithromycin and at the melting of crystalline roxithromycin obtained by standard TMDSC for the first heating run (red) and second heating run (blue). The scan parameters are the underlying heating rate $q = 1 \text{ K} \cdot \text{min}^{-1}$; the amplitude of modulation $A_{Ts} = 0.5 \text{ K}$; and the period of modulation $p = 60 \text{ s}$. Vertical arrows mark the locations of the glass-transition and melting temperatures. (b) Reversing heat capacity of crystalline and amorphous roxithromycin by standard TMDSC and quasi-isothermal TMDSC. For quasi-isothermal TMDSC, the scan parameters are the underlying heating rate $\langle q \rangle = 0$; amplitude of modulation $A_{Ts} = 0.5 \text{ K}$; period of modulation $p = 60 \text{ s}$; and temperature steps of 2 K .

isothermal TMDSC. Measurements by standard TMDSC for both crystal and amorphous phases were performed with underlying heating rate $q = 1.0 \text{ K} \cdot \text{min}^{-1}$, amplitude of sinusoidal modulation $A_{Ts} = 0.5 \text{ K}$, and period of modulation $p = 60 \text{ s}$. The experiments by quasi-isothermal TMDSC were conducted without any underlying heating rate, i.e., $\langle q \rangle = 0$, with amplitude of modulation $A_{Ts} = 0.5 \text{ K}$, period of modulation $p = 60 \text{ s}$, and 2 K temperature steps. Changes in reversing heat capacity for crystalline and amorphous RXM are similar for both techniques. A slightly lower transition temperature in the glass-transition region of amorphous RXM and at crystal melting can be observed for quasi-isothermal TMDSC compared to that for standard TMDSC. Based on these experimental results of heat capacities, it can be concluded that crystalline material exhibits cooperative molecular dynamics during melting that are analogous to those observed near the glass transition due to the same changes in large-amplitude motions (rotation and anharmonic (external) motions) as in the amorphous material. It should be noted that the step in heat capacity (ΔC_p) observed at the onset of melting reflects the progressive activation of molecular

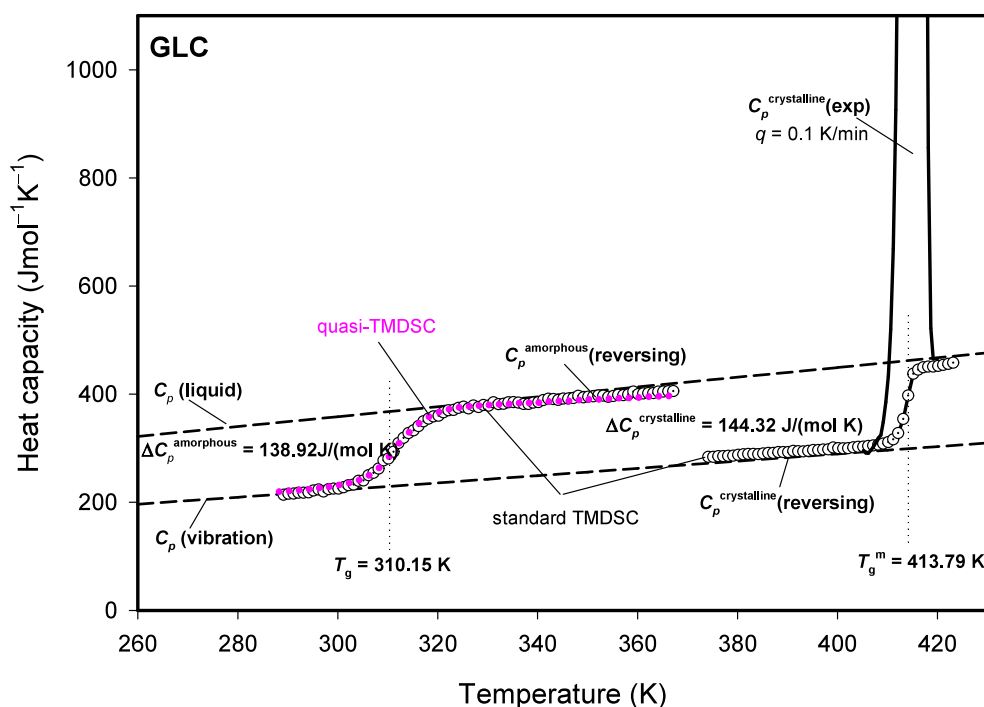


Figure 3. Comparison of total heat capacity $C_p^{\text{crystalline}}(\text{exp})$ for crystalline glucose measured by standard DSC with heating rate $q = 0.1 \text{ K} \cdot \text{min}^{-1}$ and reversing heat capacity of crystalline glucose $C_p^{\text{crystalline}}(\text{reversing})$ and amorphous glucose $C_p^{\text{amorphous}}(\text{reversing})$, measured by standard TMDSC ($q = 0.1 \text{ K} \cdot \text{min}^{-1}$, $p = 60 \text{ s}$, and $A = 0.05 \text{ K}$) and quasi-isothermal TMDSC with $q = 0$, $p = 60 \text{ s}$, and $A_{Tb} = 0.5 \text{ K}$ with temperature steps of 2 K .⁴⁹ Dashed lines represent the solid vibrational heat capacity and the liquid heat capacity.

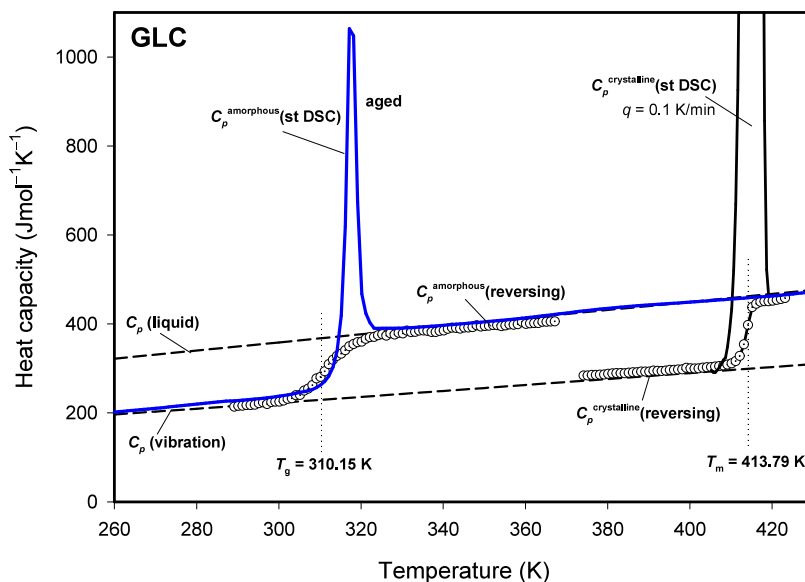


Figure 4. Comparison of the total heat capacity for crystalline glucose measured by standard DSC, $C_p^{\text{crystalline}}(\text{standard DSC})$, with heating rate $q = 0.1 \text{ K} \cdot \text{min}^{-1}$ and reversing heat capacity of crystalline and amorphous glucose measured by standard TMDSC ($q = 0.1 \text{ K} \cdot \text{min}^{-1}$, $p = 60 \text{ s}$, and $A = 0.05 \text{ K}$). Additional apparent heat capacity for amorphous glucose $C_p^{\text{amorphous}}(\text{standard DSC})$ aged for 8 days at room temperature (ca. 293 K) is presented.^{49,54} Dashed lines represent the equilibrium solid vibrational heat capacity and the liquid heat capacity.

degrees of freedom, particularly orientational and rotational/conformational motions. In contrast, the enthalpy of fusion ($\Delta_f H$) represents the total energy required to overcome intermolecular cohesive forces and to fully disrupt the crystalline lattice. These two quantities provide complementary insights: while ΔC_p captures the onset and development of molecular mobility, $\Delta_f H$ reflects the overall structural decomposition associated with the melting process.

A transition exhibiting a C_p signature similar to that of the glass transition is observed for crystalline material as shown by the total heat capacity as a function of temperature in Figure 3 for crystalline glucose (GLC). Amorphous glucose is shown for comparison. Thermal parameters of α -D-glucose are described by a glass-transition temperature of around $T_g = 308\text{--}310 \text{ K}$, an equilibrium melting temperature of around $T_m = 414 \text{ K}$, and a heat of fusion of $\Delta_f H = 31.5 \text{ kJ} \cdot \text{mol}^{-1}$ for 100% crystal.⁴⁹

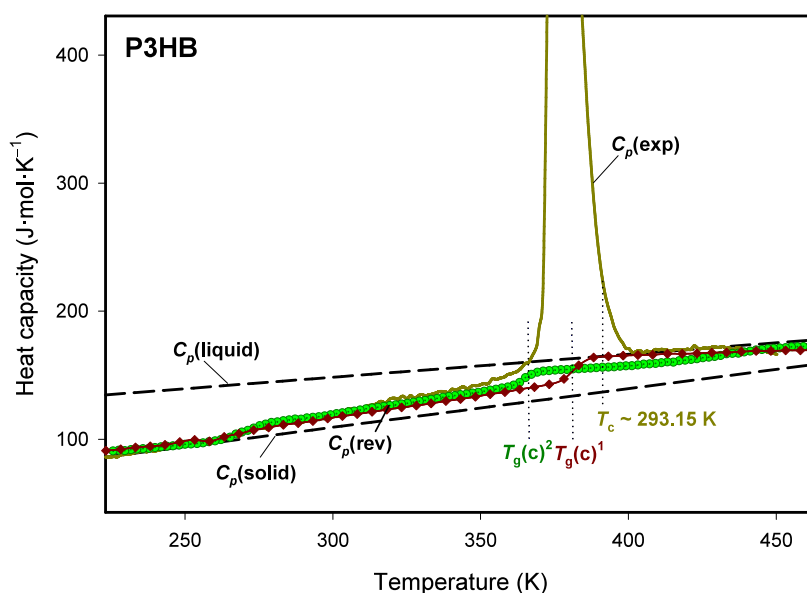


Figure 5. Apparent heat capacity $C_p(\text{exp})$ (standard DSC; $q = 10 \text{ K} \cdot \text{min}^{-1}$) and reversing heat capacity $C_p(\text{rev})$ of semicrystalline poly(3-hydroxybutyrate) on cooling from the molten state using quasi-isothermal TMDSC ($\langle q \rangle = 0$, $p = 60 \text{ s}$, and $A_{T_b} = 1.0 \text{ K}$, with temperature steps of 2 K) and standard TMDSC ($q = 0.5 \text{ K} \cdot \text{min}^{-1}$, $p = 60 \text{ s}$, and $A_{T_b} = 1.0 \text{ K}$) during crystallization.⁵⁴ Dashed lines represent the equilibrium solid vibrational heat capacity and the liquid heat capacity.

The reversing heat capacity of crystalline GLC shows C_p changes ($\Delta C_{p, \text{crystalline}} = 144.32 \text{ J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$) under the melting endotherm at $T_m = 413.79 \text{ K}$ arising from the difference among the vibrational heat capacity, $C_p(\text{vibration})$, and liquid heat capacity $C_p(\text{liquid})$, shown by the dashed equilibrium reference lines.²⁵ It should be noted that the melting peak in Figure 3 resulted from the apparent heat capacity $C_{p, \text{crystalline}}(\text{exp})$ obtained by standard DSC measured on heating with $q = 0.1 \text{ K} \cdot \text{min}^{-1}$.

The amorphous GLC was measured by standard TMDSC and quasi-isothermal TMDSC measurements (Figure 3). Reversing heat capacity from TMDSC and quasi-isothermal TMDSC data overlaps in the glass-transition region, and the change in heat capacity was estimated to be $\Delta C_{p, \text{amorphous}} = 138.92 \text{ J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$ at $T_g = 310.15 \text{ K}$.

The heat capacity in Figure 3 is referenced to the equilibrium lines of the solid $C_p(\text{vibration})$ and liquid $C_p(\text{liquid})$ heat capacities. This quantitative thermal analysis shows very close values of ΔC_p arising from the glass-transition process of amorphous GLC and the melting process of crystalline GLC. The vibrational component, originating from phonon-like lattice motions, remains nearly identical in the crystalline and amorphous states (below T_g) within the limits of experimental uncertainty.¹⁸ In contrast, the excess ΔC_p observed during melting arises predominantly from configurational contributions, associated with the activation of cooperative molecular rearrangements and the progressive release of orientational and rotation/conformational and anharmonic (external) constraints. This indicates that the C_p increase does not result from changes in the vibrational density of states but rather from the onset of large-amplitude molecular mobility. Thus, the liquid heat capacity, $C_p(\text{liquid})$, is the sum of the vibrational, rotational/conformational, and anharmonic (external) heat capacities.

During the heating of fully amorphous materials, the glass transition is marked by the overlap of two primary phenomena: a dominant change in heat capacity and enthalpy relaxation

associated with the aging process.^{50,51} Similarly, the melting process in fully crystalline materials involves the overlap of two main phenomena: the dominant endothermic heat of fusion and a change in the heat capacity around the melting peak.

In other words, in crystalline materials, the melting process is characterized predominantly by molecular disordering and the rotation and anharmonic motion of bonds or segments, which correlates with the observed change in heat capacity (ΔC_p). In contrast, the glass transition in amorphous materials is characterized primarily by a disordered glassy phase, with a relatively small effect related to structural ordering, as seen in enthalpy relaxation.^{50,52,53} Figure 4 compares these processes in the amorphous and crystalline forms of GLC. However, the transition mechanisms at T_g and T_m are different.

It is therefore pertinent to ask, why does a transition exhibiting a C_p signature similar in shape and magnitude to that observed at the glass transition appear in the melting region? The explanation proposed here is that once the crystalline structure is disrupted, the entire material volume becomes amorphous (not glassy). As a consequence, a jump in heat capacity is observed, corresponding to the transition from the vibrational heat capacity of the solid to the heat capacity of the liquid, similar to what is observed for mobile amorphous phases at T_g (refer to Figures 3 and 4). These processes, structural disordering and activation of additional molecular motions, occur simultaneously during melting. We suggest that while the melting process itself proceeds relatively rapidly, the associated change in heat capacity develops more gradually. Furthermore, Na et al. observed that in aged amorphous polymeric material⁵⁵ the disruption of short-range-ordered structures during heating occurs both in the glass-transition region and during melting, as evidenced by similar decreases in the FTIR absorbance of helical and intermolecular packing bands. This indicates that molecular motions associated with the breakdown of ordered conformations contribute to enthalpic changes in both transitions. While in their case the melting of local order occurs within the amorphous phase at

T_g , this example demonstrates that similar activation of molecular motions can also be observed during the melting of fully crystalline material, suggesting a common underlying mechanism where the extent of ordering determines the temperature at which such transitions occur.

The next example, poly(3-hydroxybutyrate) (P3HB), belongs to the homologous series of aliphatic polyesters and is a semicrystalline, biodegradable polymer. Depending on its thermal history, semicrystalline P3HB's glass-transition temperature can be between about 273 and 300 K with a ΔC_p of about 40 to 43 J·K⁻¹·mol⁻¹ for the fully amorphous polymer. The melting endotherm of semicrystalline P3HB occurs between $T_m = 443$ and 448 K with an enthalpy of fusion of 7.5 to 7.9 kJ·mol⁻¹.⁵⁶

The example of P3HB illustrates the transition exhibiting a C_p signature similar in shape and magnitude to that observed at the glass transition occurring during the crystallization process of a semicrystalline polymeric material on cooling from the molten state (Figure 5). The crystallization exotherm at around $T_c = 393.2$ –388.2 K appears alongside the mobile glass transition at $T_g = 273.15$ K on a standard DSC cooling run ($q = 10$ K·min⁻¹). By applying standard and quasi-isothermal TMDSC, the separation of ordering from the change in heat capacity is observed during cooling from the liquid. Figure 5 presents the reversing heat capacity $C_p(\text{rev})$ of semicrystalline P3HB on cooling obtained by quasi-isothermal TMDSC ($\langle q \rangle = 0$, $p = 60$ s, $A_{T_b} = 1.0$ K, and step temperature 2 K) and standard TMDSC ($q = 0.5$ K·min⁻¹, $p = 60$ s, and $A_{T_b} = 1.0$ K). Results are compared with the apparent heat capacity $C_p(\text{exp})$ measured by standard DSC on cooling at a rate of $q = 10$ K·min⁻¹ during crystallization. Heat capacity is referenced to the equilibrium solid, vibrational heat capacity $C_p(\text{solid})$, and liquid heat capacity $C_p(\text{liquid})$. The temperature corresponding to the C_p signature similar to the glass-transition temperature in the crystalline phase of P3HB obtained from quasi-isothermal TMDSC is $T_g(c)^1 = 378.2$ K, and that obtained from standard TMDSC is $T_g(c)^2 = 363.2$ K. The difference in these $T_g(c)$ values comes from the underlying cooling rates (quasi-isothermal TMDSC $\langle q \rangle = 0$ and standard TMDSC $q = 0.5$ K·min⁻¹). The change in the reversing heat capacity observed under the crystallization process is similar to the one seen in the glass-transition process of the mobile amorphous phase of a polymer.^{39,40,57} The large-amplitude motion freezes during crystallization, showing a jump in the heat capacity (ΔC_p). The values of ΔC_p during crystallization and during the glass-transition process of the mobile amorphous phase are different due to the semicrystalline nature of P3HB. The step in the reversing heat capacity under crystallization occurs at around $T_g(c) = 378.2$ K for the quasi-isothermal TMDSC measurement and at around 363.2 K for standard TMDSC. From both TMDSC techniques, the reversing heat capacity $C_p(\text{rev})$ reaches the full level of the solid vibrational heat capacity $C_p(\text{solid})$ below the mobile glass-transition temperature of around $T_g = 273.15$ K. This behavior occurs due to the gradual freezing of conformational and anharmonic (external) motions from the crystalline and amorphous phases of semicrystalline P3HB. Below the mobile glass-transition temperature, the only contribution to the heat capacity comes from vibrational motions.⁵⁴

The calculated solid heat capacity arises solely from vibrational motion, below the glass transition for a 100% amorphous sample and below the melting point for a 100% crystalline sample, and is extended into the melting region as a

reference baseline. Changes in the apparent heat capacity resulting from large-amplitude molecular motions, including conformational and rotational movements, anharmonic (external) vibrations, and latent heat, can be evaluated against this equilibrium baseline vibrational heat capacity $C_p(\text{solid})$. Similarly, during cooling from the melt, the apparent heat capacity can be analyzed throughout the crystallization process. In the liquid state, above T_g for fully amorphous material and above the melting transition, the sum of vibrational, conformational/rotational, and anharmonic (external) heat capacities provides the liquid heat capacity $C_p(\text{liquid})$. Temperature-modulated DSC and quantitative thermal analysis allow the separation of latent heat from heat capacity in the apparent heat capacity in the melting/crystallization region for materials, demonstrated here for roxithromycin, glucose, and poly(3-hydroxybutyrate).

These findings may have practical implications for the design and stability assessment of crystalline pharmaceutical compounds, where the interplay between crystal melting and molecular mobility governs the shelf life and processing stability. Similarly, in semicrystalline polymers, the ability to monitor large-amplitude molecular motions during crystallization may inform processing protocols to optimize mechanical performance. More broadly, our observations contribute to the growing understanding that large-amplitude molecular motions activated near phase transitions may serve as a unifying feature connecting classical glass transition and melting processes.

Our study suggests that the change in heat capacity (glass-like transition properties) during melting may not be restricted to specific molecular systems but could represent a general thermodynamic feature of melting in ordered materials, driven by the activation of large-amplitude molecular motions. This expands the classical understanding of the glass transition, typically reserved for amorphous systems, and highlights the potential universal aspects of molecular mobility across phase boundaries. Future studies may explore whether such phenomena can be observed in a wider class of molecular crystals, biomaterials, and inorganic crystalline systems.

New experimental evidence reveals the transition exhibiting a C_p signature similar in shape and magnitude to that observed at the glass transition in the melting process of fully crystalline materials, investigated through standard DSC, TMDSC, and quasi-isothermal TMDSC techniques. Advanced thermal analysis using TMDSC enables the separation of latent heat from the thermodynamic heat capacity, facilitating the distinction between apparent heat capacity and the reversible and irreversible processes occurring in the melting region of 100% crystalline materials. In standard DSC measurements of crystalline substances, a melting peak is observed; however, no heat capacity change is detectable. In contrast, the reversing heat-flow rates or heat capacities measured by TMDSC in fully crystalline materials do not show a melting endotherm but display a change in the heat capacity akin to the change seen at the glass transition of amorphous materials. The change in reversing heat capacity during the melting process closely resembles that seen at T_g for fully amorphous materials. This similarity suggests that the molecular large-amplitude motions, such as rotational/conformational and anharmonic (external) movements, are the likely origin of the heat capacity changes in both the amorphous and crystalline phases during the glass and melting transitions. It should be clearly emphasized that during melting the crystalline structure is disrupted and simulta-

neously the material transforms into the amorphous liquid state. The observed change in heat capacity, from $C_p(\text{solid})$ to $C_p(\text{liquid})$, reflects the activation of additional large-amplitude molecular motions, similar to those observed during the glass transition of fully amorphous materials. However, these heat capacity changes occurring during melting differ from the conventional glass transition in several aspects, including its higher transition temperature, lower packing density, lower viscosity, and other distinct thermodynamic and dynamic properties.

This research provides a detailed thermal characterization of crystalline and amorphous material forms, introducing a novel perspective on interpreting melting and crystallization transitions. The findings indicate that fully crystalline materials can exhibit behaviors traditionally associated with glass transitions in amorphous states, which could redefine the way we understand phase transitions in solids. These findings extend previous theoretical and experimental work on glass-like- C_p change phenomena by providing direct experimental evidence that such behavior can occur even during the melting of fully crystalline low-molecular-weight molecular solids. Moreover, these results imply that the thermal properties of crystalline materials may be more complex and dynamic than previously thought, with significant implications for applications requiring precise thermal management, such as pharmaceuticals, polymer processing, and material engineering. By uncovering these glass-like transition properties in crystalline materials, the study not only deepens the theoretical framework for phase transitions but also opens new avenues for controlling and utilizing these properties in practical applications where thermal stability and behavior are critical factors.

EXPERIMENTAL SECTION

Samples of crystalline and amorphous roxithromycin (RXM; pharmaceutical grade, $M_w = 837.06 \text{ g}\cdot\text{mol}^{-1}$; POL-NIL SA, Warsaw, Poland), glucose (GLK; α -D-glucose, $M_w = 180.16 \text{ g}\cdot\text{mol}^{-1}$; Sigma-Aldrich, St. Louis, MO, USA), and semicrystalline poly(3-hydroxybutyrate) (P3HB; $M_w = 1.6 \times 10^4$ to $3.8 \times 10^5 \text{ g}\cdot\text{mol}^{-1}$; $99.2 \pm 0.2\%$ purity, supplied by Prof. A. Mansour, University of Cairo, Egypt) were measured using a heat-flux DSC Q1000 or DSC 2920 (TA Instruments, USA) under a nitrogen purge of $50 \text{ mL}\cdot\text{min}^{-1}$ with heating rates of between 0.1 and $10 \text{ K}\cdot\text{min}^{-1}$. Typical sample masses ranged from 10 to 30 mg (DSC) and 2 to 8 mg (TMDSC). Full experimental details are provided in the [Supporting Information](#).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jpclett.5c03072>.

Experimental details on materials; description of DSC, TMDSC, and quasi-isothermal TMDSC methodologies; thermogravimetric analysis of roxithromycin; and powder X-ray diffraction patterns of crystalline and amorphous roxithromycin (PDF)

AUTHOR INFORMATION

Corresponding Authors

Marek Pyda – Department of Chemistry, University of Tennessee, Knoxville, Tennessee 37996-1600, United States; Chemical Sciences Division, Oak Ridge National Laboratory,

Oak Ridge, Tennessee 37831-6197, United States;

Email: mpyda@utk.edu

Marcin Skotnicki – Industrial Pharmacy Division, Chair and Department of Pharmaceutical Technology, Poznan University of Medical Sciences, 60-806 Poznan, Poland; orcid.org/0000-0002-3325-4109; Email: marcskot@ump.edu.pl

Authors

Anna Czerniecka-Kubicka – Department of Pharmaceutical Technology and Medical Physics, Medical College of Rzeszow University, The University of Rzeszow, 35-310 Rzeszow, Poland

Peggy Cebe – Department of Physics and Astronomy, Tufts University, Medford, Massachusetts 02155, United States; orcid.org/0000-0002-8721-644X

Complete contact information is available at:

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Author Contributions

^vRetired.

Notes

The authors declare no competing financial interest.

DEDICATION

In memory of Professor Bernhard Wunderlich.

REFERENCES

- (1) Bridgman, P. W. *The Logic of Modern Physics*; The Macmillan Company: New York, 1927.
- (2) Stillinger, F. H. A Topographic View of Supercooled Liquids and Glass Formation. *Science* **1995**, 267 (5206), 1935–1939.
- (3) Wunderlich, B. The Glass Transition of Polymer Crystals. *Thermochim. Acta* **2006**, 446 (1–2), 128–134.
- (4) Wunderlich, B. Glass Transition as a Key to Identifying Solid Phases. *J. Appl. Polym. Sci.* **2007**, 105 (1), 49–59.
- (5) Wunderlich, B. Thermodynamic Description of Condensed Phases. *J. Therm. Anal. Calorim.* **2010**, 102 (2), 413–424.
- (6) Miyazaki, Y.; Matsuo, T.; Suga, H. Glass Transition of Myoglobin Crystal. *Chem. Phys. Lett.* **1993**, 213 (3–4), 303–308.
- (7) Suga, H. Thermodynamic Studies of Glassy Crystals. *Annu. Rep. Res. Inst. Sci. Technol. Kinki Univ.* **1994**, 6, 31–38.
- (8) Havranek, A.; Marvan, M. Glass Transition in Inorganic Glasses, Polymers, and Crystals. *Ferroelectrics* **1996**, 176 (1), 25–32.
- (9) Angell, C. A. Glass Formation and Glass Transition in Supercooled Liquids, with Insights from Study of Related Phenomena in Crystals. *J. Non-Cryst. Solids* **2008**, 354 (42–44), 4703–4712.
- (10) Martinez, L.-M.; Angell, C. A Thermodynamic Connection to the Fragility of Glass-Forming Liquids. *Nature* **2001**, 410 (6829), 663–667.
- (11) Krzakala, F.; Zdeborová, L. On Melting Dynamics and the Glass Transition. I. Glassy Aspects of Melting Dynamics. *J. Chem. Phys.* **2011**, 134 (3), 034512.
- (12) Krzakala, F.; Zdeborová, L. On Melting Dynamics and the Glass Transition. II. Glassy Dynamics as a Melting Process. *J. Chem. Phys.* **2011**, 134 (3), 034513.
- (13) Zacccone, A.; Samwer, K. Fragility and Thermal Expansion Control Crystal Melting and the Glass Transition. *J. Chem. Phys.* **2025**, 162 (11), 114502.
- (14) Wunderlich, B. *Macromolecular Physics: Crystal Structure, Morphology, Defects*; Academic Press: New York, 1973.
- (15) Royall, C. P.; Williams, S. R. The Role of Local Structure in Dynamical Arrest. *Phys. Rep.* **2015**, 560, 1–75.
- (16) Wunderlich, B.; Jin, Y.; Boller, A. Mathematical Description of Differential Scanning Calorimetry Based on Periodic Temperature Modulation. *Thermochim. Acta* **1994**, 238, 277–293.

- (17) Schawe, J. Principles for the Interpretation of Modulated Temperature DSC Measurements. Part 1. Glass Transition. *Thermochim. Acta* **1995**, 261, 183–194.
- (18) Wunderlich, B. *Thermal Analysis of Polymeric Materials*; Springer Science & Business Media: Berlin, 2005.
- (19) Gardner, C. R.; Walsh, C. T.; Almarsson, Ö. Drugs as Materials: Valuing Physical Form in Drug Discovery. *Nat. Rev. Drug Discovery* **2004**, 3 (11), 926–934.
- (20) Florence, A. T.; Attwood, D. *Physicochemical Principles of Pharmacy: In Manufacture, Formulation and Clinical Use*; Pharmaceutical Press: London, 2015.
- (21) Zhang, R.; Jariyavidyanont, K.; Zhuravlev, E.; Schick, C.; Androsch, R. Physical Aging and Glass Transition Dynamics of Semicrystalline Poly (Lactic Acid) for 3D-Printing Applications Investigated by Fast Scanning Calorimetry. *Macromolecules* **2024**, 57 (1), 32–41.
- (22) Donth, E. *The Glass Transition: Relaxation Dynamics in Liquids and Disordered Materials*; Springer Science & Business Media: Berlin, 2013.
- (23) Pionteck, J.; Pyda, M. In *Part 2: Thermodynamic Properties – pVT-Data and Thermal Properties*; Arndt, K.-F., Lechner, M. D., Eds.; Springer: Berlin, 2014.
- (24) Schawe, J. E. Vitrification in a Wide Cooling Rate Range: The Relations between Cooling Rate, Relaxation Time, Transition Width, and Fragility. *J. Chem. Phys.* **2014**, 141 (18), 184905.
- (25) Magoń, A.; Pyda, M. Melting, Glass Transition, and Apparent Heat Capacity of α -D-Glucose by Thermal Analysis. *Carbohydr. Res.* **2011**, 346 (16), 2558–2566.
- (26) Wunderlich, B. *Macromolecular Physics: Crystal Melting*; Elsevier Science: St. Louis, MO, 1980.
- (27) Wunderlich, B. The ATHAS Database on Heat Capacities of Polymers. *Pure Appl. Chem.* **1995**, 67 (6), 1019–1026.
- (28) Pyda, M.; Bartkowiak, M.; Wunderlich, B. Computation of Heat Capacities of Solids Using a General Tarasov Equation. *J. Therm. Anal. Calorim.* **1998**, 52 (2), 631–656.
- (29) Pyda, M.; Wunderlich, B. Computation of Heat Capacities of Liquid Polymers. *Macromolecules* **1999**, 32 (6), 2044–2050.
- (30) Angell, C. A. Formation of Glasses from Liquids and Biopolymers. *Science* **1995**, 267 (5206), 1924–1935.
- (31) Ediger, M. D.; Angell, C. A.; Nagel, S. R. Supercooled Liquids and Glasses. *J. Phys. Chem.* **1996**, 100 (31), 13200–13212.
- (32) Schoenholz, S. S.; Cubuk, E. D.; Sussman, D. M.; Kaxiras, E.; Liu, A. J. A Structural Approach to Relaxation in Glassy Liquids. *Nat. Phys.* **2016**, 12 (5), 469–471.
- (33) Schawe, J. A Description of the Glass Transition Measured by Temperature Modulated Differential Scanning Calorimetry. *Colloid Polym. Sci.* **1998**, 276, 565–569.
- (34) Di Lisio, V.; Gallino, I.; Riegler, S. S.; Frey, M.; Neuber, N.; Kumar, G.; Schroers, J.; Busch, R.; Cangialosi, D. Size-Dependent Vitrification in Metallic Glasses. *Nat. Commun.* **2023**, 14 (1), 4698.
- (35) Pyda, M.; Wunderlich, B. Reversing and Nonreversing Heat Capacity of Poly(Lactic Acid) in the Glass Transition Region by TMDSC. *Macromolecules* **2005**, 38 (25), 10472–10479.
- (36) Schawe, J.; Bergmann, E.; Winter, W. A Method for Analysis of the Measured Curves of TMDSC Investigation in the Melting Region of Polymers. *J. Therm. Anal. Calorim.* **1998**, 54 (2), 565–576.
- (37) Merzlyakov, M.; Schick, C. Complex Heat Capacity Measurements by TMDSC Part 1. Influence of Non-Linear Thermal Response. *Thermochim. Acta* **1999**, 330 (1–2), 55–64.
- (38) Merzlyakov, M.; Schick, C. Complex Heat Capacity Measurements by TMDSC. Part 2. Algorithm for Amplitude and Phase Angle Correction. *Thermochim. Acta* **1999**, 330 (1–2), 65–73.
- (39) Wunderlich, B. Reversible Crystallization and the Rigid–Amorphous Phase in Semicrystalline Macromolecules. *Prog. Polym. Sci.* **2003**, 28 (3), 383–450.
- (40) Righetti, M. C.; Tombari, E. Crystalline, Mobile Amorphous and Rigid Amorphous Fractions in Poly (L-Lactic Acid) by TMDSC. *Thermochim. Acta* **2011**, 522 (1–2), 118–127.
- (41) Wunderlich, B.; Boller, A.; Okazaki, I.; Ishikiriya, K.; Chen, W.; Pyda, M.; Pak, J.; Moon, I.; Androsch, R. Temperature-Modulated Differential Scanning Calorimetry of Reversible and Irreversible First-Order Transitions. *Thermochim. Acta* **1999**, 330 (1–2), 21–38.
- (42) Wurm, A.; Schick, C. Reversing and Nonreversing Contributions to Polymer Melting. *Colloid Polym. Sci.* **2003**, 281 (2), 113–122.
- (43) Ishikiriya, K.; Wunderlich, B. Melting of Poly(Oxyethylene) Analyzed by Temperature-Modulated Calorimetry. *Macromolecules* **1997**, 30 (14), 4126–4131.
- (44) Qiu, W.; Pyda, M.; Nowak-Pyda, E.; Habenschuss, A.; Wunderlich, B. Reversibility between Glass and Melting Transitions of Poly(Oxyethylene). *Macromolecules* **2005**, 38 (20), 8454–8467.
- (45) Cheng, S. Z. D.; Wunderlich, B. Molecular Segregation and Nucleation of Poly(Ethylene Oxide) Crystallized from the Melt. I. Calorimetric Study. *J. Polym. Sci., Part B: Polym. Phys.* **1986**, 24 (3), 577–594.
- (46) Pak, J.; Pyda, M.; Wunderlich, B. Temperature-Modulated Calorimetry of Hexacontane and Oligomer Fractions of Poly-(Oxyethylene) and Poly(Oxytetramethylene). *Thermochim. Acta* **2003**, 396 (1–2), 43–56.
- (47) Williams, M. L.; Landel, R. F.; Ferry, J. D. The Temperature Dependence of Relaxation Mechanisms in Amorphous Polymers and Other Glass-Forming Liquids. *J. Am. Chem. Soc.* **1955**, 77 (14), 3701–3707.
- (48) Adam, G.; Gibbs, J. H. On the Temperature Dependence of Cooperative Relaxation Properties in Glass-forming Liquids. *J. Chem. Phys.* **1965**, 43 (1), 139–146.
- (49) Magoń, A.; Pyda, M. Melting, Glass Transition, and Apparent Heat Capacity of α -D-Glucose by Thermal Analysis. *Carbohydr. Res.* **2011**, 346 (16), 2558–2566.
- (50) Hutchinson, J. M. Physical Aging of Polymers. *Prog. Polym. Sci.* **1995**, 20 (4), 703–760.
- (51) Cangialosi, D.; Boucher, V. M.; Alegría, A.; Colmenero, J. Physical Aging in Polymers and Polymer Nanocomposites: Recent Results and Open Questions. *Soft Matter* **2013**, 9 (36), 8619–8630.
- (52) Struik, L. C. E. *Physical Aging in Amorphous Polymers and Other Materials*; Elsevier: Amsterdam, 1978.
- (53) Skotnicki, M.; Gawel, A.; Cebe, P.; Pyda, M. Thermal Behavior and Phase Identification of Valsartan by Standard and Temperature-Modulated Differential Scanning Calorimetry. *Drug Dev. Ind. Pharm.* **2013**, 39 (10), 1508–1514.
- (54) Magon, A. *Termodynamiczne właściwości polimerów biodegradowalnych i biomateriałów badane metodami analizy termicznej (Thermodynamic properties of biodegradable polymers and biomaterials studied by thermal analysis)*. Ph.D. Thesis Technical University of Rzeszow: Rzeszow, Poland, 2012.
- (55) Na, B.; Lv, R.; Zou, S.; Li, Z.; Tian, N.; Fu, Q. Spectroscopic Evidence of Melting of Ordered Structures in the Aged Glassy Poly(L-Lactide). *Macromolecules* **2010**, 43 (4), 1702–1705.
- (56) Czerniecka, A.; Magoń, A.; Schliesser, J.; Woodfield, B. F.; Pyda, M. Heat Capacity of Poly(3-Hydroxybutyrate). *J. Chem. Thermodyn.* **2014**, 73, 76–84.
- (57) Pak, J.; Pyda, M.; Wunderlich, B. Rigid Amorphous Fractions and Glass Transitions in Poly (Oxy-2, 6-Dimethyl-1, 4-Phenylene). *Macromolecules* **2003**, 36 (2), 495–499.