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Changing the Tendency of Glass-Forming Liquid To Crystallize by Moving Along Different Isolines in the $T-p$ Phase Diagram

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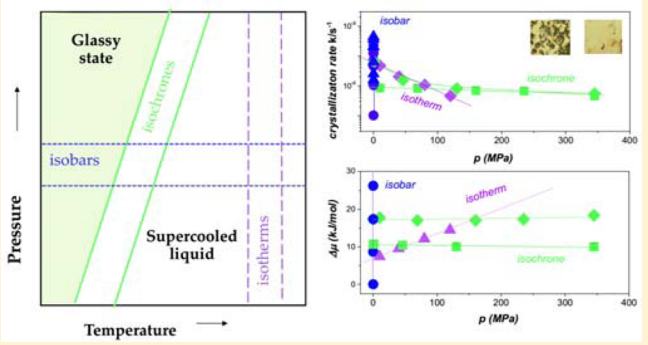
Supporting Information

ABSTRACT: Controlling crystallization and glass-forming tendencies of molecular liquids is of great scientific and practical importance. In the present work, we show that a lot can be learned regarding this process by introducing temperature and pressure as thermodynamic control variables. For the glass-forming liquid ketoprofen and its non-hydrogen bonded analogue, we have investigated changes in the crystallization rate along different isolines located in the two-dimensional $T-p$ phase space. This has included isobaric (p = const), isothermal (T = const), and isochronal (τ_α = const) data. Our results reveal that the crystallization tendency of the investigated liquids can be tuned by moving along specific thermodynamic pathways. In particular, we highlight that among considered isolines the overall crystallization rate is the least affected by the density increase for the isochronal (T, p) state points. Interestingly, for various thermodynamic conditions with the same τ_α the estimated value of the thermodynamic driving force toward crystallization $\Delta\mu$ was found to be almost constant.



INTRODUCTION

When a liquid is cooled down below the melting temperature, it can either crystallize or become supercooled. On further cooling, a supercooled liquid will eventually solidify and form a glassy state, which is a solid state without the long-range order characteristic for crystalline materials. Controlling the crystallization and glass-forming ability is important from a fundamental as well as a practical perspective.[1−6] However, it is by no means easy to understand what makes a liquid crystallize in one case and form a stable glass in another.[7−10] Since crystallization and glass-formation are two sides of the same coin, by understanding what governs crystallization in supercooled liquids, we can learn how to make good glass-formers.

Considering the crystallization process, a good starting point is always the classical nucleation theory that serves as a guiding picture of the crystal formation.[7,11−14] According to the classical nucleation theory and the crystal growth models, crystallization is a two-step process that involves (i) formation of the nuclei of the critical size, and (ii) its growth in the macroscopic dimension. As a rule, nucleation and growth rates exhibit complex temperature dependences with the maxima located below the melting point.[15,16] Their location with respect to each other (i.e., the overlapping zone) determines whether a liquid is susceptible to crystallization, or a glass formation upon cooling. The general expression for the nucleation rate I, defined as the number of nuclei formed per volume unit per unit of time, is $I = C_1 \exp[-(W^* + \Delta G_D)/k_B T]$, where W^* and ΔG_D define thermodynamic and kinetic barriers to nucleation, respectively. The growth rate describes the increase of the characteristic crystal size per unit of time and can be expressed as $G = C_2[\exp(-(\Delta E/k_B T)][1-\exp(\Delta G/k_B T)$ where ΔE and ΔG are kinetic and thermodynamic barriers to crystal growth, respectively. So at every given state the crystallization process is controlled by two fundamental forces: kinetic (i.e., molecular mobility) and thermodynamics. On lowering the temperature, the two factors lead to completely different effects on the crystallization progress; i.e., thermodynamic driving force favors the crystal formation, but at the same time slowing down of the molecular movements retards it. Therefore, depending on the significance, or the interplay between these factors, it is possible to alter the crystallization behavior of the supercooled liquids. In experimental reality, by varying only temperature it is difficult, if not impossible, to determine the individual

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contributions of the kinetic and thermodynamic factors to the overall crystallization behavior of the glass-forming liquids. Consequently, it is also not possible to face the instability problem of glass-forming liquids in a fully aware manner.

Recently, we have demonstrated that a key to a get better understanding of the crystallization behavior of glass-forming liquids must involve introducing pressure as another thermodynamic variable to control.[17−19] This has included the first pioneering experiments aimed at controlling the mobility factor upon the crystallization progress.[17−20] By considering crystallization at isochronal states, that is, at different combinations of (T, p) while keeping the same time scale of the α-relaxation, we have studied changes in the crystallization rate affected exclusively by the thermodynamics. This effect cannot be achieved by changing only temperature at constant (atmospheric) pressure or pressure at a fixed temperature. Here we have looked at this aspect from a broader perspective and investigated the tendency of glass-forming liquids to crystallize along different isopaths in the two-dimensional $T-p$ phase space. We demonstrate that among various isocurves, the crystallization rate changes the least when the time scale of the α-relaxation (τ_α) is kept constant. The most surprising finding is, however, that for various (T, p) conditions with identical τ_α the estimated value of the thermodynamic driving force toward crystallization $(\Delta\mu)$ was found to be practically constant. This indicates that there should be some hidden link between kinetic and thermodynamic factors governing the crystallization behavior of the supercooled liquids. The materials under investigation are molecular liquids: *RS*-ketoprofen and methyl ester of *RS*-ketoprofen of a very similar molecular structure (see Figure 1)

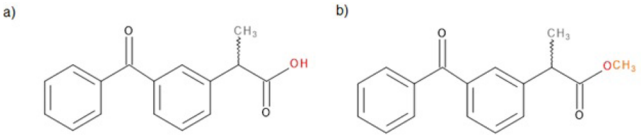

Figure 1. Chemical structure of (a) *RS*-ketoprofen and (b) methyl ester of *RS*-ketoprofen.

but differing in the propensity to form hydrogen bonds. As confirmed via molecular dynamics simulation, the former one has a strong tendency to form hydrogen bonded dimeric structures,[21,22] whereas the latter one is a typical van der Waals liquid with no capability to form intermolecular hydrogen bonds.

EXPERIMENTAL METHODS

Materials. The studied materials include racemic *RS*-ketoprofen (Sigma-Aldrich, >98%), *S*-ketoprofen (Sigma-Aldrich, >99%), and the methyl ester of racemic *RS*-ketoprofen. A detailed synthesis protocol of the methyl ester of racemic *RS*-ketoprofen is given elsewhere.[32] For ketoprofen and its methylated derivative the glass transition temperature T_g determined based on the dielectric studies is T_g = 266.5 K and T_g = 228.3 K, respectively.[32]

Dielectric Measurements. Dielectric relaxation and crystallization studies at atmospheric pressure were carried out by using a Novocontrol Alpha analyzer. For high pressure experiments we used a Unipress system (Institute of High Pressure Physics, Polish Academy of Sciences) connected to an impedance analyzer (Novocontrol GmbH) with a homemade capacitor. The pressure was generated by a pump and transmitted with the use of nonpolar silicon oil via a system of capilars (Nova Swiss) to a high pressure vessel. The measured sample was separated from the silicon oil by Teflon. For temperature stabilization, we use a thermal bath (Julabo) connected to a heating jacket on the pressure chamber. The longest hold time upon isochronal crystallization studies on increased pressure was studied for 5 days (at p = 345 MPa and T = 324 K).

Pressure−Volume−Temperature Measurements. Pressure−volume−temperature (PVT) measurements were performed using Gnomix dilatometer operating within the range of pressure from 0.1 to 200 MPa. Isobaric dependences of the specific volume for Me-*RS*-ketoprofen and *RS*-ketoprofen can be found in our recent paper.[32,35] In order to describe evolution of the specific volume V_{sp} (T, p) in the supercooled liquid regime we have parametrized PVT data with the use of the equation of state. These results can be also found in the literature. For crystallization studies, the V_{sp} values were recorded in the time intervals of 600 s at isothermal conditions T = 304 K and pressures: 10 MPa, 40 MPa, 80 and 120 MPa. The longest crystallization hold time reached 5 days.

Calorimetric Measurements. To determine the accurate temperature dependences of the isobaric heat capacity for glassy, liquid, and crystalline samples we exploited the stochastic temperature-modulated differential scanning calorimetry (TMDSC) technique implemented by Mettler-Toledo (TOPEM). The quenched samples were heated at rate of 0.5 K/min. In the experiment, a temperature amplitude of the pulses of 0.5 K was selected with a switching time range with minimum and maximum values of 15 and 30 s, respectively. We have adjusted our evaluation of the temperature dependence of the quasi-static heat capacity $C_p(T)$ using a sapphire reference curve.

RESULTS AND DISCUSSION

We start by discussing the molecular mobility aspect of the crystallization process. The kinetic term embedded in the rates of nucleation and crystal growth determines the molecular rearrangement in the liquid phase necessary to form a crystal. In agreement with the classical school of crystallization, molecular diffusion controls the rate at which molecules can organize into a crystal. In practice, it is very difficult to provide reliable experimental data of the diffusivity in supercooled liquids as well as a satisfactory model that relates it to the other physical properties.[23] Therefore, the kinetic barriers to nucleation and crystal growth are often discussed in terms of the viscosity. The diffusion coefficient D can be easily related to the macroscopic viscosity η via the Stokes−Einstein relation, $k_BT/6\pi r\eta$, where r is a hydrodynamic radius.[24] In this way, D changes with the temperature the same as the inverse of η. It is also well-known for glass-forming materials that the temperature dependences of the α-relaxation time τ_α and the viscosity η typically follow each other via the Debye−Stokes−Einstein relation, $\tau_\alpha^{-1} = k_BT/8\pi r^3\eta$,[25] even on increased pressure.[26] Therefore, we can link the α-relaxation dynamics (reflecting cooperative reorientational movements) to the translational motions reflected by the self-diffusion coefficient. However, the proportionality between τ_α-D and η-D is often invalidated in the deeply supercooled region (typically at $T < 1.2T_g$) where a decoupling phenomenon takes place.[27−29] In such a case, the fractional exponents provide a more appropriate description of the relationship between the dynamic quantities, $D = k_BT/6\pi r\eta^{-s}$ where s quantifies the magnitude of decoupling. For *RS*-ketoprofen and its methylated derivative, we have recently demonstrated that the temperature dependences of the α-relaxation time (viscosity) and the self-diffusion coefficient follow each other at temperatures $T > T_g + 40-60$ K. However, on approaching the glass transition the translational diffusion was recognized to change more weakly with decreasing temperature than does the viscosity or molecular dipole reorientations (s = 0.72).[32] We assume that the decoupling between η-D and τ_α-D is independent of pressure. In the

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supercooled liquid regime, this cannot be experimentally validated so far. However, for some simple liquids (except water) there are no signs of the breakdown of the SE relation on increased pressure.[30,31]

At this point, we wish to note that it is not completely recognized whether the formation of crystal involves rearrangement of molecules of the reorientational or translational character. At very high temperatures this is probably less important, as η and D (similarly τ_α-D) dependences follow each other. On the other hand, in the supercooled liquid regime the temperature dependences of both quantities start to deviate from each other. As a matter of fact, selected in this study crystallization isochrones are located in the temperature range where decoupling between τ_α-D might potentially occur (at least at atmospheric pressure). In such a case, identifying whether the overall crystallization rate k correlates better with the translational, or either reorientational movements is essential for providing an adequate description of the kinetic barrier of the crystallization process.

In Figure 2 we present a qualitative test of the relationship between τ_α-k and D-k based on the atmospheric pressure data

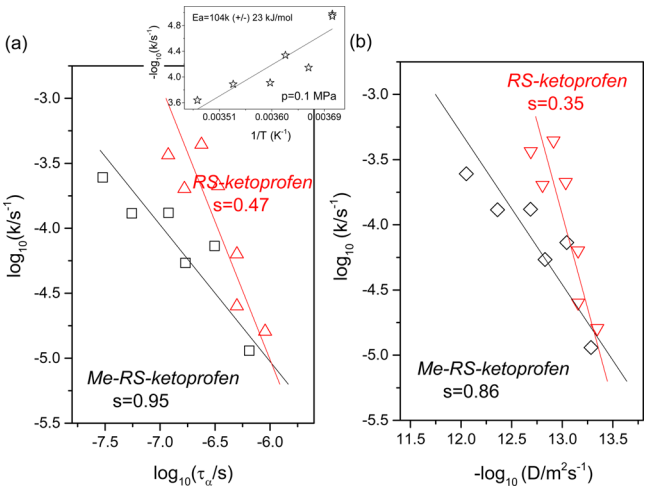

Figure 2. Overall crystallization rate k for Me-*RS*-ketoprofen and *RS*-ketoprofen plotted as a function of the α-relaxation time (a) and the self-diffusion coefficient D (b). Data refer to atmospheric pressure conditions. The inset shows temperature dependence of the overall crystallization constant rate as determined for Me-*RS*-ketoprofen. The solid line is the fit the Arrhenius equation. Crystallization data cover the same range of temperatures as the dielectric relaxation and NMR studies.

available for both investigated samples. The temperature dependences of τ_α and D were taken from our recent paper,[32] whereas the overall crystallization constant rate k measured at 0.1 MPa was obtained from this work. The inset in Figure 2a shows the evolution of k with temperature for supercooled Me-*RS*-ketoprofen. Herein, we wish to note that the choice of the experimental technique used to probe the isothermal crystallization kinetics does not have a significant impact on the activation barrier of the crystallization process.[33] As can be seen in Figure 2a,b, in the studied range of temperature plotting τ_α or D versus k on a log−log scale gives a straight line. If the considered observables are coupled to each other their temperature dependences should follow each other (slope $s = 1$). For Me-*RS*-ketoprofen, the cooperative reorientational motions, as described by α-relaxation dynamics, correlate almost perfectly with k ($s = 0.95$), whereas the translational self-diffusion coefficient changes slightly weaker with the temperature than the crystallization constant rate ($s = 0.86$). On the other hand, for *RS*-ketoprofen τ_α and D are loosely coupled to k. This might indicate a bit more complex crystallization mechanism, possibly because of the presence of the hydrogen bonds. While for both investigated samples we can expect a decoupling between translational diffusion and α-relaxation (or viscosity) in the supercooled liquid state,[32] the crystallization process seems to correlate to a greater extent with the reorientational dynamics rather than the translational motions. Therefore, if we wish to keep constant the kinetic term embedded in the overall crystallization rate, the choice of the isorelaxation time (isochronal conditions) seems to be more justified than the isodiffusive points. This explains why in the further part of this paper we have used the dielectric α-relaxation time as a measure of the molecular mobility related to the crystallization process.

For the methylated derivative of ketoprofen, the crystallization kinetics was investigated along isobar $p = 0.1$ MPa, isotherm $T = 304$ K and isochrone $\log_{10}(\tau_\alpha/s) = -5.7$. The selected relaxation time matches quite well the crystallization isochrone $\log_{10}(\tau_\alpha/s) = -6.0$ studied previously for *RS*-ketoprofen.[19] This enables us to explore the effect of changes in the intermolecular hydrogen bonds on the crystallization tendency of the investigated liquids. Using dielectric spectroscopy, isochronal conditions are recognized as having the same frequency of the α-loss maximum when changing the temperature and pressure. For Me-*RS*-ketoprofen we have considered the following set of (T, p) pairs with the same time scale of α-relaxation: ($T = 261$ K, $p = 10$ MPa), ($T = 281$ K, $p = 69$ MPa), ($T = 297$ K, $p = 160$ MPa), ($T = 309$ K, $p = 235$ MPa), ($T = 324$ K, $p = 345$ MPa). On the other hand, for isobaric (or isothermal) data the α-peak shifts with changing the temperature (or pressure). This means that while moving along isobaric or isothermal lines it is not possible to control the time scale of the molecular motions and hence the kinetic factor governing the crystallization process.

In Figure 3a, a typical evolution of the real ε' and imaginary ε'' parts of the complex dielectric permittivity ε^* upon a crystallization progress is presented. A systematic decrease of the dielectric strength of the α-relaxation with time signifies ongoing crystallization. By following these changes, we can analyze the kinetics of the crystallization progress at varying thermodynamics conditions. Crystallization on increased pressure was also monitored by using volumetric data, as seen in Figure 3b. At any given (T, p) condition, the specific volume of the studied sample decreases with time as the effect of the crystallization. In addition to that, the initial values of the specific volume for the liquid and crystalline phases drop off with increasing pressure due to densification. This is by approximately 3.5% and 1.5% for the liquid and crystalline phases, respectively.

To express changes in the dielectric and volumetric responses of the sample upon crystallization we have introduced the normalized quantities $Xc_N(t) = (Xc_{initial} - Xc(t))/(Xc_{initial} - Xc_{final})$, where Xc denotes the crystalline fraction. In the case of the volumetric data, Xc refers to the specific volume V_{sp}, while for dielectric data we have used the real part of the complex dielectric permittivity from the low-frequency range. The evolution of the normalized specific volume V_{sp_norm} with crystallization progress is shown in the inset in Figure 3b. The representative evolution of the

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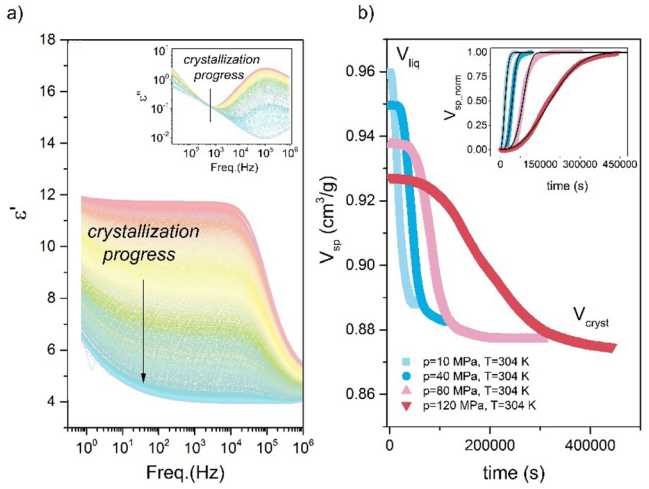

Figure 3. (a) Real part ε' of the complex dielectric permittivity ε^* measured as a function of the crystallization time at T = 324 K and p = 345 MPa for Me-*RS*-ketoprofen. The inset shows identical evolution of the imaginary part ε'' with the crystallization progress. (b) Changes in the specific volume V_{sp} for Me-*RS*-ketoprofen upon isothermal crystallization at pressures: 10 MPa, 40 MPa, 80 MPa, and 120 MPa. The inset shows evolution of the normalized specific volume, V_{sp_norm}, at T = 304 K. Solid lines denote Avrami fits.

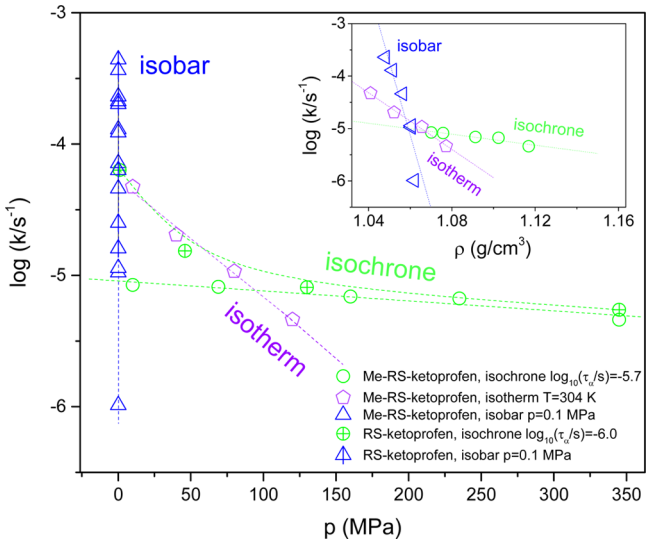

Figure 4. Crystallization rate k measured for (i) Me-*RS*-ketoprofen along isotherm (T = 304 K) and isochrone $\log_{10}(\tau_\alpha/s) = -5.7$ and (ii) *RS*-ketoprofen along isochrone $\log_{10}(\tau_\alpha/s) = -6.0$ plotted versus the corresponding pressures p. Isobaric data from 0.1 MPa were included as well. Isothermal data comes from volumetric studies, whereas isobaric and isochronal crystallization results from the dielectric relaxation measurements. Dashed lines show the trend and were drawn to guide the eye. Inset demonstrates variation of k as a function of the density ρ.

normalized dielectric permittivity ε'_N as a function of the crystallization time is shown in Supporting Information. For low-molecular glass-forming liquids, the degree of crystallinity calculated from dielectric and volumetric measurements are expected to be comparable. To determine the rate of crystallization along different isopaths the normalized quantities for each (T, p) condition were then fitted with the use of the Avrami equation, $Xc_N(t) = 1 - \exp(-kt^n)$.[34] Variation of the crystallization constant rate k for Me-*RS*-ketoprofen with pressure along various isolines is shown in Figure 4. It can be seen that each crystallization line spans in the two-dimensional $T-p$ space in a different way, signifying that the crystallization tendency of the studied liquids can be modified by choosing an adequate thermodynamic pathway. For example, a systematic slowing down of the crystallization is observed when lowering the temperature at a fixed pressure, or increasing pressure at a fixed temperature. However, by comparing the slopes of the isochronal, isobaric, and isothermal crystallization data it can be seen that the changes in the crystallization rate are the lowest when both thermodynamic variables T and p are changed to maintain the same time scale of the molecular motions. This finding is also evident when the crystallization rate is analyzed versus the density, as demonstrated in the inset in Figure 4. The density for *RS*-ketoprofen and Me-*RS*-ketoprofen at various thermodynamic conditions was determined from volumetric data. The specific volume measurements for investigated samples are attainable in the 295−430 K and 0.1−130 MPa range,[35] while crystallization data on increased pressure cover a much broader $T-p$ range. To calculate densities, PVT data were described with the use of the equation of state for supercooled liquids (see ref 35) and extrapolated to the range of temperature and pressure of the crystallization measurements.

As can be seen, the change of the liquid's density is definitely the most pronounced when moving along isochrone. Interestingly, this corresponds to its very slight effect on the crystallization tendency of the studied liquids. Therefore, keeping the same time scale of the molecular motions has indeed a great impact on the overall crystallization progress of the studied samples. Plotting isochronal data together with T-invariant and p-invariant crystallization data enable us to recognize this striking finding. Since the same effect was observed for *RS*-ketoprofen and its non-hydrogen bonded derivative, we conjecture that the differences in the hydrogen bonding propensity of the investigated samples have essentially no effect on their overall crystallization behavior at varying thermodynamic conditions.

Unfortunately, there is no general trend in the evolution of the Avrami parameter along different isopaths for both investigated samples. For *RS*-ketoprofen we have observed a decrease of the Avrami parameter with increasing temperature from 2.4 ± 0.3 at 314 K to 1.6 ± 0.2 at 331 K at atmospheric pressure. Meanwhile, for Me-*RS*-ketoprofen the Avrami parameter has turned out to fluctuate around 1.5 ± 0.2. For Me-*RS*-ketoprofen, we have observed increase of the Avrami parameter from 2.8 at 10 MPa up to 5.3 at 345 MPa along studied isochrone. On the other hand, for *RS*-ketoprofen it remains almost constant (2.4 ± 0.1). Along isotherm T = 304 K the Avrami parameter increases with increasing pressure from approximately 2 at 10 MPa to 4 at 80 MPa. At the highest pressure (120 MPa) the Avrami parameter suddenly drops to 2.5.

Isobaric and isothermal paths are the easiest to approach from the experimental point of view. This corresponds to numerous experimental studies on the high-pressure crystallization of glass-forming materials.[36−38] However, from such isolines it is not possible to obtain any relevant information regarding the kinetic and thermodynamic factors governing the crystallization progress. Therefore, when considering crystallization behavior of the glass-forming liquids, the phase space should be also supplemented by the paths along which the kinetic (or thermodynamic) driving force toward crystallization

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remains invariant. This gives an exceptional opportunity to see what is the actual effect of one factor, when the other one is being fixed. Controlling the time scale of the molecular motions along an isochrone implies that the changes in the crystallization rate reported for investigated liquids can be exclusively assigned to the variation of the thermodynamic factor. Therefore, in the next step of this study we have analyzed the behavior of the thermodynamic driving force toward crystallization along all considered isolines. Thermodynamic driving force toward crystallization is typically discussed in terms of the difference in the chemical potential of the liquid and crystalline phases, $\Delta\mu$. We have defined it in the following way[18]

$$\Delta\mu(T, p) = -\int_{T_m(0)}^{T} \Delta S(T, p)\, dT + \int_{p_0}^{p} \Delta V(T_m(0), p)\, dp \quad (1)$$

where ΔS is the difference in the entropy of the liquid and crystalline phases at (T, p), while ΔV is the difference in the specific volume of the liquid and crystalline phases at $(T_m(0), p)$. Parameters p_0 and $T_m(0)$ are atmospheric pressure (0.1 MPa) and melting temperatures of the investigated samples at 0.1 MPa, respectively. Equation 1 implies that ΔS and ΔV are expected to be temperature- and pressure-dependent.

Here, we wish to note that for spherical nuclei $\Delta\mu$ is directly related to the thermodynamic barrier for nucleation $W^* = \frac{16\pi V_m^2 \sigma^3}{3\Delta\mu^2}$ where σ is the surface energy and V_m the molar volume of the crystallizing phase. The difference in the chemical potential between the liquid and crystal phases $\Delta\mu$ can be also explicitly used to define the thermodynamic barrier to crystal growth ΔG.

In contrast to dielectric relaxation time, $\Delta\mu$ cannot be measured directly. It can be only estimated based on some assumptions that require specific heat capacity and volumetric data. For example, the difference in the entropy of the liquid and crystalline phases at various thermodynamic conditions is estimated using the heat capacity data, whose pressure dependence is calculated from the Maxwell's thermodynamic relations. In addition, to estimate the Kauzmann temperature T_K on increased pressure the Vogel temperature T_0 parameter from the isobaric VFT fits was used. Such a procedure of calculating configurational entropy values at various thermodynamic conditions has been also applied by us in some previous studies. However, $\Delta\mu$ (T, p) dependences given in this paper can be treated only as an approximation of the most possible trend, rather than the precise values at given (T, p) conditions. In Supporting Information, we describe a procedure allowing us to estimate the magnitude of $\Delta\mu$ on increased pressure. Changes of $\Delta\mu(T, p)$ along considered isolines are presented in Figure 5. The thermodynamic driving force toward crystallization increases with (i) decreasing temperature at constant pressure and (ii) increasing pressure at fixed temperature. This rationalizes numerous experimental evidence that the pressure favors crystallization progress, as also expected based on the classical theory of nucleation and crystal growth. However, it is remarkable that $\Delta\mu$ changes only very little with increasing pressure/density along an isochrone. This surprising finding indicates that both fundamental factors governing the crystallization follow each other closely, even though only one of them is being experimentally controlled.

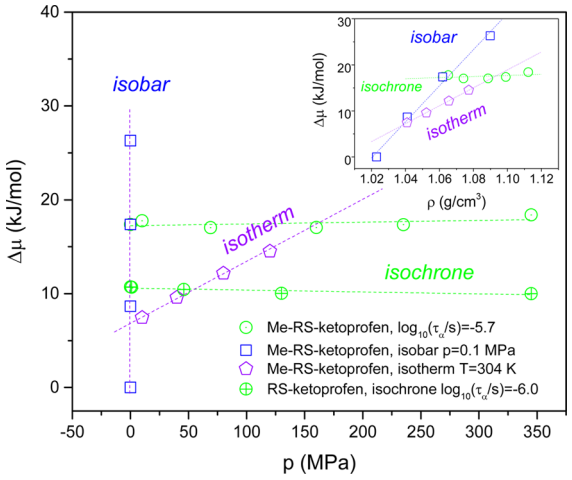

Figure 5. Evolution of the thermodynamic driving force toward crystallization for Me-*RS*-ketoprofen plotted as a function of pressure along different isobaric (0.1 MPa), isothermal (T = 304 K) and isochronal ($\log_{10}(\tau_\alpha/s)$ = −5.7) lines. Isochronal data for *RS*-ketoprofen are shown as well. Dashed lines are linear fits to the data. Inset demonstrates variation of $\Delta\mu$ as a function of the density along considered isolines.

In summary, this study has shown that the crystallization in supercooled liquids can be effectively tuned by moving along specific thermodynamic pathways in the two-dimensional phase space. By changing both temperature and pressure, one can favor or disfavor crystallization progress. However, only by recognizing isochronal state points in the $T-p$ phase diagram of a glass-forming liquids is it possible to keep the same time scale of the molecular movements related to the crystallization. This is immediately reflected in the crystallization behavior of studied samples showing a smaller variation of k with increasing pressure. In the case of the isochronal conditions, the crystallization tendency of the studied liquids seems to be also the least affected by the density change. Another remarkable result is the behavior of the thermodynamic driving force toward crystallization which remains nearly temperature and pressure invariant when τ_α is kept fixed at various thermodynamic conditions. Finding k and $\Delta\mu$ to change only very little when moving along isochrones is our original idea, so far not reported elsewhere. From a future perspective, our finding could be possibly rationalized better in terms of the isomorph theory which describes a specific case of simple liquids called Roskilde liquids. Isomorph theory predicts that for Roskilde simple liquids a number of structural and dynamic properties are invariant along so-called isomorphs,[39,40] which in practice coincide with the isochrones.[41] Though thermodynamics are not in general invariant along the isomorphs, the melting line is an approximate isomorph,[42,43] and it is possible that the difference in chemical potential between the solid and the liquid phase is also close to being constant along an isomorph. It is surprising in this context that we find no difference in the behavior between the van der Waals bonded liquid and the hydrogen-bonded liquid as isomorph theory is not expected to hold for the latter. Understanding some of these aspects in terms of the isomorph theory is still not fully established and requires more theoretical development. In any case, our finding that the thermodynamic driving force is constant when the time scale of the molecular movements is controlled suggests an intimate link between the dynamics and the thermodynamics of the supercooled liquid. Thus, the results

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of this study are of the vital importance for the understanding of crystallization phenomenon, dynamics of the supercooled liquid, and the glass formation.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.cgd.6b00798.

Description of the procedure allowing us to estimate the magnitude of the thermodynamic driving force toward crystallization on increased pressure, representative normalized dielectric permittivity ε'_N plotted versus crystallization time along isochrone $\log_{10}(\tau_\alpha/s) = -5.7$ (for Me-*RS*-ketoprofen) and $\log_{10}(\tau_\alpha/s) = -6$ (for *RS*-ketoprofen) (PDF)

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Notes

The authors declare no competing financial interest.

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