

Plastic and Glassy Crystal States of Caffeine

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The present paper focuses on the high temperature form I of caffeine and on its low temperature metastable form. Structural, dynamic, and kinetic information has been obtained by X-ray, dielectric, and calorimetric investigations. This study shows the following features: (1) The high temperature phase (I) of caffeine is in a state of dynamically orientationally disordered crystalline state (so-called “plastic, or rotator, phase”). (2) This high-symmetry hexagonal phase can be maintained at low temperature in a metastable situation. (3) Under deep undercooling of form I a glass transition occurs in the disordered crystalline state near room temperature. It is associated with the orientational freezing in of the molecular motions. Otherwise stated, the metastable state I enters into a nonergodic unstable state, so-called “glassy crystal” state. These findings rationalize the difficulties seen with caffeine in pharmaceutical science.

I. Introduction

Caffeine is an important agrochemical and therapeutic compound. However, the physical state of solid caffeine has resisted years of investigation in pharmaceutical science, which come up against the apparent impossibility to isolate phases of the compound which are crystallographically pure. This situation is the archetype of pharmaceutical challenges in solid-state drug processing with direct involvement in bioavailability. It requires a fundamental understanding of the stable and metastable states of the compound. The aim of the present paper is to gain insight into the physical understanding of the solid states of caffeine.

Caffeine is known either as an anhydrous or a hydrated form (there is no full agreement on the stoichiometry of the hydrated form^{1–3}). This latter form dehydrates easily at room temperature. We are here concerned with the anhydrous form. In 1980, Cesàro and Starec⁴ have shown that it undergoes a phase transformation at $T_i \approx 150$ °C (426 K) before melting at $T_m \approx 240$ °C (512 K). On the base of calorimetric measurements, it was suggested that the high temperature phase (called I in the following) is structurally disordered.

Sublimation of caffeine is easy above 170 °C. Sublimation energy and vapor pressure analysis at different temperatures allowed Griesser et al.⁵ to characterize the relative stability of the crystalline phases. It has also been shown⁶ that it is difficult to obtain crystallographically well identified low temperature “form II”.⁷ Depending on the preparation mode and history of the sample, it is found⁶ that a proportion of form I always seems to poison the room temperature form II in a rather unpredictable way. Evidence of the instability of the low temperature apparently mixed state has been shown by time-resolved microcalorimetry and X-ray diffraction.^{8,9} From these experiments it appears that below 150 °C the undercooled form I slowly converts to form II. The intermingled structural and

kinetic complexities have prevented any definitive crystal structure identification of the different forms. The structure of the high temperature form I has not already been solved. Several propositions of rhombohedral space groups have been made for this form I.¹⁰ It has been suggested that molecules in form I could be linked by very weak hydrogen bonds to form a crystallographic ordered array. Nevertheless, it has also been suspected that form I could be highly disordered.^{4,6} Nothing is still assessed about the static or dynamic nature of this possible disorder.

The crystallographic structure for the low temperature form of caffeine is also very confusing. The presence of some molecular disorder has been claimed for this form which could be only tentatively modeled assuming an extremely large cell with as large as 10 independent molecules in the asymmetric unit.¹¹ In a recent computer generation study Carlucci and Gavezzotti have proposed an energetically optimized ordered structure for caffeine.¹²

In the present paper, we mainly focus on the high temperature form I and its low temperature metastable situation in order to obtain structural and dynamic information. We also paid attention about the phase transformation kinetics through isothermal real time studies. This was achieved by coupling calorimetric, X-ray, and dielectric investigations. The latter technique is especially suitable since the molecule carries a sizable dipole moment. More generally it is hoped to gain some insight into the origin of the apparent phase complexity and instability of caffeine.

II. Experimental Details

Samples. Caffeine ($C_8H_{10}N_4O_2$) was purchased from Acros Organics. Before the experiments, commercial caffeine was purified by “cold sublimation”, i.e., caffeine was sublimated at 493 K and 10^{-3} Torr onto a coldfinger (at 285 K). For comparison, some experiments were also performed starting with the as received commercial samples.

Dielectric. Dielectric measurements were performed with a TA Instruments dielectric analyzer DEA 2970, which supplied more than 7 decades of frequency (1 mHz to 300 kHz). A liquid

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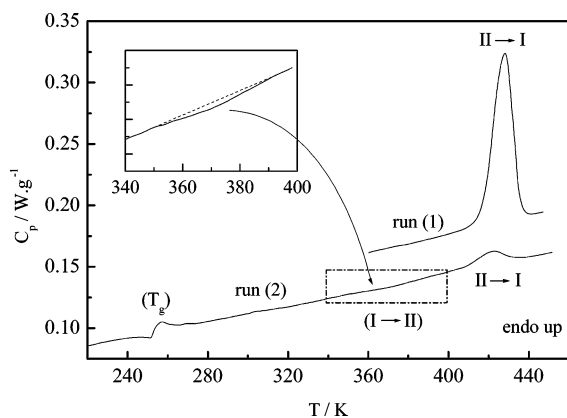


Figure 1. DSC scans obtained upon heating at 5 K min^{-1} . Run 1: Heating curve of form II from 353 to 453 K. Run 2: Heating curve measured after form I had been cooled to 220 K. The inset evidences a partial exothermic ($\text{I} \rightarrow \text{II}$) back-transformation.

nitrogen cooling accessory provided the testing capability from 120 to 700 K. Temperature control is performed within $\pm 0.01 \text{ K}$. A constant flow of nitrogen ($\sim 300 \text{ mL min}^{-1}$) was used to purge the measuring cell and to prevent water condensation on the measuring head and sample. The samples were prepared in parallel plate capacitor geometry. They were subjected to a constant compressive force (50 N) during the experiments, which ensured that the sensor maintained good contact with the sample. Samples were used in the form of a disk (25 mm of diameter and 2 mm of thickness) prepared by compressing $\sim 1.3 \text{ g}$ of caffeine form II under a pressing force of $\sim 50 \text{ kN}$. The value of the spacing between the top and bottom electrodes is known at each time of the experiment. This is important to get a proper estimate of the filling factor ($\theta = 0.95$ at room temperature). The analyzer calculates the real (ϵ') and imaginary part (ϵ'') of the dielectric function with an accuracy of 0.01. The complex dielectric permittivity was measured by both isochronal temperature ramps and isothermal scans. The isochronal measurements gave a general overview of the different relaxation processes, whereas isothermal scans yielded a more precise description of the relaxations.

X-ray Diffraction. The powder X-ray diffraction (XRD) experiments were performed with an Inel CPS 120 diffractometer ($\lambda_{\text{Cu K}\alpha} = 1.540 \text{ \AA}$) equipped with a 120° curved position sensitive detector coupled to a 4096 channel analyzer. Some experiments were also performed with a Phillips X-Pert Pro diffractometer. The samples were placed into Lindemann glass capillaries ($\phi = 7 \text{ mm}$).

Calorimetry. Thermal behavior was studied preliminary by means of differential scanning calorimetry with a Perkin-Elmer DSC7 calorimeter. Figure 1 (run 1) shows the heating curve of form II measured at a rate of 5 K min^{-1} from 353 to 453 K using a hermetic capsule completely filled with 16.8 mg of commercial caffeine. An endothermic peak with maximum at $T = 428 \text{ K}$ identifies the II to I phase transformation. The enthalpy of transition is 3.9 kJ mol^{-1} in agreement with previous measurements.^{4,13} The cooling curve measured after the conversion to form I does not show any noticeable exothermic peak which demonstrates the large supercooling ability of form I. Only a small anomaly can be detected near 256 K. On subsequent heating (run 2) this “anomaly”, which appears in the form of a heat capacity jump, is found again. It looks like the calorimetric glass transition signature found in the under-cooled situation of a liquid. An exothermic event follows around 360 K. The endothermic transition $\text{II} \rightarrow \text{I}$ is recognized around 420 K with an intensity depending of the time spent at lower

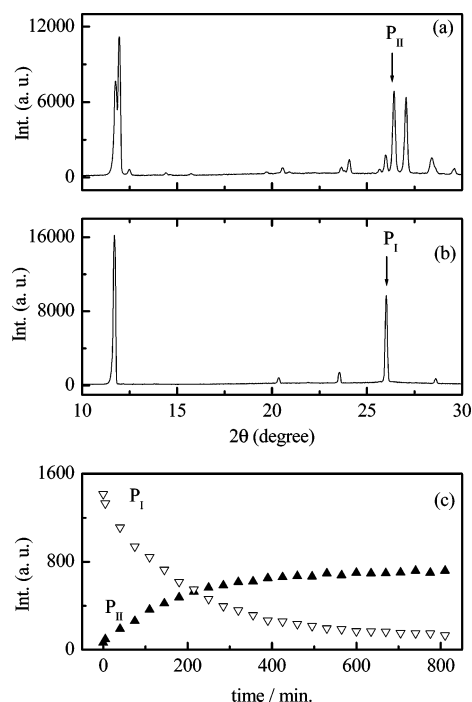


Figure 2. (a) X-ray diffraction patterns of caffeine powder at 290 K (form II) and (b) at 425 K (form I). (c) Isothermal time evolution ($T = 363 \text{ K}$) of the X-ray intensity of one characteristic peak of form I, P_I , and one of form II, P_{II} .

temperature. From this, it is concluded that the exotherm around 360 K locates the temperature range of slow back-transformation from the metastable form I toward the form II. A similar calorimetric behavior was obtained with the sublimated sample.

III. X-ray Diffraction Investigation

The structural changes associated with forms II and I are illustrated in the X-ray diffraction patterns from caffeine powder taken at different temperatures and different times (Figure 2). The powder pattern of the purified sample at 290 K is shown in Figure 2a. We note that the X-ray diffraction pattern of the as received commercial sample (“form II”) is analogous to that one shown here for the purified sample by “cold sublimation”. After heating above 425 K, the diffraction pattern of form I (Figure 2b) shows noticeable changes appearing mainly in a diminution of the number of peaks. This reveals an evolution to a phase of higher symmetry.

After quenching form I to 100 K the overall high temperature diffraction pattern remains unchanged (see Figure 3) as could be expected from the DSC results. Slight changes in the positions of the Bragg reflections and variation of their intensities only indicate a thermal contraction and the reduction of the molecular disorder on cooling. The pattern of the quenched phase was analyzed with the N-Treor program.¹⁴ It is consistent with a hexagonal setting description of the structure. The lattice parameters at 278 K are $a = 14.9372(5) \text{ \AA}$, $c = 6.8980(2) \text{ \AA}$, and the density $D_c = 1.452 \text{ g/cm}^3$ with six molecules per unit cell. The best space group estimated with the program CHEKCELL¹⁵ was found to be $R3c$. Further discussion about the crystallographic structure of the form I is done in another paper.¹⁶ At room temperature, it is known from pharmaceutical investigations⁸ that any evolution of the physical properties may only occur on extremely long periods of time—from weeks to years. To specify the optimal condition for investigating the metastable situation of form I, a search for rapid conversion kinetics was made at higher temperatures.

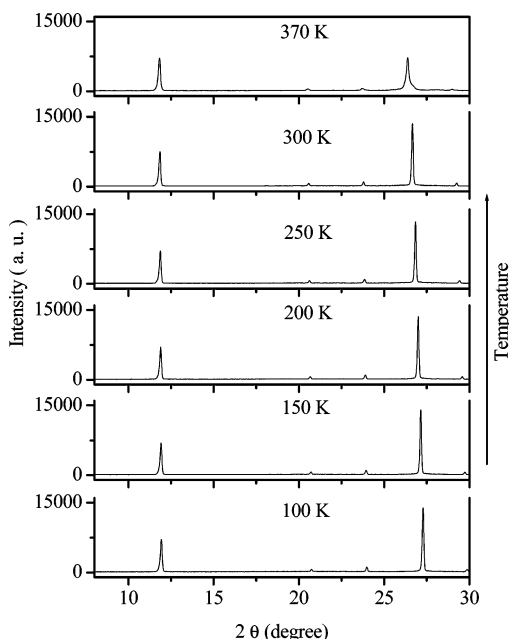


Figure 3. Temperature evolution of the X-ray diffraction pattern of the undercooled form I upon reheating from 100 up to 370 K. For clarity only some temperatures are shown.

Faster transformation from I to II was found near 363 K where we observe a slow recovery of the diffraction pattern of Figure 2a with a progressive splitting of the hexagonal peaks. Figure 2c shows the isothermal time evolution of one characteristic peak of each form (P_I characteristic of the hexagonal form I, and P_{II} characteristic of form II), after undercooling the form I at $T = 363$ K. This picture reveals slow, nonsigmoidal kinetics by which these peaks evolve in opposite way. It provides an idea of the very long time scale generally involved in the phase transformation process converting undercooled state I to form II. At this temperature, where the transformation is fastest, it is found that the conversion is not completed after 13 h. The considerable slowing down of the kinetics observed at lower temperature indicates that the thermodynamic driving force of the transformation $I \rightarrow II$ is certainly strongly counterbalanced by dynamics at low temperature. This situation makes it possible to follow the evolution of the different structural parameters of form I on a wide undercooling temperature range.

The evolution of the diffraction pattern of undercooled form I upon reheating from 100 up to 370 K is shown in Figure 3. The full recording process takes about 11 h (1 h per single pattern). This figure demonstrates that transformation to form II does not practically spoil the initial pattern during the whole reheating process. At 370 K, a gentle additional bump with very small intensity can only be detected in the foot of one of the main hexagonal reflection. This guarantees that the evolution of the pattern observed in the covered temperature range is to be ascribed to structural changes occurring in the undercooled hexagonal state I only. The data on the temperature variation of the structural parameters were obtained by fitting the position of the peaks on the hexagonal space group which matches the observed set of Bragg reflections. The resulting temperature evolution of the cell volume (log scale) of form I in its undercooled situation is depicted in Figure 4a. It is clear from this figure that a break in the temperature evolution of the cell volume occurs at about 253 K. The change of slope results in a step rise increment of the thermal expansion coefficient ($\alpha = (1/V)(\partial V/\partial T) = \partial \ln(V)/\partial T$) by about 40% at this temperature (Figure 4b). This step change of α does not accompany any

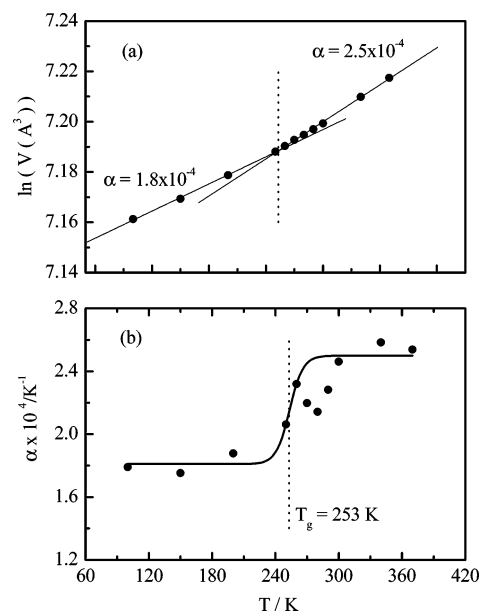


Figure 4. Temperature evolution: (a) cell volume, V (log scale), and (b) thermal expansion coefficient, α . The error bars are smaller than the dot size.

change of structure and rather suggests a rapid change in the degree of anharmonicity or molecular mobility amplitude, i.e. a glass transition. This is coherent with the interpretation proposed for the C_p jump found at the same temperature (Figure 1).

IV. Dielectric Relaxation Investigation

Dielectric relaxation is suitable to characterize the molecular mobility of a compound like caffeine whose molecule is asymmetric and carries a sizable permanent dipole moment ($\mu_D = 3.70$ D).¹⁷ We have characterized caffeine with this technique in the different states previously identified and explored with X-ray diffraction. Additionally, we have checked by X-ray diffraction that the compressing procedure used to obtain the disks for the dielectric measurements does not change the initial crystalline structure—form II—of caffeine. On the basis of X-ray diffraction studies, it is not possible to conclude about whether a molecular disorder has a static or dynamic origin. The investigation was first performed in isochronal mode in order to get global information on the dielectric signature of the detected transformations. Isothermal investigation is then achieved to get an insight into the kinetics of the transformation. This allows fixing the procedure for an accurate isothermal characterization of the dielectric response in the metastable domain of form I.

Overall Behavior. First, isochronal mode investigation was performed upon heating the purified sample form II (fully similar results were obtained with the as received commercial sample). Real and imaginary parts of the dielectric function $\epsilon_\omega(T) = \epsilon' - i\epsilon''$ are shown in Figure 5, parts a and b (solid lines), respectively, at three selected frequencies. A dispersion is observed in $\epsilon'_\omega(T)$ which increases from a low-temperature plateau value $\epsilon_\infty \sim 2.8$ to a higher temperature value. At the lowest frequency (1 Hz), a new plateau ascribable to a static value ϵ_s is nearly reached at 360 K. Correspondingly, the dielectric losses $\epsilon''_\omega(T)$ show clear dipolar peaks for which the maxima shift toward higher temperatures with increasing frequency (T^{peak} (1 Hz) ~ 318 K, T^{peak} (100 Hz) ~ 360 K, T^{peak} (1 kHz) ~ 420 K). This demonstrates that a thermally activated relaxation with low-frequency exists in form II of caffeine

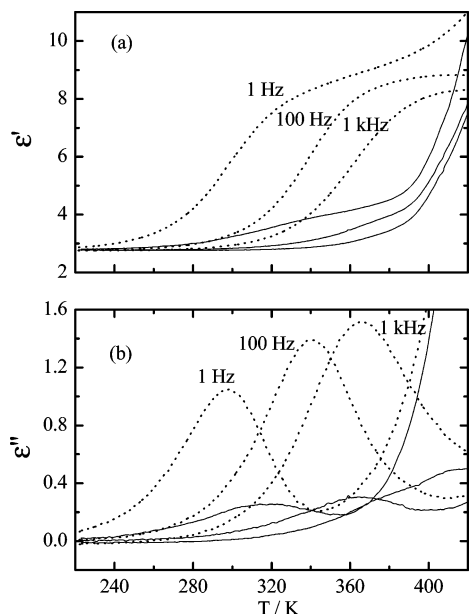


Figure 5. Temperature dependence of the real (a) and imaginary part (b) of dielectric function at fixed frequencies. Solid lines were obtained upon heating caffeine form II. Dotted lines were obtained upon cooling after an annealing at 423 K to obtain form I.

either coming from purification by cold sublimation or from a commercial sample. Approaching the calorimetric transition temperature ϵ' abruptly increases for all investigated frequencies. (At the lowest frequency (1 Hz) the conductivity even gives rise to a more pronounced effect.) In the temperature domain of form I and for the two highest frequencies, which are not contaminated by any conductivity effect, the same common value $\epsilon_s \sim 8.5$ is reached. After annealing form I (at 423 K), the sample has been cooled to 220 K. Figure 5 (dotted lines) shows the isochronal dielectric relaxation pattern of form I all along the undercooling process of this phase. The three selected frequencies are the same as that used for the above-described experiments on form II. We can check that the dielectric strength is much higher than in this latter case. This shows that a high degree of dynamic dipolar mobility has been gained crossing the $\text{II} \rightarrow \text{I}$ transition. This mobility is preserved in the undercooled situation. It can also be checked that in the cooling run the maxima in $\epsilon''_{\omega}(T)$ are shifted down by about 20 K with regard to the corresponding maxima recorded in form II upon heating. This is more than expected by the effect of just reversing the temperature sweeping rate in the exploration of the same dielectric relaxation pattern. Dielectric relaxations are thus observed to exist both in form II and I but on slightly different time scale.

Isothermal Measurements in the Equilibrium and Metastable Form I. To perform a more accurate investigation, isothermal measurements were carried above T_i and on a wide range of metastability of form I during the undercooling of the sample. Parts a and b of Figure 6 show the real and imaginary part of the isothermal dielectric function at several temperatures as well as the temperature evolution of the static dielectric constant (inset in Figure 6b). The strong dispersions seen in $\epsilon'(\omega)$ and the well-defined loss peaks of $\epsilon''(\omega)$ confirm the existence of relaxation motions of the molecular dipoles in form I which persist upon cooling below T_i . No indication of a decrease of ϵ_s is noticed when passing the transition temperature. As the temperature is decreased, one notes an important increase of the most probable value of the relaxation time τ_{\max} corresponding to the peak value of $\epsilon''(\omega)$ ($\tau_{\max} = 1/(2\pi\nu_{\max})$).

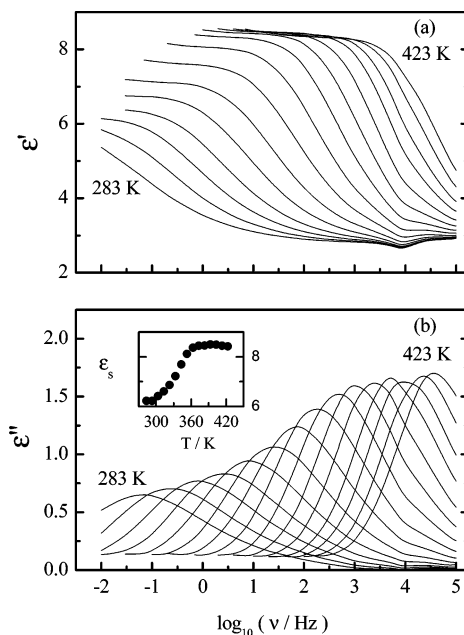


Figure 6. Real (a) and imaginary part (b) of the isothermal dielectric function of caffeine (form I) at the studied temperatures between 423 and 283 K (in steps of 10 K). The inset shows the corresponding temperature evolution of the static dielectric constant, ϵ_s . The error bars are smaller than the dot size.

Relaxation times as high as 1 s are reached at room temperature. The $\epsilon''(\omega)$ peak width is greater than the 1.14 frequency decade expected for an exponential Debye behavior. Because of the presence of a glass transition, in the following we try to fit the data using the phenomenological laws which describe results obtained on glass forming systems. Broadened dielectric data can usually be well fitted using the Havriliak–Negami (HN) equation¹⁸

$$\epsilon_{\text{HN}}^*(\omega) = \epsilon_{\infty} + \frac{\Delta\epsilon}{(1 + (i\omega\tau_{\text{HN}})^{\alpha})^{\gamma}} \quad (1)$$

where the parameters α and γ are related, respectively, to the low and high-frequency side of the relaxation peak and represent the dissymmetry of the peak. (The Debye behavior is recovered for $\alpha = \gamma = 1$). For caffeine, with decreasing temperature, we effectively observe such an asymmetric broadening of the relaxation peak. Below 363 K α decreases while γ increases. We find values $0.5 < \alpha < 0.85$ and $0.5 < \gamma < 0.73$. If we convert the frequency domain data into the time domain, the HN representation used is consistent with a stretched exponential relaxation function $\varphi(t) \sim \exp[-(t/\tau_{\text{WW}})^{\beta}]$.¹⁹ We find the value of the nonexponential coefficient $\beta \approx 0.5$ almost independent of the temperature. Such a low value of β reveals an effective important distribution of relaxation times. A plot of the most probable relaxation time of the distribution, $\log \tau_{\max}$ vs $1000/T$ (Figure 7), shows an almost perfect Arrhenius behavior. In the case of a molecule with a sizable dipole moment like caffeine, dipolar orientation plays the major role. The dielectric measurements thus reveal a dipolar rotation in form I that is surviving in the undercooled state but with relaxation times increasing strongly. The extrapolation of the plot gives the relaxation time of 100 s at $T = 260$ K. This is the usual way to locate the glass transition for an undercooled liquid.

The inset of Figure 6b displays the static values ϵ_s as a function of temperature. One may notice a very pronounced decrease during cooling. The height of the peak in $\epsilon''(\omega)$ shows

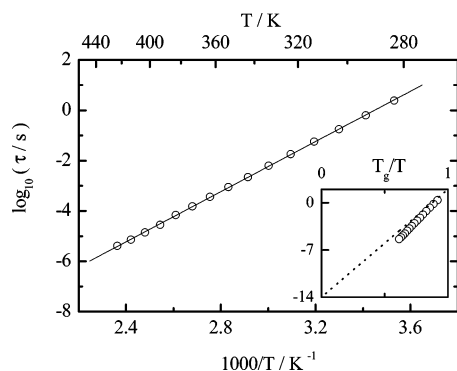


Figure 7. Temperature dependence of the average dielectric relaxation time as obtained from the frequency maximum of $\epsilon''(\omega)$. The solid line is the result of fitting the experimental data to the Arrhenius equation: preexponential factor $\tau_0 = (6.5 \pm 0.7) \times 10^{-18}$ s and activation energy $E_a = 95.4 \pm 0.4$ kJ mol $^{-1}$ (straight line correlation coefficient $R^2 = 0.9999$). The inset shows the deviations of the relaxation times from the maximal strong behavior (dotted line).

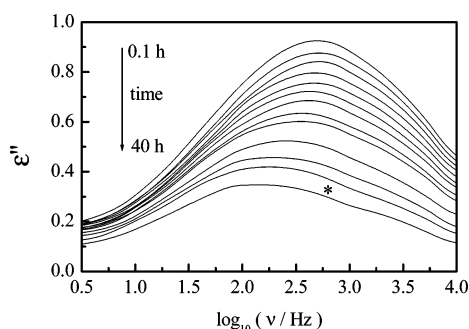


Figure 8. Time evolution of the imaginary part of the dielectric function during an isothermal transformation process ($T = 363$ K). The asterisk locates the shoulder in $\epsilon''(\omega)$, seemingly developing in the late stage of the annealing.

the same behavior. This decrease is more noticeable between 363 and 283 K. The decrease of the quasi-static permittivity with decreasing temperature is contrary to the $1/T$ behavior which is expected if correlations between dipoles are negligible (the situation is described by the value $g = 1$ in formula (2) below). Since the decrease occurs in the domain of metastability of form I we may wonder if it is not linked to a transformation mechanism toward the more stable form II and thus to a decrease of the fraction of molecules which contribute to the relaxation. To elucidate this point, the evolution of the dielectric spectrum has been followed isothermally during an annealing at 363 K where it was shown that kinetics are fastest. The isothermal time evolution of $\epsilon''(\omega)$ is shown in Figure 8. We observe a slow collapse of the peak which indicates that rotating dipoles are less and less contributing to the polarization as transformation toward II is progressing.

The time scales involved in the low temperature measurements and that involved in the cooling process are however considerably smaller than that of the kinetics of transformation. As a consequence the observed temperature decrease of ϵ_s cannot be ascribed to a conversion process but rather to an intrinsic dielectric property of metastable form I. This is confirmed by the fact that the more pronounced decrease of ϵ_s occurs in the temperature domain where the kinetics of conversion slows down enormously.

Some interesting information about the short-range organization of the dipoles can be drawn from the slope value of the $\epsilon_s(T)$ curve.²⁰ A positive slope indeed indicates that an external electric field increases the dipolar disorder. This may be understood if the dipoles tend toward antiparallel orientation

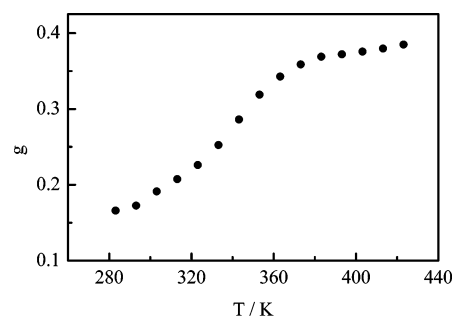


Figure 9. Temperature dependence of the Kirkwood correlation factor, g , as obtained from eq 2.

with decreasing temperature. Since ϵ_∞ is nearly independent of temperature, the relaxation strength $\Delta\epsilon = \epsilon_s - \epsilon_\infty$ is clearly decreasing when the temperature decreases. Intermolecular correlation effect on the dielectric strength is taken in the Kirkwood correlation factor g :²¹

$$\epsilon_s - \epsilon_\infty = \frac{\epsilon_s}{2\epsilon_s + \epsilon_\infty} \left(\frac{\epsilon_\infty + 2}{3} \right)^2 \left(\frac{N\mu^2}{V\epsilon_0 kT} \right) g \quad (2)$$

where N/V is the density of dipoles, k is the Boltzmann constant, and ϵ_0 is the dielectric permittivity of vacuum. For $g > 1$ ($g < 1$) we expect a ferroelectric (antiferroelectric) tendency in the short-range organization of dipoles. The dielectric measurements were carried on compressed powder samples. A proper estimate of g thus needs an evaluation of the filling factor at each temperature in order to get a correct density of dipoles. This is made possible due to the capability of the instrument to provide the thickness of the sample and thus of its volume at each temperature. This way to evaluate the density has been found correct by confrontation to the theoretical density value deduced from X-ray diffraction measurements. Figure 9 thus shows the temperature evolution of g deduced from that of ϵ_s . It reveals a remarkable increasing tendency toward antiparallel orientation between the dipoles of neighboring molecules when temperature decreases.

V. Discussion

High-Temperature Rotator State. The points which have to be considered in order to interpret the experimental results on caffeine (X-ray diffraction and Dielectric Relaxation) are the following:

- The caffeine molecule has a low symmetry while the crystalline class of form I has a hexagonal high symmetry.
- The low symmetry molecule carries a permanent electric dipole moment ($\mu_D = 3.70$ D¹⁷), and a prominent dielectric relaxation is observed in form I.

To obtain full hexagonal symmetry a random distribution of molecules between equivalent orientations around the hexagonal c axis must be assumed. Our results demonstrate furthermore that this disorder is dynamic in nature. These results can be reasonably associated with a dynamical rotation of the caffeine molecules in form I. The rotation allows accommodating the low molecular symmetry to the high symmetry of the site. Since the molecule is sterically flat and the crystallographic structure hexagonal, it is reasonable to assume that the rotation of molecules occurs axially around the c direction of the hexagonal cell. The best found space group $R3c$ generates 18 positions. Since there are six molecules in the hexagonal cell, we may temporarily accept the picture by which each molecule on its site can jump randomly among three preferred orientations. The orientations of dipoles in the lattice have no long range order.

The determination of the structure is in progress and will be described in a next paper.¹⁶ Caffeine belongs to the family of the so-called “plastic crystals”.²² These are usually crystals of nearly spherical molecules which become rotationally disordered below the melting point, while the translational order is retained. This is the situation found for CH₄, adamantane, C₆₀, In these compounds there is a first order transition from an ordered crystalline phase to a disordered crystalline phase in which the molecules rotate rapidly around their center of mass. Usually the high-temperature crystalline phase has higher symmetry than the low-temperature phase. Often the high temperature phase is of cubic symmetry when globular molecules are involved. When molecules are sterically flat, like for benzene derivatives, only axial rotations are unlocked and the rotator phase is hexagonal. This is the situation effectively found for caffeine. The exact nature of the molecular motions in the plastic phase of caffeine will deserve further study as well as the phase transition which are certainly influenced by the translation–rotation coupling.²³

Metastability and Orientational Glassy State of Caffeine.

An undercooling ability such that found for caffeine is common with plastic crystals. Upon undercooling, the kinetics of transformation from I to form II have their maximum rate at about 360 K. Below this temperature kinetics become extremely slow and form I of caffeine can be safely undercooled. The slow dynamics of molecular motions are certainly one of the major motives for the general slowness of the kinetics at low temperature. At a higher temperature, close to the transition, the temperature evolution of the thermodynamic driving force usually controls the kinetics. The specificities of this thermodynamic driving force are determined by the nature of the phase transition and also by that of the ultimate stable state below T_i . Some information can be captured in the specificity of the kinetic law itself. It must be noticed that the kinetics (see Figure 2c) are monotonic in time. They are thus fundamentally different from the sigmoidal Avrami law which is expected in an isothermal nucleation-and-growth process. The situation rather looks similar to that of a nucleation mechanism without growth. This is however difficult to conciliate with the fact that the growing Bragg diffraction peaks do not appear really broad as they should be if nanocrystals were involved. Further analysis of the kinetics could probably help understanding the true nature of the phase transition between II and I. Caffeine offers an interesting new possibility to study the “orientational crystallization”²⁴ on time scales accessible to X-ray diffraction.

The temperature range of the most rapid transformation being bypassed, the undercooled form I can be investigated in detail. The results show that the dynamic orientational disorder of the caffeine dipoles persists on temperatures far below the II → I transition. The dipoles undergo increasing slower reorientational motions about their lattice site. The symmetry of the latter however remains perfectly hexagonal. At room temperature the average dipolar relaxation time is of about 1 s. Upon further cooling, the reorientation time rapidly becomes comparable with the laboratory experimental time scale. A glasslike transition is finally reached at $T_g \approx 260$ K when relaxation times are of a few hundreds of seconds. The signatures of this glass transition are the jumps in heat capacity shown in Figure 1 and in expansivity shown in Figure 4. Such jumps are also observed for conventional glass-forming liquids. Below T_g the large configurational motions associated with dipolar rotations are effectively frozen out. The contribution of these degrees of freedom to the expansivity effectively disappears. There only remains the usual vibrational anharmonicity contributing to the

expansivity of crystals. At T_g , supercooled plastic caffeine thus enters the so-called “glassy crystal”^{25–27} state as named by Suga and co-workers. Cyclohexanol,²⁸ ethanol,^{29,30} and cyano-adamantane^{31,32} crystals are prominent examples of the situation by which the freezing phenomenon, which is typical of glasses, occurs in an orientationally disordered crystal.

Glass forming systems are usually classified according to the degree of non-Arrhenius behavior of their dynamics.³³ This is rationalized in the Angell fragility index defined as

$$m = \frac{d(\log_{10}(\tau))}{d(T_g/T)} \bigg|_{T=T_g} \quad (3)$$

In caffeine, we find $m = 19$ (see Figure 7 inset). This value is close to the strong limit ($m = 16$). Such a strong character is shared by almost all glassy crystals. In conventional glass formers, a correlation has been found between the value of m and that of the nonexponential coefficient β .³⁴ It is usually expected that a high value of m corresponds to a low value of β . Such a correlation can be understood as resulting from an increasing intermolecular coupling and cooperativity,³⁵ which is more pronounced in the fragile glass formers. Such a correlation is however currently found to be violated in supercooled plastic crystals for unknown reason.³⁶ Since β is as low as 0.5, caffeine is found to comply with this behavior of plastic crystals. A very interesting feature shown by caffeine which could lead to resolve this violation is the strongly pronounced antiferroelectric local organization of dipoles found when temperature is reaching T_g . This behavior is shared with cyanoadamantane glassy crystal state.³¹

Toward an Understanding of the Equilibrated Room Temperature State. Looking closely at Figure 8, we may notice that the relaxation peak does not totally disappear even after a 40 h annealing at 363 K. The situation which is reached looks similar to that shown in Figure 5 for form II. Obviously form II does not comprise complete orientational order of the dipoles, and the disorder is also dynamic in nature. To explain this feature, we may expect either that the physical state, which is reached at a long time, is a mixed state of untransformed disordered form I and ordered form II or that the dynamical disorder is an intrinsic property of the low temperature form II. In the latter case, we would have to presume a structural restriction of the reorientational molecular motions in form II with regard to that occurring in form I. This is necessary to explain the lower value found for the dielectric strength. Upon annealing, we may also notice in Figure 8 a 1 decade shifting toward lower frequency in the positioning of the maximum of $\epsilon''(\omega)$. In the end a slight structuration in the peak profile may also be observed in the form of a shoulder on the high frequency side. This may be an indication that some dynamic disorder is proper to form II, with a time scale slightly larger than that of metastable form I at the same temperature. Closer inspection of this problem is needed to accede a full understanding of solid-state caffeine.

Conclusion

Calorimetric, dielectric, and X-ray diffraction analyses of the phase transformations in caffeine have shown the following:

(1) The high temperature phase I of caffeine is in a state of dynamically orientationally disordered crystalline state (the so-called “plastic, or rotator, phase”).

(2) The dynamical disorder is compatible with a high symmetry–hexagonal–crystallographic structure. This disordered state can be maintained at low temperature in an

undercooled metastable situation. At room temperature the frequency associated with molecular reorientations slows down to about 1 Hz.

(3) Under deep undercooling of form I, a glass transition occurs in the disordered crystalline state at a temperature not far below the room temperature. It is associated with the orientational freezing in of the molecular motions. Otherwise stated, the metastable state I enters into a nonergodic unstable state, the so-called “glassy crystal” state. The calorimetric glass transition is observed through both heat capacity and expansivity jumps at temperature where the dielectric relaxation time is about 100s.

This study further suggests that the low temperature form II is also dynamically disordered. With regard to phase I, the dielectric strength is significantly smaller, while the characteristic frequency is shifted down about one decade. An (not yet observed but theoretically predicted¹²) ultimately stable ordered phase in caffeine, differing from form II, can thus be expected.

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