

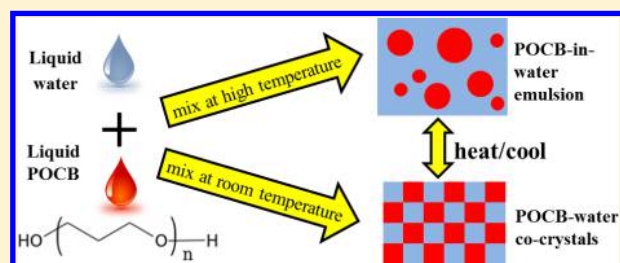
Liquids That Freeze When Mixed: Cocrystallization and Liquid–Liquid Equilibrium in Polyoxacyclobutane–Water Mixtures

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Supporting Information

ABSTRACT: We show that liquid polyoxacyclobutane $-\text{[CH}_2\text{-CH}_2\text{-CH}_2\text{-O]}_n\text{-}$ when mixed with water at room temperature precipitates solid cocrystals of the polymer and water. Cocrystals can also be formed by simply exposing the liquid polymer to saturated humidity. This appears to be the only known example of nonreacting liquids combining to form a solid cocrystal, also known as a clathrate, at room temperature. At high temperatures, the same polymer–water mixtures phase separate into two coexisting liquid phases. This combination of cocrystal formation and LCST-type liquid–liquid equilibrium gives rise to an unusual, possibly unique, type of phase diagram.



1. INTRODUCTION

Polyoxacyclobutane (POCB), repeat unit $-\text{[CH}_2\text{CH}_2\text{CH}_2\text{O]}_n\text{-}$, is an unusual polymer. Of the polyoxyalkene series $-\text{[(CH}_2\text{)}_m\text{O]}_n\text{-}$ as m is varied, PO CB with $m = 3$ has the lowest melting point, lowest enthalpy of melting, and smallest size of random chains (i.e., smallest r_0/\sqrt{M} ratio where M is molecular weight).^{1–3} The size of PO CB chains in theta solvents is also nearly independent of temperature.¹ Many of these characteristics have been attributed to the fact that PO CB has two backbone bonds that prefer the *trans*-rotational conformation and two that prefer the *gauche* conformation.¹ Perhaps the most unusual aspect of PO CB is that it can combine with water to form a crystalline hydrate.^{3–8} Formally such cocrystals form from two distinct molecules are known as clathrates. Only a few polymers (notably syndiotactic polystyrene and poly(ethylene oxide)) can form clathrates,^{9–18} and only two—POCB and linear polyethylenimine—are known to form clathrates with water.^{9,10} Here we show that PO CB of low molecular weight displays even more unusual behavior: its mixtures with water show a rare, and possibly unique, type of phase diagram that combines cocrystallization with liquid–liquid equilibrium (LLE).

Research on PO CB has been in progress for decades, but different researchers have used different names for the same polymer: polyoxacyclobutane, polytrimethylene oxide (or glycol), polyoxetane, and poly(1,3-propanediol). Incidentally we note that the term “poly(propylene oxide)” (or glycol) is generally reserved for the polymer with the repeat unit $-\text{[CH}_2\text{CH}(\text{CH}_3)\text{O]}_n\text{-}$, which is entirely different from PO CB. The earliest research on PO CB was initiated in the late 1960s as a part of fundamental studies of semicrystalline

polymers.^{3–8} In most of those and later studies,^{1,2,19–22} PO CB was prepared by ring-opening polymerization of oxacyclobutane (also known as oxetane) and had molecular weights ranging from several thousand to over 10^5 g/mol. More recently (~ 2007), DuPont commercialized much lower molecular weight grades of PO CB, prepared by condensation polymerization of 1,3-propanediol.^{23–26} Since the 1,3-propanediol was obtained from cereal (corn), this product was given the brand name Cerenol. The chief application was as a soft segment of multiblock copolymer elastomers, and hence the grades available had modest molecular weight (300–5000 g/mol) with hydroxyl end groups. The polymer used in the current paper is such a DuPont material with a nominal molecular weight of 650 g/mol, henceforth denoted PO CB650.

Three crystal forms of PO CB were discovered in early research⁵ and one more later.²⁷ Forms II, III, and IV were all crystals of pure PO CB. Form I, which is most relevant to this paper, appeared only in the presence of water and was found to be a hydrate^{3,7} with one water molecule per monomer. At this 1:1 monomer:water ratio, the PO CB:water weight proportion is 58:18 (i.e., 1:0.31), and hence the crystal has 23.6 wt % water. The unit cell⁷ was shown to have the PO CB chain in a planar, all-*trans* backbone with the water molecules located along channels so that they hydrogen-bond with the ether oxygen of PO CB as well as with neighboring water molecules. The unit cell⁷ has been reproduced in Figure S1 for convenience. All of this early research on crystallization was conducted using PO CB of molecular weights exceeding 10 000 g/mol. These

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relatively high molecular weight polymers, which were solid at room temperature, were heated until molten and then combined with liquid water to induce hydrate crystallization.

Separately, Lee et al.²⁸ examined the phase behavior of water–POCB mixtures at a much lower molecular weight. The experiments used a hydroxyl-terminated PO CB of mean molecular weight 300 g/mol, which corresponds to only about 5 repeat units per chain. The polymer, which is liquid at room temperature, is partially miscible with water. The cloud point data (reproduced in Figure 3) show indications of both a lower and an upper consolute solution temperature (LCST and UCST) although the temperature range was not sufficiently wide to identify either. LCST behavior is common among polymer–solvent or polymer–polymer mixtures, and indeed the immediate neighbor of PO CB, poly(ethylene oxide), is well-known to show an LCST (as well as a UCST) with water.^{29,30} The article by Lee et al.²⁸ did not mention the formation of PO CB hydrate crystals. However, our own experiments with the same grade of material show that it can also crystallize to form hydrates when mixed with water, but only if cooled below room temperature.

These two behaviors have been investigated at the two extremes of molecular weight: crystalline hydrate formation has been noted only in high molecular weight PO CB, whereas liquid–liquid equilibrium only in a low molecular weight (300 g/mol) oligomer of PO CB. Here we show that these two kinds of behavior can combine to produce a phase diagram that is to our knowledge, altogether unique.

2. RESULTS

Most of the experiments used the polymer DuPont Cerenol grade H650, with a nominal molecular weight of 650 g/mol. All the experiments in sections 2.1–2.3 use this material. Section 2.4 compares this material with two other molecular weights: 300 g/mol (data from Lee et al.²⁸ measured using DuPont Cerenol H250) and 2480 g/mol (our own data). All these materials are liquid at room temperature. All the materials used here, and although the polydispersity does not affect the qualitative results of this paper, it is expected to affect the various phase transitions quantitatively, as discussed in section 2.5.

The chief goal of this paper is to explore the coupling between LLE and cocrystallization in PO CB–water mixtures. The existence of a crystal hydrate itself is not a new finding.^{3,7} Yet, we conducted limited experiments to verify that the solid phase formed by mixing PO CB and water is indeed a cocrystal. Figures 1a,b show optical images of the solid phase formed by placing a drop of PO CB + water onto a microscope slide. The birefringent spherulitic structure is a strong indicator that crystals are actually formed. Figure 1c compares the wide-angle X-ray scattering patterns of a 1:0.31 mixture of PO CB:water vs the dry PO CB crystals. These scattering patterns establish beyond doubt both that the PO CB hydrate is actually a crystalline structure and that the structure of the hydrate is different from that of the pure PO CB crystal.

2.1. Phase Behavior of PO CB650–Water Mixtures. The phase diagram for mixtures of PO CB650 and water is shown in Figure 2. Three phases can be identified for the PO CB650–water mixtures: L_p and L_w , the polymer-rich and water-rich liquid phases respectively, and S_c is the solid crystal hydrate mentioned above. The crystal hydrate is indicated by a solid vertical line drawn at 23.6% water, and it melts at 37 °C. Several two-phase regions can be identified experimentally. Further-

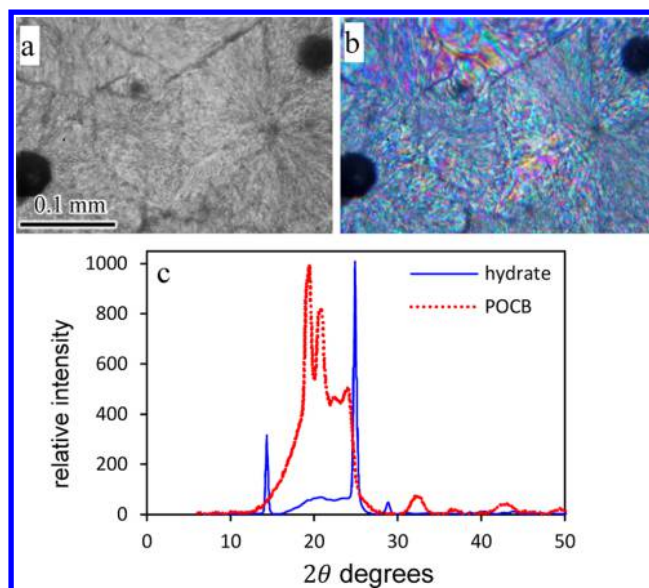


Figure 1. Appearance of the solid phase when a drop of PO CB + water mixture was cooled on a glass slide under (a) bright field and (b) polarization showing birefringence. (c) Wide-angle X-ray diffraction patterns of pure PO CB and PO CB hydrate measured at 2 °C (Cu K α radiation of 0.154 nm wavelength).

more, the lower two schematic graphs in Figure 2 show additional two-phase regions whose existence is expected on thermodynamic grounds although we have not attempted to prepare samples in these regions.

Pure Species. Figure 2 notes the melting points of the pure species as 0 °C for water and 14 °C for pure PO CB650 in the absence of water. The latter was measured by cooling dry PO CB650 in a refrigerator to 1–5 °C and then reheating slowly in a water bath. Crystallization studies of water-free PO CB of much higher molecular weight^{20–22} suggest an equilibrium melting temperature of roughly 50 °C, which is the same as the value quoted in the *Polymer Handbook*.³¹ The much lower melting temperature noted here is likely due to the low molecular weight of the material of Figure 2.

LLE Behavior. PO CB650–water mixtures show a miscibility gap with coexistence between the L_p and L_w phases. The LLE coexistence curve can be divided into two regions depending on whether the LLE is stable or metastable.

For $T > 37$ °C, i.e., above the hydrate melting temperature, LLE is thermodynamically stable. The polymer-rich boundary of the LLE region, i.e., the boundary of the single-phase L_p region, was quantified by cloud point measurements. Its negative slope in Figure 2 suggests a LCST at lower temperatures. The water-rich boundary of the LLE, i.e., the boundary of the single phase L_w region was not quantified because it is very nearly pure water. Specifically, mixtures with a PO CB650:water ratio of 1:99 were found to be two-phase liquids above 37 °C; i.e., the water-rich L_w phase contains less than 1% PO CB650.

For $T < 37$ °C, i.e., below the hydrate melting temperature, the LLE behavior is metastable. At water content exceeding ~35%, mixtures of PO CB and water cooled from above 37 °C to below 37 °C remain liquid for some time until they eventually crystallize. At temperatures not too far below 37 °C, crystallization is slow, and hence the boundary of the metastable LLE region can be mapped. However, at temperatures far below 37 °C, crystallization is rapid, making it

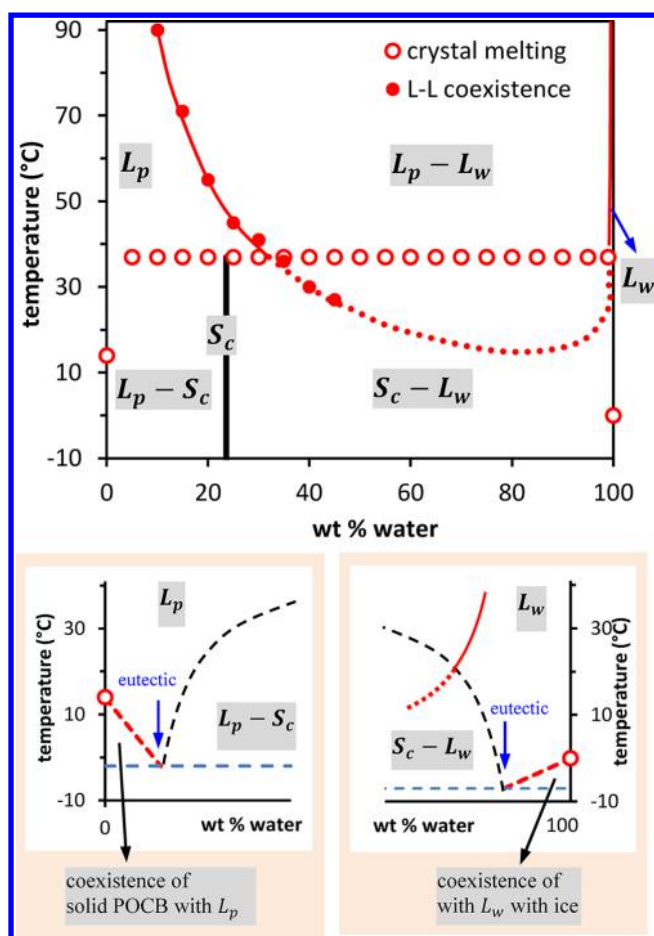


Figure 2. Phase diagram for PO CB650–water mixtures for PO CB of molecular weight 650 g/mol. Filled circles are experimental cloud points, and open circles denote melting points. The solid and dotted red lines indicate the stable and metastable portions of the LLE curve. The lower two graphs are schematics of the phase diagram at very low and very high water content. The dashed red lines indicate the boundaries of the homogeneous L_p and the L_w phases.

difficult to judge with confidence whether a mixture is cloudy due to suspended crystals or due to suspended drops. For this reason, we are not able to establish the composition and temperature of the LCST.

SLE Behavior. For $T < 37$ °C, which is below the hydrate melting temperature, almost the entire range of compositions is spanned by the two solid–liquid coexistence regions. On the right-hand side of Figure 2, crystallization occurs readily even at 0.1 wt % PO CB650 in water, i.e., the single-phase L_w region can exist only at extremely dilute polymer loadings. On the left-hand side of Figure 2, i.e., at dilute water loading, samples are single-phase immediately upon mixing, but they crystallize eventually. The crystallization kinetics can be slow, making it difficult to establish with confidence the “right boundary” of the single-phase L_p region. The lowest water loading examined here, mixtures with 5% water, showed hydrate crystallization, implying that achieving the homogeneous L_p phase requires less than 5% water.

The lower portion of Figure 2 shows the phase behavior expected theoretically at the extremes of the composition range. At the dilute–water extreme (lower left sketch in Figure 2), one expects melting point depression of the pure PO CB crystals, terminating in a eutectic, which is the lowest temperature at

which the L_p phase can exist. Similarly at the dilute-PO CB extreme (lower right sketch in Figure 2), one expects melting point depression of ice, also terminating in a eutectic. We have not attempted to quantify the temperature or composition of these eutectics since in the present case, they occur only when one species is very dilute. Nevertheless, Guenet¹⁰ cites several cases^{14–18} of polymer–solvent cocrystallization in which both eutectics are quantified. As illustration, we have reproduced (Figure S2) data from Point and Coutelier¹⁴ on mixtures of poly(ethylene oxide) (PEO) + *p*-dibromobenzene which also show analogous cocrystallization, along with eutectic behaviors.

Across this entire range of PO CB650:water ratios, the crystal melting temperature was found to be constant at 37 °C. The independence of melting temperature on composition is a signature of crystallization from an LLE state.^{32–34} Indeed, some of our samples did crystallize from the LLE state (discussed further in Figure 3); however, Figure 2 shows the melting temperature to be independent of composition even outside the LLE region. This absence of melting point depression at compositions far from the 23.6 wt % water corresponding to the S_c phase is puzzling.

Finally, we point out a remarkable feature: for PO CB650, the crystal hydrate has higher melting temperature than either of the two species, pure PO CB650 (14 °C) and water (0 °C). This behavior is extremely unusual. The example from Point and Coutelier¹⁴ reproduced in Figure S2 shows exactly such behavior, as do mixtures of PEO and urea.¹⁷ Even outside of polymeric systems, it is unusual for a cocrystal to melt at a temperature higher than both of its constituents. Some metal alloys, notably aluminum alloys³⁵ (e.g., Ni/Al³⁶ and Ti/Al³⁷), form intermetallic compounds with melting points exceeding the pure-species melting points. Furthermore, in Figure 2, the pure species melting points are below room temperature, whereas the hydrate melts at 37 °C. This unusual confluence of facts leads to a visually dramatic result: liquid PO CB650 and liquid water, when mixed in equal proportions at room temperature, rapidly turn in to an opaque nonflowing paste—a transformation that involves only a phase change and no chemical reaction.

We close this section by noting two ways in which the hydrate crystallization of PO CB650 likely differs from the more common crystallization of high molecular weight polymers. First, the determination of equilibrium melting temperatures of high molecular weight polymers can sometimes be fraught with uncertainty due to very slow crystallization kinetics at small undercooling, the wide range of melting temperatures due to the wide thickness distribution of crystalline lamellae, and the decrease of melting temperature with crystallization temperature. However, except at low water contents, for most of the compositions of Figure 2, a mixture of PO CB650 and water held at 36 °C shows clearly visible crystals within a few minutes to hours (depending on composition), whereas complete melting has been verified at 38 °C. Thus, we believe that 37 °C is very close to the equilibrium melting temperature of the hydrate crystals (however see comments on molecular weight effects and polydispersity section 2.5). This sharp melting behavior, with little or no hysteresis between melting and crystallization temperature, resembles the behavior of small molecule compounds rather than of polymers. Second, PO CB650 with a molecular weight of 650 g/mol has an average of only 11 monomers per chain. Past research on crystallization of small molecule alkanes,³⁸ poly(ethylene oxide),³⁹ or other polymers⁴⁰ suggests that at such short

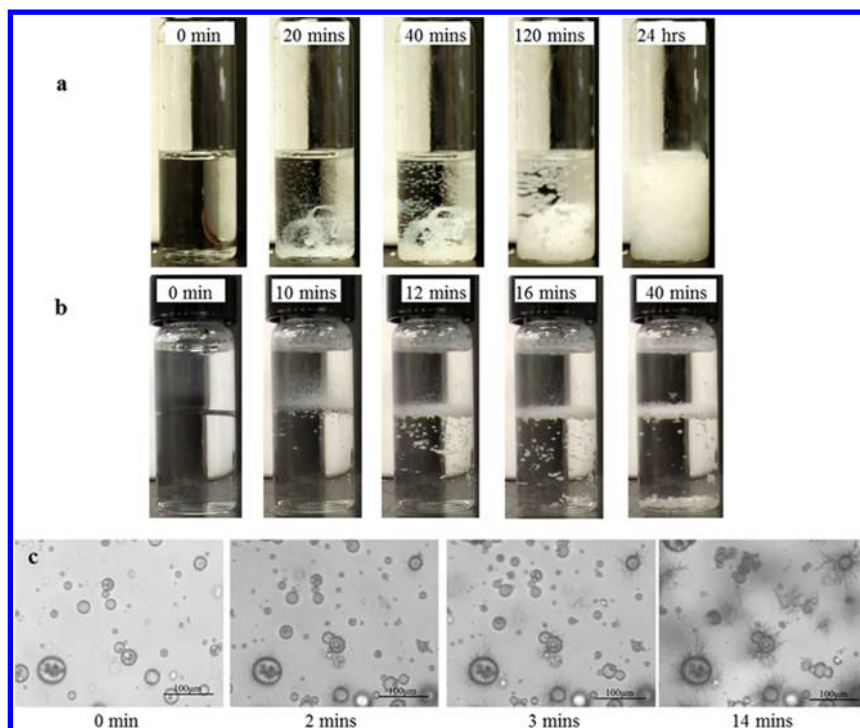


Figure 3. Crystallization process on mixtures of POCB and water at (a) 20% water, (b) 50% water, and (c) 99% water.

length the crystals have extended chain conformations rather than folded conformations. This may be a further reason for the sharp melting point.

2.2. Crystallization. Figure 2 is concerned with equilibrium phase behavior. We will now briefly discuss the crystallization process, which, owing to the unusual phase diagram, can be distinctly different from standard polymer crystallization. The phase diagram suggests three distinct regimes: crystallization from the single phase L_p solution, from a two-phase S_c-L_w region, and from single-phase L_w solution. Here we will discuss only the first two cases; the third is not accessible due to the exceedingly low polymer content necessary to reach the L_w phase. Figure 3a shows the sequence of crystallization for a mixture with a POCB:water ratio of 1:0.25 (i.e., 20 wt % water) from the single-phase L_p solution. The solution was preheated to 50 °C and then allowed to cool over several minutes to room temperature. Under these conditions, crystallization is slow; spherulites formed gradually with nucleation occurring primarily on the walls of the glass vial. Eventually the entire vial was found to crystallize. The chief conclusion then is that, qualitatively at least, the crystallization in the homogeneous L_p phase resembles standard polymer crystallization under quiescent conditions, although the kinetics may be slow.

The situation is quite different when crystallizing from two phase LLE conditions since the POCB:water ratio in the crystal is generally different from the POCB:water ratio of the individual liquid phases. Thus, as crystallization proceeds, the species must transfer from one phase to another, both to maintain LLE and to continue crystallization. The crystallization is therefore coupled to interfacial exchange of the species and hence must depend on the phase sizes or mixing conditions. This can be illustrated with two cases of quiescent crystallization that differ in the extent to which the two fluids separate macroscopically. Figure 3b corresponds to a mixture with a POCB:water weight ratio of 1:1. The mixture was shaken and allowed to separate into two layers at 50 °C, followed by

cooling to room temperature. Crystals appeared after a few minutes, mainly near the interface, but also some in the upper L_w phase and the lower L_p phase. Subsequent crystallization was primarily at the interface; however, large crystals were observed to sediment from the interface into the lower phase and accumulate on the bottom of the vial. We speculate that such interfacial growth is a consequence of mass transport limitations: since water can likely diffuse into the polymer-rich phase much faster than POCB650 can diffuse into the water-rich phase, crystallization occurs primarily in the polymer-rich phase near the interface. A secondary effect may be nucleation: Schaaf et al.,⁴¹ in their studies of polyethylene crystallization out of a two-phase liquid, suggested that the interface between the polymer-rich and solvent-rich phase may act as a nucleation site, and the same may be true here.

A somewhat different scenario was found for a mixture with a POCB:water ratio of 1:99 (Figure 3c). In this case, upon cooling to room temperature, the sample was composed of drops of the L_p phase suspended in the L_w phase. The vial was then tipped on its side and observed through an inverted optical microscope. Since the L_p drops were dilute, they remained well-separated and did not coalesce. Thermodynamically the situation is identical to Figure 3b; however, large-scale phase separation was avoided. The higher resolution of the optical microscope (compared to Figure 3b) makes individual crystallites visible. Dendritic crystallites were found to grow rapidly in the L_w phase *outside* the drops—surprising considering the very dilute concentration of polymer in the L_w phase. At later times, crystallization also occurs inside the L_p drops as evidenced by the transition from an initial perfectly spherical drop shape to a slightly distorted shape, simultaneously with a sharp change in the clarity of the drop. In Figure 3c, some dendritic crystals are also seen that are not attached to drops; we believe that these are crystals nucleated on the glass surface. The early crystal growth in the L_w phase outside the drops suggests that crystallization can proceed rapidly in the L_w

phase even though it is very dilute in POCB since the polymer can diffuse from the proximate interface.

2.3. Humidity-Induced Crystallization. Samples of POCB650 can also crystallize into hydrates simply by exposure to saturated humidity. Petri dishes with POCB650 were placed in a closed container at room temperature. The bottom of this container was covered with a pool of water to ensure an atmosphere saturated with water vapor. The dish was photographed daily to judge crystallization and also weighed to quantify water uptake. The images in Figure 4b show that

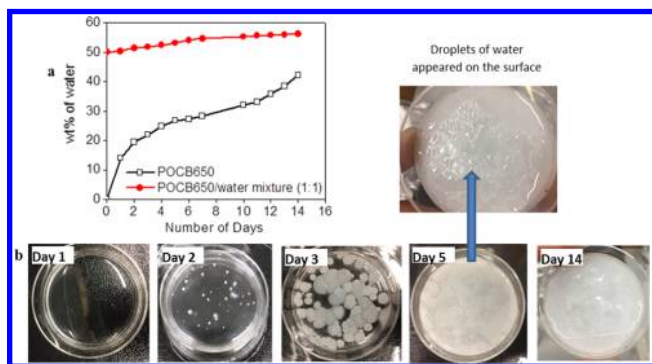


Figure 4. (a) Water uptake by pure POCB or by POCB/water mixture at 1:1 weight ratio when exposed to saturated humidity. (b) Change in appearance of samples with time.

crystallization initiates on day 2, and a spherulitic morphology develops until the sample appears fully crystallized. The corresponding weight measurements (open black squares in Figure 4a) suggest that water absorption clearly precedes crystallization. For instance, on day 2, the weight gain is already 15% water (based on the original POCB650 mass). If this water was completely used to form hydrate crystals (which have a POCB:water ratio of 1:0.31), 48% of the original POCB mass would have crystallized. This would lead to a total crystal mass fraction of 63.5% within the sample. Yet the corresponding image has only a few sparse crystallites, suggesting that most of the water is dissolved into the POCB and not yet crystallized. These observations suggest that as water absorbs into the sample, the crystallization rate remains low until the water fraction becomes 10–20 wt % of the POCB650. Beyond this water loading, the crystallization rate is sufficiently high that crystals become apparent.

Figure 4b shows another remarkable feature of these mixtures: after complete crystallization, water absorption continues until the surface of the dish is covered by a film of liquid water. This is indicated by images taken on day 5 and on day 14, both of which show free-flowing water at the surface. To verify this hygroscopic nature of the fully crystallized samples, a second experiment was conducted. A POCB–water mixture with a 1:1 weight ratio was prepared and allowed to crystallize. Since the water content of this sample far exceeds the 1:0.31 POCB:water ratio corresponding to the hydrate crystal, this sample has excess water even when fully crystallized. Nevertheless, upon exposure to saturated humidity, it absorbed more water as indicated by the filled red circles in Figure 4a, confirming its hygroscopic nature.

Finally we note that at any stage of Figure 4, if the crystallized hydrate is exposed to dry air, it gradually loses water and melts back to form a liquid. In effect, the chemical potential

of water in low-humidity air appears to be lower than of the water in the crystal.

2.4. Effect of Molecular Weight. The entire discussion thus far has concerned the single POCB650 material. Figure 3 compares the phase diagram at three different molecular weights: H250 with a quoted molecular weight of 300 g/mol (LLE data taken from Lee et al.²⁸), 650 g/mol (same data as Figure 2), and 2480 g/mol (prepared by chain extension with dibromopropane as described in the Experimental Section). At 2480 g/mol, the pure POCB melting temperature was found to be 18 °C, whereas the hydrate melting temperature increases modestly to 39 °C. However, the LLE region expands to fill almost the entire composition range. Mixtures with POCB2480:water ratios of 99:1 to 1:99 were both found to be in LLE upon melting, and hence the equilibrium cloud points are not accessible. We have not attempted to quantify the metastable portion of the LLE below 39 °C. At 300 g/mol, the data of Lee et al.²⁸ have quantified cloud points along both branches of the LLE curve, and as mentioned above, the shape of the curve suggests the existence of both LCST and UCST.

Qualitatively, the data of Figure 5 suggest the LLE region expands as molecular weight increases. However, Figure 5 shows a distinct peculiarity: the polymer-rich branch of H250/water LLE, when extrapolated, appears to intersect the polymer-rich branch of the POCB650. Such an intersection would suggest that at certain compositions of POCB/water

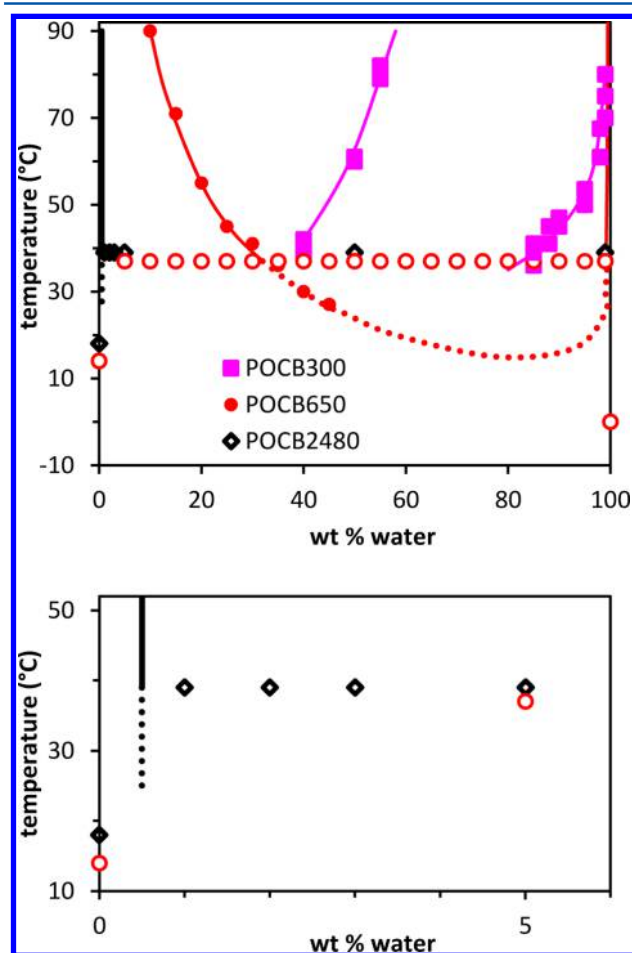


Figure 5. Effect of molecular weight on the phase diagram. The data low water content have been magnified in the graph below. The data for 300 g/mol have been reproduced from Lee et al.

mixtures, reducing the molecular weight would lead to phase separation. While not impossible, this seems unlikely. In an attempt to clarify this, we sought to reproduce the data of Lee et al.²⁸ but were unsuccessful. We found that mixtures of H250 and water to be miscible at all compositions from room temperature up to 80 °C. Although our H250 polymer was nominally the same grade as that of Lee et al.,²⁸ it was not the same batch, and furthermore it had also been stored for several years. This very significant discrepancy may be attributable to polydispersity effects which are likely severe at these low molecular weights. Polydispersity effects are discussed in detail in the following section 2.5.

Lee et al.²⁸ did not mention hydrate crystallization at 300 g/mol molecular weight. Using a sample of DuPont Cerenol H250 (once again, the same grade as used by Lee et al.,²⁸ but not the same batch), we prepared mixtures with water. Upon cooling in a refrigerator to 1–5 °C, these mixtures did crystallize into hydrates. Upon heating, the hydrate phase steadily melted as room temperature was approached and no crystals were evident above 27 °C. Therefore, we tentatively conclude that the hydrate melting temperature reduces as the PO CB molecular weight decreases. This is not surprising; since the monomer 1,3-propanediol is not known to form a hydrate with water, once the degree of polymerization becomes sufficiently low, the hydrate cannot be a stable phase.

In summary then, at low molecular weights, any possible LLE behavior occurs well above the hydrate melting temperature, and hence LLE and SLE occur independently. At high molecular weights, the two behaviors “intersect” each other.

2.5. Comments on Polydispersity Effects. All the samples examined here are polydisperse. The fact that mean molecular weight significantly affects the phase behavior (section 2.4) immediately suggests that sample polydispersity might affect the reported phase diagrams (Figures 1 and 4). We will discuss the possible effects on LLE and SLE separately.

Polydispersity is likely to reduce the extent of the LLE region. A cloud point appears when *any* species precipitates, and if each molecular weight precipitates independently, the reported cloud points would represent precipitation of the high molecular weight tail of the molecular weight distribution. In fact, each species may not precipitate independently; the lowest molecular weight species may also act as solubilizing agents for the higher molecular weight species. Indeed, Lee et al.²⁸ noted that the cloud points of PO CB300–water mixtures increased sharply upon addition of 1,3-propanediol (PDO), the monomer from which PO CB300 was prepared. The PDO, similar to other small alcohols tested in that paper,²⁸ is miscible with water. Therefore, the corresponding PDO-containing aqueous phase is better able to dissolve the higher molecular weight fractions of PO CB. Lee et al.²⁸ comment that it is possible to tune the phase behavior of PO CB–water mixtures “by simply controlling residual monomer in the purification process”. From this, one may then infer that polydispersity in the form of very low molecular weight species (e.g., monomer, dimer, etc.) may shrink the LLE region, both because they are themselves miscible with water and because they improve the miscibility of higher molecular weight species. We believe the discrepancy between our experiments with H250 vs Lee et al. is likely attributable to polydispersity.

Analogously, the solid–liquid region may be overestimated as well. Since we determine the presence or absence of crystals visually, the mixture is deemed to be in SLE as long as at least some crystal fraction is visible. Since the higher molecular

weights form hydrates with a higher melting temperature, if the different molecular weight species crystallize independently, the extent of the SLE is determined by crystallization of the longest chains. In this case, however, PDO was not found to affect the melting temperature. From this we tentatively infer that very low molecular weight species do not themselves crystallize, but they likely do not depress the melting point of the hydrate formed from the longer chains.

In summary then, if monodisperse samples of the same molecular weights as those in Figure 3 were prepared, it is likely that the cloud points would be higher and the melting temperatures would be lower than noted in Figures 1 and 2.

3. CONCLUSION

In summary, we show that mixtures of low molecular weight polyoxacyclobutane (PO CB) and water have highly unusual phase behavior. First, the cocrystal hydrate has a higher melting temperature than the pure PO CB and water—a feature that appears to be rare among polymeric systems. Second, since PO CB has poor miscibility with water, under liquid conditions, PO CB–water mixtures can also show liquid–liquid equilibrium. This interplay of cocrystal solid–liquid equilibrium and liquid–liquid equilibrium creates a phase diagram that, to our knowledge, has not been seen in any other two-component mixture, within or outside of polymeric systems. Third, the hydrate melting temperature appears to be independent of the mixture composition, regardless of whether the hydrate is formed from a two-phase or single-phase PO CB–water mixture. Finally, PO CB can crystallize by absorbing water from humid air at room temperature, behavior which, to our knowledge, is also unique among polymers. PO CB was already recognized to be an unusual polymer owing to its low melting point and chain size as compared to its polyether homologues, a chain size that is nearly independent of temperature, and an ability to cocrystallize with water to form a hydrate. This paper shows that the extraordinary characteristics of PO CB also extend to its mixtures with water.

4. EXPERIMENTAL SECTION

4.1. Materials. Polyoxacyclobutane was obtained from DuPont under the trade name of Cerenol. Most of the experiments used grade H650 with a manufacturer-quoted molecular weight was 650 g/mol. The grade H250 was used chiefly to test whether it cocrystallizes with water. As mentioned in the text, a limited number of LLE experiments were also conducted with this material, but we were not able to reproduce the LLE data of Lee et al.²⁸ Potassium *tert*-butoxide (98% pure), anhydrous benzene, and 1,3-dibromopropane were all obtained from Fischer Scientific.

4.2. Chain Extension of PO CB650. 10 g of PO CB was dried thoroughly in a round-bottom flask at 60 °C under vacuum for 2 h followed by purging with nitrogen. 20 mL of anhydrous benzene was added to it. In a separate small conical flask, 4.1 g of potassium-*tert*-butoxide was dispersed in 20 mL of anhydrous benzene to form a slurry. The slurry was added dropwise into the PO CB–benzene solution at 35 °C under a nitrogen blanket and stirred for 2 h. A solution of 1.8 mL of 1,3-dibromopropane in 15 mL of benzene was then added slowly to this reaction mixture at 50 °C under constant stirring. The reaction was allowed to continue for 48 h, during which the mixture turned slightly orange. The product obtained from this reaction was filtered to remove most of the insoluble salt, potassium bromide. Finally, the benzene was removed from the reaction mixture by a rotovap. Roughly 100 mL of cold water was then added to the hydrate crystals, the crystals were centrifuged, and the supernatant water (which contains KBr salt) was discarded. This process was repeated two more times. Finally, the mixture was heated to 60 °C to

melt the hydrate, upon which the mixture separated into two layers. The upper water-rich layer was discarded and the lower polymer-rich layer (which contains some dissolved water) was dried thoroughly.

4.3. NMR Spectroscopy. NMR measurements (^1H , ^{13}C , and HMBIC) were conducted using a Bruker Avance III and 500 MHz (11.7 T) spectrometer. Roughly 30 mg of polymer was dissolved in deuterated benzene, and the hydroxyl end groups reacted with roughly 30 mg of trifluoroacetic anhydride (TFAA) following Harmer et al.²³ The peaks were assigned as indicated in Figure S3. The molecular weights, calculated from the peak areas of the terminal CH_2 protons vs the CH_2 groups adjacent to the ether oxygens, were determined to be 653 g/mol for the H650 material material supplied by DuPont and 2480 g/mol for the material chain-extended with 1,3-dibromopropane.

4.4. Cloud-Point Determination. POCB–water mixtures (roughly 3 g total) were placed in glass vials and immersed in a water bath whose temperature was maintained by a temperature-controlled hot plate. The actual water temperature was measured by a thermometer immersed in the bath. Temperatures were gradually raised until the onset of cloudiness and then lowered again to verify that the cloudiness disappeared.

4.5. Melting Point Determination. The same vials were allowed to crystallize at room temperature. In some cases, stirring was necessary to ensure that the mixtures did not separate into layers. At low water content, crystallization at room temperature was slow, and hence vials were cooled to roughly 1–4 °C to accelerate crystallization. Crystallized samples were then immersed in a water bath and heated until melting. A minimum of 5 min equilibration time was imposed at each temperature during heating. To verify that the crystallization temperature did not affect melting temperature, a limited number of samples were allowed to crystallize at 36 °C. These yielded the same melting temperature as those crystallized at room temperature.

4.6. Crystallization of POCB under Humid Conditions. Roughly 3 g of POCB was poured in a polystyrene Petri dish to form a layer about 1 mm thick. The dish was left uncovered in an enclosed glass container whose bottom was covered with a pool of water to ensure saturated humidity. Samples were removed from the enclosure daily for weighing and photographing.

4.7. Differential Scanning Calorimetry. A DSC TA Instruments Q200 DSC was used for examining the hydrate crystals. A mixture of POCB650 and water in a 1:1 ratio was allowed to crystallize, and 5 mg was sealed in a DSC pan. The pan was left in the refrigerator overnight to ensure complete crystallization. The sample was then cooled to 2 °C in a DSC at 2 °C/min, held isothermal for 10 min, and then heated to 45 °C at 10 °C/min. The corresponding data are shown in Figure S4.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.macromol.8b00239.

Figures S1–S4 (as mentioned in the main text) (PDF)

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Notes

The authors declare no competing financial interest.

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NOTE ADDED IN PROOF

Additional experiments show that solubility of POCB650 in water at 65C is less than 50 ppm. Moreover hydrate crystallization can occur at room temperature even at 10 ppm POCB. Thus, the L_w phase in Figure 2 is nearly pure water.