Highly Stable Indomethacin Glasses Resist Uptake of Water Vapor

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Mass uptake of water vapor was measured as a function of relative humidity for indomethacin glasses prepared using physical vapor deposition at different substrate temperatures. Highly stable glasses were produced on substrates at 265 K ($0.84T_g$) by depositing at 0.2 nm/s while samples similar to melt-cooled glasses were produced at 315 K and 5 nm/s. Samples deposited at 315 K absorb approximately the same amount of water as glasses prepared by supercooling the melt while stable glasses absorb a factor of 5 less water. Unexpectedly, the diffusion of water in the stable glass samples is 5−10 times faster than in the glass prepared by cooling the liquid.

Introduction

Glasses represent an important class of materials that combine the mechanical properties of a crystal with the molecular disorder of a liquid. This leads to properties that make glasses the best materials for a wide variety of everyday applications, including compact discs, structural materials, optical fibers, electrical transformers, golf clubs, and of course windows. While a substance may have a few different crystal structures (polymorphs), it has essentially an infinite number of glassy structures. Glasses are not in thermodynamic equilibrium and the properties of a particular glass depend upon exactly how it was made. Glasses are most commonly prepared from the liquid state (by cooling a liquid) but can also be prepared from solutions (by freeze drying[1] or spray drying[2]), from crystals (by milling,[3] pressurization,[4] or dehydrating a crystalline hydrate,[5,6] and from gases (by chemical[7] or physical vapor deposition[8]). Additionally, once a glass is prepared, annealing (or aging) the glass for long periods of time causes a very slow evolution in its properties as the glass evolves toward the equilibrium liquid.[9]

To illustrate why it might be useful to prepare different types of glasses from the same molecule, consider the use of glasses in the pharmaceutical field.[10] It has been shown that the solubility[11] and bioavailability of an amorphous drug can be orders of magnitude greater than that of the same drug in a crystalline form. A difficult aspect of formulating amorphous drugs is that stability against crystallization is required for several years. Some glasses will be more stable against crystallization than others and it is important to understand how to manipulate preparation methods to produce glasses with a wide range of properties.

While it has been previously reported that physical vapor deposition (VD) produces unstable glasses as compared to glasses made by cooling a liquid,[12,13] recent work has challenged that view.[8] Under certain deposition conditions, glassy films of small organic molecules with low enthalpies and high densities can be produced.[14−16] Relative to their melt-quenched counterparts, these glasses are thought to be the most stable glasses

ever produced in a laboratory. For example, glasses vapor-deposited under optimal conditions have enthalpies and densities that could be obtained only by aging an ordinary glass for thousands of years or by slowly cooling a supercooled liquid over an equivalently long time period.[14] Under other deposition conditions, vapor deposition can produce glasses that are similar to glasses produced by cooling a supercooled liquid at typical laboratory rates (ordinary glasses).

Of key interest for this paper is the difference between stable and ordinary glasses in terms of gas uptake. It has been shown that the amount of gas sorption decreases as a glass is aged. For example, for the low-molecular-weight glass former trehalose,[1] aging for 120 h decreases the water uptake by almost a factor of 2. For various polymer membranes[17−21] it has been shown that sorption of a variety of gases can decrease by up to 35% with aging. The increase in density of a glass as it ages apparently decreases the space available for gas molecules. Since stable glasses produced by vapor deposition are thought to be similar to glasses that would result from extremely long aging far below T_g, one might speculate that these glasses would absorb much less water than ordinary glasses. Such a result might be important in the field of amorphous pharmaceuticals. For example, Zografi and co-workers showed that, for glasses formed from the drug indomethacin, decreasing water content decreases the rate of crystallization.[22]

Here we report measurements of water absorption by vapor-deposited glasses of indomethacin (IMC), an aromatic carboxylic acid. By controlling the deposition conditions, stable and ordinary glass samples were created. Additionally, ordinary glass samples were prepared by annealing stable glasses above the glass transition temperature, T_g, and then cooling back down into the glass. The mass of water vapor absorbed by these samples was measured as a function of time in environments within a range of relative humidities. From this information, equilibrium water uptake values and diffusion coefficients for water in stable and ordinary IMC glasses were determined.

We find that stable IMC glasses absorb 5 times less water than ordinary glasses at the same relative humidity. To our knowledge, this is the largest difference in gas uptake properties ever reported for a given substance prepared in different glass

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states. The changes in water content with time were consistent with the Fickian model of diffusion and water uptake in both samples occurred by a bulk mechanism. Unexpectedly, water diffusion in the stable IMC glass was 5−10 times *faster* than in the ordinary glass.

Experimental Methods

Materials. Indomethacin (IMC, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-3-indoleacetic acid, T_{melt} = 434 K) of greater than 99% purity was purchased from Sigma (St. Louis, MO) and used as received. This starting material was completely crystalline and in the γ polymorphic form.[14] When dispersed in mineral oil and examined under a microscope, the average crystal size (longest dimension) was found to be about 40 μm.

Vapor Deposition. Vapor deposition was performed in a vacuum chamber with the pressure maintained between 10^{-7} and 10^{-8} torr.[15] Crystalline IMC was loaded into a quartz crucible, the temperature of which could be controlled with a resistive wire heater. All depositions were monitored with a quartz crystal microbalance (QCM, Sycon Instruments) with the temperature of the crucible varied to achieve the desired deposition rate. The temperature of the sample stage was controlled using a LakeShore 340 temperature controller and a 4-wire resistive temperature detector (Omega).

IMC was vapor-deposited onto cleaned aluminum disks that were approximately 7.4 mm in diameter. The disks were attached to the sample stage using double-sided carbon black mounting tape (SPI Supplies) developed for SEM studies. The chamber is designed with a movable crucible and heater. During the initial heating of the crucible, it was held beneath the QCM; minimal deposition occurred onto the Al disks during this period or at the end of the deposition. When the desired deposition rate was achieved, the crucible was moved beneath the Al disks. The deposition rate was periodically checked during the deposition by moving the crucible under the QCM. For the preparation of stable glasses,[15] the sample stage was held at 265 K ($0.84T_g$) and a rate of 0.2 nm/s was used. For preparation of ordinary glasses, the sample stage was held at the T_g of IMC (315 K) and a deposition rate of 5 nm/s was used. During all depositions the sample stage temperature was constant within 1 K and the measured deposition rate was within 15% of the reported value.

After the deposition was complete, the sample stage was allowed to return to room temperature before the chamber was brought up to atmospheric pressure using dry nitrogen. The total time for this process was 45−60 min. The disks were then carefully removed from the chamber so that the deposited films did not flake off. Samples were stored in a low humidity environment with anhydrous calcium sulfate at 250 K prior to water uptake measurements. To calculate the average film thickness, the mass of the disk after deposition was measured and the mass of the blank disk (∼2.5 mg) was subtracted. The IMC mass was then converted into thickness using the disk diameter of 7.4 mm and assuming a density of 1.31 g/cm^3.[23] The crucible was sufficiently close to the Al disks (3 cm) that the film thickness was not uniform, but varied by less than 30% from one side of the disk to another; this in turn lead to a range of deposition rates of less than 30% for any given disk.

Water Vapor Uptake Measurements. The sample disks were loaded into an automated moisture sorption apparatus (model Q5000SA, TA Instruments) that measures sample mass (and thus water uptake) as a function of relative humidity and time. For all uptake experiments, nitrogen at 1 bar was used as a carrier gas. For almost all experiments, the temperature was

held at 298 K. This instrument has a very low balance noise (∼±0.05 μg) and a correspondingly low detection limit for water uptake. As a control experiment, we measured the water uptake of an uncoated Al disk; no mass uptake could be detected given the signal noise of ±0.05 μg.

As an initial step in all experiments, water absorbed during environmental exposure in storage or loading was removed by holding the samples at 0% relative humidity (RH) for 360 min or until the mass (Al disk + IMC) changed by less than 0.005% for 40 min. There were three different experimental procedures utilized for measuring water uptake, as described below. In all three procedures, it was assumed that equilibrium had been achieved if the mass changed by less than 0.005% over 40 min.

0% to 50% in 10% RH Steps. After the initial equilibration at 0% RH, the humidity was brought up to 50% in steps of 10% RH. The humidity was adjusted to the next RH level after 240 min or if the equilibrium criterion had been met. The humidity was then brought back down to 0% again using steps of 10% RH. This entire humidity cycle was then repeated a second time. Each humidity cycle typically required less than 1200 min.

0% to 50% RH Jump. After the initial equilibration at 0% RH, the humidity was jumped directly to 50% and held there for 300 min (sample thicknesses <45 μm) or 360 min (89 μm samples). The humidity was then directly jumped to 0% and held until the equilibrium criterion was met or until 180 min had passed. This humidity cycle was then repeated a second time.

0% to 20% RH Jump. After the initial equilibration at 0% RH, the humidity was jumped directly to 20% and held there for 360 min. The humidity was then jumped back to 0% and held until the equilibrium criterion was met or until 180 min had passed. This humidity cycle was then repeated a second time.

Annealing of Stable Glasses. To convert a stable IMC glass sample into an ordinary glass, the sample was heated in the TGA Q5000SA to 325 K at 0% RH for 120 min and then cooled back down to room temperature at a rate of 1.25 K/min. DSC experiments performed on stable IMC samples have shown that this annealing protocol converts a stable IMC glass into the supercooled liquid.[24] Subsequent cooling of the liquid forms an ordinary glass.

Results

Equilibrium Water Uptake as a Function of Relative Humidity. Figure 1 shows representative results for the equilibrium uptake of water vapor by various forms of IMC as a function of relative humidity. The mass % uptake was calculated by dividing the increase in mass due to water sorption by the mass of the dry IMC after the initial equilibration at 0% RH, and multiplying by 100. As shown by the open symbols, the uptake of stable IMC glasses produced by vapor deposition at 265 K is significantly reduced compared to that of ordinary IMC glasses produced by vapor deposition at 315 K (closed triangles and circles). The average water uptake for six stable glass samples at 50% RH was 0.16 ± 0.05% while six ordinary glass samples had an average uptake of 0.88 ± 0.05%. For comparison the water uptake of a crystalline powder is included in Figure 1; such samples had the lowest water uptake at 0.040 ± 0.003%.

Andronis et al. previously reported water uptake measurements of the crystalline powder and an ordinary glass of IMC.[22] They held an IMC glass (prepared by cooling the supercooled liquid) for 12 h at 303 K and 43% RH; under these conditions,
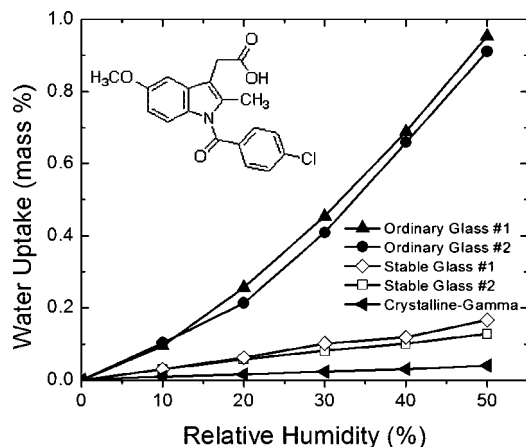
Figure 1. Equilibrium water uptake of ordinary glass, stable glass, and crystalline IMC as a function of relative humidity at 298 K. The measurement error for the glasses was ±0.05% while the error for the crystal was ±0.003%. The structure of IMC is shown as an inset.

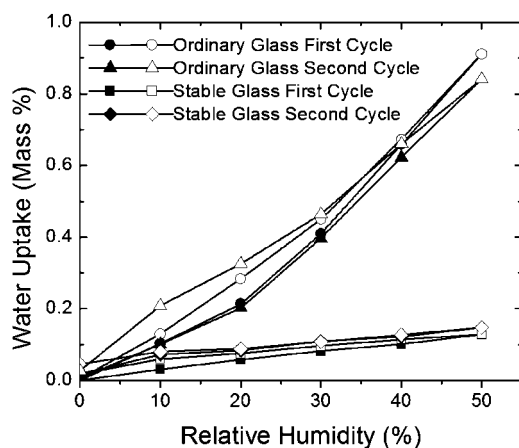**Figure 2.** Sorption/desorption of ordinary and stable IMC glass samples during two consecutive humidity cycles.

Figure 3. Water uptake of a stable IMC glass before and after annealing converted it to an ordinary glass. The uptake for an ordinary glass made by VD at 315 K is included for comparison.

Figure 4. Water uptake by a 42 μm stable IMC glass as a function of time during a 0% to 50% RH step at 298 K. The glass was subsequently annealed to produce an ordinary glass and then retested. Also shown is the humidity in the sample chamber.

the equilibrium supercooled liquid state was attained with a 1.0% water content by mass. This is similar to the water uptake values reported here for ordinary IMC glasses at 298 K. Precise agreement should not be expected considering the difference in measurement temperature and equilibration procedures. As we discuss below, under our measurement conditions, the ordinary glass does not tranform into the supercooled liquid. For the crystalline powder, Andronis et al. reported that water uptake was below their detection limits and they estimated an uptake of 0.01% based upon the adsorption of a single monolayer of water upon the crystal surface. Given the size of the nonspherical crystals in our sample (42 μm for the longest dimension), we assume that the specific surface area of the crystalline IMC powder is 0.4 m^2/g; this is in good agreement with the value reported in ref 22. Assuming a cross-sectional area of 0.1 nm^2 for a water molecule, our measured 0.04% water uptake translates into a surface adsorption of about 3 monolayers on the IMC crystals, which is in reasonable agreement with the conclusion of ref 22.

Figure 2 illustrates the reversibility and reproducibility of water uptake for both a stable glass and an ordinary glass of IMC. Two complete cycles of relative humidity changes are shown for each sample with the closed symbols showing absorption and the open symbols indicating desorption. No significant hysteresis is observed and thus the data are consistent with reversible water uptake and loss in the glassy state. Clearly
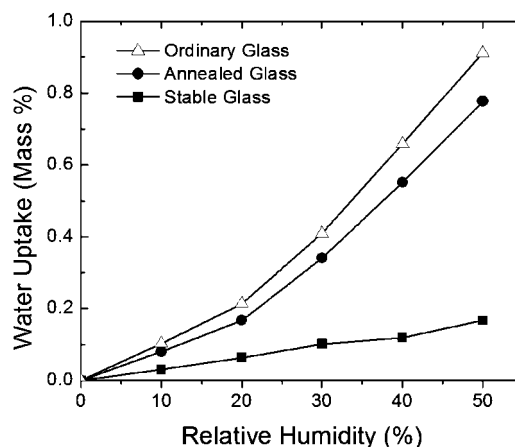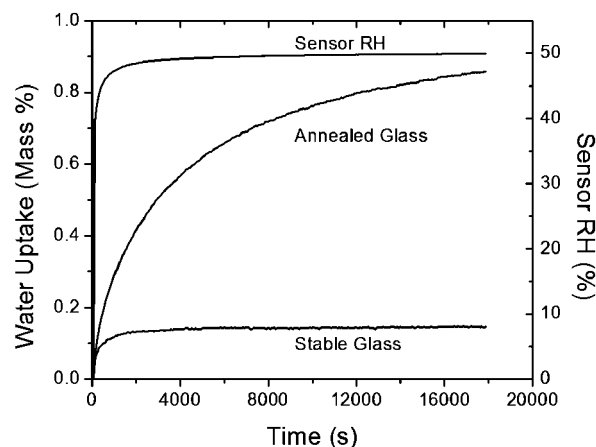
relative humidity cycling to 50% is not sufficient to convert the stable glass into an ordinary glass.

Figure 3 shows the water uptake behavior of a stable glass that has been annealed above T_g long enough to transform into the supercooled liquid and then cooled back into the glass state. As expected, the glass produced in this manner (solid circles) has very similar water uptake properties to the ordinary glass prepared by vapor deposition at 315 K. The slightly lower water uptake of the annealed glass relative to the VD ordinary glass is likely explained by surface crystallization that occurs during annealing.[25] Observations made with an optical microscope indicate that about 25% of the surface of the annealed glass appeared to be covered by crystals after the RH cycling.

Water Uptake as a Function of Time. Figure 4 shows the time dependence of water uptake for a stable glass sample subjected to a RH jump from 0% to 50%. For comparison, data is also shown for the same sample after annealing converted it to an ordinary glass. In addition, the signal from the RH sensor in the sample chamber is plotted. The RH change is sufficiently sharp as to be regarded as a step function in our subsequent analysis; it is likely that the actual RH change is even faster than the signal recorded by the sensor. The first data point for which the relative humidity was greater than 5%, as measured by the RH sensor, is defined as $t = 0$ for the RH jump.

Besides the large difference in equilibrium uptake values between the stable and annealed glasses, the most striking
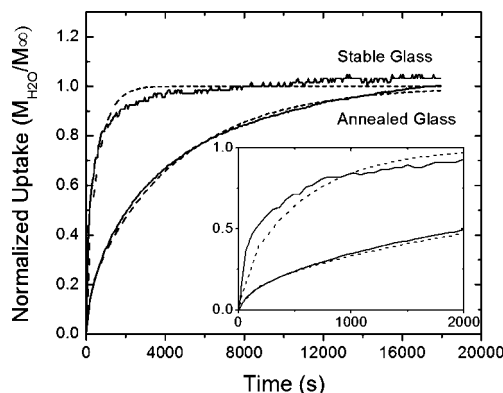
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Figure 5. Water uptake data fit to the Fickian diffusion model. Fits to eq 1 are shown by dashed lines. The data from Figure 4 is shown, scaled by the fitted parameter M_∞. The inset shows the comparison between the fit and the data at early times.

TABLE 1: Water Diffusion Coefficients for Stable and Ordinary IMC Glasses at 298 K

glass type	preparation	RH step (%)	thickness (μm)	D (cm²/s)[a]	% uptake[a]
stable	VD (265 K)	0 → 50	89	11 × 10⁻⁹	0.08
			38	10 × 10⁻⁹	0.14
		50 → 0	38	8 × 10⁻⁹	−0.13
ordinary	annealed	0 → 50	89	2.0 × 10⁻⁹	0.61
	annealed		38	1.3 × 10⁻⁹	0.86
	VD (315 K)		24	1.3 × 10⁻⁹	0.92
	annealed	50 → 0	38	1.5 × 10⁻⁹	−0.84
	annealed	0 → 20	38	1.2 × 10⁻⁹	0.18
	annealed	0 → 20	36	0.9 × 10⁻⁹	0.24

[a] Determined by a least-squares fit to eq 1.

feature of Figure 4 is the difference in rate of uptake between the two samples. The water content of the stable glass apparently reaches its equilibrium value about 10 times faster than does the annealed sample, indicating faster water diffusion in the stable glass.

We have used the Fickian model of diffusion to fit the water uptake data; in this model, the diffusion coefficient is independent of water concentration. We model the RH change as an instantaneous jump at $t = 0$ to a constant value. We assume that the Al substrate is impermeable, thus allowing water vapor to enter the sample from only one side. With the initial condition that the concentration equals zero at $t = 0$, Crank has shown for this situation that the mass uptake at any given time is given by eq 1.[26]

$$M_{H_2O}/M_\infty = 1 - \sum_{n=0}^{\infty} \left\{ \frac{8}{\pi^2(2n+1)^2} \exp\left[\frac{-D(2n+1)^2\pi^2 t}{4L^2} \right] \right\} \tag{1}$$

Here M_{H_2O} is the mass of the water at time t, M_∞ is the equilibrium water mass, L is the thickness of the film, and D is the diffusion coefficient. Diffusion coefficients were obtained by performing a least-squares fit on the data using Origin 8 graphing software (Origin Laboratories). For the purposes of the fit, the infinite sum in eq 1 was truncated at $n = 6$ and D and M_∞ were allowed to vary simultaneously. The film thickness was fixed at the value calculated from the sample mass.

Figure 5 shows fits to the Fickian diffusion model for water uptake data for the stable glass and for the ordinary glass obtained by annealing the stable glass; the fitting parameters
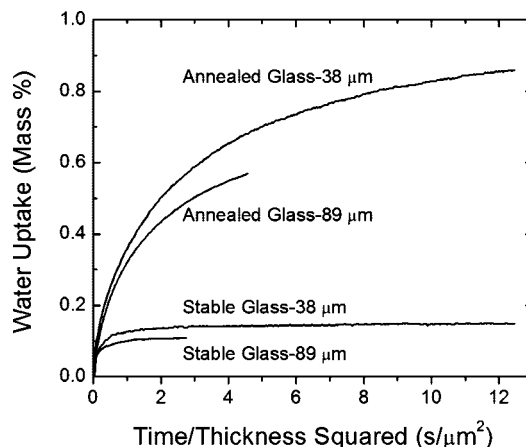

Figure 6. Water uptake by 89 and 38 μm IMC glasses during a 0% to 50% RH step, with time scaled by thickness squared.

(with M_∞ converted to % uptake) can be found in Table 1. The Fickian fit is quite good for the annealed glass at all times. Unfortunately, diffusion coefficients for water through ordinary IMC glass could not be found in the literature. However, diffusion coefficients of water in amorphous carbohydrates are on the order of $10^{-9}-10^{-10}$ cm²/s near room temperature, in good agreement with our results.[27,28]

Figure 5 shows systematic deviations in the fit to the stable glass water uptake data and below we discuss some potential reasons for this. Nevertheless, the diffusion coefficients obtained from the fits adequately specify the rate of water uptake to within about a factor of 2. Table 1 indicates that water diffusion in stable IMC glasses is 5–10 times faster than in the ordinary glass. The equilibrium mass uptake values obtained from the fits are in reasonable agreement with the data shown in Figures 1–3.

The uptake kinetics of the crystalline powder could not be studied with any reasonable precision due to the low uptake amount and the rate at which uptake occurred. Our qualitative observation is that water uptake by the crystalline sample is very fast and appears to be limited by the rate at which the relative humidity could be changed in the experimental chamber.

Check on Assumptions of Fickian Diffusion Model. A fundamental feature of Fickian diffusion is that the time required to equilibrate the water content within a film scales as the film thickness squared. In Figure 6, we test this directly for two stable glasses and for the two ordinary glasses formed by annealing the stable glasses. For both stable and ordinary glasses, the kinetics of water uptake are very similar after scaling the time by the square of the film thickness. We suspect that the slightly lower equilibrium uptake values for the thicker samples are due to these samples not being completely dry prior to the jump to 50% RH. As shown in Table 1, for both stable and annealed films, the fitted D values are reasonably independent of film thickness.

Another assumption of the Fickian diffusion model is that the diffusion coefficient is independent of water concentration. To check this, an annealed glass was tested using an RH jump from 0% directly to 20%. As shown in Table 1, there is no significant change in D between the 0 to 50% and 0 to 20% RH tests for the ordinary glass, showing that a concentration independent D provides a reasonable description of our data. This procedure could not be repeated with the stable glass due to the small amount of water absorbed and the limited sensitivity of the instrument. However, for both stable and ordinary IMC glasses, we note that similar D values were obtained for jumps

from 0 to 50% RH and for jumps from 50% to 0% RH. If D were a strong function of water concentration, different results would have been expected from these two experiments. Given the results in Table 1, the uncertainty in D for ordinary IMC glass is less than a factor of 2.

The Fickian model is appropriate for our data only if diffusion takes place in a glass whose structure is fixed on the time scale of the experiment. If water diffusion is coupled to structural recovery of the glass, then a much more complex description of water uptake would be needed.[29] Figure 1 shows clearly that water uptake for the stable glass is not coupled to structural recovery. If structural recovery were occurring, repeated cycles of RH would systematically increase the water uptake toward the value reported (1% uptake[22]) for the equilibrium liquid at the testing temperature, 298 K. For the ordinary glass, the interpretation of Figure 1 is ambiguous, since the water uptake is similar to that reported for the equilibrium liquid. For this reason, we performed further experiments that show that water uptake by ordinary and annealed stable glasses occurs without structural recovery. Experiments on ordinary glass samples at 288 K indicate water uptake values and water diffusion coefficients similar to those observed at 298 K. As structural recovery is a very strong function of temperature, this result indicates that structural recovery is not playing a role at either temperature. Thus, we interpret the results presented in this paper as reversible water uptake into a glass whose structure is not evolving on the time scale of the sorption measurements.

Discussion

We have shown that vapor deposition can prepare glasses of IMC that display significantly different water uptake properties. Very stable IMC glasses absorb about 5 times less water than ordinary IMC glasses. In this section, we discuss whether the water uptake observed in the stable glass occurs through a surface or bulk mechanism. We then place our observations of equilibrium uptake and the rate of uptake into the context of results previously reported for other glasses.

Surface or Bulk Mechanism. Zografi and co-workers[22] previously showed that ordinary IMC glass absorbs water into the bulk while crystalline IMC only adsorbs water onto the surface of the crystal. Because of the very limited water uptake of the stable IMC glass, one might ask whether stable IMC glasses also only adsorb water at the surface. Three experimental observations in this study indicate that, like ordinary IMC glass, the stable glass absorbs water into the bulk. First, the amount of water sorption measured is far too large for a surface mechanism, amounting to an unrealistic ∼100 monolayers of water on the stable glass. Second, the D values obtained for stable glass samples of differing thicknesses are very similar. A surface mechanism, if forced to fit to the bulk diffusion model, would lead to inconsistent D values. In contrast to our observations on stable glasses, surface adsorption would be expected to occur so quickly that we could not resolve it with our apparatus. Third, the water uptake percentages obtained for stable glass samples of different thicknesses are reasonably consistent, as expected for a bulk uptake mechanism; we concede that this argument is not as conclusive as the first two.

Decrease in Water Uptake for the Stable Glass. The decrease in water sorption for stable IMC glasses as compared to ordinary glasses has a simple qualitative explanation. Previous X-ray reflectivity measurements on vapor-deposited stable glasses of 1,3,5-tris(naphthylbenzene) have shown that the stable glass has a higher density (by 1−2%) than the ordinary glass.[8,16] While density has not yet been measured for vapor-deposited

stable and ordinary IMC glasses, it is a reasonable supposition that the stable IMC glass has the higher density.[23] At a qualitative level, more dense glasses have less available space (e.g., free volume) and therefore absorb less water. The striking magnitude of this effect (a factor of 5 decrease in water uptake for an expected 1−2% density increase) is reasonably interpreted as follows: even ordinary glasses have very little open space for gas molecules. In stable glasses, most of that open space has been eliminated.

It is reasonable to compare these results on IMC glasses with literature results for ordinary and aged glasses. Physical aging increases the density and lowers the enthalpy of a glass. These same changes occur to a greater extent in stable vapor-deposited glasses. Thus, it might be fair to regard a stable vapor-deposited glass as similar to an ordinary glass that has been subjected to much longer aging times than are possible in laboratory experiments. Indeed, we have previously estimated that the most stable vapor-deposited glasses are similar to what could be achieved by aging for thousands of years or more.[14]

The most relevant example for water uptake in a low-molecular-weight glass is trehalose.[1] When trehalose was aged for 120 h at 373 K, it was observed that the water uptake decreased from 1.4% to 0.8% at 10% RH.[1] As expected, this is a smaller change than the factor of 5 that we report here for stable and ordinary IMC glasses.

More attention has been paid to the effect of aging on the gas uptake properties of polymer glasses. Aging has been seen to decrease equilibrium gas uptake by as much as 35%.[17−21] For example, uptake of water by a high T_g polyimide (Matrimid) was diminished by 35% with 12 h of aging. A high T_g polysulfone studied in ref 21 shows that aging had a smaller effect on water uptake. In summary, aging has been reported to have a much smaller effect on equilibrium water uptake than the difference that we observe between stable and ordinary IMC glasses. This is consistent with the view that stable IMC glasses may be regarded as "superaged" systems.

Faster Diffusion in the Stable Glass. Since the density of the stable IMC glass is assumed to be higher than that of the ordinary glass, the observation of a larger water diffusion coefficient for the stable glass seems counterintuitive. Indeed, a review of the literature indicates that many aging studies have found that the diffusion coefficient[17,20,30,31] or permeability (linearly related to D)[32−34] decreases with aging. However, there are a few reports of increases of gas diffusion coefficients due to aging. For the polymer bisphenol A polycarbonate (BPA-PC), Kirchheim and co-workers reported that the diffusion coefficient for a number of gases increases upon aging.[18,35] In the most dramatic case, the diffusion coefficient of propane in BPA-PC increased by a factor of 2.5 after aging for an unspecified length of time.[35] Interestingly, this behavior depended strongly on the size of the gas molecule, with both smaller and larger penetrants showing less dramatic behavior; diffusion of water, for example, was not influenced by aging. Similarly, Laot et al. found that more stable BPA-PC glasses (prepared by cooling more slowly from the melt) had larger gas diffusion coefficients.[36] Cooling 80 times more slowly caused a 35% increase in the diffusion coefficient for nitrogen. In these papers, this seemingly counterintuitive behavior is explained by models in which the rate of diffusion is dependent upon the activation energy associated with particular sites and not wholly dependent on the density of the sample.[36−38]

In this work, we report that diffusion of water in stable IMC glasses is 5−10 times faster than in the ordinary glass. To our knowledge, no previous work has shown that different methods

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of preparing glasses can modulate the diffusion coefficients of gas molecules by such a large extent.

Possible Molecular Interpretation. One possible interpretation of these results emphasizes the importance of hydrogen bonding in IMC. IMC is a carboxylic acid and hydrogen bonding is an important feature in its crystalline polymorphs.[39] We imagine that ordinary IMC glasses absorb water primarily because sites exist in the glass where water can hydrogen bond with IMC. It is also likely that other sites for water absorption exist, but we imagine that these are fewer in number and that water is not so tightly bound in this second type of site. From calorimetry, we know that stable IMC glasses have a significantly lower enthalpy than ordinary glasses.[14,15] We speculate that the stable glass has more hydrogen bonds between IMC molecules and as a result fewer hydrogen-bonding sites are available for water molecules. This obviously would explain the lower water uptake by the stable glass. It can also explain the faster diffusion in the stable glass since the remaining sites for water binding do not bind water as well, on average. Less stable binding means a smaller activation barrier for escape from a site, leading to faster diffusion.

Although the above idea goes far beyond what is directly established by these experiments, it does suggest a number of additional experiments that may be insightful. Raman and IR studies of these glasses, with and without water, could check important aspects of these ideas. Vapor uptake measurements on stable and ordinary glasses in which hydrogen bonding plays no role would also be very useful.

Conclusion

Physical vapor deposition onto substrates at 265 K has been used to create highly stable glasses of indomethacin. Water vapor uptake by these stable glasses has been compared to ordinary IMC glasses prepared either by vapor deposition at 315 K or by annealing the stable glasses above T_g. Stable glasses absorb about 5 times less water than ordinary glasses. Unexpectedly, the diffusion coefficient for water in stable glasses is 5−10 times higher than for ordinary glasses. Stable glasses prepared by vapor deposition can be regarded as "superaged" glasses. Consistent with this description, the observed difference in the water uptake behavior of stable and ordinary IMC glasses is larger than any previous reports of the effect of aging on water uptake of molecular or polymeric glasses. Future work will determine if other deposition conditions decrease gas uptake even further.

We expect that detailed modeling of the diffusion coefficients and the equilibrium water uptake values for stable and ordinary glasses might give rise to considerable insight into the mechanism of gas diffusion in molecular glasses. The large differences between stable and ordinary glasses would likely place strong constraints on theoretical descriptions of gas diffusion.

In many applications it is important to limit the gas uptake of glasses. In the production of organic light emitting diodes (OLED),[40,41] for example, vapor deposition is often used to prepare sub-100 nm films of organic glasses. Uptake of water and oxygen by these glass layers has been implicated in the failure of such devices. For amorphous pharmaceuticals, water uptake has been shown to lead to faster crystallization.[22] Stable glasses prepared by vapor deposition may have an important role in controlling gas uptake of such amorphous materials.

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