Soft Matter

Surface diffusion in glasses of rod-like molecules posaconazole and itraconazole: Effect of interfacial molecular alignment and bulk penetration

1   **Surface diffusion in glasses of rod-like molecules posaconazole and itraconazole:**

2   **Effect of interfacial molecular alignment and bulk penetration**

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8

9   **Abstract.** The method of surface grating decay has been used to measure surface diffusion in the glasses

10   of two rod-like molecules posaconazole (POS) and itraconazole (ITZ). While structurally similar

11   antifungal medicines, ITZ forms liquid-crystalline phases while POS does not. Surface diffusion in these

12   systems is significantly slower than in the glasses of quasi-spherical molecules of similar volume when

13   compared at the glass transition temperature T_g. Between the two systems, ITZ has slower surface

14   diffusion. These results are explained on the basis of the near-vertical orientation of the rod-like

15   molecules at the surface and their deep penetration into the bulk where mobility is low. For molecular

16   glasses without extensive hydrogen bonds, we find that the surface diffusion coefficient at T_g decreases

17   smoothly with the penetration depth of surface molecules and the trend has the double-exponential form

18   for the surface mobility gradient observed in simulations. This supports the view that these molecular

19   glasses have a similar mobility vs depth profile and their different surface diffusion rates arise simply

20   from the different depths at which molecules are anchored. Our results also provide support for a

21   previously observed correlation between the rate of surface diffusion and the fragility of the bulk liquid.

22

23   **Keywords**. Glass, surface diffusion, posaconazole, itraconazole, rod-like molecule, liquid crystal,

24   mobility gradient.

25

26

Introduction

Surface mobility plays an important role in the physical stability of molecular glasses. Surface molecules can diffuse much faster than bulk molecules,[1,2,3] and this has been attributed to reduced local caging effect and smaller elastic penalty for rearrangement.[4,5] Surface mobility enables fast crystal growth in molecular glasses, reducing the shelf life of amorphous drugs[6,7] and motivating coating technologies for stabilization.[8] Surface mobility allows preparation of "ultra-stable glasses" by physical vapor deposition, taking advantage of the fast equilibration of just-deposited molecules before they are firmly embedded in the bulk.[9,10]

Surface diffusion can be measured by observing the evolution of surface contours driven by surface tension. [1,2,11,12,13,14] Previous work in this area has focused on molecular glasses containing quasi-spherical molecules or slightly elongated molecules.[3] Motivated by recent attention to highly anisotropic glasses prepared with non-spherical molecules,[15] we have studied surface diffusion in the glasses of two rod-like molecules, posaconazole (POS) and itraconazole (ITZ) (see Scheme 1), both antifungal drugs.[16,17] While having similar structures, the two molecules differ in that ITZ forms liquid crystals (LC), [18] while POS does not.[19] This provides an opportunity to study the effect of bulk LC structure on surface diffusion. We find that surface diffusion is significantly slower in the glasses of POS and ITZ than in the glasses of quasi-

Scheme 1. Molecular structures of posaconazole (POS) and itraconazole (ITZ).

spherical molecules of similar volume. This is attributed to the near-vertical orientation of the rod-like molecules at the surface and their deeper penetration into the bulk where mobility is low. Between the two systems studied, ITZ has slower surface diffusion, likely a result of the deeper penetration of surface molecules in this system.

Apart from investigating new types of molecules, this work was motivated by developing capabilities to predict surface diffusion rates. Chen et al. have analyzed all published surface diffusion results on molecular glasses and noted that the surface diffusion coefficient decreases smoothly with molecular size for van der Waals systems (no extensive hydrogen bonds).[3] They attributed this to a steep and generic mobility gradient beneath the surface of a molecular glass. Larger molecules insert themselves

58   deeper into the bulk where mobility is lower, slowing down their center-of-mass diffusion. In this work

59   we extend their investigation to even deeper bulk penetration using the rod-like molecules and observe a

60   greater retardation of diffusion. Our results uphold the previous conclusion and our mobility vs depth

61   profile displays the double-exponential form characteristic of surface mobility gradient seen in

62   simulations.[20,21] This finding is useful for predicting surface diffusion from molecular structures. We

63   also examine a previously observed correlation between the rate of surface diffusion and the fragility of

64   the bulk liquid.

65

Experimental Section

67   Posaconazole (POS, purity $> 98\%$) was obtained from Biochempartner and itraconazole (ITZ, purity

68    $> 99\%$) from Alfa Aesar. The materials were used as received. To make a surface grating, a master

69   pattern was placed on a viscous liquid of POS or ITZ at 363 K and was peeled off after vitrifying the

70   liquid at 298 K. This yielded a glass film with a sinusoidal surface contour. Master gratings of different

71   wavelengths were obtained as follows: for $\lambda = 1000$ nm and 1984 nm, plastic gratings purchased from

72   Rainbow Symphony were used; for $\lambda = 334$ nm, the masters were duplicated from a Blue-ray disc

73   through a UV-curing polymer (Norland Optical Adhesive 61); for $\lambda = 553$ nm, the masters were

74   duplicated from a glass grating (Spectrum Scientific) through the same polymer. All masters were

75   coated with 10 nm gold before use (Sputter deposition system, Leica ACE600). The thickness of each

76   embossed glass film was $50 - 100$ μm, much larger than the wavelength of any surface grating used,

77   ensuring that the evolution of the top surface was unaffected by the substrate.

78

79   The flattening of a surface grating over time was monitored by Atomic Force Microscopy (AFM, Bruker

80   Veeco Multiple Mode IV) or laser diffraction. AFM was performed in the tapping mode at room

81   temperature; the height profile was Fourier transformed to obtain the amplitude of the sinusoidal surface.

82   Laser diffraction was measured in transmission and used to determine faster decay than feasible with

83   AFM. A HeNe laser ($\lambda = 632.8$ nm, Uniphase Corp.) passed through a sample film perpendicularly and

84   the first-order diffraction in transmission was recorded with a silicon amplified detector (Thorlabs)

85   interfacing with a National Instruments LabVIEW program. The grating amplitude was verified to be

86   proportional to the square root of diffraction intensity. The diffraction method was used only for POS

87 since the cloudiness of LC phases made transmission experiments difficult for ITZ. The two methods

88 yielded identical results within experimental error when applied to the same decay process. During

89 grating decay, the sample was purged with dry nitrogen and its temperature was controlled within 0.1 K

90 with a Linkam microscope temperature stage or a custom-made mini-oven.

91

92 **Mullins' Theory of Surface Evolution**

93 According to Mullins,[22] the amplitude h of a sinusoidal surface contour decreases exponentially over

94 time, $h = h_0 \exp(-Kt)$, and the decay rate K is given by:

95
$$K = Fq + Aq^2 + (A' + C)q^3 + Bq^4 \qquad (1)$$

96 where

97
$$q = 2\pi/\lambda$$

98
$$F = \frac{\gamma}{2\eta}$$

99
$$A = \frac{p_0 \gamma \Omega^2}{(2\pi m)^{1/2}(kT)^{3/2}}$$

100
$$A' = \frac{\rho_0 D_G \gamma \Omega^2}{kT}$$

101
$$C = \frac{D_v \gamma \Omega}{kT}$$

102
$$B = \frac{D_s \gamma \Omega^2 \nu}{kT}$$

103 In eq. (1), λ is the grating wavelength, γ is the surface tension, η the viscosity, p_0 the vapor pressure at

104 equilibrated state, Ω the molecular volume, m the molecular weight, ρ_0 the vapor density at equilibrated

105 state, D_G the diffusion coefficient of the vapor molecules in an inert atmosphere, D_v the self-diffusion

106 coefficient in the bulk, ν the areal density of molecules on the surface, and D_s the surface diffusion

107 coefficient. The different terms in eq. (1) correspond to different mechanisms of surface evolution:

108 viscous flow (the F term), evaporation-condensation (A and A'), bulk diffusion (C), and surface

109   diffusion (B). For each decay mechanism, the decay
110   rate has a characteristic dependence on the grating
111   wavelength, useful for identifying the mechanism; for
112   example, $K \propto \lambda^{-1}$ for viscous flow and $K \propto \lambda^{-4}$ for
113   surface diffusion. Mullins' method has been applied to
114   measure the surface diffusion of many materials, both
115   crystalline[23] and amorphous.[1,3] In the case of a glass-
116   forming Lennard-Jones liquid, Malshe et al. showed by
117   simulations that the surface diffusion constant
118   determined by Mullins' method agrees with that
119   calculated from the mean squared displacement of
120   particles.[24]

121

122   Results

123   Figure 1 shows the DSC traces of POS and ITZ. The
124   two liquids have similar T_gs with the value for ITZ
125   being slightly lower. The lower T_g of ITZ is consistent
126   with the dielectric spectroscopy results,[18,19] which show
127   that ITZ has a shorter structural relaxation time at the
128   same temperature. Different from POS, ITZ undergoes
129   two phase transitions in the liquid state.[18] Cooling from
130   a high temperature, an isotropic liquid of ITZ
131   transforms into a nematic phase ($T_{N/I}$ = 363 K) and then
132   to a smectic phase ($T_{Sm/N}$ = 347 K).

133

134   Posaconazole (POS). Figure 2 shows the typical decay
135   kinetics of a POS surface grating recorded by laser
136   diffraction (Figure 2a) and by AFM (Figure 2b). In
137   each case, the decay was exponential, consistent with
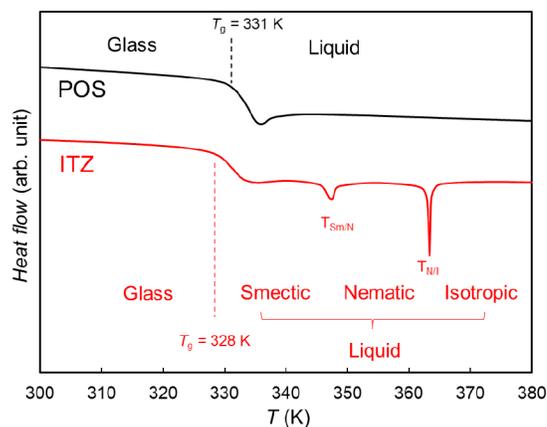
Figure 1. DSC traces of POS and ITZ during heating at 10 K/min. Both systems show a glass transition (T_g) and ITZ shows two LC
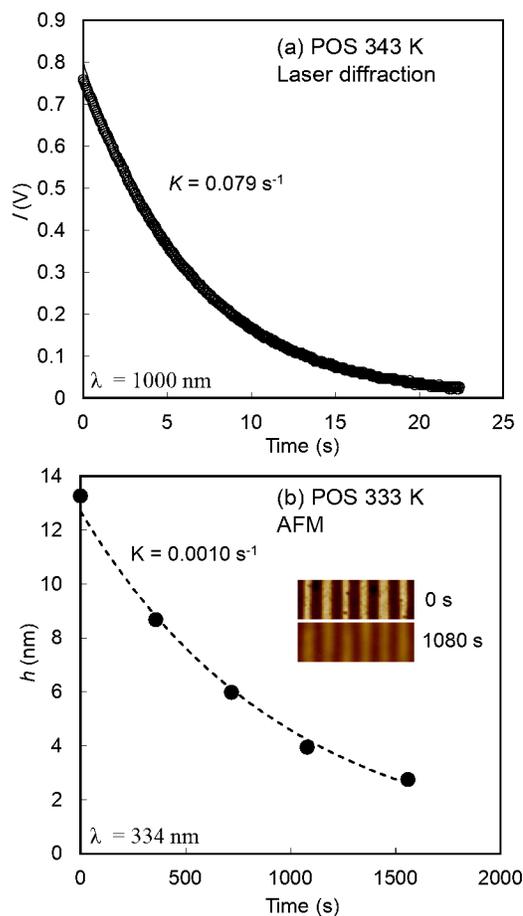
Figure 2. Typical decay kinetics of POS surface gratings. (a) At 343 K, recorded by laser diffraction (λ = 1000 nm). I is the diffraction intensity. (b) At 333 K recorded by AFM (λ = 334 nm). Inset: AFM images at two time points.

138   Mullins' theory.[22] The data were fit to the function $\phi = exp(-Kt)$, where ϕ is h/h_0 for AFM

139   measurements and $(I/I_0)^{1/2}$ for diffraction measurements and K is the decay constant.

140

141   Figure 3a shows the decay constant K of POS at $\lambda = 334$

142   nm as a function of temperature. The structural

143   relaxation time of the POS liquid[18] is also shown for

144   comparison; for this plot, we have extrapolated the

145   experimental data below 331 K using the Vogel-Fulcher-

146   Tammann (VFT) equation. At high temperatures, K

147   closely tracks the structural relaxation time, $K \propto \tau_\alpha^{-1}$.

148   Given that viscosity is generally proportional to τ_α, this

149   indicates that viscous flow is the mechanism of surface

150   flattening (the F term in eq. (1)). For this mechanism,

151   the decay rate should be inversely proportional to the

152   surface grating wavelength, $K \propto \lambda^{-1}$, and this was found

153   to be the case (Figure 3b, see the 338 K result). This

154   relation has been used to convert the K values measured

155   at longer wavelengths to the values at $\lambda = 334$ nm so

156   they can be included in Figure 3a to extend the

157   measurement to higher temperatures.

158

Figure 3. (a) Decay constant K of a POS surface grating at $\lambda = 334$ nm as a function of temperature. At high temperatures, K tracks the structural relaxation time τ_α (second y axis) indicating viscous flow controls surface evolution. Decay becomes faster below T_g + 2 K, indicating a change of surface flattening mechanism. (b) Wavelength dependence of K at two temperatures indicating decay by viscous flow at high temperatures and by surface diffusion at low temperatures.

159   Although viscous flow accounts for the decay rates

160   observed at high temperatures, it does not at low

161   temperatures (Figure 3a). The observed decay rate is

162   "too fast" relative to viscous relaxation below 333 K (T_g

163   + 2 K). This suggests a change of mechanism for surface evolution, as observed in other systems.[1]

164   Figure 3b shows that in this lower temperature region, K has a stronger dependence on the surface

165   grating wavelength, $K \propto \lambda^{-4}$, which is expected for the surface diffusion mechanism. Thus, we assign the

166   mechanism of surface evolution to surface diffusion at low temperatures and use the observed decay

167   rates to calculate the surface diffusion coefficients D_s (Figure 4). For this calculation, we assume $\gamma =$

168   0.05 N/m, a typical value for organic liquids, and obtain $\Omega = 0.92$ nm^3 (molecular volume) from the

169   density of a POS glass (1.27 g/cm^3, assumed to be the same as that an ITZ glass[25]) and its molecular

170   weight (700.8 g/mol). For this rod-like molecule, we estimate its areal density at the liquid/vapor

171   interface by taking into account its preferred orientation. Bishop et al. used NEXAFS to show that POS

172   molecules are nearly vertical at the liquid/vapor interface.[26] Thus we estimate the areal density using:

173    $\nu \approx L/\Omega = 2.8$ nm^{-2}, where L is the length of a POS molecule (2.6 nm, taken from its crystal structure).[27]

174   If POS is treated as a spherical molecule at the surface as opposed to an oriented rod, we obtain $\nu \approx$

175    $\Omega^{-2/3} = 1.0$ nm^{-2} and the calculated D_s would be larger by a factor of 3; given the 5 order of magnitude

176   spread of surface diffusion coefficients (Figure 4), this is

177   a relatively small effect.

178   Figure 4 compares the surface diffusion coefficient D_s of

179   POS and other molecular glasses: *ortho*-terphenyl

180   (OTP),[28] *tris*-naphthyl benzene (TNB),[29] griseofulvin

181   (GSF),[30] indomethacin (IMC),[1] and polystyrene (PS)

182   oligomers (1110 and 1700 g/mole).[31] Figure 4 also

183   shows the bulk diffusion coefficients D_v of the same

184   systems when available.[32,33,34,35] After scaling the

185   temperature by T_g, the D_v values cluster to a "master

186   curve". Relative to this, the D_s values are all larger and

187   do not collapse into a single curve. Note that of all the

188   systems studied to date, POS has the slowest surface

Figure 4. Surface diffusivity in POS and other molecular glasses. T_g is the onset temperature measured by DSC during heating at 10 K/min after cooling at the same rate.

189   diffusion in this comparison: its D_s at T_g, $\sim10^{-17}$ m^2/s (estimated by extrapolation), is 5 orders of

190   magnitude smaller than the value for OTP. In addition, the D_s of POS has the strongest temperature

191   dependence, with an activation energy (389 kJ/mol) close to that for bulk diffusion. The slow surface

192   diffusion of POS will be discussed later and attributed to the near-vertical orientation of the surface

193   molecules and their deep penetration into the bulk.

194

195

Itraconazole (ITZ). Figure 5a shows the surface-grating decay constant K of ITZ at λ = 334 nm as a function of temperature. The bulk structural relaxation time[18] is also shown for comparison. As in the case of POS, the relation $K \propto \tau_\alpha^{-1}$ is observed at high temperatures, indicating surface evolution by viscous flow. This is confirmed by wavelength tests (Figure 5b). At both 323 K and 333 K, we observe the relation $K \propto \lambda^{-1}$, as expected for the viscous-flow mechanism.

The key difference between ITZ and POS is that in ITZ, viscous flow controls surface evolution down to a lower temperature relative to T_g. In ITZ, K tracks τ_α down to $T_g - 5$ K (Figure 5a), whereas in POS, this is the case only down to $T_g + 2$ K (Figure 3a), below which surface diffusion is fast enough to be the decay mechanism (Figure 3b). Thus, surface diffusion in ITZ must be slower than that in POS at the same temperature relative to T_g.

To see the point above more clearly, in Figure 6, we plot the decay constant K against the bulk relaxation time τ_α for both systems. This allows a comparison of the two surface processes at the same bulk mobility. At high temperatures (short τ_α), we find $K \propto \tau_\alpha^{-1}$, confirming surface evolution by viscous flow. In this region, the two systems have very similar decay rates at a common τ_α (bulk mobility), as expected for this mechanism. At low temperatures (long τ_α), the
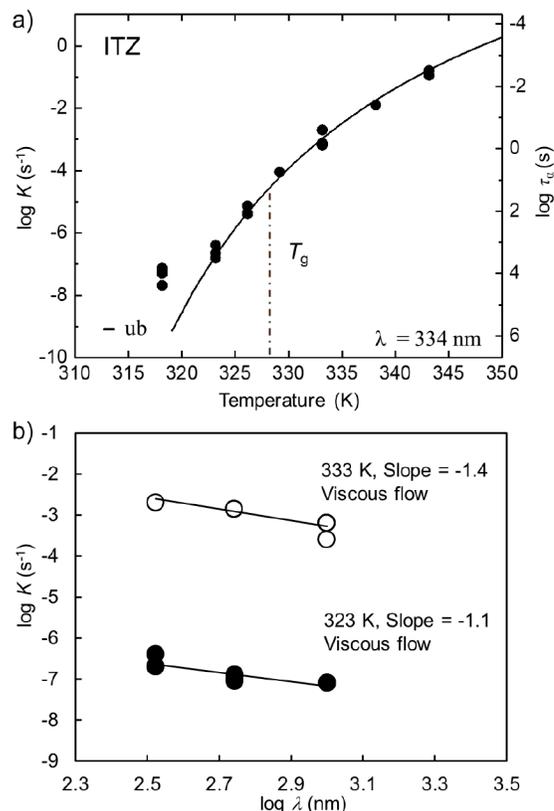
Figure 5. (a) Surface grating decay rate K of ITZ at λ = 334 nm as a function of temperature. "ub" indicates an upper bound from no significant decay in 250 days. (b) K as a function of grating wavelength λ at 323 K and
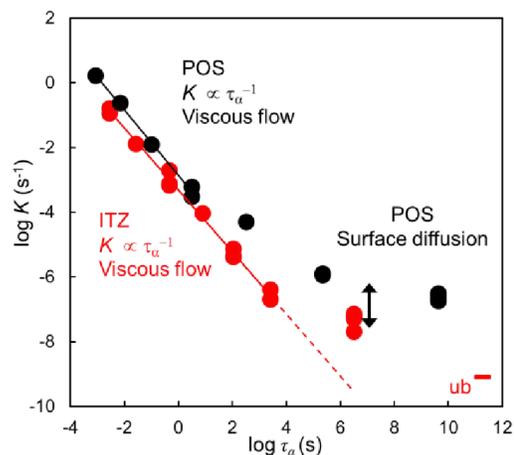
Figure 6. Surface-grating decay constant K at λ = 334 nm plotted against the bulk relaxation time τ_α for ITZ and POS. At high temperatures (short τ_α), $K \propto \tau_\alpha^{-1}$ holds, indicating surface evolution by viscous flow. At low temperatures (long τ_α), faster decay is observed signaling a new decay mechanism.

225   observed decay is faster relative to viscous flow, suggesting a change of decay mechanism. For POS, the

226   new decay mechanism was shown to be surface diffusion by a wavelength test (Figure 3b). It is likely

227   that the ITZ undergoes the same transition to surface diffusion at the lowest temperature studied (we

228   have not verified this by wavelength test due to the very slow decay rates). Under this assumption, we

229   can assess the relative rates of surface diffusion in the two systems: in POS, the transition from viscous

230   flow to surface diffusion occurs at a much higher bulk mobility ($\tau_\alpha \approx 3$ s) than in ITZ ($\tau_\alpha \approx 3000$ s). Thus,

231   surface diffusion in POS is fast enough to be the decay mechanism when bulk mobility is relatively high,

232   but this does not happen in ITZ even at a much lower bulk mobility. From Figure 6, we estimate surface

233   diffusion in ITZ to be ~ 20 times slower than that of POS at $\tau_\alpha \approx 10^7$ s (double-sided arrow).

234

235   **Discussion**

236   The main result of this work is that surface diffusion is significantly slower in the glasses of the rod-like

237   molecules POS and ITZ than in the previously studied systems (Figure 4). Between POS and ITZ,

238   surface diffusion is slower in ITZ (Figure 6). We now discuss these results and suggest that the slow

239   surface diffusion is a consequence of the deep penetration of the nearly vertically orientated surface

240   molecules. We also use the new results to test a previously reported relation between surface mobility

241   and bulk liquid fragility.

242

243   In Figure 7, we illustrate the essential difference

244   between the surface structures of liquids composed

245   of quasi-spherical molecules and rod-like molecules

246   (POS and ITZ). For a liquid of quasi-spherical

247   molecules, each surface molecule penetrates into the

248   bulk by approximately its diameter $d \approx \Omega^{1/3}$, where

249   Ω is the molecular volume. In the case of POS,

250   Bishop et al. have shown by NEXAFS that the rod-

251   like molecules tend to be vertically aligned with $\theta_z \approx$

252   33°, where θ_z is the average angle between the long

253   axis of the molecule $\boldsymbol{n}_L$ and the surface normal $\boldsymbol{n}_z$.[26]

Figure 7. Different surface molecular structures of liquids of quasi-spherical molecules and rod-like molecules POS and ITZ. While both rod-shaped, ITZ molecules form a smectic LC phase whereas POS molecules produce an isotropic liquid. For quasi-spherical molecules, the depth of penetration of a surface molecule is approximately its diameter, $z = d$. The depth of penetration can be significantly larger for vertically oriented rod-like molecules. This anchors them deeper in the bulk where mobility is low, hindering their center-of-mass diffusion.

254   (For this discussion, we take each rod-like molecule as centrosymmetric and θ_z to be positive.) Preferred

255 orientation at interfaces has been observed for many non-spherical molecules and is a result of free-

256 energy minimization in an environment lacking translational symmetry.[36, 37, 38] We estimate the depth of

257 penetration for a surface molecule as $z = L \cos \theta_z$, where $L \approx 2.6$ nm is the length of a POS molecule in

258 its crystals.[27] This yields a penetration depth of 2.2 nm, more than twice the value for a spherical

259 molecule of the same volume ($d = 0.97$ nm), a direct result of preferred orientation.

260

261 In the case of ITZ, the bulk liquid is a smectic LC

262 in the temperature range of our study, and this can

263 influence the orientational order of surface

264 molecules. In the bulk smectic phase, rod-like ITZ

265 molecules tend to be parallel with the LC director

266 forming an average angle of 27°.[18] At the vapor

267 interface, the LC director favors a vertical

268 orientation (homeotropic alignment); this is seen

269 from the annealing behavior of a vapor-deposited

270 glass film.[39] The surface anchoring effect has been

271 observed with other rod-like, LC-forming

272 molecules.[40] Furthermore, simulations have shown

273 that surface molecules of a LC can be slightly more

274 vertically aligned than in the bulk.[41] Together,

275 these results indicate that ITZ molecules favor a

276 vertical orientation at the free surface and that their

277 orientational order should be higher than that of

278 POS molecules. From its bulk orientational order

279 and its length of 2.8 nm (in crystals),[42] we estimate

280 the depth of penetration for an ITZ surface

281 molecule to be 2.5 nm.

282

283 Our central hypothesis is that the diffusion rate of

284 surface molecules is determined by their depth of

285 penetration into the bulk. Because mobility
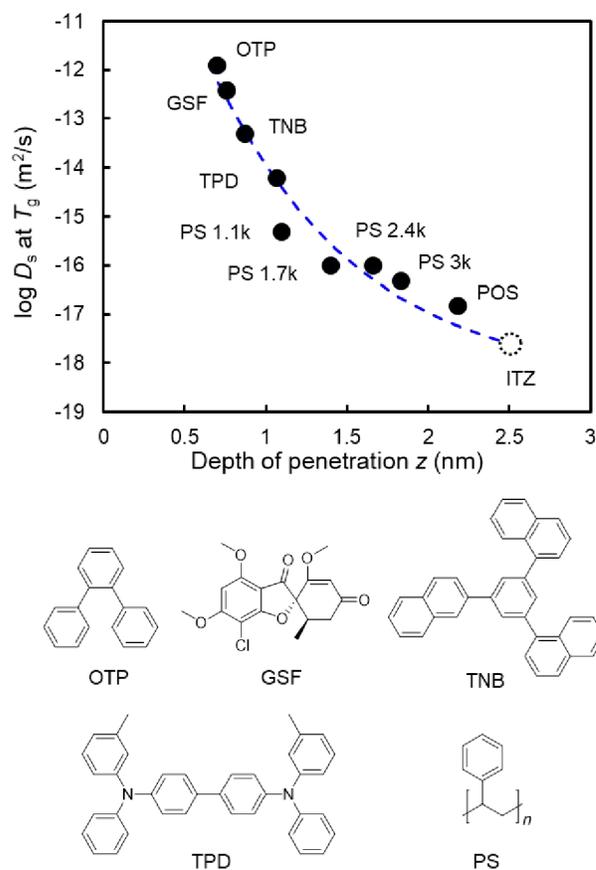
Figure 8. Surface diffusion coefficient D_s at T_g as a function of the penetration depth z. For quasi-spherical molecules OTP, GSF, and TNB, $z \approx d$ (mean molecular size). For rod-like molecules TPD, POS, and ITZ, $z = L \cos \theta_z$, where L is the length of the molecule and θ_z is the average angle between the molecular long axis and the surface normal. For chain-like PS oligomers, $z = R_{ee} \cos \theta_{zee}$, where R_{ee} is the end-to-end distance and θ_{zee} the average angle between the R_{ee} vector and the surface normal. The curve is a fit of the experimental data using a double-exponential form (eq. (2)) thought to represent the surface mobility gradient of a molecular glass. The arrow indicates the estimated D_s for ITZ based on extrapolation of the fitting curve.

286   decreases rapidly across a vapor/glass interface, we expect the translational mobility of a surface

287   molecule to be limited by its bottom part where mobility is the lowest, even if its top part is in a region

288   of higher mobility. We test this idea in Figure 8 by plotting the surface diffusion coefficient at T_g as a

289   function of the penetration depth of surface molecules, using data from this work and the literature. The

290   molecular structures of the systems included are shown at the bottom of Figure 8 and in Scheme 1;

291   Table 1 contains the numerical values. In this analysis, we regard OTP, GSF, and TNB as quasi-

292   spherical molecules and use the mean molecular size $d = \Omega^{1/3}$ to represent the depth of penetration. For

293   the mildly elongated TPD, penetration depth is estimated in the same way as POS and ITZ: $z = L \cos \theta_z$,

294   where $L \approx 1.7$ nm and $\theta_z \approx 51°$ is obtained by atomistic MD simulations.[48] This yields $z = 1.1$ nm,

295   slightly larger than the mean molecular size ($d = 0.9$ nm). For chain-like PS oligomers, penetration depth

296   is calculated from $z = R_{ee} \cos \theta_z$, where R_{ee} is the end-to-end distance [43] and θ_z the average angle between

297   the R_{ee} vector and the surface normal.[50] Given that hydrogen bonds have an independent effect on

298   surface diffusion from molecular dimensions,[3] Figure 8 only includes systems without extensive

299   hydrogen bonds. Though hydrogen bonds might be present in a POS liquid, their contribution to the total

300   vaporization energy is negligible (~ 5%, based on a group-additivity calculation[3,44]) and we include this

301   system in the analysis.

302

303   **Table 1.** Surface diffusion coefficients D_s of molecular glasses and other properties.

	T_g (K)	M (g/mol)	ρ (g/cm³)	d (nm)	L or R_{ee} (nm)	S_z	θ_z (deg.)	z (nm)	$\log D_s$ at T_g (m²/s)
OTP	246	230.3	1.12[45]	0.70	—	—	—	0.70[a]	-11.9[28]
GSF	361	352.8	1.35[46]	0.76	—	—	—	0.76[a]	-12.4[30]
TNB	347	456.6	1.15[47]	0.87	—	—	—	0.87[a]	-13.3[29]
TPD	330	516.7	1.19[2]	0.90	1.7[48]	0.1[48]	51	1.1	-14.2[2]
PS1100	307	990	1.03[49]	1.17	2.1[43]	-0.1[50]	58	1.1	-15.3[31]
PS1700	319	1600	1.03[49]	1.37	2.6[43]	-0.1[50]	58	1.4	-16.0[31]
PS2400	337	2264	1.03[49]	1.54	3.1[43]	-0.1[50]	58	1.7	-16.0[13]
PS3000	343	2752	1.03[49]	1.64	3.5[43]	-0.1[50]	58	1.8	-16.3[11]
POS	331	700.8	1.27[b]	0.97	2.6[27]	—	33[26]	2.2	-16.8
ITZ	328	705.6	1.27[25]	0.97	2.8[42]	0.7[c]	27[18]	2.5	(-17.8)[d]

304   [a] The penetration depth of these quasi-spherical molecules are assumed to be the same as their mean molecular size, $z = d$.
305   [b] Assumed to be the same as that of ITZ.
306   [c] Calculated from the S_z value from Ref. 18 (bulk value).
307   [d] Estimated based on trends in Figures 8 and 9.
308

309   Based on our hypothesis, we expect the rate of surface diffusion to decrease with the depth of

310   penetration. This is indeed observed in Figure 8. We see a smooth falling trend starting from the three

311   quasi-spherical molecules (OTP, GSF, and TNB), to the mildly elongated TPD, to the chain-like PS

312   oligomers, and finally to the rod-like POS. These systems cover a 5 orders of magnitude in D_s and a

313   penetration depth from 0.7 nm (OTP) to 2.2 nm (POS). The open circle indicates the estimated D_s for

314   ITZ by extrapolation (see below).

315

316   The smooth trend observed in Figure 8 suggests that the molecular glasses considered have a similar

317   mobility vs depth profile when compared at T_g and that the different surface diffusion rates simply

318   reflect the different depths at which surface molecules are anchored. In principle, each system in Figure

319   8 has its own mobility vs depth profile. But given the smooth trend observed, a reasonable first

320   approximation is to treat it as a generic mobility profile for van der Waals molecular glasses at T_g. One

321   support for this notion is that the profile in Figure 8 is consistent with the "double-exponential" form for

322   surface mobility gradient observed in simulations: [20,21]

323          $$\tau(z) = \tau_\alpha \exp[-A \exp(-z / \xi)] \qquad\qquad (2)$$

324   where τ_α is the bulk relaxation time, A is a "surface-enhancement" factor, and ξ is the dynamical

325   correlation length. This form is thought to arise from an activation barrier for local relaxation that

326   increases exponentially with depth. Phan and Schweitzer have rationalized this as a consequence of

327   geometric-like, layer-wise transfer of caging constraint from the surface to the bulk.[51,52] The curve in

328   Figure 8 is a fit of the data to eq. (2). In this fitting, we assume $\tau_\alpha = 10$ s at T_g and estimate $\tau(z)$ from the

329   equation: $D_s(z) = d^2/[4\,\tau(z)]$. In essence, the last equation assumes the observed D_s is determined by the

330   local mobility at the depth of penetration z. Figure 8 shows that eq. (2) can accurately describe the

331   experimental data. This argues that despite their different chemistry, the molecular glasses considered

332   have a similar mobility profile $\tau(z)$ at T_g. From this fitting, we obtain $\xi = 1$ nm, consistent with the

333   values obtained from simulations.[20,21]

334

335   We now turn to the slower surface diffusion of ITZ relative to POS. Based on the ideas developed above,

336   the simplest explanation is that the deeper penetration of ITZ surface molecules (2.5 nm vs 2.2 nm)

337   anchor them deeper in the bulk where mobility is lower. This leads to slower center-of-mass diffusion.

338   In Figure 8, we extrapolate the double-exponential fit of the experimental data points to the penetration

339   depth of ITZ to estimate its surface diffusion rate. This yields log D_s (m²/s) = -17.6 at T_g, in agreement

340   with our finding that surface diffusion is slower in ITZ than in POS (Figure 6).

341

342   Chen et al. have performed a similar analysis to that presented in Figure 8 using the mean molecular size

343   d to represent the penetration depth.[3] Their D_s vs d plot includes all the systems in Figure 8 except for

344   POS and ITZ. Their plot shows a smooth decreasing trend, but when included in their plot, the rod-like

345   molecules are outliers. For example, the D_s of POS is 30 times smaller than that of PS1110, but the two

346   molecules have similar d values (Table 1). This is because d can represent the penetration depth of

347   quasi-spherical molecules but not rod-shaped molecules like POS. Because of its near vertical

348   orientation, POS penetrates deeper into the bulk than a spherical molecule of the same volume. It is

349   interesting to note that for the chain-like PS

350   oligomers, d is not greatly different from the

351   estimated depth of penetration z (Table 1). This is

352   because the R_{ee} vector of PS tends toward a parallel

353   orientation at the surface,[50] reducing the depth of

354   penetration.

355

356   **Correlation between Surface Diffusion and Bulk**

357   **Fragility.** Chen et al.[53] reported a correlation between

358   the rate of surface diffusion and the fragility of the

359   bulk liquid, with stronger liquids having slower

360   surface diffusion when compared at T_g. This

361   correlation is useful for predicting surface mobility

362   from the dynamics of bulk liquids. In Figure 9, we

363   test this correlation using the data from this work and

364   the recently reported data on GSF.[30] We plot the D_s

365   value at T_g against the viscosity of the bulk liquid at

366   1.25 T_g (Figure 9a), used as a measure of fragility.[53]

367   While the m index (slope of each curve in Figure 9a

368   taken at T_g) is often used to measure fragility, it is
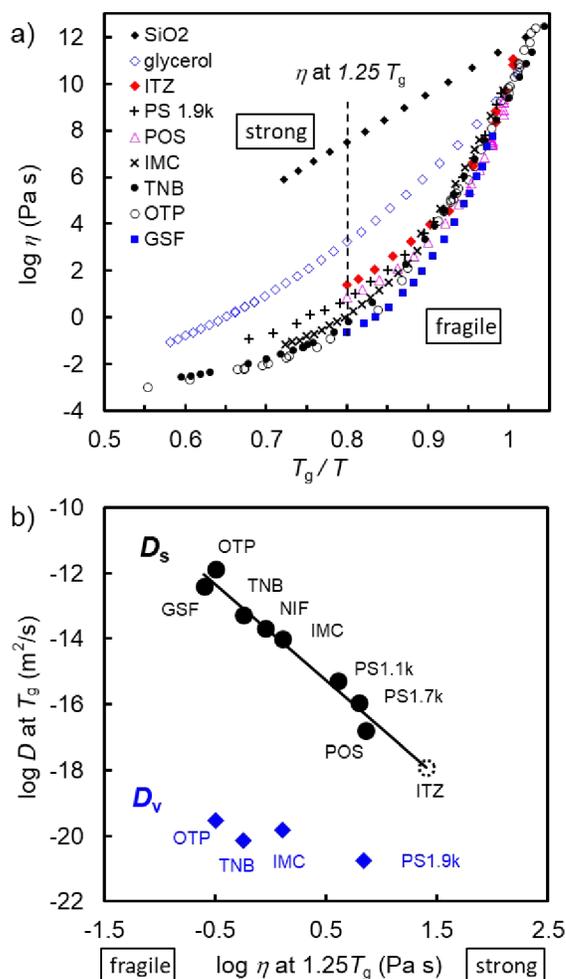
Figure 9. (a) Angell plot of viscosity of glass-forming liquids as a function of temperature scaled by DSC T_g. Viscosity at 1.25 T_g is used as a measure of fragility. (b) Correlation between diffusion coefficients and bulk liquid fragility. The ITZ point (open circle) is estimated by extrapolating the trend for the other data points to the viscosity of ITZ at 1.25 T_g.

369   sensitive to errors of slope-taking in a temperature region where viscosity varies rapidly.[54] Our choice

370   has the advantage of comparing experimental viscosity at a temperature at which displacement from the

371   Arrhenius behavior is large. For GSF, the viscosity data are from Ref. 55, with a small extrapolation to

372   high temperature through a VFT fit (Figure S1). For POS and ITZ, the literature viscosity is extrapolated

373   with the aid of τ_α assuming the two have the same temperature dependence (Figures S2 and Figure

374   S3).[19] Figure 9b shows that the new data points for GSF and POS both fall on the trend of the previous

375   data, confirming the conclusion that stronger liquids have slower surface diffusion. In contrast to the

376   strong dependence of D_s on fragility, the bulk diffusion coefficient D_v has a much weaker dependence (if

377   at all). The surface diffusion coefficient of ITZ can be estimated by extrapolating the trend to the

378   viscosity of ITZ at1.25 T_g. This yields log D_s (m^2/s) = -17.9, in good agreement with the estimate in

379   Figure 8, log D_s (m^2/s) = -17.6, using the penetration depth of ITZ molecules. The average of these two

380   values is entered in Table 1 as a preliminary result for ITZ.

381

382   According to Chen et al.,[53] the correlation in Figure 9 is interpreted as follows. Fragility measures how

383   easily a liquid's dynamics is excited when temperature is raised above T_g; strong liquids resist this

384   excitation, while fragile liquids is excited easily. The change of molecular environment from the bulk to

385   the surface can also be regarded as a form of excitation (loss of nearest neighbors and decrease of

386   density) and a stronger liquid might be expected to resist this excitation more than a fragile liquid. In its

387   application to polymer melts, the elastically collective nonlinear Langevin equation (ECNLE) theory

388   makes a connection between fragility and the relative importance of cage constraint and elastic penalty

389   in segmental rearrangement and associates high fragility with dominance by elastic penalty.[56]

390   Application of the theory to surface dynamics[51,52] could provide a quantitative understanding of the

391   observed correlation in Figure 9.

392

393   **Conclusion**

394   In summary, the method of surface grating decay has been used to measure surface diffusion in the

395   glasses of two rod-like molecules POS and ITZ. Despite their similarity, the two systems differ in that

396   ITZ forms liquid-crystalline phases while POS does not. We find that surface diffusion in these systems

397   is significantly slower than in the glasses of quasi-spherical molecules of similar volume when

398   compared at T_g. This is attributed to the near-vertical orientation of the rod-like molecules at the surface,

399   allowing deep penetration into the bulk where mobility is low. At the same bulk mobility, ITZ has

400   slower surface diffusion than POS. This is attributed to a deeper penetration of the ITZ surface

401   molecules into the bulk.

402

403   We find that for van der Waals molecular glasses (without extensive hydrogen bonds), the surface

404   diffusion rate slows down smoothly with the depth of penetration of surface molecules (Figure 8). The

405   mobility vs depth profile is in good agreement with the double-exponential form observed by

406   simulations and explained by the ECNLE theory. This argues for a generic surface mobility gradient for

407   molecular glasses and the different surface diffusion rates simply reflect the different depths at which

408   surface molecules are anchored. This picture, if valid, allows the use of surface diffusion rate as a probe

409   for the surface mobility gradient, a topic of considerable current interest[20] and a challenging target for

410   direct experimental investigations.

411

412   The smooth trend of surface diffusivity as a function of the penetration depth of surface molecules is

413   potentially useful for predicting surface mobility (Figure 8). For quasi-spherical molecules, the

414   penetration depth is simply the molecular size. For chain-like and rod-like molecules, the penetration

415   depth depends on the orientation of surface molecules relative to the interface and this can be

416   determined by experimental techniques such as NEXAFS[26] and SFG[57] and by MD simulations.[48] For the

417   purpose of predicting surface mobility, another intriguing prospect is to use the correlation between the

418   rate of surface diffusion and the fragility of the bulk liquid (Figure 9).

419

420   The surface mobility trend allows contact with recent studies of physical vapor deposition. During vapor

421   deposition, surface mobility allows equilibration leading to formation of high stability, high density

422   glasses.[9] While the measure of surface mobility most relevant for vapor deposition may not be surface

423   diffusion,[3] Figure 8 allows the speculative conclusion that the best possible glass packing (the "ideal

424   glass") would be most easily approached with small molecules. Indeed, recent experiments have shown

425   that ethylbenzene and toluene can closely approach ideal glass packing when prepared by vapor

426   deposition.[58,59,60]

427

428   To our knowledge, this work is the first to study the surface diffusion of an anisotropic organic solid (the

429   vitrified liquid crystal of ITZ). We find that surface diffusion in ITZ is slower than that in the similar but

430 non-LC system POS. At present it is unclear whether the effect is purely a result of the deeper

431 penetration of ITZ molecules or reflects further constraints by the bulk crystalline phase. Further work in

432 this area will provide insight on surface mobility in crystalline solids.

433

Supporting Information

434

435 Viscosity and structural relaxation time for GSF, POS and ITZ.

436

437 **Conflicts of interest**

438 There are no conflicts of interest to declare.

439

440 **Acknowledgements**

443

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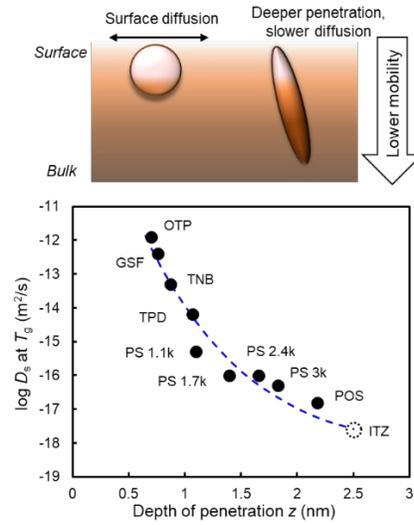
Vertical orientation of rod-like molecules at glass/vapor interface allows deep penetration into the bulk, slowing surface diffusion.