Competing Forces in Chiral Surface Chemistry: Enantiospecificity versus Enantiomer Aggregation

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S Supporting Information

ABSTRACT: The enantiospecific adsorption of enantiomer mixtures on surfaces is dictated by two competing forces: the enantiospecificity of adsorption energetics and the propensity of enantiomers to aggregate into homochiral (conglomerate) or heterochiral (racemate) clusters. These phenomena have been studied by measuring the surface enantiomeric excess, ee_s , of chiral amino acid mixtures adsorbed on Cu single-crystal surfaces and in equilibrium with gas-phase mixtures of varying enantiomeric excess, ee_g . Alanine adsorption on Cu $\{3,1,17\}^{R\&S}$ surfaces is non-enantiospecific, $ee_s = ee_g$, because alanine enantiomeric do not interact with either the



surface or with one another enantiospecifically. Aspartic acid adsorbs enantiospecifically on the Cu{3,1,17}^{*R&S*} surfaces; $ee_s \neq ee_g$, even during exposure to a racemic mixture in the gas phase, $ee_g = 0$. Exposure of the achiral Cu{111} surface to nonracemic aspartic acid, $ee_g \neq 0$, results in local amplification of enantiomeric excess on the surface, $|ee_s| > |ee_g|$, as a result of homochiral aggregation. Finally, despite the fact that the Cu{653}^{*R&S*} surfaces are chiral, the adsorption of aspartic acid mixtures yields $|ee_s| > |ee_g|$, indicating that homochiral aggregation dominates enantiospecific adsorbate—surface interactions. All of these types of behavior are captured by a Langmuir-like adsorption isotherm that includes competition between enantiospecific adsorption and both homochiral (conglomerate) and heterochiral (racemate) aggregation of chiral adsorbates.

1. INTRODUCTION

The importance of enantioselective chemical processing for the production of pharmaceuticals and other bioactive molecules arises from the fact that the biologically relevant molecules of terrestrial living organisms are chiral and exist in only one enantiomeric form.^{1,2} When both enantiomers of chiral pharmaceuticals are ingested by a living organism, the physiological impacts of the two can be significantly different because of the homochirality of the in vivo environment. In other words, one enantiomer of a pharmaceutical may be therapeutically effective while the other can be inactive or even toxic.^{3–5} As a consequence, enantioselective chemical processes are required for the production of chiral compounds with enantiomeric purity. Enantioselectivity can be achieved by exploiting the enantiospecific differences in the physical or chemical properties of two enantiomers interacting with a chiral medium such as a chiral solvent or sorbent.^{6,7} In particular, heterogeneous enantioselective processes utilizing chiral surfaces have attracted a great deal of attention over the past decade due to the inherent ease of separation of reaction products from heterogeneous chiral media.⁸⁻¹¹ Chiral surfaces can be used for separations processes such as chromatography.³ Catalysts with chiral surfaces can convert prochiral reactants into chiral products enantioselectively.¹²⁻¹⁴ A key step in the mechanisms of these processes is enantioselective adsorption on chiral surfaces. Therefore, a fundamental understanding of enantioselective adsorption and chemistry on chiral surfaces is essential for the rational design of enantioselective heterogeneous processes.

The most widely studied chiral surfaces are the chirally modified surfaces of achiral materials.^{9,11,15-19} Such chirally modified surfaces are prepared by the adsorption and tethering of enantiomerically pure chiral organic molecules onto achiral surfaces. Adsorption of a second chiral species leads to enantiospecific diastereomeric interactions with the tethered chiral surface modifier. Less well studied are the enantiospecific interactions of chiral adsorbates with naturally chiral surfaces. Such surfaces can be obtained from materials such as quartz, which have chiral bulk structures and they exhibit enantiospecific interaction with chiral molecules.²⁰ Counterintuitively, chiral surfaces can also be created from achiral bulk materials by exposing high Miller index planes with no mirror symmetry.^{21,22} Figure 1 illustrates the atomic structures of the $Cu{3,1,17}^{S}$, $Cu{653}^{S}$, and $Cu{111}$ surfaces. The achiral Cu{111} surface has mirror-symmetry planes perpendicular to the surface. The Cu{3,1,17}^S and Cu{653}^S surfaces lack mirror symmetry and, as a result, they are chiral and exist in two enantiomorphic forms denoted Cu{hkl}^{R&S}. The sense of rotational order of the (111), (100), and (110) microfacets forming the kink sites on the $Cu{3,1,17}^{S}$ and $Cu{653}^{S}$ surfaces impart a handedness, rendering these surfaces naturally chiral. 22-24

Although most chiral surfaces used in practical applications are chirally modified, $^{3,6-8,25,26}$ naturally chiral single-crystal

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Figure 1. Ball-model depictions of the ideal structures of the naturally chiral Cu{3,1,17}^S, Cu{653}^S, and achiral Cu{111} surfaces. The naturally chiral Cu{3,1,17}^S and Cu{653}^S surfaces have kinked steps, separated by (100) and (111) terraces, respectively. The kinked step structures break surface symmetry, rendering those surfaces chiral. The rotational orientation of the (111), (100), and (110) microfacets forming the kink sites determines the chirality of the surface. Surfaces with clockwise and counterclockwise rotations, (111) \rightarrow (100) \rightarrow (110), are designated *R* and *S*, respectively. The atoms along the step edges have been colored according to coordination number (highest to lowest = lightest to darkest). At right are the structures of aspartic acid and alanine used in this work as chiral probes of enantiospecific adsorption.

surfaces offer a platform for study of fundamental aspects of chiral surface chemistry that are not readily observable when using more complex materials or surfaces modified with chiral organic adsorbates.²⁷⁻³⁰ The structures of chiral single-crystal surfaces and their enantiospecific interactions with chiral molecules have been studied by various methods. Scanning tunneling microscopy (STM) images of the Cu{643}^{R&S} and the $Cu{531}^{R\&S}$ surfaces show that the absolute chirality of the surface is preserved, despite the partial loss of kink sites by thermal roughening.^{31,32} Low-energy electron diffraction (LEED) patterns and near-edge X-ray absorption fine structure (NEXAFS) spectra of enantiomerically pure D- and L-alanine (Ala) on the $Cu{531}^{R}$ surface reveal enantiospecific adsorption geometries and long-range order. 33,34 Temperature-programmed desorption or reaction (TPD or TPR) studies have demonstrated that chiral molecules exhibit enantiospecific adsorption energetics and reaction kinetics on naturally chiral metal surfaces.^{14,21,35–38} Finally, enantiospecific orientations of chiral adsorbates on chiral metal surfaces have been observed by Fourier transform infrared spectroscopy and X-ray absorption spectroscopy.^{30,33,39,40}

The vast majority of studies of chiral species on surfaces have been limited to the use of pure enantiomers or the use of racemic mixtures, often generated by adsorption of prochiral species onto achiral surfaces. Note that prochiral molecules are rendered into the two enantiomers of a chiral species simply by adsorption onto an achiral surface. The study of mixtures of adsorbed enantiomers has been thwarted by the lack of means for enantiodiscrimination of chiral molecules once adsorbed onto a surface. Until recently, the only viable approach was the use of large chiral adsorbates whose enantiomers can be distinguished using STM, provided that imaging conditions are ideal.^{41,42} Recently, we have developed the use of enantiospecific ¹³C isotopic labeling for enantiodiscrimination of chiral molecules or their decomposition products desorbing from a surface.^{27,28,43,44} If one enantiomer of the adsorbed mixture is isotopically labeled, then mass spectrometry can be used to determine the enantiomeric origin of species desorbing from the surface during heating. This is only practical for molecules that can be obtained in enantiomerically pure forms that are also isotopically enriched. The most obvious candidates are the amino acids $(HO_2C-CH(NH_2)-R)$ for which the Lenantiomers are readily available in a wide variety of isotopically labeled forms.

All studies of enantiospecific surface chemistry require three elements: a chiral surface, a chiral probe molecule, and a

physical property measurement that reveals the diastereomeric relationship among the four possible adsorbate/surface combinations.²⁵ In a study of enantiospecific adsorption on naturally chiral Cu $\{3,1,17\}^{R\&S}$ surfaces, we used mixtures of Dand isotopically labeled *L-amino acids (herein, *L denotes an isotopically labeled L-enantiomer).^{28,43,44} Doing so allowed quantification of the enantiomeric excess on the surface, $ee_{s} = \frac{\theta_{D} - \theta_{L}}{\theta_{D} + \theta_{L}}$, versus that in the gas phase, $ee_{g} = \frac{P_{D} - P_{L}}{P_{D} + P_{L}}$, under equilibrium adsorption conditions. That work showed that enantiospecific adsorption arises from strong interactions between the chiral surfaces and the functional groups of the amino acid side chains. On the $Cu{3,1,17}^R$ surface, mixtures of unlabeled D-aspartic acid (D-Asp) and ¹³C-labeled *L-Asp exhibited enantiospecific adsorption equilibrium constants, $\frac{K_{*L/R}}{K_{D/R}} = \frac{P_{\rm D}}{P_{*L}} \frac{\theta_{*L/R}}{\theta_{\rm D/R}} = 2.29 \pm 0.1, \text{ corresponding to an enantio-}$ $K_{\mathrm{D}/R}$ specific difference in adsorption free energies of $\Delta\Delta G_{D^*L} = 3.15$ \pm 0.29 kJ/mol.⁴³ That system exhibits diastereomerism in that *L-Asp adsorption is preferred on the $Cu{3,1,17}^R$ surface, while D-Asp adsorption is preferred on the $Cu{3,1,17}^{S}$ surface. Equally importantly from the perspective of the work reported herein, the enantiospecific adsorption equilibrium constant ratios are independent of the enantiomer ratios in the gas phase, $\frac{K_{D/S}}{K_{*L/S}} = \frac{P_{L}}{K_{D/R}} = \frac{P_{D}}{P_{*L}} \cdot \frac{\theta_{*L/R}}{\theta_{D/R}} = \frac{P_{*L}}{P_{D}} \cdot \frac{\theta_{D/S}}{\theta_{*L/S}}$. This is consistent with a simple Langmuirian description of competitive equilibrium adsorption. As we show in this work, this is not always the case on other surfaces.

On the achiral Cu{111} surface, equilibrium adsorption of D-/*L-Asp mixtures revealed fundamentally different enantio-specific behavior from that observed on the chiral Cu-{3,1,17}^{R&S} surfaces.^{27,43} As expected for achiral surfaces, exposure of Cu{111} to a racemic D-/*L-Asp mixture, $\frac{P_D}{P_L} = 1$, resulted in $\frac{\theta_D}{\theta_{r_L}} = 1$. In other words, adsorption on the Cu{111} surface is not enantiospecific when it is exposed to a racemic mixture of enantiomers. However, despite the fact that Cu{111} is achiral, equilibrium adsorption of nonracemic mixtures of D-/*L-Asp, $\frac{P_D}{P_L} \neq 1$, leads to local amplification of enantiomeric excess on the surface, $|ee_s| > |ee_g|$.²⁷ Similar behavior has been observed during separations of nonracemic mixtures of enantiomers by chromatographic processes using achiral stationary phases.⁴⁵⁻⁴⁷ This adsorption-induced local amplification of ee can be explained by enantiomer self-

aggregation on achiral surfaces. In previous work, we have developed a Langmuir-like adsorption isotherm that successfully captures this phenomenon by accounting for the formation of homochiral D_n and L_n clusters of Asp on the achiral Cu{111} surface.²⁷

Recent studies of the adsorption of chiral propylene oxide (PO) on the Pt{111} surface have also revealed an apparently anomalous dependence of ee_s on ee_g .^{48–50} In that case, the initial adsorption of R- and S-PO mixtures leads to local amplification of ee_s versus ee_g but then transitions to suppression of ee_s versus ee_g as the coverage approaches one monolayer. While the net effect is very similar to our observations for D-/*L-Asp on Cu{111},²⁷ the behavior of R-/S-PO at low coverage on Pt{111} is clearly attributable to enantiospecific adsorption kinetics rather than equilibrium adsorption.

Our prior work has demonstrated that enantiomer mixtures can adsorb enantiospecifically on chiral surfaces such as Cu{3,1,17}^{R&S} and that enantioselectivity can be induced by enantiomer aggregation on achiral surfaces such as Cu{111}.^{27,28} Herein we make the case that enantiospecific adsorption and enantiomer aggregation must both be active forces in adsorption on all chiral surfaces and that these two forces can compete to suppress ees versus eeg or cooperate to amplify ee_s versus ee_g . To make this case, we present new data for adsorption of D-/*L-Asp mixtures on chiral Cu{653}^{R&S} surfaces and show that despite their chirality, enantiomer aggregation competes with and dominates enantiospecific adsorption. To describe these observations we present a simple Langmuir-like model for an adsorption isotherm that reproduces the competition between enantiomer aggregation and enantioselective adsorption.

2. EXPERIMENTAL SECTION

Adsorption of D-/*L-Asp mixtures on chiral Cu{653}^{*R&S*} surfaces was studied in an ultrahigh vacuum (UHV) surface analysis chamber with a base pressure of 2×10^{-10} Torr. The chamber is equipped with an Ar⁺ ion sputter gun to clean the Cu{653}^{*R&S*} surfaces, LEED optics to examine the ordering of clean surfaces, a homemade evaporator to deposit D-/*L-Asp mixtures onto the Cu single crystal surfaces, and an Extrel quadrupole mass spectrometer to detect chemical species in the gas phase and those desorbing from the surface.

The Cu{653}^{R&S} single-crystal sample (Monocrystals Company) was ~10 mm in diameter and 2 mm thick. The Cu single-crystal disk exposed the $Cu{653}^{R}$ surface on one side and the $Cu{653}^{\hat{S}}$ surface on the other side. The temperature of the sample was controlled over the range 90-1000 K by resistive heating and liquid-nitrogen cooling and was measured using a K-type chromel-alumel thermocouple spotwelded to its edge. The temperature was controlled by a computer adjusting the heating current to give the desired temperature or heating rate. The $Cu\{653\}^{\breve{K}\&S}$ sample was cleaned by repeated cycles of 1 keV Ar⁺ ion sputtering while annealing at 850 K for 500 s. To obtain a well-ordered surface structure, the sample was cooled at a controlled rate of -1 K/sat a pressure of <1 × 10⁻⁹ Torr in the final step of the sputtering-annealing procedure. The long-range order and the chirality of the clean $Cu\{653\}^{R\&S}$ surfaces were verified by LEED before adsorption of D-/*L-Asp mixtures.

Unlabeled D-Asp (Sigma-Aldrich, 99% chemical purity) and isotopically labeled $*_{L}$ -Asp (HO₂¹³C-CH(NH₂)-CH₂¹³CO₂H, Cambridge Isotope Laboratories, 98% chemical

purity, 99 atom % $1,4^{-13}C_2$) were vapor-deposited onto the $Cu{653}^{R\&S}$ surfaces by sublimation from a homemade evaporator with two glass vials, one for each enantiomer. The glass vials were wrapped with resistive heating wires, and their temperatures were measured by thermocouples bonded to their exteriors. The fluxes of D- and *L-Asp from each vial were controlled independently by heating the vials to different temperatures. The relative fluxes (pressures) of the two Asp enantiomers generated by given sublimation temperatures were determined by exposing the Cu surface at 400 K to each enantiomer for periods of time short enough that the resulting Asp coverages were linear in the exposure time. The coverage was estimated following each exposure by heating the surface at a constant rate and using the mass spectrometer to measure the yield of CO₂ desorbing from the surface as a result of Asp decomposition.

Measurements of equilibrium adsorption were conducted with total coverages of one monolayer. The $Cu{653}^{R\&S}$ singlecrystal sample was held at 400 K during the initial exposure to D-/*L-Asp mixtures. Following saturation of the surface with Asp, the temperature was held at 460 K to allow rapid enantiomer displacement without thermal decomposition during continued exposure. The exposure times of the $Cu{653}^{R\&S}$ surfaces to the vapors were controlled by opening and closing a shutter placed in front of the glass vials. After exposure to D-/*L-Asp mixtures, the sample was positioned in front of the aperture to the mass spectrometer and then heated from 250 to 670 at 1 K/s to conduct temperature-programmed reaction spectroscopy (TPRS) of the adsorbed species. The relative coverages of D-Asp and *L-Asp on the Cu{653}^{R&S} surfaces were determined by monitoring the CO₂ (m/z = 44)and ${}^{13}\text{CO}_2$ (m/z = 45) signals with the mass spectrometer and then integrating the signals over the temperature range in which Asp decomposed.

3. RESULTS

The primary experiment conducted in the course of this and related work has been one in which Cu surfaces are exposed to gas phase mixtures of D- and $*_{L}$ - amino acids (D-AA or $*_{L}$ -AA) with various enantiomeric excesses, ee_g .^{27,28,43} As the mixtures adsorb, the enantiomeric excess on the surface, ees, is initially equal to that of the gas phase, until the total coverage on the surface reaches $\theta \approx 1$. The surface temperature of 460 K during further exposure prevents the coverage from exceeding $\theta \approx 1$. Amino acids impinging on the saturated surface are only adsorbed transiently; however, their residence time is sufficient to allow exchange with amino acids adsorbed in their anionic state.⁴³ As with many alcohols and acids adsorbed in their deprotonated states on Ag, Cu, or Au surfaces, exchange of adsorbed species with other gas-phase alcohols and acids is quite facile.^{51,52} Our experiments have identified coverage ratios of adsorbed amino acids, $\frac{\theta_{\rm D}}{\theta_{\rm s_{\rm L}}}$ for which exposure to gas-phase mixtures with a given pressure ratio, $\frac{P_{\rm D}}{P_{\rm el}}$, leads to no change in

 $[\]frac{\theta_{\rm D}}{\theta_{*\rm L}}$. These pressures and coverages are in equilibrium with one

another. It is important to remember that the acids in their adsorbed state are typically deprotonated, so the true nature of the equilibrium process is $D-AAH_{(g)} + *L-AA_{(s)} \leftrightarrow D-AA_{(s)} + *L-AAH_{(g)}$, where the subscripts indicate gas-phase or surface-phase species. In the case of Asp, which is likely deprotonated

at both ends, the equilibrium involves transfer of two protons between the adsorbed and gas-phase species.

3.1. Adsorption of D-/*L-Asp Mixtures on Cu{653}⁵. The adsorption of D-/*L-Asp mixtures on Cu{653}^S surface has been studied at partial pressure ratios of $\frac{P_{\rm D}}{P_{\rm st}} = 1/2$, 1, and 2 and using exposure times of 0-80 min with fluxes that saturated the surface after ~15 min. After exposures of varying duration, the composition of the adsorbed layer, $\frac{\theta_{\rm D}}{\theta_{\rm w}}$, was determined by TPRS experiments in which the surface was heated to decompose the adsorbed mixture of D- and *L-Asp into CO₂, $CH_3C\equiv N_1$ and H_2 and measuring the yields of CO_2 and ${}^{13}CO_2$ using the mass spectrometer. The decomposition process appears to lead stoichiometrically to these gas-phase products, leaving little contamination on the surfaces. Mutual displacement of the two enantiomers has been demonstrated previously on the Cu $\{3,1,17\}^{R\&S}$ and Cu $\{111\}$ surfaces, resulting in the evolution of the enantiomer coverages toward equilibrium with increasing exposure time.^{27,43}

Despite the fact that the Cu{653}^S surface is chiral and the fact that D- and *L-Asp have been shown to adsorb enantiospecifically on the chiral Cu{3,1,17}^{R&S} surfaces, there is no evidence of enantiospecific adsorption on Cu{653}^S. Figure 2 shows that when Cu{653}^S at 460 K is exposed to a



Figure 2. D-/*L-Asp coverage ratios, θ_D/θ_{*L} on Cu{653}^S at 460 K as a function of exposure time to D-/*L-Asp gas mixtures with $P_D/P_{*L} =$ 1/2 (red symbols), 1 (black symbols), and 2 (blue symbols). The data represented by solid circles were obtained by starting with the clean Cu{653}^S surface. The downward red triangles, red diamonds, and upright red triangles show the data obtained by starting with a monolayer of D-/*L-Asp having $\theta_{D/S}/\theta_{*L/S} = 0.3$, 0.18, and 0.1, respectively. The blue diamonds are data obtained by starting with $\theta_{D/S}/\theta_{*L/S} = 5.5$. The thick solid lines at the right represent equilibrium coverage ratios for exposure to D-/*L-Asp mixtures with $P_D/P_{*L} = 1/2$, 1, and 2.

racemic mixture of D-/*L-Asp (black circles), the coverage ratio on the surface remains $\frac{\theta_{D/S}}{\theta_{*L/S}} = 1$ for all exposure times. In contrast, the same experiment on the Cu{3,1,17}^{*R&S*} surfaces revealed that, once the surfaces were saturated, the coverage ratio diverged from unity enantiospecifically to reach $\frac{\theta_{D/S}}{\theta_{*L/R}} = \frac{\theta_{*L/R}}{\theta_{D/R}} = 2.29 \pm 0.17$.⁴³ Note also that as shown in previous studies, the fact that the coverage ratio remains unity indicates that there is no observable ¹³C isotope effect differentiating the adsorption energies of *L-Asp and D-Asp.²⁷

Although adsorption of the racemic D-/*L-Asp mixture does not show enantiospecificity on the Cu{653}^S surface, the adsorption behavior of nonracemic D-/*L-Asp mixtures does reveal evolution of the coverages as a result of enantiomer displacement. During exposure to D-/*L-Asp mixtures with $\frac{P_{\rm D}}{P_{\rm r}}$ = 2 (solid blue circles), the initial (<15 min) coverage ratio is $\frac{\theta_{\rm D/S}}{\theta_{*{\rm L/S}}}$ = 2 but begins to increase once the surface is saturated with Asp. Conversely, when $\frac{P_{\rm D}}{P_{\rm r}} = 0.5$ (solid red circles) the value of $\frac{\theta_{\mathrm{D}/S}}{\theta_{\mathrm{v}_{\mathrm{L}/S}}}$ decreases once the surface becomes saturated. If the Cu{653}^S surface is initially saturated with $\frac{\theta_{D/S}}{\theta_{*L/S}} = 0.3$ (solid, red, downward triangles) and then exposed to the gas mixture with $\frac{P_{\rm D}}{P_{\rm rL}}$ = 0.5, the value of $\frac{\theta_{\rm D/S}}{\theta_{\rm rL/S}}$ continues to decrease with exposure time. However, when the initial coverage is $\frac{\theta_{\mathrm{D/S}}}{\theta_{*\mathrm{L/S}}} = 0.1$ (solid, red, upright triangles), it increases with further exposure. These measurements bound the value of the coverage ratio in equilibrium with $\frac{P_{\rm D}}{P_{\rm e_{\rm L}}}$ = 0.5. A steady-state coverage ratio is achieved when the surface is initially covered with $\frac{\theta_{\text{D}/S}}{\theta_{s_{\text{L}/S}}} = 0.18$ (solid, red diamonds); the coverage ratio does not change during exposure to $\frac{P_{\rm D}}{P_{\rm D}}$ = 0.5. Similarly, there is no change in the value of $\frac{\theta_{D/S}}{\theta_{*L/S}}$ during exposure to $\frac{P_D}{P_{*L}} = 2$ when the surface is initially covered with $\frac{\theta_{D/S}}{\theta_{*L/S}}$ = 5.5 (solid, blue diamonds). This implies that $\frac{\theta_{\text{D/S}}}{\theta_{*\text{L/S}}} = 0.18$ and 5.5 are the equilibrium coverage ratios for D-/*L-Asp mixtures having $\frac{P_{\rm D}}{P_{\rm eL}}$ = 0.5 and 2, respectively. The fact that these coverage ratios differ from the corresponding pressure ratios must arise from enantiomer aggregation rather than enantiospecific interaction of the adsorbates with the chiral surface; the value of $rac{ heta_{
m D/S}}{ heta_{^{
m e_{L/S}}}}=1$ resulting from exposure of $Cu{653}^{S}$ to racemic D-/*L-Asp discounts enantiospecific interactions with the surface. Finally, control measurements on the $Cu{653}^R$ surface (Figure 3) reveal diastereomerism; the values of the equilibrium coverage ratios obey $\frac{\theta_{\mathrm{D/S}}}{\theta_{\mathrm{*L/S}}} = \frac{\theta_{\mathrm{*L/R}}}{\theta_{\mathrm{D/R}}} \neq \frac{\theta_{\mathrm{*L/S}}}{\theta_{\mathrm{D/S}}} = \frac{\theta_{\mathrm{D/R}}}{\theta_{\mathrm{*L/R}}}$

The data in Figure 2 characterize adsorption equilibria in which the enantiomeric excess on the surface, $ee_{\rm s} = (\theta_{\rm D} - \theta_{*\rm L})/(\theta_{\rm D} + \theta_{*\rm L})$, is determined by the enantiomeric excess in the gas phase, $ee_{\rm g} = (P_{\rm D} - P_{*\rm L})/(P_{\rm D} + P_{*\rm L})$, rather than the chirality of the surface. This is revealed by the fact that the equilibrium value of $\frac{\theta_{\rm D/S}}{\theta_{*\rm L/S}} = 0.18$ during exposure to a nonracemic D-/*L-Asp mixture with $\frac{P_{\rm D}}{R_{\rm L}} = 0.5$ is the inverse of the value of $\frac{\theta_{\rm D/S}}{\theta_{*\rm L/S}} = 5.5$ resulting from exposure to the D-/*L-Asp mixture with $\frac{P_{\rm D}}{R_{\rm L}} = 2$. Also, the lack of enantiospecific adsorption is demonstrated clearly by the comparison of results on Cu{653}^S (solid symbols) with those on Cu{653}^R (open symbols) in Figure 3 (lower right). The values of $\frac{\theta_{\rm D/S}}{\theta_{*\rm L/S}}$ and $\frac{\theta_{\rm D/R}}{\theta_{*\rm L/R}}$ are unity for all exposures to nonracemic D-/*L-Asp. However, for exposures to nonracemic mixtures with $\frac{P_{\rm D}}{R_{\rm L}} \neq 1$ the values of

P_0:P*

1:1

2



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Figure 3. D-/*L-amino acid coverage ratios, θ_D/θ_{*L} on Cu{3,1,17}^{*R&S*}, Cu{653}^{*R&S*}, and Cu{111} surfaces at 460 K as functions of exposure time to gas mixtures with $P_D/P_{*L} = 0.5$ (red symbols), 1 (black symbols), and 2 (blue symbols). For the chiral surfaces, solid symbols and solid lines are used for the *S*-enantiomer and open symbols and dashed lines for the *R*-enantiomer. The thick lines at the right of each graph indicate the estimated values of the equilibrium coverage ratios. (Upper left) D-/*L-Ala/Cu{3,1,17}^{*R&S*}. (Upper right) D-/*L-Asp/Cu{3,1,17}^{*R&S*}. (Lower left) D-/*L-Asp/Cu{111}. (Lower right) D-/*L-Asp/Cu{653}^{*R&S*}.

 $\frac{\theta_{\mathrm{D/S}}}{\theta_{*\mathrm{L/S}}}$ and $\frac{\theta_{\mathrm{D/R}}}{\theta_{*\mathrm{L/R}}}$ evolve in the same direction and converge on the

same equilibrium values with increasing exposure. Note that purely enantiospecific adsorption for which ee_s is determined by only the chirality of the surface would result in equilibrium coverages related by diastereomerism, $\frac{\theta_{D/S}}{\theta_{eL/S}} = \frac{\theta_{eL/R}}{\theta_{D/R}}$ (the inverse of our observation). Our observations on Cu{653}^{R&S} reveal adsorption behavior very similar to that observed on achiral Cu{111} (Figure 3 lower left). Thus, despite the fact that Cu{653}^{R&S} surfaces are chiral and that Asp has been shown to adsorb enantiospecifically on the chiral Cu{3,1,17}^{R&S} surfaces, the adsorption behavior of D-/*L-Asp mixtures on the Cu{653}^{R&S} surfaces suggests that enantiomer aggregation competes with and dominates any enantiospecific interactions between D- and *L-Asp and the Cu{653}^{R&S} surfaces.

3.2. Adsorption of Amino Acid Mixtures on Cu{653}^{*R&s*}, Cu{3,1,17}^{*R&s*}, and Cu{111}. The various types of adsorption behavior observed for enantiomer mixtures on chiral and achiral Cu surfaces are illustrated by the data in Figure 3, which compares the evolution of $\frac{\theta_D}{\theta_{e_L}}$ with duration of Cu{653}^{*R&s*}, Cu{3,1,17}^{*R&s*}, and Cu{111} exposure to mixtures of D-/*L-Ala and D-/*L-Asp. In all four cases, we plot $\frac{\theta_D}{\theta_{e_L}}$ versus time of exposure to gas phase D-/*L-enantiomer mixtures with values of $\frac{P_D}{P_{e_L}} = 0.5$ (red symbols), 1 (black symbols), and 2 (blue symbols). The solid and open symbols (solid and dashed lines) represent the data on the *S* and the *R* enantiomorphs of the surfaces, respectively. The thick dashed and solid bars at the right of each plot represent the equilibrium values of $\frac{\theta_D}{\theta_{e_L}}$ for given values of $\frac{P_D}{P_L}$ and have been determined by finding initial coverage ratios that do not change with

subsequent exposure to D-/*L-Ala or D-/*L-Asp (see Figure 2). The data for D-/*L-Ala/Cu $\{3,1,17\}^{R\&S}$, D-/*L-Asp/Cu $\{3,1,17\}^{R\&S}$, and D-/*L-Asp/Cu $\{111\}$ are reproduced from prior publications.^{27,43,44}

The adsorption of D-/*L-Ala mixtures on the Cu{3,1,17}^{R&S} (Figure 3 upper left) exhibits competitive adsorption behavior that is entirely consistent with nonenantiospecific adsorption describable by a classical competitive Langmuir adsorption isotherm.⁴⁴ The key point is that $\frac{\theta_{D/R}}{\theta_{*L/R}} = \frac{\theta_{D/S}}{\theta_{*L/S}} = \frac{P_D}{P_L}$, which implies that $K_{D/S} = K_{*L/S} = K_{*L/R} = K_{D/R}$, where $K_{D/S}$ is the adsorption equilibrium constant for D-amino acid on S-surface. The interactions of D-/*L-Ala with the chiral $Cu{3,1,17}^{R\&S}$ surface must be enantiospecific at some level; however, given that the R group on alanine is a $-CH_3$ that interacts only weakly with the Cu surface, it is not too surprising that the adsorption of Ala is not measurably enantiospecific. The structure and energetics of deprotonated D- and L-Ala on the Cu{3,1,17}^S surface has been determined using DFT.⁴⁴ These calculations predicted a preference for L-Ala adsorption by only 1.1 kJ/mol. On the basis of the accuracy of our measurements using D- and L-Asp on the Cu $\{3,1,17\}^{R\&S}$, we suggest that the enantiospecific difference in the adsorption energetics of D- and L-Ala is <0.3 kJ/mol.⁴³

The adsorption of D-/*L-Asp mixtures on the Cu{3,1,17}^{*R&S*} surfaces in Figure 3 (upper right) exhibits behavior that can be described simply in terms of enantiospecific, competitive Langmuir adsorption.^{28,43} The D-/*L-Asp coverages ratios equilibrated with racemic D-/*L-Asp (black symbols) have $\frac{\theta_{D/S}}{\theta_{rL/S}} = \frac{\theta_{*L/R}}{\theta_{D/R}} = 2.2$; in other words, the equilibrium values of $\frac{\theta_D}{\theta_{*L}}$ differ from unity and are inverted on the two enantiomorphs of the chiral Cu{3,1,17} surface. Equally importantly, the ratios of the enantiospecific adsorption equilibrium constants,

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 $\frac{K_{\text{D/S}}}{K_{*\text{L/S}}} = \frac{K_{*\text{L/R}}}{K_{\text{D/R}}} = \frac{P_{\text{D}}}{P_{\text{L}}} \cdot \frac{\theta_{*\text{L/R}}}{\theta_{\text{D/R}}} = \frac{P_{\text{H}}}{P_{\text{D}}} \cdot \frac{\theta_{\text{D/S}}}{\theta_{*\text{L/S}}}$, are independent of the gasphase pressure ratio, $\frac{P_{\text{D}}}{P_{\text{H}}}$, as predicted by a competitive Langmuir isotherm with equilibrium constants that are independent of the enantiomer coverages. The fact that Asp has two carboxylate groups, both of which can deprotonate to interact with the surface, thereby restricting the interaction of the amine group with the surface, is likely to be the cause of the different behaviors and enantiospecificities of Ala and Asp on the Cu{3,1,17}^{R&S} surfaces.

Adsorption of D-/*L-Asp mixtures on Cu{111} cannot be enantiospecific simply because the surface is achiral. This is demonstrated clearly in Figure 3 (lower left), which shows that during exposure to racemic D-/*L-Asp, $\frac{P_{\rm D}}{R_{\rm L}} = 1$, the adsorbate coverage ratio remains $\frac{\theta_{\rm D}}{\theta_{\rm r_L}} = 1$ (black symbols).²⁷ This has also been demonstrated on the achiral Cu{100} surface.⁴³ Critically, these experiments demonstrate that there is no ¹³C-isotope effect that is differentiating *L-Asp adsorption from that of D-Asp. The extraordinary observation on Cu{111} is that when exposed to a D-/*L-Asp mixture with $\frac{P_{\rm D}}{P_{\rm L}} = 2$, the coverage on the surface increases from a value of $\frac{\theta_{\rm D}}{\theta_{\rm e_L}}$ = 2 at low exposures to an equilibrated value of $\frac{\theta_{\rm D}}{\theta_{*\rm L}}$ = 16. Similarly, the exposure of Cu{111} to a mixture with $\frac{P_{\rm D}}{P_{\rm eL}}$ = 0.5 results in an equilibrated coverage ratio of $\frac{\theta_{\rm D}}{\theta_{\rm el}}$ = 0.06. This process of enantiomer partitioning is driven by the enantiomeric excess in the gas phase and results in a local amplification of enantiomeric excess on the surface, lee_s|>lee_g|. We have previously developed a simple, Langmuir-like adsorption isotherm that accounts for these results in terms of an enantiomer aggregation mechanism that results in the formation of homochiral D_n and L_n clusters on the Cu{111} surface.²⁷ While we have shown for D-/*L-Asp/Cu{111} that the local amplification of enantiomeric excess on the surface occurs under equilibrium adsorption conditions, it has been shown that similar behavior in another system, R- and S-PO/Pt $\{111\}$, can be attributed to enantiospecific adsorption kinetics.⁴⁸⁻⁵⁰ This type of apparent symmetry breaking and amplification of enantiomeric excess has been observed in a number of other types of systems including sublimation of enantiomers, crystallization, and autocatalysis.53-5

Despite the fact that Cu{653}^{*R&S*} surfaces are chiral, the data shown in Figure 2 and 3 (lower right) reveal that D-/*L-Asp adsorption is consistent with enantiomer aggregation dominating enantiospecific adsorption. Exposure of the Cu{653}^{*R&S*} surfaces to racemic D-/*L-Asp results in the equilibrium adsorption of a racemic monolayer. This implies that the enantiospecific difference in the adsorption free energies of the two enantiomers is <0.3 kJ/mol. Although there must be some enantiospecificity to the equilibrium constants for D- and *L-Asp adsorption on Cu{653}^{*R&S*}, $\frac{K_{D/S}}{K_{*L/S}} \neq \frac{K_{*L/R}}{K_{D/R}}$, it is undetectable; whereas, the effects of enantiomer aggregation are clearly observed. Adsorption of nonracemic D-/*L-Asp results in local amplification of enantiomeric excess on the surface. It is worth noting that this case is also different from adsorption of D- and *L-Ala on Cu{3,1,17}^{*R&S*} (Figure 3 upper left) in which D-/*L-Ala mixtures reveal neither enantioselective adsorption nor enantiomer aggregation. For all gas phase ratios of enantiomers $\frac{\theta_{\text{D/R}}}{\theta_{\text{e}_{\text{L/R}}}} = \frac{\theta_{\text{D/S}}}{\theta_{\text{e}_{\text{L/S}}}} = \frac{P_{\text{D}}}{P_{\text{e}_{\text{L}}}}$, or equivalently, $ee_{\text{s}} = ee_{\text{g}}^{44}$.

Equilibrium adsorption of enantiomer mixtures on surfaces is best captured by expression of ee_s as a function of ee_g , as shown in Figure 4 for D-/*L-Asp adsorption on Cu{653}^{R&S},



Figure 4. Plots of e_s versus e_g for equilibrium adsorption at 460 K of gas phase mixtures of amino acid enantiomers on chiral and achiral Cu surfaces. The equilibrium adsorption of D-/*L-Ala on Cu{3,1,17}^{R&S} (blue squares) follows $ee_s^R = ee_s^S = ee_g$, showing neither enantiospecificity nor enantiomer aggregation. The equilibrium adsorption of D-/*L-Asp on Cu{3,1,17}^R (solid red triangles) and Cu{3,1,17}^S (open red triangles) results in $ee_s^R(0) = -ee_s^S(0) \neq 0$, revealing enantiospecific adsorption. The equilibrium adsorption of D-/*L-Asp on Cu{111} (green diamonds) and Cu{653}^{R&S} (black circles) leads to $ee_s(0) = 0$ but $ee_s \neq ee_g$ otherwise, revealing enantiomer aggregation.

Cu{3,1,17}^{*R&S*}, and Cu{111} and for D-/*L-Ala adsorption on Cu{3,1,17}^{*R&S*}. It is worth noting that the data in this Figure are only made possible by the fact that we can control the fluxes of enantiomers independently and thus span the range of $-1 \le ee_g \le 1$. The vast majority of surface science studies of chiral adsorbates have adsorbed either the pure enantiomer or the racemic mixture and thus only accessed $ee_g = -1$, 0, or 1.

The equilibrium values of $ee_s(ee_g)$ (Figure 4) for D-/*L-Ala on Cu{3,1,17}^{R&S} (open blue symbols) show the result expected for a system that exhibits neither enantiospecificity nor enantiomer aggregation, $ee_s^R = ee_s^S = ee_g$, where superscripts R and S denote surface chirality. The data for D-/*L-Asp on Cu{3,1,17}^{R&S} (red symbols) show the adsorption behavior expected for purely enantiospecific adsorption with no influence of aggregation, $ee_s^R(0) = -ee_s^S(0) \neq 0$. The data for D-/*L-Asp on Cu{111} (green symbols) exhibit the characteristics expected for adsorption dominated by enantiomer aggregation, $ee_s(0) = 0$ but $ee_s \neq ee_g$ otherwise. It is clear in this regard that despite the fact that Cu{653}^{R&S} (black symbols) behaves like a system in which enantiomer aggregation dominates.

Finally, note that in Figure 4 D-/*L-Asp on Cu{111} and D-/ *L-Asp on Cu{653}^{*R&S*} both exhibit characteristics of enantiomer aggregation with $|ee_s| > |ee_g|$. In other words, the local ee_s on the surface is amplified relative to that in the gas phase. This is attributed to the formation of homochiral clusters, D_n and L_n, by enantiomer self-aggregation on the surface.^{27,45-47} This is equivalent to conglomerate formation during crystallization of enantiomer mixtures from solution. One could also imagine that it is possible to form heterochiral clusters, $(DL)_n$, or racemate phases. Such heterochiral enantiomer aggregation on the surface would result in the local suppression of enantiomeric excess with respect to that in the gas phase, $|ee_s| < |ee_g|$. Thus homochiral cluster and heterochiral clustering should be readily distinguishable based

on the slope of $ee_s(ee_g)$ evaluated at $ee_g = 0$; that is, $\frac{dee_s}{dee_g}\Big|_0 > 1$ implies homochiral (conglomerate) clustering while $\frac{dee_s}{dee_g}\Big|_0 < 1$

implies heterochiral (racemate) clustering.

4. DISCUSSION

The key point of the work presented herein is that both enantiospecific adsorption and enantiomer aggregation must, in general, be active driving forces in chiral surface chemistry. Depending on the system, they can augment one another to amplify $ee_s(ee_{\sigma})$ or compete to suppress $ee_s(ee_{\sigma})$. In prior work, we have successfully described the local amplification of chirality observed during adsorption of D-/*L-Asp on Cu{111} through considering the role of homochiral cluster formation via enantiomer self-aggregation.²⁷ The solid green curve in Figure 4 is the fit of a Langmuir-like adsorption isotherm that accounts for the formation of homochiral clusters of 10 D- or *L-Asp molecules on the Cu{111} surface. Fits of the isotherm for 8 or 12 molecule clusters were also equally acceptable. In the following, we generalize this model to include two additional features that must be relevant to equilibrium adsorption of enantiomer mixtures on surfaces. One is the fact that on chiral surfaces the equilibrium constants for processes involving chiral species must be enantiospecific. The other feature is the formation of heterochiral clusters, $(DL)_{n}$ in addition to homochiral clusters, D_{2n} and L_{2n} . Although we have not observed behavior that would result from the formation of heterochiral clusters in our work, there have been observations of heterochiral clusters or racemate phases forming during the adsorption of racemic mixtures on surfaces.^{48,49,5}

As with all Langmuir-like models, ours says nothing about the structure of the surface other than that it consists of undescribed and identical adsorption sites. Ours makes the distinction between sites being either chiral or achiral but nonetheless identical on any surface. It is certainly the case that there are other models that might describe the phenomenology that we have observed. It is possible and even probable that the amino acids induce some level of reconstruction of the surfaces so that they no longer have their ideal structures, as pictured in Figure 1.^{60–62} Our model does not address these details and their impact on enantiomer adsorption. We pose it as one framework for describing our observations. Validating it relative to other adsorption models that might be posed in the future will require additional investigation.

4.1. Adsorption Isotherm for Enantiomeric Mixtures on Surfaces. Our generalized Langmuir-like model describing equilibrium adsorption of D- and L-enantiomers on a surface is depicted in Figure 5. Two enantiomers adsorb on a chiral surface competitively as monomers, D_1 and L_1 , with enantiospecific adsorption equilibrium constants, $K_a^D \neq K_a^L$. If the surface is achiral, then $K_a^D = K_a^L$. The adsorbed D- and Lmonomers can undergo heterochiral aggregation to form racemate (DL)_n clusters with a nonenantiospecific equilibrium constant, K_r^{DL} , or they can undergo homochiral aggregation to



Figure 5. Equilibrium adsorption of D- and L- enantiomers of a chiral adsorbate. The monomers, D₁ and L₁, adsorb with adsorption equilibrium constants, K_a^D and K_a^L , that are enantiospecific if the surface is chiral but equal otherwise. Monomers can form racemate (DL)_n clusters with a nonenantiospecific equilibrium constant, K_r^{D} , and they can form conglomerate D_{2n} and L_{2n} clusters with equilibrium constants are enantiospecific, if the surface is chiral, but equal otherwise.

form conglomerate D_{2n} and L_{2n} clusters. The equilibrium constants K_c^D and K_c^L are enantiospecific ($K_c^D \neq K_c^L$) if the surface is chiral but equal otherwise. One of the assumptions of the pure Langmuir model is that adsorbed species do not interact with one another. Thus it does not allow for the formation of cluster that inherently requires adsorbate–adsorbate attractions.

The equilibrium coverages of all adsorbed species $(\theta_{D_l}, \theta_{L_l}, \theta_{D_{2a'}}, \theta_{L_{2a'}}, \theta_{D_{2a'}}, \theta_{D_{2a'}},$

$$\theta_{\mathrm{D}_{1}} = K_{\mathrm{a}}^{\mathrm{D}} P_{\mathrm{D}} \delta \tag{1}$$

$$\theta_{L_1} = K_a^L P_L \delta \tag{2}$$

$$\theta_{\mathsf{D}_{2n}} = K_{\mathsf{c}}^{\mathsf{D}} \theta_{\mathsf{D}_{1}}^{2n} \tag{3}$$

$$\theta_{\mathrm{L}_{2n}} = K_{\mathrm{c}}^{\mathrm{L}} \theta_{\mathrm{L}_{1}}^{2n} \tag{4}$$

$$\theta_{\mathrm{DL}_{n}} = K_{\mathrm{r}}^{\mathrm{DL}} \theta_{\mathrm{D}_{1}}^{n} \theta_{\mathrm{L}_{1}}^{n}$$
⁽⁵⁾

where δ is the vacancy coverage. The vacancy coverage in eqs 1 and 2 is given by

$$\delta = 1 - \theta_{\mathrm{D}_1} - \theta_{\mathrm{L}_1} - 2n\theta_{\mathrm{D}_{2n}} - 2n\theta_{\mathrm{L}_{2n}} - 2n\theta_{\mathrm{D}_{\mathrm{L}_n}}$$
(6)

In these terms, the ee_s on the surface is

$$ee_{s} = \frac{(\theta_{D_{1}} + 2n\theta_{D_{2n}} + n\theta_{DL_{n}}) - (\theta_{L_{1}} + 2n\theta_{L_{2n}} + n\theta_{DL_{n}})}{(\theta_{D_{1}} + 2n\theta_{D_{2n}} + n\theta_{DL_{n}}) + (\theta_{L_{1}} + 2n\theta_{L_{2n}} + n\theta_{DL_{n}})}$$
(7)

For simplicity we redefined the equilibrium constants

$$K_{\rm a}^{\rm D} = \Delta_{\rm a} K_{\rm a} \tag{8}$$

$$K_{\rm a}^{\rm L} = \Delta_{\rm a}^{-1} K_{\rm a} \tag{9}$$

$$K_{\rm c}^{\rm D} = x \Delta_{\rm c} K_{\rm c} \tag{10}$$

$$K_{\rm c}^{\rm L} = x \Delta_{\rm c}^{-1} K_{\rm c} \tag{11}$$

$$K_{\rm r}^{\rm DL} = (1 - x)K_{\rm c}$$
 (12)

In these terms, Δ_a determines the enantiospecificity of the adsorption equilibrium constants; $\Delta_a = 1$ implies nonenantiospecific adsorption (or adsorption on an achiral surface). Similarly, Δ_c determines the enantiospecificity of the



Figure 6. 2D and 3D plots of ee_s versus ee_g obtained from a Langmuir-like model describing equilibrium adsorption of D- and L-enantiomer mixtures on a surface. All were calculated with $K_aP = 1000$, which ensures that $\theta \approx 1$. (Left) Enantiospecific adsorption without aggregation ($K_c = 0$, Δ_c and nare not applicable). (Middle) Nonenantiospecific adsorption with homochiral aggregation ($\Delta_a = 1$, $K_c = 1000$, x = 1). The 3D plot is calculated for n= 4. (Right) Nonenantiospecific adsorption with both conglomerate and racemate aggregation ($\Delta_a = 1$, $K_c = 1000$, $\Delta_c = 1$, n = 4).

equilibrium constants for conglomerate (homochiral) clustering; $\Delta_c = 1$ implies nonenantiospecific conglomerate clustering (or conglomerate clustering on an achiral surface). Finally, *x* is the contribution of conglomerate versus racemate clustering; *x* = 0 implies purely racemate clustering. Note that the full range of possible behavior can be described by limiting $\Delta_{a'} \Delta_{c'}$ and *x* to the range $0 \rightarrow 1$. These equations can now be solved to yield ee_s versus ee_g for any given choice of the parameters *n*, $K_{a'}$, $K_{c'}$, *P* = $P_D + P_L$, $\Delta_{a'} \Delta_{c'}$ and *x* (see Supporting Information for details). The positive real roots of the following expression yields the vacancy concentration, δ , for all values of ee_g

$$0 = 1 - \left\{ 1 + \frac{K_{a}P}{2} [\Delta_{a}(1 + ee_{g}) + \Delta_{a}^{-1}(1 - ee_{g})] \right\} \delta$$

- $2n \left(\frac{K_{a}P}{2} \right)^{2n} \{ K_{c} \Delta_{c} x [\Delta_{a}(1 + ee_{g})]^{2n} + K_{c} \Delta_{c}^{-1} x [\Delta_{a}^{-1}(1 - ee_{g})]^{2n} + K_{c}(1 - x) [(1 + ee_{g})^{n}(1 - ee_{g})]^{n} \} \delta^{2n}$ (13)

Given that the experimental conditions dictate that the total coverage of the adsorbate is close to saturation, $\theta \approx 1$, the physically relevant vacancy concentration must have a value of $\delta \approx 0$. So for our purposes eq 13 is solved for its smallest positive real root. The values of ee_s are then given by

$$(1 - \delta)ee_{s} = \left(\frac{K_{a}P}{2}\right) \{\Delta_{a}(1 + ee_{g}) - \Delta_{a}^{-1}(1 - ee_{g})\}\delta + 2n\left(\frac{K_{a}P}{2}\right)^{2n} K_{c}x\{\Delta_{c}[\Delta_{a}(1 + ee_{g})]^{2n} - \Delta_{c}^{-1}[\Delta_{a}^{-1}(1 - ee_{g})]^{2n}\}\delta^{2n}$$
(14)

As applied to our data, the model described above implicitly assumes that the equilibrium constants are independent of enantiomer coverage on the surface. In principle, one could relax this constraint and solve this model numerically, assuming that one had access to the coverage dependence of the equilibrium constants. There are certainly observations of chiral adsorbate clustering in which the formation of homochiral versus heterochiral clusters is coverage-dependent. In our case, the total coverage on the surface is $\theta \approx 1$, and so the coverage dependence would only be an issue if the equilibrium constants were dependent on the specific coverages of the two enantiomers.

4.2. Nonenantiospecific Adsorption without Aggregation: Ala on Cu{3,1,17}^{R&S}. To explore the influences of the enantiospecificity of the equilibrium constants for adsorption and clustering on ees, the solutions to our model for variations of Δ_a , Δ_c , and *x* have been obtained (Figure 6) by solving eqs 13 and 14, where other parameters were fixed at n =1 or 4 (dimer or octamer formation) and $K_{a}P = 1000$. Note that $K_{a}P$ appears as a product throughout eqs 13 and 14 and thus represents a single independent variable. Although we do not measure the absolute pressure of the amino acids directly, we have chosen to use sublimation temperatures at which the monolayer is saturated in ~15 min. Assuming that the sticking coefficients are $S \approx 1$, this means that the fluxes correspond to a pressure of $\sim 10^{-9}$ Torr. Although we do not measure K_a directly, it must be $\gg 10^9$ Torr⁻¹ to yield $K_a P \gg 1$ and coverages that are $\theta \approx 1$. Once $K_a P \gg 1$, the solutions become insensitive to it value. Solution of the isotherm equations with $K_{a}P = 1000$ yields a total coverage on the surface of $\theta \approx 1$ and a vacancy coverage of δ < 0.001, consistent with our experiments. Under these conditions the results are insensitive to increases in the value of $K_{a}P$.

Equilibrium adsorption of D-/*L-Ala on Cu{3,1,17}^{*R&S*} (Figure 3 upper left) behaves like an ideal competitive Langmuir adsorption system with nonenantiospecific adsorption equilibrium constants despite the fact that the adsorbate and the surface are both chiral, and there is no evidence of enantiomer aggregation. This implies that $\Delta_a = 1$ (nonnantiospecific adsorption) and that $K_c = 0$ (no cluster formation). With these values the adsorption isotherm predicts that $ee_s = ee_{g'}$ as observed for D-/*L-Ala on Cu{3,1,17}^{*R&S*} in Figure 4.

4.3. Enantiospecific Adsorption without Aggregation: Variation of Δ_a **with** $K_c = 0$. Equilibrium adsorption of D-/*L-Asp on Cu{3,1,17}^{*R*&S} exhibits prototypical behavior consistent with competitive enantiospecific adsorption on a chiral surface, $\Delta_a \neq 1$, but without enantiomer aggregation, $K_c = 0$. The key observation is that for a racemic mixture in the gas phase, $ee_g =$ 0, the enantiomeric excess on the surface is $ee_s(0) \neq 0$, as illustrated for D-/*L-Asp on Cu{3,1,17}^{*R*&S} in Figure 3 upper right panel and in Figure 4.

The general behavior of $ee_s(ee_g)$ for enantiospecific adsorption on a chiral surface without aggregation is illustrated in the left-hand panels of Figure 6. The lack of aggregation is imposed by $K_c = 0$ and renders ee_s insensitive to x, Δ_{c^2} and n. The functional form of $ee_s(ee_g)$ has been plotted for values of Δ_a = 0.25 to 4, the variable quantifying enantiospecificity of the adsorption equilibrium constants. As expected, $ee_s = ee_g$ for conditions of nonenantiospecific adsorption, $\Delta_a = 1$, as on an achiral surface. For all other values of Δ_a , $ee_s \neq ee_g$ for $-1 < ee_g$ < 1.

4.4. Nonenantiospecific Adsorption with Homochiral Aggregation: Variation of Δ_c with $\Delta_a = 1$ and x = 1. Enantiomer aggregation on a chiral surface can lead to enhancement of enantiomeric excess, $ee_s \neq ee_g$. This arises because the equilibrium constants for conglomerate cluster formation can be enantiospecific, $\Delta_c \neq 1$, even if the adsorption equilibrium constants are not, $\Delta_a = 1$. The middle two panels of Figure 6 show $ee_s(ee_g)$ calculated at values of the cluster size, n = 1 or 4, and for values of $\Delta_c = 0.25$ to 4. The value of $K_aP = 1000$ ensures almost monolayer coverage, and the value of $K_c = 1000$ ensures that most molecules are present in the clusters rather than as monomers. The quantity x = 1 implies that all clusters are homochiral.

The examples of D-/*L-Asp on Cu{653}^{*R&S*} and on Cu{111} match the behavior illustrated in the middle panels of Figure 6, implying adsorption equilibrium constants that are nonenantiospecific, $\Delta_a = 1$, and conglomerate equilibrium constants that are also nonenantiospecific, $\Delta_c = 1$. Thus there is no enhancement of enantiomeric excess during exposure to a racemic mixture in the gas phase, $ee_s(0) = 0$. In general, however, the isotherm indicates that $ee_s \neq ee_g$ even with nonenantiospecific adsorption equilibrium constants, if $\Delta_c \neq 1$.

4.5. Conglomerate versus Racemate Aggregation on an Achiral Surface: Variation of x with $\Delta_a = \Delta_c = 1$ and K_c = 1000. The equilibrium constants for adsorption and for conglomerate aggregation on an achiral surface cannot be enantiospecific, $\Delta_a = \Delta_c = 1$. Nonetheless, the competition between conglomerate and racemate aggregation has a significant impact of *es*_s(*ee*_g). The right-hand panels of Figure 6 show the impact of varying contributions of racemate and conglomerate aggregation on *ee*_s(*ee*_g) by varying x across the range $0 \rightarrow 1$. These have been calculated for conditions of monolayer coverage, $K_aP = 1000$, with adsorption dominated by aggregation, $K_c = 1000$, into clusters with n = 4 that interact nonenantiospecifically with the surface, $\Delta_a = \Delta_c = 1$.

The case of D-/*L-Asp on Cu{111} (Figure 4) is well described by the condition that aggregation is purely homochiral, x = 1. This results in local amplification of ee_s relative to ee_{g} , and the slope of $ee_s(ee_g)$ evaluated for exposure to a racemic mixture in the gas phase is $\frac{dee_s}{dee_g}\Big|_{ee_g=0} > 1$. Although

we have not yet observed an example of amino acid adsorption on Cu surfaces resulting in aggregation into racemic clusters, there is no reason to exclude the possibility. STM images of other systems have revealed examples of racemate cluster formation.⁵⁹ It is well known that crystallization in 3D results predominantly in the formation of racemic crystals rather than conglomerates.⁶³ It has been suggested that the opposite holds true in 2D and that conglomerates should be prevalent.^{64,65} One of the interesting observations to be made from Figure 6 is that for racemate formation, x = 0, the slope of $ee_s(ee_g)$ evaluated for exposure to a racemic mixture in the gas phase is

$$\frac{dee_s}{dee_g}\Big|_{ee_g=0}$$
 < 1. For conglomerate clusters $\frac{dee_s}{dee_g}\Big|_{ee_g=0}$ > 1. This

implies that the slopes through $ee_g = 0$ of the adsorption isotherms measured for enantiomer mixtures on achiral surfaces can be used to distinguish between conglomerate and racemate formation. Experiments of the type illustrated in this work could thus serve as a general means of resolving whether conglomerate formation in 2D crystallization or self-assembly is more or less common than in 3D.

5. CONCLUSIONS

The observations reported herein demonstrate a variety of different behaviors that are observed during the adsorption of enantiomer mixtures of varying ee_g onto chiral and achiral surfaces. The two primary forces dictating the relationship between ee_s and ee_g are those of enantiospecific adsorption from the gas phase and enantiomer aggregation into homochiral or heterochiral clusters on the surface. These can both compete and augment one another in enhancing the ee_s versus ee_g . Even during adsorption on naturally chiral surfaces, enantiomer aggregation can dominate over enantiospecific adsorption. It is likely that these two forces are generally active and must be considered in modeling of all enantioselective chemical processes occurring on chiral or achiral surfaces. Because aggregation is the direct result of adsorbate-adsorbate interactions, purely Langmuir adsorption models cannot be used to describe these processes. Nonetheless, a simple treatment of the formation of adsorbate clusters has allowed us to develop an isotherm for competitive, enantiospecific adsorption that captures the impact of aggregation.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpcc.6b07758.

Derivation of eqs 13 and 14 that define the enantiomeric excess on the surface, ee_s , in terms of the enantiomeric excess in the gas phase, ee_e . (PDF)

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Notes

The authors declare no competing financial interest.

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