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Formation and Reaction of Interchain Carboxylic Anhydride Groups on Self-Assembled Monolayers on Gold

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This paper demonstrates a new method for the synthesis of mixed self-assembled monolayers (mixed SAMs) by reaction of a reactive intermediate—an interchain carboxylic anhydride—with alkylamines. The interchain anhydride was prepared in high yield from a SAM of 16-mercaptohexadecanoic acid ($HS(CH_2)_{15}COOH$) on gold by treatment with trifluoroacetic anhydride. Alkylamines reacted cleanly with the interchain anhydride to generate a mixed SAM, which comprised a mixture of acids and amides in approximately 1:1 ratio on the surface. The SAMs of the interchain anhydride and the mixed SAM were characterized using polarized infrared external reflectance spectroscopy, X-ray photoelectron spectroscopy, contact angle, and ellipsometry. Control of the wettability of the SAMs was demonstrated by allowing the interchain anhydride to react with alkylamines having different alkyl groups; this model system gave wetting data consistent with earlier studies of mixed monolayers and verified the ability of this method to manipulate interfacial physical properties. In certain circumstances, this method is experimentally simpler as a method to produce mixed SAMs than are conventional methods involving coadsorption of two thiols from a mixture in solution. It also assures two other characteristics of the mixed SAM: that the composition of the SAM is roughly 1:1 in carboxylic acid and amide groups, and that these two groups are well mixed on the surface.

Introduction

This paper describes a new method of synthesizing mixed, functionalized self-assembled monolayers (mixed SAMs) of carboxylic acids and amides by reaction of a reactive intermediate—an interchain carboxylic anhydride—with amines. The interchain anhydride is easily prepared by dehydration of a SAM of 16-mercaptohexadecanoic acid ($HS(CH_2)_{15}COOH$) on gold (Scheme 1). There are three general strategies to synthesize mixed SAMs: (1) to synthesize the differently functionalized alkanethiols and prepare mixed SAMs by coadsorption from a solution containing two different thiols;[1] (2) to prepare asymmetric dialkyl disulfides[1,2] and asymmetric dialkyl sulfides[3] with requisite functional groups and then self-assemble them on gold; (3) to introduce the desired functionality into a SAM *after* its assembly. While the first two strategies have been widely used to synthesize a variety of functionalized SAMs for a broad range of applications, such as biocompatibility,[4] wetting,[5] adhesion,[6] corrosion preventing,[7] and micro- and nanofabrication,[8,9] the last method has been less used. It would be especially valuable for generation of patterned SAMs,[10,11] formation of three-dimensional multilayers,[12−14] synthesis of two-dimensional arrays for combinatorial libraries,[15] immobilization of DNA for rapid sequencing,[15,16] preparation of certain types of biosensors and enzymatic microreactors,[17] and attachment of functional molecules and polymers to surfaces.[18−21]

Efforts to manipulate functional groups on SAMs have focused on alkylsiloxanes on Si/SiO_2, because this class of SAMs is believed to be (and probably often is) more stable than SAMs on gold.[22−28] Development of new methods to modify SAMs on gold is, however, important because: (1) many analytical systems and sensors are being developed

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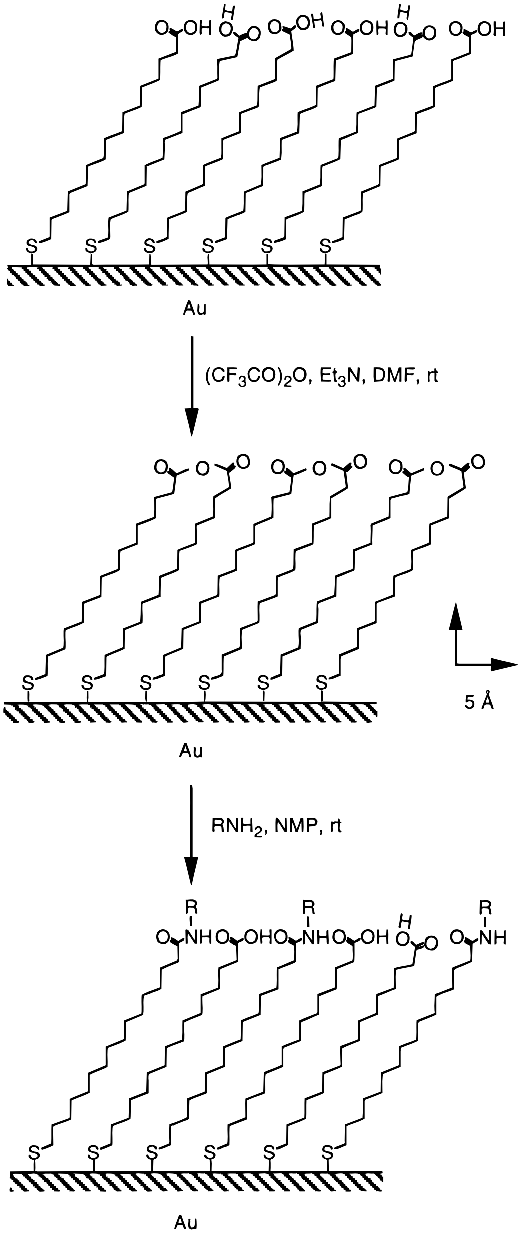
Scheme 1. Schematic Representation of Formation of the Interchain Anhydride and Reaction of the Interchain Anhydride with an Alkylamine[a]



[a] The alkyl chains of the original SAM of the carboxylic acid in these three SAMs are in trans conformation; the methylene groups near the functional groups may adapt gauche conformation and are less ordered. Carboxylic acids in the SAMs of the carboxylic acid and in the mixed SAMs of amides and carboxylic acids involve in hydrogen bonding. The interchain anhydrides orient largely perpendicular to the surface.

that are based on combinations of SAMs on gold and surface plasmon resonance,[29,30] electrochemistry,[31−33] mass measurement using the quartz crystal microbalance,[33,34] or surface acoustic wave devices;[19] (2) SAMs of alkanethiolates on gold are substantially better defined structurally than other classes of SAMs.[35−37]

Why are there so few methods available for the modification of SAMs on gold after their assembly? There are, at present, only few synthetic methods that are used, and are more or less restricted in their generality. Terminal aryl azide groups[10] have been activated photochemically to produce nitrenes and perhaps other reactive intermediates; the chemistry and yield of this type of coupling are not easy to predict. Terminal amino groups react with isocyanates in solution.[33] Amines on the surface of SAMs react at significant rates with atmospheric CO_2 and other environmental components, and this chemistry is difficult to control. Three methods are known for modification of the SAMs of carboxylic acid groups: formation of acyl chlorides;[38] generation of mixed anhydrides;[19] *in situ* activation with carbodiimide reagents for amide coupling[39] and ester formation.[40] In more general terms, many organic reactions do not transpose easily from solution to the surface for a number of reasons: the surface is a very sterically hindered environment and backside reactions (e.g., the S_N2 reaction) and reactions with large transition states (e.g., esterification or saponification) often proceed slowly. In addition, the technical problems of establishing the identities of products, and their yields, for organic reactions proceeding on the surface remain substantial.

Here we report a new method for preparation of mixed SAMs that has three steps: (1) preparation of a well-ordered homogeneous SAM of 16-mercaptohexadecanoic acid on gold; (2) conversion of the terminal carboxylic acid groups into interchain anhydrides by reaction with trifluoroacetic anhydride; (3) reaction of the interchain anhydride with an alkylamine to give a mixed SAM presenting carboxylic acids and amides on its surface. The SAMs of the interchain anhydride and mixtures of carboxylic acids and alkylamides were studied and characterized by X-ray photoelectron spectroscopy (XPS), polarized infrared external reflectance spectroscopy (PIERS), contact angle, and ellipsometry. All three of these steps take place rapidly and in high yield; the last step will, we believe, have broad generality. This reaction thus seems a very good sequence to use in introducing organic functionality into SAMs. The organic amines required are readily available and compatible with most other organic structures. The one characteristic of this reaction that will restrict it from some applications is that it produces a 1:1 mixture of functional groups on the surface of the SAM ($-CO_2H$ and $-CONHR$ or $-CONRR'$), rather than a single species. In some circumstances, when a mixed SAM containing CO_2H groups is required, this characteristic may be an advantage.

Results and Discussion

Preparation of the Interchain Anhydride. SAMs of 16-mercaptohexadecanoic acid were prepared by immersing precleaned gold slides in a 2 mM ethanolic solution of the thiol as described previously.[41] Terminal

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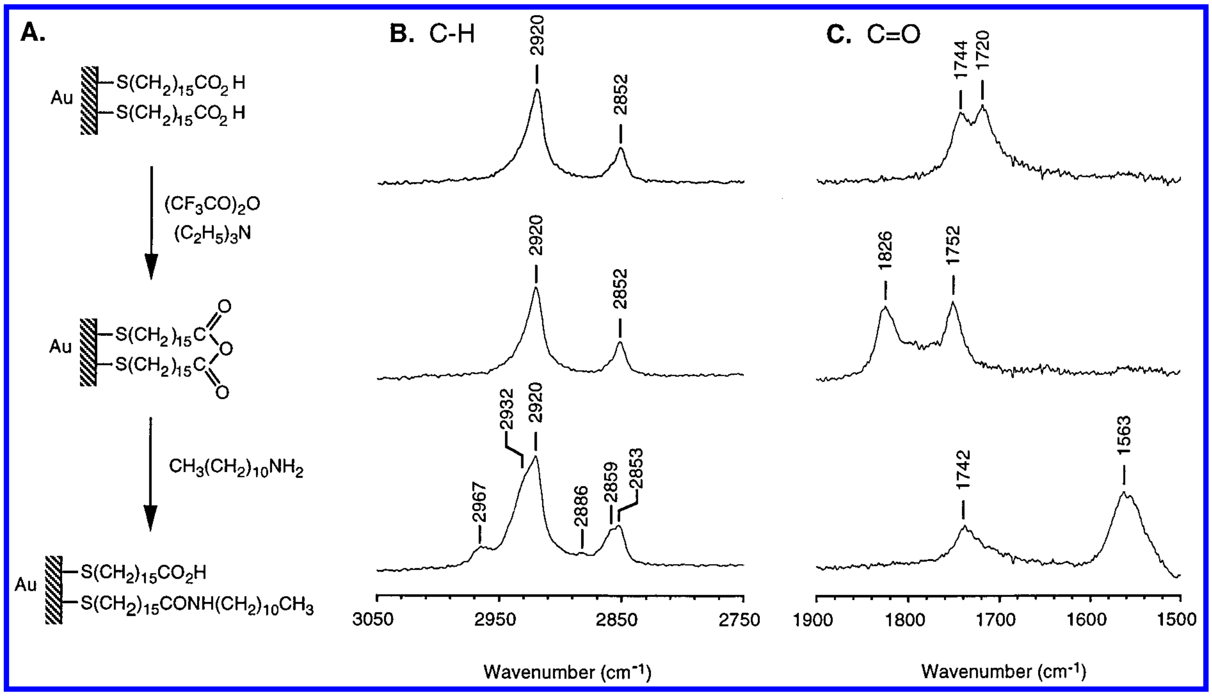

Figure 1. Comparison of PIERS spectra of the SAMs of the carboxylic acid, the interchain anhydride, and a mixture of carboxylic acids and *n*-undecylamides on gold: (A) schematic representation of the formation of the interchain anhydride and the reaction of the interchain anhydride and *n*-undecylamine; (B) PIERS spectra of these SAMs in the C−H stretching region; (C) PIERS spectra of these SAMs in the C=O stretching region.

carboxylic acid groups were converted into surface anhydrides by treatment with trifluoroacetic anhydride and triethylamine in anhydrous *N*,*N*-dimethylformamide. Since there was no evidence for mixed anhydride incorporating trifluoroacetyl moieties by XPS, we inferred that these surface anhydrides were derived from carboxylic acids on adjacent chains (Scheme 1). Related interchain structures, such as bridged thioether and disulfide groups that connect two adjacent chains of siloxanes in SAMs on Si/SiO_2, have been reported previously.[22]

Characterization of the Interchain Anhydride. PIERS. PIERS provides information both about the presence of IR-active functional groups and also about the order and orientation of the hydrocarbon chains within a SAM.[42] In PIERS, the vibrational modes whose transition dipole moments are perpendicular to the surface show maximal absorbances; the vibrational modes whose transition dipole moments are parallel or nearly parallel to the surface show zero or minimal absorbances.[43,44] In this paper, all the absorption bands are assigned according to literature precedent.

Figure 1 shows the PIERS spectra of the SAMs of the carboxylic acid and the interchain anhydride. The spectrum of the SAM of the carboxylic acid shows two C=O stretching bands at 1744 and 1720 cm^{-1}, which arise from the free and hydrogen bonded carboxylic acids, respectively.[45] After treatment of the SAM of the carboxylic acid with trifluoroacetic anhydride, these two C=O stretching bands disappeared completely. Two new absorption bands at 1826 and 1752 cm^{-1} appeared instead; this doublet is characteristic of the C=O stretching absorption of a carboxylic anhydride, and are assigned to in-phase and out-of-phase stretching modes of the two coupled carbonyl groups, respectively.[46] The position and the similar intensities of these bands are characteristic of a unconjugated open-chain aliphatic carboxylic anhydride[47] and suggest that the interchain anhydride is similar to an unstrained, acyclic aliphatic carboxylic anhydride. Furthermore, the high intensities of these bands suggest that the interchain anhydride groups are oriented largely perpendicular to the surface. The complete disappearance of the C=O stretching bands for carboxylic acid groups on treatment with trifluoroacetic anhydride suggests that the transformation of carboxylic acids at the interface to interchain anhydrides occurs in high yield (that is, by the criterion of PIERS spectroscopy, quantitative yield).

The position of the C−H stretching bands of the methylene groups of the alkyl chains indicates the order of the alkyl chains within a SAM.[48,49] In the spectrum of the SAM of the carboxylic acid (Figure 1), two absorption bands at 2920 and 2852 cm^{-1} are assigned to asymmetric and symmetric C−H stretching bands of the methylene groups, respectively. The positions of these peaks are the same as those in crystalline polyethylene and suggest that most of the polymethylene chains are fully extended in *trans* conformations and exist in quasi-crystalline state; they do not, however, give much information about the terminal methylene units, since small shifts in these groups are not easily detected against the large background of absorption from the remaining methylene groups of the chains. The C−H stretching bands of the methylene groups of the SAM of the interchain anhydride are indistinguishable from those of the carboxylic acid; this observation indicates that the majority of the polymethylene chains remain trans-extended but again does not define the order immediately at the surface.

XPS. The survey spectrum of the interchain anhydride is similar to that of the carboxylic acid (Figure 2). The high-resolution core-level spectra of these SAMs in the

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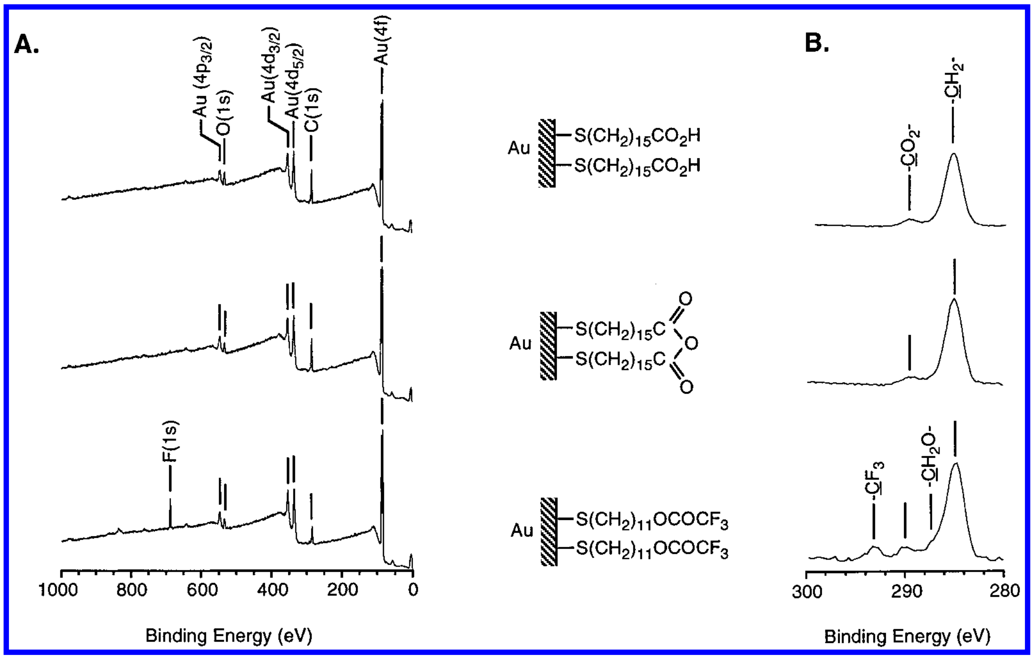

Figure 2. Comparison of XPS spectra of the SAMs of the carboxylic acid and the interchain anhydride and of a model compound containing a trifluoroacetate group on gold: (A) survey spectra of these SAMs; (B) high-resolution spectra of these SAMs in the C(1s) region.

C(1s) region show a similar profile. The spectrum of the carboxylic acid exhibits a slightly asymmetric photoelectron peak centered at 284.7 eV and a small high-energy photoelectron peak at 289.5 eV, which arises from the carbonyl group of the carboxylic acid.[41] The spectrum of the interchain anhydride shows a peak centered at 284.7 eV and a small high-energy peak at 289.3 eV, which arises from the carbonyl group of the interchain anhydride. The position of the photoelectron peak of the carbonyl group of the interchain anhydride is in good agreement with the data reported for organic polymers containing carboxylic anhydride groups.[50]

The area under the photoelectron peak of O(1s) (as normalized to the intensity of the C(1s) peak) of the interchain anhydride is 0.35 and that of the carboxylic acid is 0.44. The normalized content of oxygen on the SAM of the carboxylic acid is 1.23 times that of the interchain anhydride (the theoretical value is 1.33, based on a complete conversion from the carboxylic acid to the interchain anhydride); these values are compatible with dehydration of the carboxylic acid groups on conversion to the interchain anhydride groups. The small difference (*ca.* 7%) between observed and theoretical oxygen contents may reflect instrumental errors.

The plausible products of the reaction of the carboxylic acid groups and trifluoroacetic anhydride under the reaction conditions are a mixed trifluoroacetic carboxylic anhydride ($CF_3COOC(=O)(CH_2)_{15}S/Au$), an interchain carboxylic anhydride, or a mixture of both. Since the mixed trifluoroacetic carboxylic anhydride contains a trifluoroacetyl group, which can be readily identified by XPS, we recorded the XPS spectra of the SAM of trifluoroacetates[51,52] and that of the carboxylic acid before and after reaction with trifluoroacetic anhydride (Figure 2). The survey spectrum of the SAM of the interchain anhydride shows no observable F(1s) signal. If the newly formed functional group on the surface is an anhydride, and since it is not a mixed trifluoroacetic carboxylic anhydride, it must be an interchain anhydride.

Contact Angle. Examination of the advancing contact angle of water on the SAM of the interchain anhydride showed that its surface is more hydrophobic than that of the SAM of the carboxylic acid.[53] (The stability of the interchain anhydride in contact with water is sufficient to allow the contact angle to be measured; see below.) The advancing contact angle of distilled, deionized water (pH = 6.0) on the SAMs of the interchain anhydride is *ca.* 72°, whereas it is less than 15° on that of the carboxylic acid. This observation is compatible with the lower polarity of a carboxylic anhydride compared to that of the corresponding acid (or, at neutral pH, a mixture of carboxylic acid and carboxylate anion).[54]

The results of PIERS, XPS, and contact angle together establish that an interchain anhydride is formed on the surface under these reaction conditions and that the transformation of the carboxylic acid to the interchain anhydride occurs in high yield. Although these interchain anhydrides bridge two adjacent alkyl chains, they are similar to open-chain, unconjugated carboxylic anhydrides, and the underlying alkyl chains are well-ordered and closely packed.

Figure 3 shows a tentative mechanism proposed for the formation of the interchain anhydride on the surface of the SAM of carboxylic acid. Triethylamine deprotonated the carboxylic acid, and the resulting carboxylate anion reacted with trifluoroacetic anhydride to form a reactive and perhaps unstable intermediate, a mixed trifluoroacetic carboxylic anhydride. The mixed anhydride further reacted with an adjacent carboxylate anion to produce an interchain anhydride. It is probable that the trifluoro-

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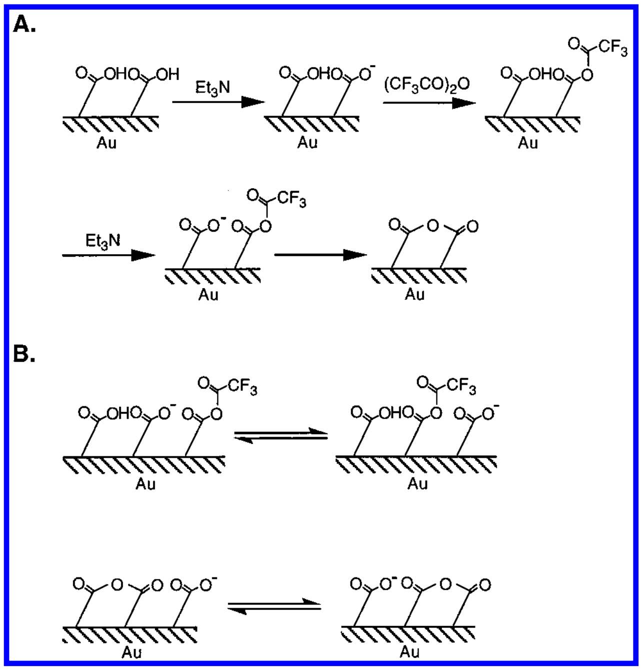

Figure 3. Schematic representation of a tentative mechanism proposed for the formation of the interchain anhydride on the surface of the SAM of carboxylic acid: (A) a mixed trifluoroacetic carboxylic anhydride was generated as a reactive intermediate on conversion of carboxylic acid groups into interchain anhydrides; (B) during the reaction, both mixed trifluoroacetic carboxylic anhydrides and interchain anhydrides could migrate reversibly on the surface.

acetyl group can translocate reversibly on the surface; the interchain anhydride group can react with an adjacent carboxylate anion and therefore the interchain anhydride group can "walk" on the surface. Such reversible migration of the trifluoroacetyl group and the interchain anhydride avoids the statistical isolation of unreacted carboxylic acid or mixed trifluoroacetic carboxylic anhydride on the surface and also assures completion of the conversion of carboxylic acid groups into interchain anhydrides.

Characterization of the Mixed SAMs of Amides and Acids. PIERS. After the reaction of the interchain anhydride and *n*-undecylamine (taken as a representative *n*-alkylamine), the two C=O stretching bands characteristic of the interchain anhydride disappeared completely and two new absorption bands appeared at 1742 and 1563 cm^{-1} (Figure 1). The former band is assigned to the C=O stretching absorption of a carboxylic acid. The position of this band is between the two C=O stretching bands of the SAM of the carboxylic acid; this position suggests that this carboxylic acid is also hydrogen bonded, perhaps weakly, to the neighboring carbonyl groups of either an amide or a carboxylic acid. No absorption band characteristic of a carboxylate anion was observed around 1420−1300 cm^{-1}.[55,56] The carboxylic acids generated during the reaction are thus *protonated*, and they appear not to transfer protons to *n*-undecylamine and form stable ammonium salts.[57] We suggest that the failure of the formation of the stable salts probably reflects the low dielectric constant of the interior of the SAM.

The absorption band at 1563 cm^{-1} is assigned to the amide II band.[58] This absorption band is characteristic of a monosubstituted amide in *trans* configuration.[59] The amide I band, which generally appears as a relatively strong absorption band around 1680−1630 cm^{-1} due to the C=O stretching mode, was absent.[60−62] The transition dipole moment of this vibrational mode is probably oriented parallel to the surface and thus is inactive in PIERS. The presence of a strong amide II band and the absence of an amide I band indicate that the carbonyl groups of the amides are oriented parallel to the surface and the amide bonds are in the expected *trans* configuration. This spatial arrangement allows the C=O and N−H groups to participate in hydrogen bonding with the neighboring amide or carboxylic acid groups without obvious steric strain.

Absorption bands corresponding to an imide were not observed.[58] Efforts to convert the carboxylic acid and adjacent amide groups of the mixed SAMs into interchain imides using trifluoroacetic anhydride were unsuccessful. This reaction would require initial deprotonation of the carboxylic acids, followed by reaction of the carboxylate anions with trifluoroacetic anhydride. These processes would, again, be suppressed by the low dielectric constant in the interior of the monolayer.

After the reaction of the interchain anhydride with *n*-undecylamine, new absorption bands appeared in the C−H absorption region: The band at 2967 cm^{-1} is assigned to the asymmetric C−H stretching vibration of the terminal methyl group; the band at 2886 cm^{-1} is assigned to the symmetric C−H stretching vibration of the methyl group of the *n*-undecyl group.[49] The methylene vibrations at 2920 and 2853 cm^{-1} are significantly broader than those of the original SAM of the interchain anhydride. The low-frequency shoulder peaks at 2932 and 2859 cm^{-1} that appear on the formation of amides are the bands arising from the methylene groups of the *n*-undecyl chain.[63] From the peak shapes, we infer that the alkyl chains of the original SAM remain in *trans* conformation but that the new alkyl chains are *disordered* (Figure 4).

XPS. XPS spectra of the mixed SAMs of mixtures of acids and amides show a photoelectron peak for N(1s) at 399.9 eV. The ratio of the intensities of the photoelectron peaks for N(1s) and O(1s) provides semiquantitative information about the yield of the reaction. We have allowed the interchain anhydride to react with three structural isomers of butylamine (*n*-, *sec*-, and *tert*-butylamine). The interchain anhydride groups are in a highly structured and sterically demanding environment, and we had anticipated large differences in yield of the amides derived from these three amines; in fact, the yields are similar.

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(59) In *trans* configuration of a monosubstituted amide bond, the interaction between N−H bending and C−N stretching gives rise to a strong amide II absorption band; however, in *cis* configuration, there is much less interaction between them and therefore there is no absorption band in the 1600−1500 cm^{-1} region comparable to the amide II band in *trans* configuration. For example, lactams ($\overline{\mathrm{CONH(CH_2)_n}}$) do not show amide II absorption when $n < 9$ and do show amide II absorption when $n > 9$; it is conceivable that the amide bond adapts *trans* configuration in large rings and *cis* configuration in small rings. Schiedt, U. *Angew. Chem.* **1954**, *66*, 609.

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(61) Tam-Chang, S.-W.; Biebuyck, H. A.; Whitesides, G. M.; Nuzzo, R. *Langmuir* **1995**, 4371−4382.

(62) Clegg, R. S.; Hutchison, J. E. *Langmuir* **1996**, *12*, 5239−5243.

(63) The positions of these shoulders were determined by subtracting the spectrum of the interchain anhydride from that of the mixed SAM of carboxylic acids and 11-undecylamides. Although subtraction of reference spectra has no mathematical justification, it allowed us to estimate the position of these shoulders.

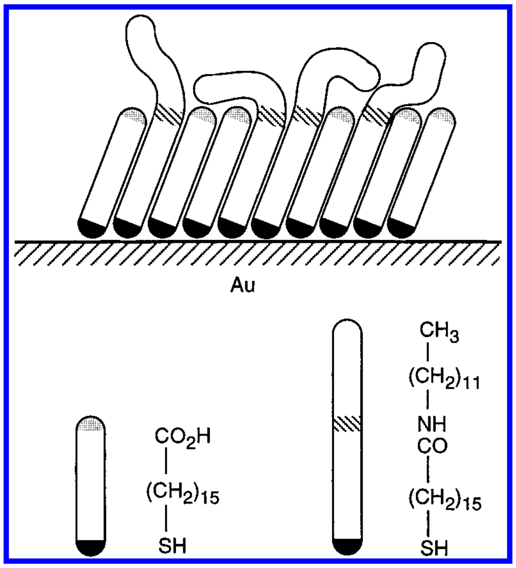

Figure 4. Schematic representation of a mixed SAM of carboxylic acids and *n*-undecylamides on gold. The alkyl chains of the amides are disordered in liquid-like state; the polymethylene groups of the original SAM of the carboxylic acid are closely packed in quasi-crystalline state. Since alkanethiolates containing amides are either positioned next to each other or separated by one or two alkanethiolates terminated at carboxylic acids, large-scale phase separated domains may not exist.

Table 1. Ratios of N(1s)/O(1s) of Butylamines with Different Structural Isomers Modified Carboxylic Acid-Terminated SAMs

R	N(1s)/O(1s)	relative yield (%)[a]
n-C_4H_9	0.40	100
s-C_4H_9	0.32	80
t-C_4H_9	0.34	85

[a] The uncertainty in this number is at least ±5%.

The reactions of the interchain anhydride with those isomeric butylamines were carried out using the same procedure as that used for the reaction of other *n*-alkylamines. Table 1 lists the estimated yields of these reactions on the basis of the ratios of N(1s)/O(1s) of these samples. The relatively high ratios of N(1s)/O(1s) in the samples generated by the reactions of *tert*-butylamine and *sec*-butylamine with the interchain anhydride suggest that although these alkyl groups are sterically bulkier than *n*-butyl, the interchain anhydride readily reacts with them in high yield.

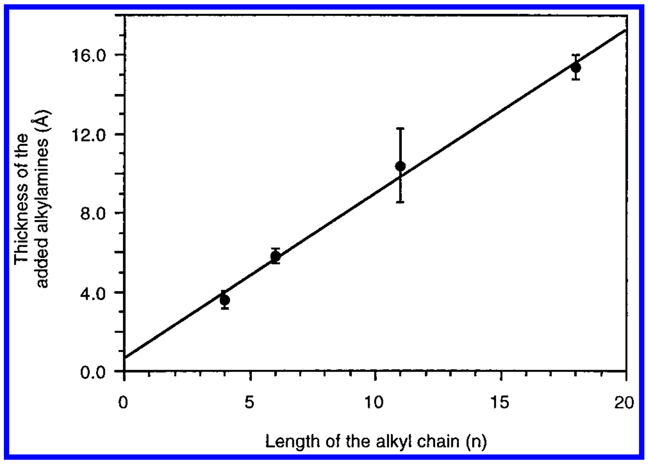

Figure 5. Reaction of the interchain anhydride and *n*-alkylamine (*n*-$C_nH_{2n+1}NH_2$, $n = 4, 6, 11$, and 18) generates a mixed SAM containing a mixture of carboxylic acids and amides. The thicknesses of the added hydrocarbon layers were measured by ellipsometry: Linear regression analysis gives an increment of the thickness of 0.84 Å/CH_2 of added amine. Error bars represent the standard deviation of the mean for at least three individual substrates.

Ellipsometry. The thicknesses of the SAMs were calculated from ellipsometric data that were obtained and analyzed by procedures described previously.[64] Figure 5 presents the thicknesses measured by ellipsometry for the mixed SAMs generated by reaction of the interchain anhydride and four homologous *n*-alkylamines (*n*-$C_nH_{2n+1}NH_2$, $n = 4, 6, 11$, and 18). Linear regression analysis of the experimental data yields a slope of 0.84 Å/CH_2 and an intercept of 0.65 Å. The increment of thickness per methylene unit is approximately 70% that of the SAMs of carboxylic acid-terminated alkanethiolates ($\Delta h = 1.16$ Å/CH_2).[41] The PIERS data indicate that the alkyl groups of the amides are disordered. Assuming that a hydrocarbon layer comprising alkyl chains of the amides is homogeneous, the surface density (σ, mol/cm^2) of the alkyl chains is simply related to the density (ρ, g/cm^3) and the thickness (h, cm) of this hydrocarbon layer by eq 1

$$\sigma = h\rho/m \tag{1}$$

where m (g/mol) is the molecular weight of the alkyl chain. This relation holds if we replace the total thickness (h) by the increment of thickness of the hydrocarbon layer per methylene unit (Δh), and the molecular weight of the chain (m) by the molecular weight of one methylene group (Δm). A similar relation can be written for the surface density of the alkanethiolates on gold. The ratio of the surface densities of the alkyl chains in a well-ordered SAM and in a disordered hydrocarbon layer of the amides of the mixed SAM generated by this method is thus given by eq 2

$$\frac{\sigma_{\mathrm{HC}}}{\sigma_{\mathrm{SAM}}} = \frac{\Delta h_{\mathrm{HC}}\rho_{\mathrm{HC}}}{\Delta h_{\mathrm{SAM}}\rho_{\mathrm{SAM}}} \tag{2}$$

where subscript "HC" stands for the hydrocarbon layer of the amides and "SAM" for that of the SAM of the carboxylic acid. Since the *n*-undecyl groups of the amides are disordered and liquid-like and the alkyl groups of the SAM of the carboxylic acid on gold are highly ordered and crystalline on the basis of the PIERS data, we assume that the density of the hydrocarbon layer of the amides is similar to that of the liquid *n*-undecane ($\rho = 0.740$ g/cm^3) and the density of that of the SAM of the carboxylic acid is similar to that of the crystalline polyethylene ($\rho = 1.00$ g/cm^3),[65] then the surface density of the alkyl groups of the amide is *ca.* 0.5 times that of the original SAM of the carboxylic acid. This estimate is compatible with our inference that the reaction of the interchain anhydride and alkylamines proceeds in high yield. It also reinforces the conclusion that the transformation of the carboxylic acids to the interchain anhydrides occurs in close to quantitative yield.[66]

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(64) Wasserman, S. R.; Whitesides, G. M.; Tidswell, I. M.; Ocko, B. M.; Pershan, P. S.; Axe, J. D. *J. Am. Chem. Soc.* **1989**, *111*, 5852−5861.

(65) We used the density of liquid *n*-undecane ($\rho = 0.740$ g/cm^3, *Handbook of Chemistry and Physics*, 71st ed.; CRC Press: Boca Raton, FL, 1990−1991) for the density of the hydrocarbon layer of *n*-undecyl groups since both of them are highly disordered. We used the density of crystalline polyethylene ($\rho = 1.000$ g/cm^3, *Polymer Handbook*, 3rd ed.; John Wiley & Sons: New York, 1989) for that of the ordered $(CH_2)_n$ region of the SAM, since we infer that it is in the quasi-crystalline state.

(66) A lower yield of this transformation would result in a smaller amount of the interchain anhydride groups and subsequently a lower surface density of the hydrocarbon layer.

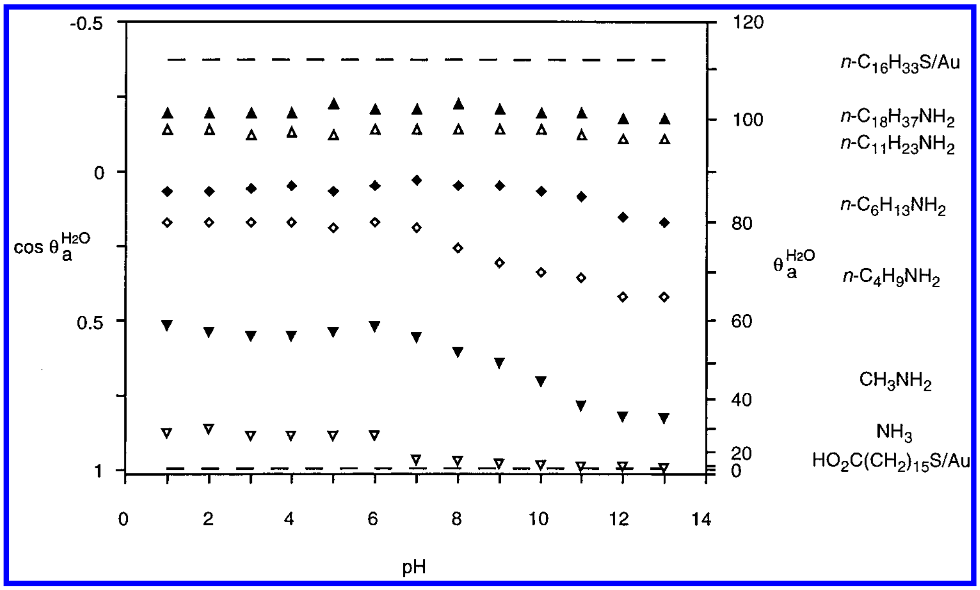

Figure 6. Dependence of the advancing contact angle (θ_a) of buffered aqueous solutions of pH on the SAMs comprising a mixture of carboxylic acids and amides, generated by reactions of the interchain anhydride and alkylamines (n-$C_nH_{2n+1}NH_2$, $n = 0$, 1, 4, 6, 11, and 18). The curves are labeled by the respective alkylamines on the right side of the plot. Two dashed lines on the top and the bottom of the plot are the reference data for θ_a of $CH_3(CH_2)_{15}S/Au$ and $HO_2C(CH_2)_{15}S/Au$ as indicated, respectively, on the right side of the plot.

Contact Angle. Previous, extensive studies of carboxylic acid functionalized polyethylene films (PE−CO_2H),[67−70] of SAMs terminated in ionizable acids and bases,[71] of mixed SAMs of carboxylic acid- and methyl-terminated alkanethiolates,[72] and of SAMs of dialkyl sulfides[3] on gold have established the utility of contact angle titration in characterizing the interfaces. We have determined the advancing contact angle of water, θ_a, as a function of pH, for several mixed monolayers obtained by allowing the interchain anhydride to react with several homologous n-alkylamines (n-$C_nH_{2n+1}NH_2$, $n = 0$, 1, 4, 6, 11, and 18) (Figure 6). These mixed SAMs comprise mixtures of amides and carboxylic acids, with the polar carboxylic acid groups buried beneath hydrocarbon layers of different thickness.

The values of θ_a for the n-undecyl- and n-octadecylamine-modified SAMs did not change with pH. The carboxylic acid groups of these two amine-modified systems were buried beneath *ca.* 10 and *ca.* 15 Å of hydrocarbon layers, respectively; these saturated hydrocarbon films thus prevented their direct contact with water. The values of θ_a for the n-undecyl- and n-octadecylamine modified SAMs are slightly smaller than that of a SAM of hexadecanethiolates on gold; the small discrepancy may reflect the disorder of the hydrocarbon layers of these modified SAMs.

The values of θ_a change with pH for mixed SAMs comprising mixtures of carboxylic acids and n-hexyl- and n-butylamides. There are two significant features of these data: First, the titration curves do not reach a plateau at high pH; the same behavior is observed for the mixed SAMs of carboxylic acid- and methyl-terminated alkanethiolates on gold prepared from mixtures of $HS(CH_2)_{10}COOH$ and $HS(CH_2)_{10}CH_3$.[73] By contrast, the carboxylic-acid functionalized material obtained by oxidizing polyethylene (PE−CO_2H) does achieve plateau values at high pH.[67] Second, the onset points of ionization are approximately pH 10 for the n-hexylamine-modified SAM and approximately pH 8 for the n-butylamine-modified SAM. The values of θ_a also change with pH for mixed SAMs comprising mixtures of carboxylic acids and methylamide and unsubstituted amides. These titration curves are very similar to that of the SAM of n-butylamides and carboxylic acids. Both the onset points of ionization are approximately at pH 7. Such shifts from the expected values on the basis of titration in aqueous solution are also similar to those observed with mixed SAMs terminated with carboxylic acid and methyl groups.[73]

Contact angle titrations of these n-alkylamine-modified SAMs suggest that these systems are more like mixed SAMs of methyl- and carboxylic acid-terminated alkanethiolates on gold than they are like PE−CO_2H.

Kinetics of Formation of the Interchain Anhydride and Its Reaction with *n*-Undecylamine. We estimated the rate of formation of the interchain anhydride and its reaction with alkylamine, in order to make this system useful in surface modification.

Since the anhydride surface was hydrophobic ($\theta_a = 75°$) and the carboxylic acid surface was hydrophilic ($\theta_a < 15°$), we estimated the formation of the interchain anhydride by measuring the advancing contact angles of water on the anhydride surfaces as a function of time of reaction. No observable hydrolysis of the anhydride occurred during the measurement (that is, over 1−2 min). Since no F(1s) was identified by XPS during the course of the reaction, and since the reaction conditions were anhydrous and the formation of the interchain anhydride on the surface was irreversible, we infer that the only two moieties on the surface are the interchain anhydride and the unreacted carboxylic acid and therefore that the hydrophobicity of the anhydride surfaces was mainly due to the generation of the interchain anhydride. Figure 7A shows that the formation of the surface anhydride is very rapid: Within the initial 30 s of the reaction, the advancing contact angle

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[67] Holmes-Farley, S. R.; Reamey, R. H.; McCarthy, T. J.; Deutch, J.; Whitesides, G. M. *Langmuir* **1985**, *1*, 725−740.

[68] Holmes-Farley, S. R.; Whitesides, G. M. *Langmuir* **1986**, *3*, 62−76.

[69] Holmes-Farley, S. R.; Bain, C.; Whitesides, G. M. *Langmuir* **1988**, *4*, 921−937.

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[73] Bain, C. D.; Whitesides, G. M. *Langmuir* **1989**, *5*, 1370−1378.

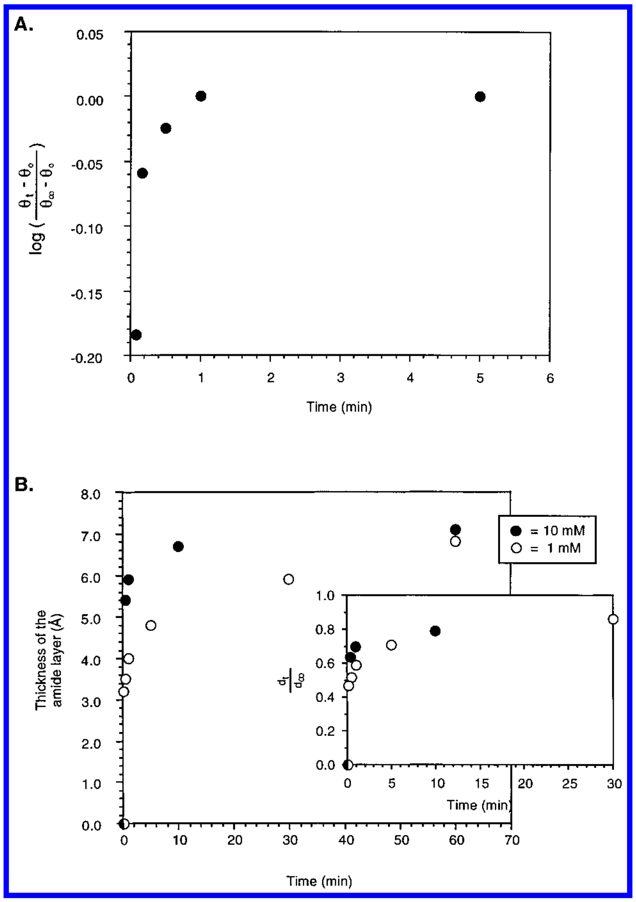

Figure 7. (A) The surface of the SAMs of the interchain anhydride is more hydrophobic than that of the carboxylic acid. Formation of the interchain anhydride was followed by contact angles. (B) The reaction of the interchain anhydride and *n*-undecylamine in anhydrous 1-methyl-2-pyrrolidinone formed a hydrocarbon layer of the amide at the surface of the original SAM of carboxylic acid. The change of the thickness of the layer was measured by ellipsometry. The inset is a plot of ratios of the thickness at time *t* and the final thickness during the initial 30 min. The solid circle (●) indicates that the concentration of *n*-undecylamine is 10 mM; the open circle (○) indicates that the concentration is 1 mM.

of water had almost reached its final value, and the reaction was complete within 5 min. These results establish that the formation of the interchain anhydride for the SAM terminated in carboxylic acid group by reaction with trifluoroacetic anhydride is a fast reaction.

We used ellipsometry to estimate the rate of the reaction of *n*-undecylamine and the surface anhydride (Figure 7B). The formation of the amide is characterized by two different phases: Within a few minutes the thicknesses have reached about 70−80% of their maxima; completion of the reaction occurs slowly. We hypothesize that this result reflects the decreasing reactivity of the functional groups on the surface as the reaction approaches completion. As the formation of amide groups on the surface proceeds toward completion, the unreacted anhydride groups become more buried by the long alkyl chains of the newly formed amides and, therefore, become less accessible and less reactive.

Conclusions

This paper demonstrates a simple, two-step method that generates mixed SAMs of carboxylic acids and amides from a well-ordered SAM of carboxylic acids on gold: dehydration of terminal carboxylic acids to form interchain anhydrides, and reaction of the interchain anhydrides with alkylamines. Conversion of the carboxylic acids into the interchain anhydrides is rapid and complete; all the acids are transformed into the interchain anhydrides and there are no mixed trifluoroacetic carboxylic anhydride groups detectable by XPS. Subsequent reaction of the interchain anhydride and alkylamine proceeds rapidly and cleanly to generate a mixture of acids and amides in approximately 1:1 ratio. The PIERS studies show that the underlying polymethylene groups of the SAMs of the interchain anhydride remain well-ordered; this order seems to be preserved in the mixed SAMs, although the alkyl groups of the amides are disordered.

This method provides a useful new synthetic route to prepare mixed SAMs, especially those comprising 1:1 mixture of acids and amides. It provides an easier and quicker route than *de novo* synthesis of the alkanethiols that contain amide groups. One important feature of the mixed SAMs generated by this method is that they are unlikely to contain large-scale phase separated domains. Such domains may complicate the interpretation of data in many types of experiments.

We believe that this method is the basis for a simple and versatile procedure for construction of complex surface structures. Other functional groups can also be readily incorporated into SAMs using this route. For example, we have allowed the interchain anhydride to react with cysteamine ($HSCH_2CH_2NH_2$) to generate a surface that presents thiol groups; this type of surface could *not* be generated by reaction of the thiol ($HSCH_2CH_2NHCO(CH_2)_{15}SH$) with gold.[74] It is likely that other functional groups that react rapidly with anhydride (e.g., alcohols, enamines, Grignard reagents, hydrazines) can be used to introduce a variety of functionalities into the interface.[75] This method also provides a simple route for grafting polymers to the surface. Finally, we also believe that this method can be readily applied to modification of SAMs and construction of two-dimensional patterns or three-dimensional structures on other metallic or semiconductor substrates. We are currently investigating applications of this new method.

Experimental Section

General Materials. Si⟨100⟩ wafers were obtained from Silicon Sense Inc., Nashua, NH. Absolute ethanol (Pharmco Products, Inc.), anhydrous *N*,*N*-dimethylformamide (HPLC grade, Aldrich), anhydrous 1-methyl-2-pyrrolidinone and trifluoroacetic anhydride (Aldrich), hydrochloric acid, sodium phosphate, citric acid, acetic acid, sodium acetate, boric acid, and sodium hydroxide (Fisher), and glycine (Sigma) were used as received. Triethylamine was dried over 3 Å molecular sieve, and methylene chloride was distilled over calcium hydride. 16-Mercaptohexadecanoic acid and 11-hydroxylundecanethiol were prepared according to the literature.[41]

Preparation and Characterization of SAMs. The gold substrates were prepared by e-beam evaporation of 5 nm of titanium and 200 nm of gold onto a silicon wafer as previously described.[76] The gold-coated wafers were cut into *ca.* 1 cm × 2 cm pieces and washed with absolute ethanol before adsorption of alkanethiol. SAMs were prepared by overnight exposure of the freshly prepared substrates to a 2 mM ethanolic solution of 16-mercaptohexadecanoic acid at room temperature in a clean 20-mL scintillation vial.[41]

PIERS spectra were obtained in single reflection mode using a dry air purged Digilab Fourier transform infrared spectrometer

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[74] XPS shows a photoelectron peak at 163.6 eV, and contact angle measurement shows an advancing contact angle of water of 60 °C. See ref 22.

[75] Treatment of the interchain anhydride with *n*-hexanol and 4-dimethylaminopyridine gives a surface having an advancing contact angle of *ca.* 85°.

[76] Folkers, J. P.; Laibinis, P. E.; Whitesides, G. M. *Langmuir* **1992**, *8*, 1330−1341.

(BioRad, Cambridge, MA).[77] The p-polarized light was incident at 80° relative to surface normal of the substrate. A narrow band mercury−cadmium−telluride (MCT) detector, cooled with liquid nitrogen, was used to detect the reflected light. A spectrum of a SAM of *n*-hexadecanethiolate-d_{33} on gold was taken as reference. Typically, 1024 scans were averaged to yield spectra with excellent signal-to-noise ratios at a resolution of 2 cm^{-1}.

XPS spectra were collected on an SSX-100 spectrometer (Surface Science Instrument) using monochromatic Al Kα X-rays ($\lambda = 8.3$ Å). The spectra were referenced to Au($4f_{7/2}$) at 84.00 eV. Survey spectra were recorded with a 150-eV pass energy, 1-mm spot size with an acquisition time of 3 min. High-resolution core level spectra were recorded with a 50-eV pass energy, 300-mm spot size with an acquisition time of 30 min. All spectra were fitted by using 90% Gaussian/10% Lorentzian function in the computer system of the spectrometer.

Ellipsometric measurements were made on a Rudolf Research Type 43603−200E ellipsometer using a He−Ne laser ($\lambda = 632.8$ nm) at an incident angle of 70.0° relative to the surface normal of the substrate. At least three separate spots were measured on each of three individually prepared substrates, and the readings were then averaged. The thickness of the monolayer was calculated using a program written by Wasserman according to the algorithm of McCrackin et al.[64] and a refractive index of 1.45 for calculation.

Advancing contact angles, θ_a, were determined on a Ramé-Hart Model 100 goniometer under ambient laboratory conditions on static drops that were applied using an Electra-Pipette dispenser (Matrix Technologies, Lowell, MA).[52] Contact angles were measured on both sides of the static drop. Data presented in this paper were averages of the measurements of at least three spots on each of three individually prepared samples. The concentrations of all the buffers used were 0.1 M. The following buffers were used for the titration: HCl (pH = 1), glycine (2, 10), sodium phosphate and citric acid (3, 4, 6, 7), acetic acid (5), boric acid (8, 9), sodium phosphate (11, 12), and sodium hydroxide (13).

Preparation of the Interchain Anhydride. In a 20-mL scintillation vial, a 10-mL solution of 0.1 M trifluoroacetic anhydride and 0.2 M triethylamine in anhydrous *N*,*N*-dimethylformamide was prepared. Precleaned substrates of the SAM of the carboxylic acid were immersed in this freshly prepared solution[78] without stirring for 20 min at room temperature, removed from the solution, rinsed thoroughly with CH_2Cl_2, and dried in a stream of nitrogen. The substrates of the interchain anhydride were used immediately.

Reactions of the Interchain Anhydride with Alkylamines. A 10-mL solution of 10 mM alkylamine in anhydrous 1-methyl-2-pyrrolidinone was prepared in a 20-mL scintillation vial (the solution of *n*-octadecylamine was above its saturation concentration at 10 mM, and used as a suspension). Precleaned substrates of the freshly prepared interchain anhydride were immersed in this solution without stirring for 30 min at room temperature, removed from the solution, rinsed with ethanol, and dried with a stream of nitrogen.

Kinetic Measurement of Formation of the Interchain Anhydride and Its Reaction with Alkylamines. Formation of the interchain anhydride was monitored by advancing contact angles of distilled, deionized water. Substrates of the SAMs of the carboxylic acid were immersed in a freshly prepared solution of trifluoroacetic anhydride and triethylamine in anhydrous *N*,*N*-dimethylformamide at room temperature. They were removed from the reaction mixtures after different periods of time and quickly rinsed with CH_2Cl_2. The contact angles of water were measured immediately by the procedure described above.

Reaction of *n*-undecylamine and the interchain anhydride was monitored by ellipsometry. The thicknesses of the SAM of the carboxylic acid of individual substrates were measured prior to the reaction. The substrates were then immersed in a freshly prepared solution of trifluoroacetic anhydride and triethylamine in anhydrous *N*,*N*-dimethylformamide at room temperature. After 20 min, the substrates were withdrawn from the mixture, quickly rinsed with CH_2Cl_2, and immersed in a 10-mM solution of *n*-undecylamine in anhydrous 1-methyl-2-pyrrolidinone. The substrates were removed from the amine solution after different periods of time, rinsed with absolute ethanol, and blown dry in a stream of nitrogen. Ellipsometric measurements were taken immediately according to the procedure described above.

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(77) Laibinis, P. E.; Bain, C. D.; Nuzzo, R. G.; Whitesides, G. M. *J. Phys. Chem.* **1995**, *99*, 7663−7676.

(78) The reaction solution has to be prepared freshly because tertiary amines can be oxidized by trifluoroacetic anhydride: Schreiber, S. L. *Tetrahedron Lett.* **1980**, *21*, 1027−1030.