# Sequence Dependent Behavior of Amphiphilic β-Peptides on Gold Surfaces

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We describe the formation of self-assembled monolayers (SAMs) on gold by helical β-peptides and show that β-peptide sequence can determine whether or not the SAM displays internal order. β-Peptide sequence isomers were designed either to be globally amphiphilic (**GA**), i.e., to display segregated hydrophilic and lipophilic surface patches, or to display an even distribution of hydrophilic and lipophilic side chains (***iso*-GA**). These isomers were compared in terms of two-dimensional self-assembly on a gold surface. β-Peptides derivatized with 3-mercapto-propionic acid, termed **GA-SH** and ***iso*-GA-SH**, display an N-terminal thiol for formation of gold-sulfur bonds. Comparison of ellipsometry measurements and the Amide I /Amide II ratios from infrared spectroscopy indicates that interactions between globally amphiphilic β-peptide molecules dictate the organization of the SAM formed from **GA-SH**. In contrast, the non-globally amphiphilic isomer ***iso*-GA-SH** formed a disordered monolayer. Comparison of the IR data for **GA-SH** and an analogue lacking a terminal thiol group, **GA-NH$_2$**, suggests that thiol-mediated chemisorption to the gold surface is not required for organization but facilitates the concentration of β-peptides at the surface. These studies suggest that sequence control among β-peptides is important for generating an ordered monolayer. Because the helices formed by appropriately designed β-peptides are more stable than helices formed by α-peptides, we suggest that β-peptide SAMs provide an avenue to the rational engineering of surfaces in which chemical groups are presented in precise and predictable arrangements.

## Introduction

The diverse properties of proteins in biological systems have inspired chemists to explore synthetic materials formed by designed α-peptides (oligomers of α-amino acids).[1−8] The behavior of α-peptides at interfaces has been studied,[3,9,10] and in some cases, peptide folding patterns evolve substantially upon transfer to an interfacial environment.[11−15] Here, we report an effort to determine whether oligomers of β-amino acids ("β-peptides")[16−19] form organized monolayers at interfaces. Short β-peptides can adopt predictable secondary structures. The use of cyclically constrained β-amino acid building blocks (Figure 1) leads to helical conformations with very high stability,[20−22] much higher than can be achieved with short α-peptides. Rigid β-peptide helices provide a predictable way to display side chains in space, which creates unique prospects for function-based design of β-peptides. The "rules" that relate β-peptide sequence and three-dimensional structure have previously been used to identify β-peptides that self-assemble in dilute aqueous solution[23] and form liquid crystalline phases at higher concentrations in

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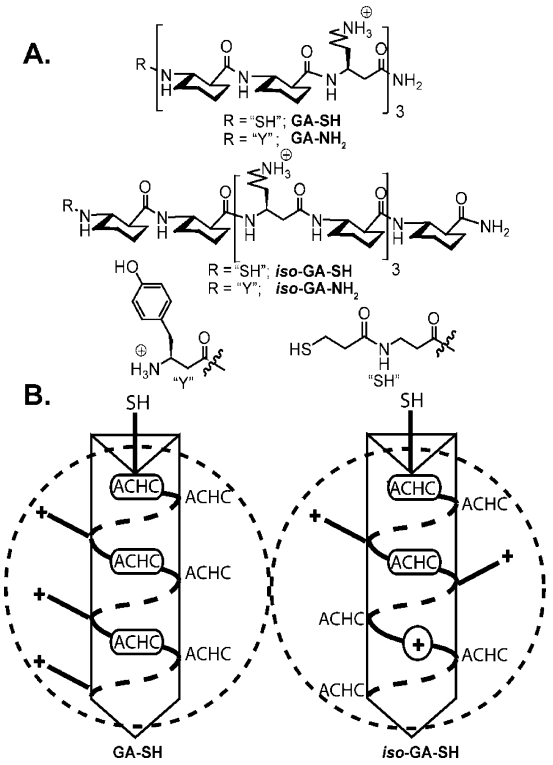


**Figure 1.** Globally amphiphilic and non-amphiphilic 14-helical β-peptides **GA** and ***iso*-GA** (A) Linear sequences of β-peptides. (B) Cylinder drawing of folded helices with predicted side-chain volume indicated by a dashed oval.

water.[24] Crucial to self-assembly is the ability of the β-peptide to adopt a globally amphiphilic helix conformation, i.e., a helix that has hydrophilic groups segregated on one side and lipophilic groups segregated on the other; in the comparisons reported to date, isomeric sequences that do not adopt globally amphiphilic conformations do not self-assemble.[23]

Here, we describe efforts to determine whether the ability of a β-peptide to adopt a globally amphiphilic helical conformation influences self-assembly when the β-peptide is constrained to a surface. This question is interesting because β-peptides with a robust and well-defined secondary structure that form organized monolayers could provide a predictable way to pattern chemical functional groups on surfaces. Such precisely defined interfaces may be useful for controlling surface-sensitive phenomena such as the wetting and spreading of liquids or the nucleation of oriented crystals. Molecularly engineered surfaces might ultimately be useful for molecular electronics or photonics applications.[25] The high proteolytic stability of β-peptides[26,27] stands in contrast to the proteolytic susceptibility of α-peptides and may be useful for biological applications.[28]

## Experimental Section

**Materials.** Fmoc-(S,S)-*trans*-2-aminocyclohexanecarboxylic acid (Fmoc-S,S-ACHC) was prepared by the method outlined by Schinnerl et al.[29] Fmoc-(S)-$\beta^3$-amino acids were prepared from their corresponding α-amino-acids (Novabiochem) or purchased from PepTech.[30] S-Trityl-3-mercaptopropionic acid was synthesized from known procedures.[31] Biotech-grade DMF was purchased from Aldrich and stored over 50W-X8 DOWEX ion-exchange resin. Methanol, $CH_2Cl_2$, tetrahydrofuran, and acetonitrile were purchased from Burdick and Jackson. *O*-Benzotriazol-1-yl-*N*,*N*,*N*′,N′-tetramethyluronium hexafluorophosphate, and NovaSyn TGR resin (0.25 mmol/g loading) were purchased from Novabiochem. $iPr_2EtN$ was distilled from calcium hydride. All other reagents were purchased from Aldrich and used without purification.

*RP-HPLC (Reverse Phase-High-Pressure Liquid Chromatography).* All β-peptides were purified via RP-HPLC on a Vydac C18 semipreparative column using a flow rate of 3 mL/min. Solvents A and B for RP-HPLC were 0.1% trifluoroacetic acid (TFA) in Millipore water and 0.1% TFA in acetonitrile, respectively. β-peptide purity was assessed using a Vydac C18 analytical column using a flow rate of 1 mL/min from 10 to 60% B over 50 min monitoring at 220 and 273 nm.

*MALDI-TOF MS (Matrix-Assisted Laser Desorption−Ionization Time-of-Flight Mass Spectrometry).* MALDI-TOF MS data were collected on a Bruker REFLEX II spectrometer with a 337 nm laser using α-cyano-4-hydroxycinnamic acid as matrix. Measurements were calibrated using peptide standards angiotensin I ($M + H^+$) = 1296.7 and neurotensin ($M + H^+$) = 1672.9.

**General Procedure for the Microwave-Assisted Solid-Phase Synthesis of β-Peptides.** All 14-helical β-peptides were synthesized on a solid phase in a CEM MARS microwave reactor. Microwave irradiation involved a maximum power of 600 W. Reaction mixtures were agitated by magnetic stirring during irradiation. Reaction temperature was monitored using a fiberoptic temperature sensor. Coupling and deprotection reactions involve the following conditions: couplings, 600 W maximum power, 80 °C, ramp 2 min, hold 4 min; deprotections, 600 W maximum power, 90 °C, ramp 2 min, hold 2 min. For difficult couplings,[32] an additional temperature ramping cycle was included: 600 W maximum power, 80 °C, ramp 2 min, 0 W, 25 °C, 10 min hold, 3×.

**Representative Example of Microwave-Assisted Synthesis of a β-Peptide (GA-SH).** β-Peptide **GA-SH** was synthesized on a 25 μmol scale on NovaSyn TGR resin. All coupling and deprotection reactions were carried out at atmospheric pressure under microwave irradiation as described above. Prior to coupling, the resin was swelled in $CH_2Cl_2$ in a solid-phase extraction tube (Alltech). The resin was washed 3 times with DMF. In a separate vial, Fmoc-β-amino acid (75 μmol) was dissolved in 1000 μL of DMF and activated with *O*-benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HBTU, 150 μL of 0.5 M solution in DMF), 1-hydroxybenzotriazole monohydrate (HOBT, 150 μL of 0.5 M solution in DMF), and $iPr_2EtN$ (150 μL of 1.0 M solution in DMF).

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The coupling solution was vortexed and added to the resin, and the mixture was irradiated at 80 °C as described above. The resin was washed (3 times with DMF, 3 times with $CH_2Cl_2$, and 3 times with DMF). Deprotection solution (1900 $\mu$L of 20% piperidine in DMF (v/v)) was added to the resin, and the mixture was irradiated at 90 °C and washed as before. All ACHC residues were double-coupled and double-deprotected. Difficult coupling reactions for ACHC-3 and ACHC-6 were subjected to the temperature ramping cycle immediately following the second coupling. The coupling/deprotection cycles were repeated until the last residue, S-trityl-3-mercaptopropionic acid, was coupled. The $\beta$-peptide was cleaved from the resin in a mixture of 92.5/2.5/2.5/2.5 TFA/ethanedithiol/thioanisole/water for 2 h, followed by evaporation of the solvent under a nitrogen stream. The crude $\beta$-peptide was then purified by RP-HPLC and lyophilized to yield a white powder, 34−44% B over 20 min. MALDI-TOF MS (*m/e*) calcd for $C_{69}H_{120}N_{14}O_{11}S$: M = 1352.9. Found: $(M + H^+) = 1353.9$; $(M + Na^+) = 1375.9$; $(M + K^+) = 1391.9$.

*β-peptide* ***iso-GA-SH****:* 22−32% B over 20 min. MALDI-TOF MS (*m/e*) calcd for $C_{69}H_{120}N_{14}O_{11}S$: M = 1352.9. Found: $(M + H^+) = 1353.3$; $(M + Na^+) = 1375.3$; $(M + K^+) = 1391.3$.

*β-peptide* ***iso-GA-NH₂****:* 21−31% B over 20 min. MALDI-TOF MS (*m/e*) calcd for $C_{73}H_{122}N_{14}O_{11}$: M = 1370.9. Found: $(M + H^+) = 1372.1$; $(M + Na^+) = 1394.1$; $(M + K^+) = 1409.8$

*β-peptide* ***GA-NH₂****:* 35−45% B over 20 min. MALDI-TOF MS (*m/e*) calcd for $C_{73}H_{122}N_{14}O_{11}$: M = 1370.9. Found: $(M + H^+) = 1371.8$; $(M + Na^+) = 1393.8$; $(M + K^+) = 1409.8$.

**Preparation of *β*-Peptide Thin Films.** Reflective gold films were prepared by sequential deposition of 10 nm of titanium and 200 nm of gold onto silicon wafers (Silicon Sense, Nashua, NH) at normal incidence with an electron beam evaporator (Tek-Vac Industries, Brentwood, NY). The rates of deposition of titanium and gold were 0.2 and 1.0 Å/s, respectively. The pressure in the evaporator was maintained below $2 \times 10^{-6}$ Torr throughout evaporation of the metals. Upon removal from the vacuum chamber, the gold-coated silicon wafers were immediately cut into approximately 7 mm × 30 mm pieces, immersed into 0.1 mM methanolic $\beta$-peptide solutions, and incubated for up to 48 h. Upon removal from solution, samples were rinsed for 20 s with methanol; dried under a stream of nitrogen; rinsed sequentially for 20 s each with 2 M NaCl in deionized water (18.2 MΩ cm), deionized water, ethanol, and methanol, and then dried again under nitrogen.

**Ellipsometry.** Ellipsometric measurements were performed with a Gaertner LSE ellipsometer ($\lambda = 632.8$ nm, $\psi = 70°$) in order to determine the optical thicknesses of the $\beta$-peptide thin films on the surface of 200 nm thick gold films. The optical thicknesses reported are the averages of three spots on a sample using a refractive index of $n = 1.46$ for the thin films. The optical thicknesses reported for the films formed by soaking for 48 h are the averages of three spots on each of five samples.

**PM-IRRAS.** IR spectra of $\beta$-peptide thin films supported on gold (200 nm) were obtained using a Nicolet Magna-IR 860 FT-IR spectrometer with photoelastic modulator (PEM-90, Hinds Instruments, Hillsboro, OR), synchronous sampling demodulator (SSD-100, GWC Technologies, Madison, WI), and a liquid-$N_2$-cooled mercury cadmium telluride (MCT) detector. All spectra were obtained at an incident angle of 83° with the modulation centered at 1500 $cm^{-1}$. For each sample, 1000 scans were taken at a resolution of 4 $cm^{-1}$. Data were collected as differential reflectance versus wavenumber, and spectra were normalized and converted to absorbance units via the method outlined by Frey et al.[33]

**ATR-IR.** IR spectra of lyophilized $\beta$-peptides were obtained using a Bruker Tensor 27 FT-IR spectrometer with an ATR-IR setup (MIRacle, PIKE technology). Powdered samples were placed on a silicon coated ZnSe crystal plate, and spectra were recorded using 8 scans at a resolution of 1 $cm^{-1}$.

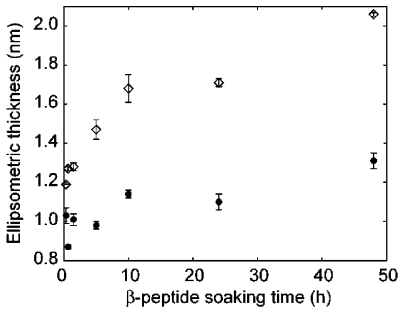


**Figure 2.** Ellipsometric thickness (nm) of $\beta$-peptide monolayers formed on gold. Film thickness for **GA-SH** (empty diamonds) and **GA-NH₂** (filled circles) from varying immersion time in $\beta$-peptide solutions.

## Results

The helical secondary structure of $\beta$-peptides used in this study is defined by 14-membered ring N−$H_i$ → O=$C_{i+2}$ hydrogen bonds between backbone amide groups; the resulting "14-helix" has approximately three residues per turn. Our $\beta$-peptides, sequence isomers **GA-SH** and ***iso*-GA-SH**, were designed to be either globally amphiphilic or non-globally amphiphilic, respectively, on the basis of this helical repeat (Figure 1). Non-globally amphiphilic sequences cannot achieve side-chain segregation in the 14-helical conformation. Approximately two-thirds of the residues in **GA-SH** and ***iso*-GA-SH** are derived from *trans*-2-aminocyclohexanecarboxylic acid (ACHC; Figure 1), which has previously been shown to confer a high degree of 14-helical folding in water for short $\beta$-peptides.[23,34] These studies showed adoption of the 14-helix by **GA-NH₂** and the enantiomer of ***iso*-GA-NH₂** as indicated by circular dichroism. The hydrophilic residues in these $\beta$-peptides are derived from $\beta^3$-homolysine ($\beta^3$-hLys), which has a side-chain amino group that can be protonated. An N-terminal thiol was attached to each of the two $\beta$-peptides to facilitate immobilization onto a gold surface, "chemisorption". **GA-NH₂** and ***iso*-GA-NH₂**, which lack the terminal thiol, were used as control compounds to assess nonspecific binding to the gold surface (Figure 1), "physisorption". All $\beta$-peptides were synthesized by standard solid-phase peptide synthesis methods using microwave irradiation.

We used ellipsometry to obtain initial evidence for formation of $\beta$-peptide films on the gold surface (Figure 2). Measurements were performed as a function of time of immersion of the gold substrates in methanolic $\beta$-peptide solutions. Inspection of Figure 2 reveals that for the amphiphilic compound **GA-SH**, the ellipsometric thicknesses of the films grew over a period of 48 h to 2.1 ± 0.1 nm. Films from control compound **GA-NH₂** also showed an increase in thickness over time, to 1.2 ± 0.1 nm, but were significantly thinner than films formed by **GA-SH**. Non-amphiphilic isomers ***iso*-GA-SH** and ***iso*-GA-NH₂** exhibited

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**Table 1. Thickness (nm) of β-Peptide Films on Gold after Immersion in β-Peptide Solutions for 48 h and Respective Amide I/Amide II Ratio**

| β-peptide | thickness (nm) | amide I/amide II (SAM) | amide I/amide II (powder) |
|---|---|---|---|
| **GA−SH** | 2.1 ± 0.1 | 0.92 ± 0.07 | 1.81 |
| **GA−NH$_2$** | 1.2 ± 0.1 | 0.62 ± 0.02 | |
| ***iso*−GA−SH** | 2.1 ± 0.1 | 1.6 ± 0.2 | 1.98 |
| ***iso*−GA−NH$_2$** | 1.5 ± 0.1 | 1.3 ± 0.2 | |

similar trends, with the thiol version leading to a thicker film (2.1 ± 0.1 nm and 1.5 ± 0.1 nm, respectively; Table 1). An 11-residue 14-helical β-peptide is predicted to be 1.7 nm in length on the basis of known dimensions of the 14-helical backbone (0.16 nm rise/residue, 0.54 nm helical diameter).[35] If we assume that the thiol-terminated linker is extended rather than participating in the 14-helix, then the ellipsometric thicknesses of immobilized β-peptides **GA-SH** and ***iso*-GA-SH** are consistent with formation of a chemisorbed monolayer. To assess the orientation of the β-peptide within the monolayer, we must consider the dimensions of the side chains. When side chains are accounted for, the aspect ratio of the 14-helical conformations expected from **GA-SH** and ***iso*-GA-SH** is close to 1[36] (the side-chain volumes are represented by a dashed oval in Figure 1). Therefore, a preferred orientation of the β-peptides cannot be inferred from the ellipsometry data.

The kinetics of monolayer formation show a rapid initial rate of formation and slower deposition at later time points (Figure 2). The decreased rate may reflect increasing density of β-peptide attached at the gold surface over time. We note that the deposition of our β-peptides is markedly slower than the deposition of alkanethiols;[37] this difference is likely due to the large size and strong interactions (e.g., electrostatic and/or dipolar interactions) among the helical β-peptide molecules. Similar behavior has been observed in SAMs formed from hydrophobic α-peptides.[38]

Because the ellipsometric measurements described above provide support for the formation of monolayers of helical β-peptides on the gold surface, we sought to characterize the level of molecular organization within the monolayers by using polarization-modulation infrared reflection−absorption spectroscopy (PM-IRRAS). When applied to thin films formed on a gold surface, this technique is sensitive to only those components of the transition dipole moment that are perpendicular to the surface, thus providing information regarding the orientations of molecules confined to these surfaces. PM-IRRAS data from β-peptide SAMs were compared to FT-IR spectra from a powdered sample; the latter represents the β-peptide in a non-oriented state.

PM-IRRAS spectra from monolayers of ***iso*-GA-SH**, which should form a non-globally amphiphilic helix, reveal amide I and amide II bands at 1661 and 1555 cm$^{-1}$,

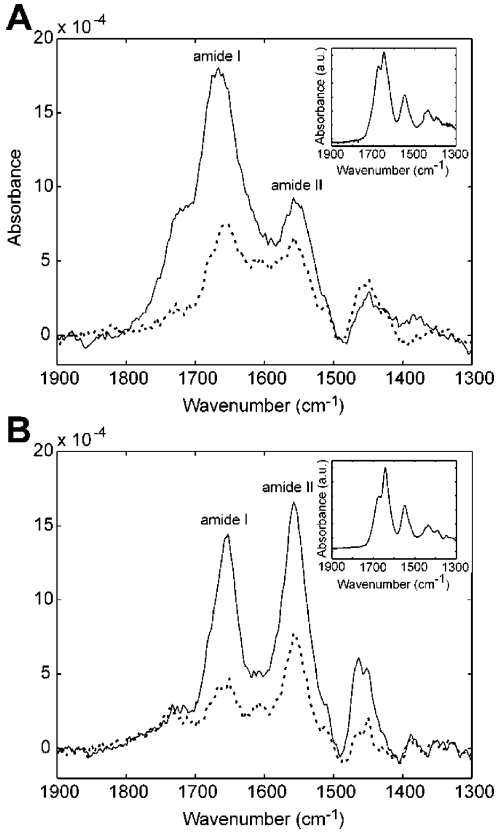


**Figure 3.** IR spectra of β-peptides on gold surfaces following 48 h immersion in β-peptide solution. (A) ***iso*-GA-SH (**solid line); ***iso*-GA-NH$_2$ (**dotted line); FT-IR data from a powdered sample of ***iso*-GA-SH** (inset). (B) **GA-SH (**solid line); **GA-NH$_2$ (**dotted line); FT-IR data from a powdered sample of **GA-SH** (inset).

respectively (Figure 3A). The positions of these bands are comparable to those reported previously for helical β-peptide polymers (poly(β-L-aspartates)) dispersed in solid films of polyethyleneoxide, 1654 ± 2 and 1552 ± 2 cm$^{-1}$.[39] The intensities of the bands for ***iso*-GA-SH** grew over time, which is consistent with ellipsometry measurements. Both bands were broad, and the amide I/amide II ratio of 1.6 ± 0.2 is similar to that of a randomly oriented powdered sample of ***iso*-GA-SH**, 1.98 (Figure 3A, Table 1). Taken together, these data indicate that although the non-amphiphilic β-peptide forms a monolayer on gold, the monolayer lacks a high level of organization. The breadth of the IR bands is consistent with a heterogeneous distribution of orientations (and thus microenvironments) on the surface (Figure 4).

Inspection of Figure 3B shows that **GA-SH**, the β-peptide that can form a globally amphiphilic 14-helix, displays markedly different behavior from that of sequence isomer ***iso*-GA-SH**. The amide I and amide II bands of **GA-SH** adsorbed to the gold surface, at 1653 and 1558 cm$^{-1}$, are much sharper than those observed for adsorbed ***iso*-GA-SH** (i.e., the peak width at half-height for the amide I band of ***iso*-GA-SH** is 83 vs 50 cm$^{-1}$ for **GA-SH**). In addition, the amide I/amide II ratio for gold-adsorbed **GA-SH** differs greatly from the ratio of the randomly oriented (powder) sample, 0.92 ± 0.07 vs 1.81, respectively (Table 1). The low value of the amide I/amide II intensity ratio for adsorbed

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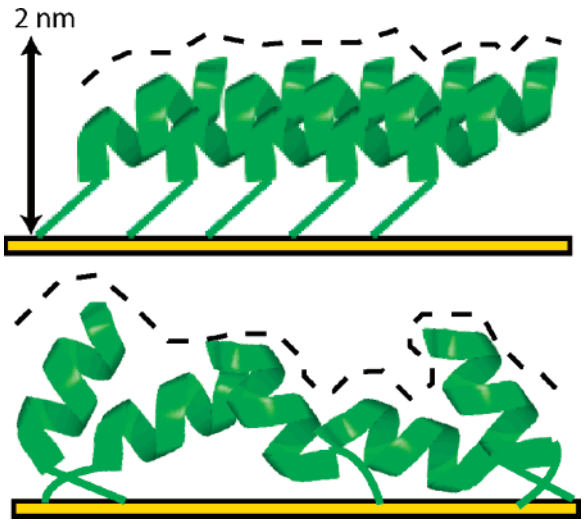


**Figure 4.** Model for organization of $\beta$-peptide SAMs on gold. Top: arrangement of globally amphiphilic sequence **GA-SH**; bottom: non-globally amphiphilic ***iso*-GA-SH**. Side chains have been omitted for clarity.

**GA-SH** is consistent with a preferred orientation of the $\beta$-peptide in which the helical axis is highly tilted away from the surface normal (Figure 4, top). We infer such an organization by assuming that the orientations of the amide I and amide II transition dipoles of the $\beta$-peptide 14-helix, relative to the helix structure, are similar to the analogous transition dipole orientations of α-helices; this assumption seems reasonable on the basis of the fact that the carbonyls of the amide bonds are oriented approxiamately parallel to the helix axis in both the α-helix and the 14-helix.[21]

Organization of the globally amphiphilic helices formed by $\beta$-peptide **GA-SH** could result from interactions between the dipoles of neighboring helices and/or from association of lipophilic surfaces on neighboring $\beta$-peptide molecules. Our data suggest that only the globally amphiphilic isomer, **GA-SH**, forms an organized assembly on the gold surface. The apparent difference in self-association between **GA-SH** and ***iso*-GA-SH** when they are immobilized on a gold surface is consistent with the comparable differences observed for **GA-NH$_2$** and ***iso*-GA-NH$_2$** in aqueous solution. **GA-NH$_2$** forms small, soluble aggregates in dilute aqueous solution, and at higher concentration this $\beta$-peptide forms larger aggregates with long-range order, whereas ***iso*-GA-NH$_2$** does not self-associate under these conditions.[23,24]

PM-IRRAS experiments were carried out with ***iso*-GA-NH$_2$** and **GA-NH$_2$**, which lack a thiol group and therefore can adsorb only noncovalently to gold. The data showed significant $\beta$-peptide adsorption to the gold surface even after extensive washing, consistent with ellipsometry observations. However, in all cases, the overall absorbance intensities from these thiol-free molecules were significantly lower than from the analogous thiol-bearing $\beta$-peptides (panels A and B in Figure 3). A significant difference in the amide I/amide II ratio was observed for the two thiol-free molecules in the gold-adsorbed state (Table 1), with the ratio for globally amphiphilic **GA-NH$_2$** significantly lower than the ratio for the sequence isomer. This amide I/amide II ratio difference between **GA-NH$_2$** and ***iso*-GA-NH$_2$** is comparable to the amide I/amide II ratio difference observed between **GA-SH** and ***iso*-GA-SH**, which suggests that the isomer capable of forming a globally amphiphilic 14-helix displays a distinctive organization at the interface even in the thiol-free series. Thus, the interactions that lead to organization of $\beta$-peptides that form a globally amphiphilic helix appear to be dictated largely by the pattern of side-chain display and not by sulfur-mediated chemisorption to the gold surface. We note that the amide I/amide II ratio of **GA-SH** is slightly higher than that of **GA-NH$_2$**, indicating that the presence of the thiol group on the globally amphiphilic 14-helix has a small but measurable impact on ordering on the gold surface. The difference between amide I/amide II ratios suggests an increased tilt of the 14-helix axis away from the surface normal for **GA-NH$_2$** relative to **GA-SH**. In contrast to the small influence of sulfur-mediated chemisorption on ordering of the globally amphiphilic helix, the difference between chemisorption and physisorption does not seem to affect the ordering of the non-globally amphiphilic 14-helices.

## Discussion

The results described above indicate that it is possible to form organized monolayers of $\beta$-peptides on surfaces, a necessary step toward our long-term goal of exploiting the precisely defined conformations of $\beta$-peptides for rational manipulation of the nanoscopic structures of interfaces and associated properties. The $\beta$-peptide sequence exerts a substantial effect on monolayer organization: the $\beta$-peptide that cannot form a globally amphiphilic helix appears to show no more order in the adsorbed state than it does in a powder form, whereas the $\beta$-peptide that can form a globally amphiphilic helix displays a distinctive ordering when adsorbed on a gold surface. Previous work showed that the ability to adopt a globally amphiphilic helix is necessary for $\beta$-peptide self-association in aqueous solution; therefore, it is tempting to speculate that ordering at the gold surface results from interhelical interactions comparable to those that occur in solution. Comparison between **GA-SH** and **GA-NH$_2$** suggests that thiol-mediated chemisorption to the gold surface has a minor influence on organization relative to the effects of sequence and amphiphilicity. However, a terminal thiol group does seem to facilitate the concentration of $\beta$-peptides at the gold surface.

Our experiments explore a new strategy for contolling molecular order within monolayers based on the use of oligomers with unnatural backbones that display strong and specific folding tendencies ("foldamers"). Related studies have been reported with α-peptides. Boncheva and Vogel[40] showed that an α-peptide capable of forming an amphiphilic α-helix displays pronounced orientation effects upon immobilization on a gold surface. Miura et al.[38] also detected orientation effects among self-assembling hydrophobic peptides. Neither study, however, compared sequence isomeric α-peptides that either could or could not adopt globally amphiphilic helical conformations. Our conclusions regarding the importance of global amphiphilicity for organization within a monolayer therefore represent a distinctive contribution to this field.

(40) Boncheva, M.; Vogel, H. *Biophys. J.* **1997**, *73*, 1056.

## Conclusions

On the basis of our ellipsometry and IR data, we propose a model for the organization within self-assembled monolayers of globally amphiphilic β-peptide **GA-SH** and non-amphiphilic β-peptide ***iso*-GA-SH** (Figure 4). The data suggests that the helical molecules of **GA-SH** are tilted away from the surface normal (Figure 4, top). In contrast to this ordered monolayer, we propose that the molecules are disordered within the monolayer formed by ***iso*-GA-SH** (Figure 4, bottom). Nanostructured interfaces such as those we propose for the globally amphiphilic sequence may find use in engineering surfaces with specific biological properties or in fundamental studies of transport processes (e.g., electron transport) at surfaces. Helical α-peptides bearing appended redox-active groups or chromophores have been used to study interfacial electron transport or photophysical processes.[25] Similar studies based on helical β-peptides may provide a higher level of control over the placement of redox-active groups or chromophores at interfaces.

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