in phases and the semiquantitative computational values, the qualitative similarity of the results is reasonable.

Conclusions

Macrocyclic polyether **3** is an unusual host for the binding of a fluoride ion. The host undergoes a number of conformational changes in order to bind the fluoride by four C-H hydrogen bonds. The fluorinated groups attached to the $-CH_2-$ groups constitute the electronic driving force for binding of the fluoride and simultaneously provide stereochemical labels in the resulting complex. Several enantiomerization processes that are nondissociative feature hydrogen bond making and breaking steps coupled with multiple bond rotations. Anti-Arrhenius behavior is associated with some of these conformational processes. This suggests that solvent and/or gegenions are involved in the conformational changes and that the complete supersystem may need to be included for a complete analysis of the data. Theoretical model calculations were useful in understanding some of the modes leading to enantiomerization and in providing insight into the bonding and energetics of the complex. Extension of these results to other systems with sufficiently low energy barriers and restricted conformational spaces should provide other examples which exhibit unusual conformational dynamics with novel temperature dependencies.

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Supplementary Material Available: Tables of fractional coordinates and thermal parameters, intramolecular bond distances and angles, and intermolecular distances for **3-5** (34 pages); listing of structure factors for **3-5** (30 pages). Ordering information is given on any current masthead page.

Oriented Crystallization as a Tool for Detecting Ordered Aggregates of Water-Soluble Hydrophobic α-Amino Acids at the Air-Solution Interface

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Abstract: The formation of two-dimensional ordered aggregates of water-soluble hydrophobic α-amino acids at the air-solution interface has been demonstrated through the induced epitaxial nucleation of α-glycine crystals at these interfaces. This crystallization method, albeit indirect, has been found to be very sensitive to small changes in the structure of the presumed aggregates. The hydrophobic-amino acids used were divided into two classes: The first, including valine, leucine, phenylalanine, norleucine, isoleucine, and α-aminooctanoic acid, induced fast oriented crystallization of α-glycine, at the solution surface, whereas the second class, *tert*-butylglycine, neopentylglycine, and hexafluorovaline, did not. The comparison between the packing arrangement of the α-glycine crystalline face attached at the interface and that of various hydrophobic α-amino acid crystals, complemented by surface tension measurements, brought evidence in favor of the formation of structured domains which must carry precise enantioselective information to generate the oriented crystallization process. These results may be relevant to any process involving structural self-aggregation.

Introduction

Information available today on the initial stages of aggregation of molecules either at interfaces or in the bulk solution is sparse. These processes are decisive for the formation of membranes, thin molecular films, and crystals and are therefore important in fields ranging from biochemistry to the material sciences.

It is well-known that water-soluble amphiphiles have a tendency to accumulate at the air-solution interface. Surface tension[1] and other modern experimental techniques such as nonlinear optic measurements[2] and X-ray[3] and neutron specular reflectivity[4,5] have been used to provide direct information both on the surface concentration and on the orientation of such molecules. None of these techniques is however sensitive to the distribution of the molecules within the surface layer.

The question we pose here is whether water-soluble hydrophobic α-amino acids form two-dimensional-ordered aggregates or are randomly distributed at the air-solution interface. It is our hypothesis that spontaneous organization of water soluble hydrophobic α-amino acids can occur at the air-solution interface, yielding aggregates with a layer structure similar to that found within the crystals of the same compound. We further obtained evidence from previous studies[6-8] that crystal nuclei assume structures similar to that of the mature crystals. If both these assumptions are true, the above-mentioned aggregates may serve as structured two-dimensional domains for epitaxial nucleation of the same compound or of other compounds, provided a structural match exists between the structures of the two crystals within the interface layer.

Following this line of thought we use here the induction of oriented floating glycine crystals of the α form by soluble hy-

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Table I. Crystallographic Data, Molecular Area, and Calculated Subcell for α-Amino Acids

α-amino acid	space group	Z	cell parameters						Molecular area:	subcell		
			a	*b*	*c*	α	β	γ	A_m	*a'*	*c'*	β'
α-glycine	$P2_1/n$	4	5.10	11.97	5.46	90	111.7	90	25.9 (*ac* sin β)			
(*S*)-leucine	$P2_1$	4	14.67	5.32	9.61	90	94.06	90	25.6 (*bc*/2)	5.3	5.5	123
(*S*)-valine	$P2_1$	4	9.71	5.27	12.06	90	90.8	90	25.6 (*ab*/2)	5.3	5.5	123
(*S*)-norleucine	*C*2	4	9.55	5.26	15.38	90	95.6	90	25.1 (*ab*/2)	5.45	5.45	122
(*S*)-isoleucine	$P2_1$	4	9.75	5.32	14.12	90	95.8	90	25.9 (*ab*/2)	5.3	5.5	122
(*S*)-α-aminooctanoic	$P2_1$	4	9.58	5.21	19.76	90	86	90	25.0 (*ab*/2)	5.3	5.5	123
(*S*)-phenylalanine	*C*2	8	8.80	6.04	31.56	90	96.6	90	26.6 (*ab*/2)	5.3	5.3	112
(*S*)-neopentylglycine·H_2O	$P2_12_12$	8	10.18	30.74	5.84	90	90	90	29.8 (*ac*/2)	5.2	5.8	126
(*S*)-*tert*-butylglycine·H_2O	*P*1	4	12.86	10.96	5.97	92.36	100.8	81.45	32.7 (*bc* sin α/2)	5.3	6.0	114
(*RS*)-*tert*-butylglycine·H_2O	$P2_1/c$	8	13.12	12.25	10.83	90	109.4	90	33.2 (*bc*/4)			
(*RS*)-hexafluorovaline	$P2_1/c$	4	11.73	6.61	10.73	90	109.4	90	34.3 (*bc*/2)			

drophobic α-amino acids[9] as a tool for studying the surface aggregation of the latter. We take advantage of the fact that one class of the hydrophobic α-amino acids forms crystalline layer structures similar to that of glycine, while the other class has been engineered so that their side chains are too bulky to form a layer structure similar to that of α-glycine. If our hypothesis on surface aggregation is indeed correct, the former class, but not the latter, is expected to induce epitaxial surface nucleation of glycine.

We had already suggested the possibility of a mechanism involving ordered aggregates in recent crystallization studies[10] related to spontaneous generation of optical activity. We had examined the crystallization of α-glycine at the air–solution interface in the presence of small amounts of the naturally occurring hydrophobic α-amino acids. We had found that they induced the formation of oriented crystals of α-glycine floating on the solution surface: When (*S*) α-amino acids were used, glycine crystals were found to float with their chiral ($0\bar{1}0$) face exposed to air, which we specify as "($0\bar{1}0$) oriented". By symmetry the hydrophobic (*R*) α-amino acids induced (010) oriented floating crystals of glycine.

Crystalline α-glycine[11] (Table I) is composed of hydrogen-bonded layers parallel to the *ac* plane in which the molecules are related only by translational symmetry (Figure 1b). The area per molecule within such a layer, *ac* sin β, is 25.9 Å^2. These layers are interlinked by N–H···O bonds via a center of inversion to form centrosymmetric bilayers. Since each layer is chiral,[12] the replacement of the C–H groups, which emerge from the (010) crystal surfaces by α-amino acid side chains, would generate a chiral amino acid layer of (*R*) configuration. By glide or inversion symmetry a layer of glycine molecules at the ($0\bar{1}0$) crystal surface may be replaced by a chiral layer of (*S*) α-amino acids. Thus, epitaxial growth of glycine on such layers is conceivable, provided the cross-sectional area of the side chains is not appreciably larger than 25.9 Å^2, the area of α-glycine.

To validate the hypotheses formulated above, the crystal structures of a series of water–soluble hydrophobic α-amino acids were analyzed as a function of the size of their hydrophobic chains and in relation to that of glycine. α-Glycine was subsequently crystallized in the presence of these α-amino acids, and the presence or absence of induced oriented crystals at the interface was monitored.

Results

The Layer Structures of Hydrophobic α-Amino Acids in Relation to That of α-Glycine. The hydrophobic optically pure α-amino acids valine,[13] leucine,[14] norleucine,[15] isoleucine,[16] phenylalanine,

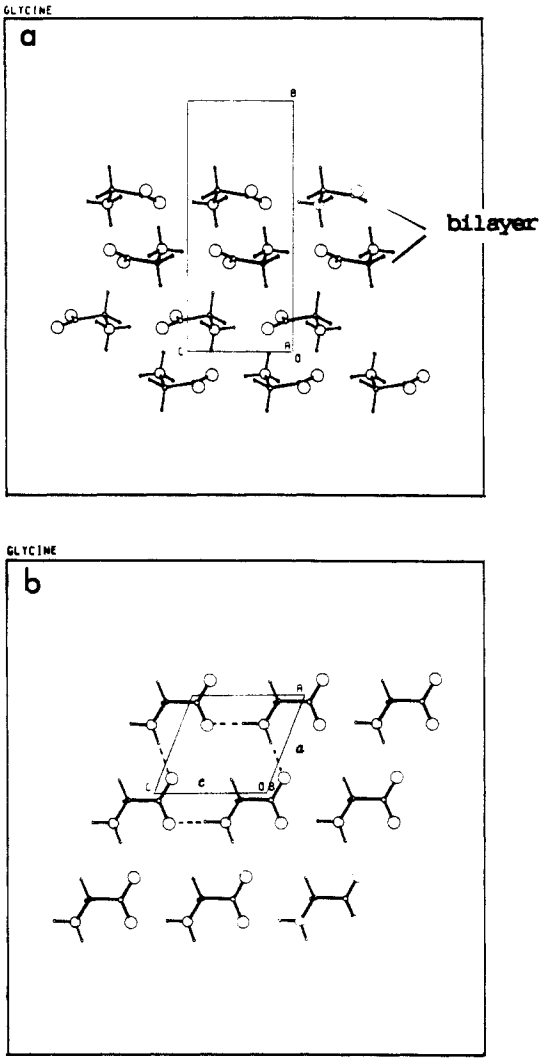

Figure 1. Packing arrangement of the α-form of glycine viewed: (a) along the *a* axis (note the bilayer of molecules) and (b) perpendicular to the layer of molecules. The characteristic hydrogen-bonded motif is depicted.

and α-aminooctanoic acid[17] all pack in hydrogen-bonded layer structures similar to that of α-glycine. This is evident from a comparison of the unit cell parameters *a*, *c*, and β of α-glycine with the corresponding subcell (*a'*,*c'*, and β') of these hydrophobic α-amino acids (Table I and Figures 2b, 3b). The similarity is manifested despite the fact that the hydrogen-bonded bilayer of these hydrophobic α-amino acids is formed via a (pseudo) two-fold axis (Figures 2a, 3a) and the bilayer of glycine via a center of inversion[18] (Figure 1a). The area/molecule within the layer ranges

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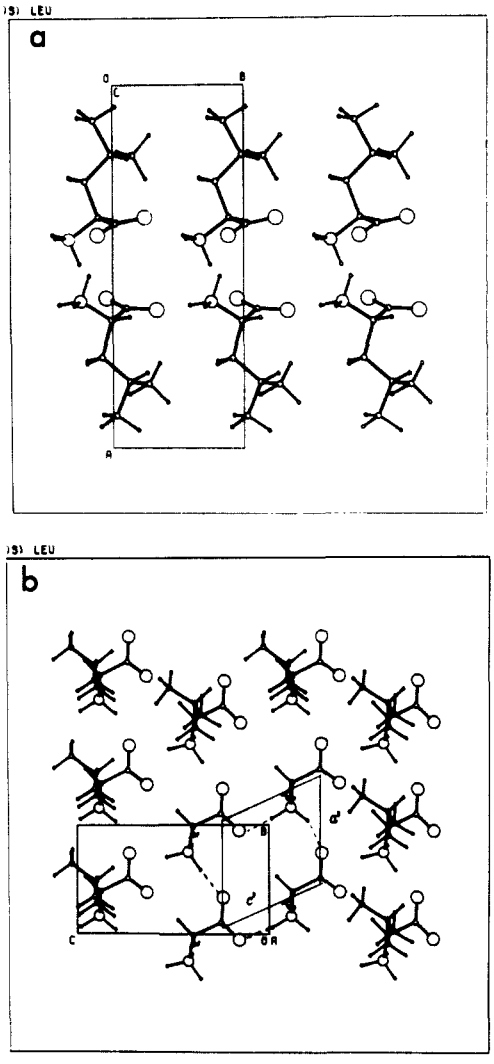

Figure 2. Packing arrangement of (*S*)-leucine crystal viewed: (a) along the *c* axis and (b) perpendicular to the layer of molecules. The hydrogen-bonded motif similar to that of α-glycine is depicted, and *a'* and *c'* are the calculated axes of the subcell (see text). The side chains of the four relevant molecules were omitted for clarity.

from 25.1 to 26.6 Å^2, close to that of α-glycine. It is noteworthy that optically pure phenylalanine has a layer structure similar to that of α-glycine despite the relatively large cross sectional area of the aromatic ring.

A distinctive feature of these compounds is their tendency, unlike gycine, to crystallize at the aqueous solution surface as plates the two faces of which are parallel to the plane of the hydrogen-bonded bilayers.

If the hydrophobic optically pure α-amino acids form an ordered aggregate on top of a supersaturated solution of glycine we expect glycine molecules to bind to it via a center of inversion resulting in a bilayer composed of a layer of chiral hydrophobic α-amino acids and a layer of glycine. Such a bilayer may eventually induce oriented crystallization of α-glycine at the air–solution interface.

In contrast to the above mentioned group of natural α-amino acids, we anticipated a mismatch between the layer structures of α-glycine and that of hydrophobic α-amino acids with bulky side chains such as neopentylglycine, *tert*-butylglycine, and hexafluorovaline. This prediction was confirmed by the crystal structure determination of these three unnatural amino acids.

Optically pure neopentylglycine and *tert*-butylglycine both crystallize as monohydrates in layer structures. In *tert*-butylglycine ($P1$, $Z = 4$, Table I), the *bc* layer (Figure 4) is formed by ribbons, two-molecules wide, and interlinked by strands of water molecules. Within each ribbon, molecules are related by a *c* translation of 5.97 Å along the ribbon and by a pseudo-translation of 5.3 Å in the $-b + c$ direction. Thus we may construct a two-dimensional

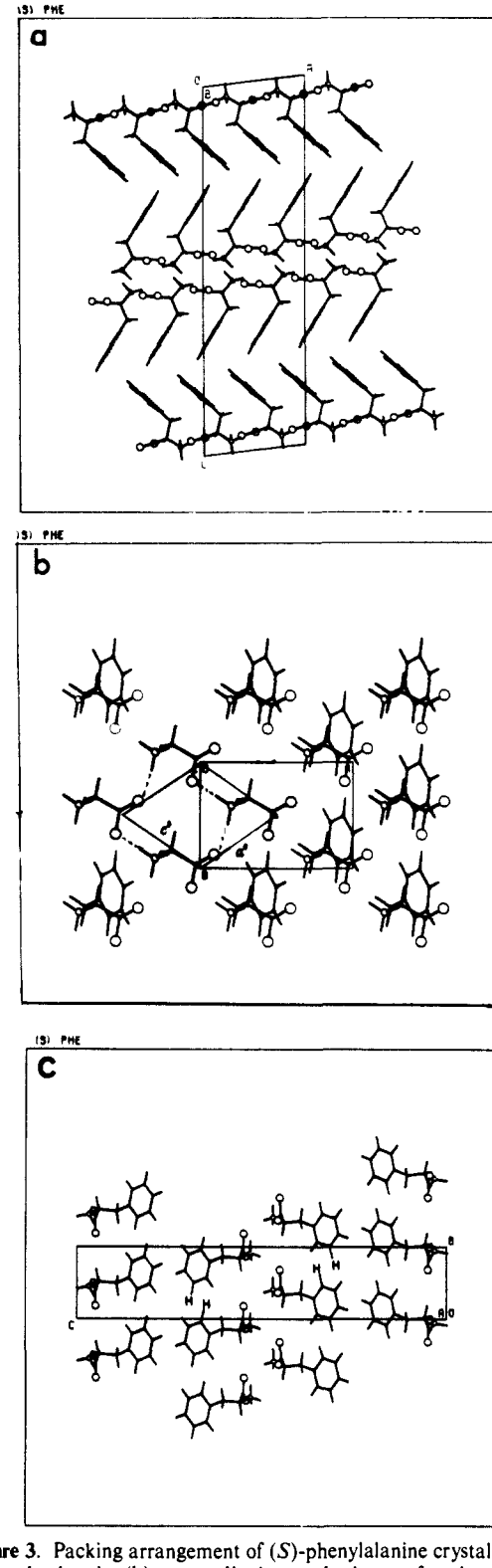

Figure 3. Packing arrangement of (*S*)-phenylalanine crystal viewed: (a) along the *b* axis, (b) perpendicular to the layer of molecules, and (c) along the *a* axis. The subcell is depicted as in Figure 2.

subcell with axes $a' = 5.3$ Å, $c' = 6.0$ Å, and $\beta = 123°$ which simulates the corresponding cell axes of α-glycine, $a = 5.1$, $a + c = 5.9$ Å with an angle of 121°. Because of steric hindrance of the *tert*-butyl side chain, the layer is substantially distorted from planarity .

The crystal structure of (*S*)-neopentylglycine ($P2_12_12$, $Z = 8$, Table I and Figure 5) also contains ribbons, two (crystallographically independent) molecules wide, running parallel to *c* in the *ac* plane and separated by chains of water molecules. Here as well a subcell with axes $c' = c = 5.8$ Å, $a' = (a - c)/2 = 5.2$ Å, $\beta' = 126°$, may be constructed to be compared to the corre-

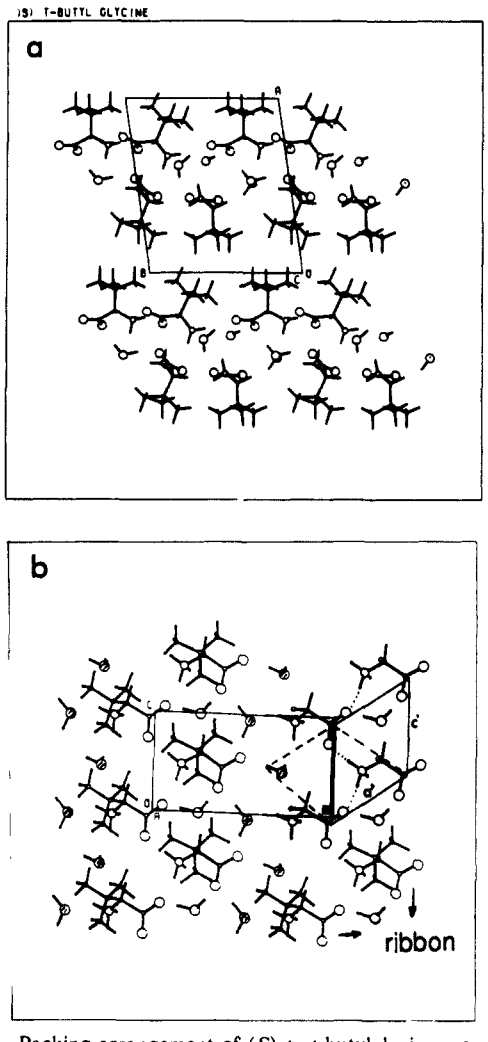

Figure 4. Packing arrangement of (*S*)-*tert*-butylglycine monohydrate crystal viewed: (a) along the *c* axis and (b) perpendicular to the layer of molecules. Subcell depicted as in Figure 2. The shaded water molecules form the strand separating the ribbons. The unshaded water molecules lie below the layer but are hydrogen bonded to it.

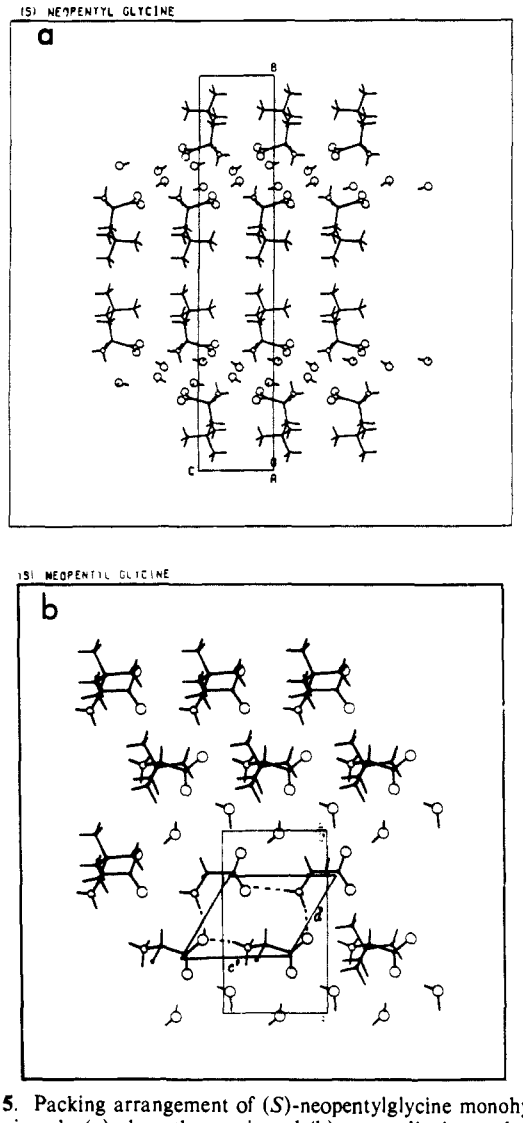

Figure 5. Packing arrangement of (*S*)-neopentylglycine monohydrate crystal viewed: (a) along the *a* axis and (b) perpendicular to the layer of molecules. Subcell depicted as in Figure 2.

sponding one in α-glycine. We note, however, that for one of the molecular chains parallel to *c*, the $N-H_1$ bond is hydrogen-bonded to O_2 rather than to O_1, as in glycine. The hydrogen-bond arrangement within the ribbon is less distorted from planarity than in *tert*-butylglycine.

We may conclude, from the above analysis, that the similarity in layer packing of *tert*-butyl- and neopentylglycine to that of α-glycine does not exist in both directions but is rather confined to one direction along the ribbon. For this reason epitaxial crystallization of glycine from such layers is hardly possible, but some induction may be expected.

The crystal structure of (*S*)- or (*R*)-hexafluorovaline was not determined because the racemic mixture has not been resolved. In the racemic structure however the molecules are arranged in *bc* bilayers interlinked by N–H···O bonds via *c* glide and twofold screw symmetry (Table I and Figure 6). The area/molecule within the layer is 34.3 Å^2. Therefore under no circumstance would it be possible for optically pure molecules to pack with an area/molecule of 25.9 Å^2 in a layer structure similar to that of α-glycine. No epitaxial growth and no induction can thus be expected.

Crystallization Experiments. Pure crystals of glycine grown from aqueous solutions are bipyramidal. They develop dominant {110} and {011} faces at which the COO^- and NH_3^+ groups are exposed and sometimes also small {010} faces at which the C-H groups emerge. The pure crystals have no tendency to grow at the water–air interface.

We have shown that glycine grown in the presence of natural hydrophilic (*S*) or (*R*) amino acids crystallizes at the bottom of the vials as pyramids with well developed (0$\bar{1}$0) or (010) faces respectively. In the presence of the corresponding racemic compounds it forms {010} plates.

Glycine, when grown in the presence of the (*R*) or (*S*) α-amino acids leucine, valine, norleucine, phenylalanine, and α-amino octanoic acid form floating pyramids with their basal (010) or (0$\bar{1}$0) faces respectively exposed at the surface (Table II). Oriented nucleation is induced above a threshold concentration of additive which varies from one amino acid to the other; the minimum concentration required is 1% wt/wt (of glycine) for valine and phenylalanine, 0.1% for leucine, norleucine and isoleucine, 0.01% for α-aminoctanoic acid. This variability can be correlated with surface tension measurements which give a measure of the 'hydrophobicity' of the α-amino acid side chains (Table III). The strongest effect and the minimum threshold concentration are observed for α-aminooctanoic acid which has the highest tendency for surface accumulation. The relatively high threshold concentration of phenylalanine, which, according to surface tension measurements, is more hydrophobic than valine, can be explained on the basis of the packing arrangement of the (*S*)-phenylalanine crystal (Figure 3c); unfavorably short H···H contacts exist between the aromatic rings along the *b* direction. Thus, the aggregates formed at the solution surface are, probably, less stable in view of the fact that we are considering only a single layer.

In contrast with the above results, the addition of up to 3% (wt/wt of glycine) of (S)-*tert*-butylglycine to the crystallizing solution of glycine resulted in few floating crystals with random

Table II. Crystallization Behavior of α-Glycine When Grown in the Presence of Hydrophobic[a] α-Amino Acids

α-amino acid additive	amount: % wt/wt of glycine	crystallization behavior	crystallization rate
(*S*)-valine	1–5		fast (min)
(*S*)-phenylalanine	1–5	(0$\bar{1}$0)-oriented	fast (min)
(*S*)-norleucine	0.1–3	floating crystals	fast (min)
(*S*)-leucine	0.1–3		fast (min)
(*S*)-α-aminooctanoic acid	0.01–0.1		fast (min)
(*S*)-*tert*-butylglycine	0.5–3	few floating crystals with random orientation	slow (h)
(*S*)-neopentylglycine	0.1–0.3	few floating crystals with random orientation	slow (h)
	0.7–1	more crystals (0$\bar{1}$0) oriented	slow (h)
(*RS*)-hexafluorovaline	0.5–3	no floating crystals	zero

[a] Hydrophilic α-amino acids do not induce crystallization of α-glycine at the air–solution interface.

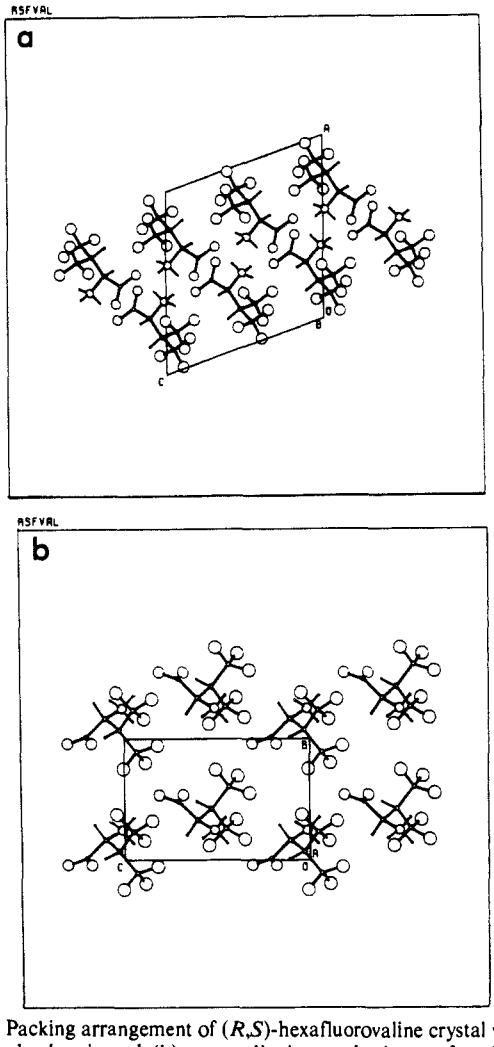

Figure 6. Packing arrangement of (*R*,*S*)-hexafluorovaline crystal viewed: (a) along the *b* axis and (b) perpendicular to the layer of molecules.

{010} orientation at the interface.

Crystallization of glycine in the presence of a mixture of (*S*)-*tert*-butylglycine and (*R*)- or (*S*)-alanine, serine, or threonine yielded still only a small number of floating glycine crystals of both orientations. In contrast, crystallization of glycine in the presence of 1:1 mixture of (*S*)-*tert*-butylglycine and (*R*)-leucine resulted in a large number of floating (010)-oriented crystalline plates, dictated by the presence of properly arranged leucine aggregates at the surface, and *tert*-butylglycine in solution. A 1:1 mixture of (*S*)-*tert*-butylglycine and (*S*)-leucine yielded a large number of (0$\bar{1}$0)-oriented pyramids. These results provide thus evidence for the high enantioselective recognition at the glycine

Table III. Surface Accumulation Parameter, $-(\Delta\gamma/\Delta c)_{T,c=0-0.1M}$,[a] Reflecting the Degree of Hydrophobicity of Various Water-Soluble α-amino Acids

α-amino acid	$-(\Delta\gamma/\Delta c)_{c=0-0.1M}$
glycine	−0.9
(*S*)-threonine	0.8
(*S*)-valine	5
(*S*)-phenylalanine	22
(*S*)-norleucine	23
(*S*)-leucine	40
(*S*)-α-amino octanoic acid	240
(*S*)-*tert*-butylglycine	22
(*S*)-neopentylglycine	162
(*RS*)-hexafluorovaline	188

[a] The tendency for surface accumulation, Γ, for a given solution concentration, *c*, can be calculated by using the $(\Delta\gamma/\Delta c)_{T,c=1-0.1M}$ parameter, determined from surface tension measurments of the hydrophobic α-amino acid solutions at various concentrations in the range 0–0.1 M, as shown by the Gibbs equation:

$$\Gamma = -(1/RT)(1/c)(d\gamma/dc)_T$$

where $(d\gamma/dc)_T \cong (\Delta\gamma/\Delta c)_{T,c=0-0.1M}$, γ surface tension (mN/m), c solution concentration (mol/L).

crystal surfaces and the inefficiency of a nucleation mechanism based on interactions between isolated hydrophobic molecules and glycine nuclei.

In the presence of (*S*)-neopentylglycine in concentrations lower than 0.6% wt/wt (of glycine) only a relatively small number of floating glycine crystals were formed. In contrast to *tert*-butylglycine however, neopentylglycine, when used in concentration of 0.7% wt/wt (of glycine) induces the formation of a relatively higher number of (0$\bar{1}$0) pyramids. Addition of other more hydrophilic α-amino acids such as (*R*)-alanine or (*R*)-threonine increases the number of thin (0$\bar{1}$0) oriented plates. We explain this effect in the following way: Glycine nuclei formed underneath surface domains of the hydrophobic α-amino acids interact enantioselectively with the hydrophilic α-amino acid molecules present in solution. This interaction causes inhibition of growth toward the solution, forcing growth in the plane parallel to the interface. The result is an overall inhibition accompanied by the formation of thin, large plate-like crystals. Both reduced growth rate and large surface-to-bulk ratio favor increased nucleation.

Crystallization of α-glycine in the presence of up to 3% wt/wt (*R*,*S*)-hexafluorovaline did not yield any floating crystals but resulted in a general bulk inhibition of the crystallization process. The inhibition was so strong that crystallization occur at the bottom of the beaker after 2 days, whereas about 30 min are required for leucine 1% wt/wt (of glycine) to induce surface crystallization at the same glycine supersaturation. Even stereospecific interactions of isolated molecules of hexafluorovaline with the {010} glycine surface layer are improbable since no {010} platelike crystals can be grown in the bulk of the solution. α-Glycine crystals grown in the bulk of the solution containing 1–2%

wt/wt (*RS*)-hexafluorovaline display destroyed {011} faces consistent with adsorption of the additive molecules at these four surfaces and strong inhibition of growth therefrom. This also proves that hexafluorovaline is not stereospecifically adsorbed at the {010} face and cannot inhibit crystal growth from these faces.

Discussion

We brought here evidence, albeit indirect, that hydrophobic α-amino acids not only accumulate at aqueous solution interfaces but spontaneously assemble in structured aggregates.

Two classes of resolved hydrophobic amino acids have been studied: Those belonging to the first, leucine, valine, phenyl alanine, norleucine, and α-aminooctanoic acid, all form in the crystalline state chiral layers, similar in structure to a corresponding chiral layer in α-glycine. They all induce fast-oriented nucleation of glycine crystals at the air–solution interface, with the appropriate layer face at the surface.

The three members of the second class, *tert*-butylglycine, neopentylglycine, and hexafluorovaline, were selected because their bulky side chains would prevent close packing of their polar head-groups within a layer arranged as in α-glycine. Thus, although the first two members form hydrogen-bonded layers with subcell motifs similar to that of α-glycine, the layers contain strands of water to counteract the steric size of the side chains. These compounds hardly, if at all, induce crystallization of α-glycine at the interface.

A one-to-one correlation thus exists between the packing of these amphiphiles in their own crystals and their capability to induce nucleation of glycine at air–solution interface, when present as cosolutes. These results have implication both to the spontaneous organization of molecules in structured domains and to the mechanism of induced nucleation.

We deduce that self-aggregation of the hydrophobic amino acids at the surface results in ordered domains that, at least in part, mimic the structure of a single layer of molecules in their crystals.[19] Because of their structural similarity to the layers of glycine, the aggregates with appropriate structures can induce epitaxial nucleation of glycine crystals. We cannot detect, and therefore cannot overrule, the possibility of formation of aggregates with different structures. We can exclude the possibility of nucleation being induced by isolated molecules at the water surface.

The presence of few floating glycine crystals of random {010} orientation induced by (*S*)-*tert*-butylglycine is attributed to a match, albeit poor, between the layer structure of glycine and that of ribbons of *tert*-butylglycine, two-molecules wide, separated by strands of water. We may attribute the presence of glycine crystals of both orientations, (010) and (0$\bar{1}$0), to the formation of the initial bilayer with glycine as the underlying molecule, followed by the second layer of glycine molecules related to the top glycine layer by a glide or pseudo-twofold axis respectively.[18]

The relatively better performance of neopentyl glycine as a nucleator of glycine can be correlated to the smaller distortion from planarity of the molecules within the ribbon, which leads to almost perfect epitaxy, albeit for a ribbon two-molecules wide. This last piece of information raises interesting questions about the size of nucleating domains and the extent of the required match between planar domains in order to allow epitaxial growth.

The indirect information on surface domain structures of hydrophobic α-amino acids is linked to the presence of glycine in the subphase and thus to the formation of an heterogeneous bilayer of oriented molecules, with the hydrophobic molecules at the solution surface and glycine bound thereto from below. At this stage, a direct confirmation of the heterogeneous bilayer, by say diffraction techniques, is not possible. Nevertheless, X-ray reflectivity experiments on compressed Langmuir monolayers of α-amino acids with long alkyl side chains (14–20 methylene or fluoromethylene groups) have recently provided direct evidence for the formation of a heterogeneous bilayer with the soluble counterparts in the aqueous phase.[20]

Further evidence in favor of ordered aggregation of the hydrophobic α-amino acids on water is provided by the results on water-insoluble α-amino acids N$^{\epsilon}$-palmitoyllysine[21] (PL) and perfluorododecyl aspartate (PFA).[22] A monolayer of PL on water both in its compressed and uncompressed states induces perfectly oriented crystallization of α-glycine.[18] The crystallinity of a compressed monolayer of PL was demonstrated by grazing incidence X-ray diffraction using synchrotron radiation.[21] The diffraction signal indicated ordered domains of approximately 500 Å in size, corresponding to about 100 lattice spacings and a packing arrangement of the glycine moieties very similar to that of the *ac* layer of α-glycine. However, the uncompressed PL monolayer did not give a diffraction signal at room temperature, indicating no observable crystallinity. On the other hand, the PFA Langmuir monolayer proved to be crystalline in its uncompressed state with a coherence length greater than 1500 Å (i.e. greater than 300 lattice spacings) as presented in the following paper.[23] This monolayer induced both (010) and (0$\bar{1}$0) oriented crystals of glycine.

Moreover, it proved indeed possible to monitor the dynamics of growth of the two-dimensional crystalline domains of PFA on the water surface by grazing incidence X-ray diffraction. This experimental result suggests that it should eventually be possible to monitor, in an analogous manner, the growth of a three-dimensional crystal.

Table IV. Agreement Factors $R(F)$ for the Refined Crystal Structures

compound	$R(F)^a$
(*S*)-*tert*-butylglycine	0.068
(*RS*)-*tert*-butylglycine	0.068
(*S*)-neopentylglycine	0.57
(*RS*)-hexafluorovaline	0.041
(*R*)-phenylalanine	0.147

$^a R(F) = \sum(|F_{obs} - F_{calc}|)/\sum F_{obs}$.

Experimental Section

All the α-amino acids were commercial analytical grade materials and were used without further purifications.

Crystallization Experiments. In a typical experiment, 10 g of glycine were dissolved by heating with the appropriate amounts of additives (see Table II) in 30 mL of double distilled water (33% supersaturation at 25 °C). The hot solutions were filtered through cotton wool in crystallizing dishes (30-mL volume, 60-mm diameter) in three 10-mL batches. Crystallizations were performed at room temperature, 25 ± 1 °C. In the presence of optically pure valine, phenylalanine, norleucine, leucine, and α-aminooctanoic acid, the floating crystals started to appear after about 20 min and after 3 h the whole surface of the solution was covered with well-developed crystals. With neopentylglycine in the high concentration regime, the time of appearance of the floating crystals was 2–8 h. With neopentylglycine in the low concentration regime and with *tert*-butylglycine very few floating crystals were observed and crystals at the bottom of the crystallizing dishes appeared after about 3 h as in the control experiments without any additive. When crystals had reached a mature size (mm) they were collected from the interface, dried, counted, and measured. The average number of floating crystals was at least 100/batch. Their orientation at the solution–air interface was determined by the methods described in a previous paper.[10]

Surface tension measurements were performed on a semiautomatic Fisher surface tensiometer by the du Nouy method with the use of a platinum iridium ring for all the α-amino acids at various concentrations of their aqueous solutions in the range of 0–0.1 mol/L. In this range of dilute solutions the surface tension varies almost linearly with concen-

(19) It is unlikely that molecules of glycine will form mixed layer aggregates with the hydrophobic α-amino acids since that would introduce very weak intermolecular contacts between the alkyl chains across intercalated glycine molecules. This deduction is in keeping with the increased surface accumulation of the hydrophobic α-amino acids from saturated glycine solutions as obtained by surface tension measurements.[10]

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tration. The slope of this line, $-(\Delta\gamma/\Delta c)_{\Gamma c=0-0.1M}$, is considered to be proportional to the surface accumulation, Γ, (described by the Gibbs equation) and thus to reflect the hydrophobicity of the water-soluble α-amino acids.

Crystal Structure Determinations. Crystals of optically pure phenylalanine, *tert*-butylglycine, neopentylglycine, and racemic *tert*-butylglycine and hexafluorovaline were grown by slow evaporation from their aqueous solutions as plates. Cell dimensions and X-ray intensity measurements were performed on a rotating anode Rigaku diffractometer using Cu or Mo Kα radiations. The space groups of all the systems were unequivocally determined (Table I). The crystal structures were solved by use of the SHELX-86 and refined by SHELX-76 programs.[24] The X-ray structure refinements of all the crystals were satisfactory but for phenylanaline. Their agreement factors R(F) varied from 0.04 to 0.069 (Table IV). The bond lengths, bond angles, temperature factors, and intermolecular distances were normal, indicating correct structure determination (available as supplementary material). The structure of optically pure phenylalanine, with two molecules per asymmetric unit, was refined to a R(F) value of 0.147. There is also too short a H···H distance of 1.8 Å between the hydrogen atoms of neighboring phenyl rings related by translation along the b axis (Figure 3c). The carbon atoms of the two independent phenyl rings show unusually large displacement parameters $U_{ii}(i = 1,3)$, as high as 0.25 Å^2, for the C(5), C(6), (C8), and C(9) (or C(52), C(62), C(82) and C(92)) atoms. We interpret these results in terms of orientational disorder of the phenyl rings: The short 1.8 Å contact may be increased to an acceptable value of 2.2 Å by rotating the phenyl rings by 15° about the C(4)-C(7) (or C(42)-C(72)) axis. The rotation may be clockwise or counterclockwise, but the direction of rotation will be the same for a row of molecules related by transition along the b axis. This would lead to abnormally high displacement parameters for the phenyl ring atoms and the "short" 1.8 Å H···H separation, since the structure was refined with only one phenyl ring per molecule. This proposed disorder of the phenyl rings does not cast doubt on the correctness of the overall packing arrangement and on the hydrogen-bonding structure which is our primary interest.

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Supplementary Material Available: Tables of crystal data, atomic coordinates, anisotropic temperature factors, hydrogen atom coordinates and isotropic temperature factors, bond lengths, and bond angles for (*S*)-neopentylglycine, (*S*)-*tert*-butylglycine, (*RS*)-hexafluorovaline, and (*R*)-phenylalanine (47 pages). Ordering information is given on any current masthead page.

Dynamics of Two-Dimensional Self-Aggregation: Pressure and pH-Induced Structural Changes in a Fluorocarbon Amphiphile at Liquid-Air Interfaces. An X-ray Synchrotron Study

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Abstract: In order to provide, on the molecular level, information on crystal nucleation of monolayers at air-water interfaces, the self-aggregation of 1H,1H,2H,2H-perfluorododecyl aspartate $CF_3(CF_2)_9(CH_2)_2OCOCH_2CH(NH_3^+)CO_2^-$ (PFA) over water subphases at various pH values was studied using synchrotron X-ray grazing incidence diffraction (GID), including Bragg rods (BR) and reflectivity (XR) measurements. Two-dimensional crystalline domains with coherence lengths exceeding 1500 Å were detected for low surfactant surface densities and zero surface pressure. GID measurements reveal structural changes with subphase pH and composition. Structural models are proposed at high, neutral, and low pH. For water subphases containing KOH at pH ≥ 11.2, the diffraction is consistent with molecules arranged in a hexagonal net and vertically aligned. Over pure water and acidic subphases containing HCl at pH = 1.5, the molecules pack in a distorted hexagonal net with the fluorocarbon chains tilted from the vertical. The growth in time of the uncompressed crystallites over aqueous glycine solutions was directly monitored by GID. Compression and subsequent decompression of the monolayers over pure water and HCl (pH = 1.5) subphases, for which the fluorocarbon chains are originally tilted, were found to reduce the crystallinity of the system considerably. By contrast, over KOH at pH ≥ 11.2, the hexagonal net with vertically aligned molecules is preserved at all surface pressures and the crystalline order of the system is reduced upon compression but increases again upon release of pressure. Estimates of the degree of crystallinity of the monolayer were made over water for various states of compression and over KOH at pH ≥ 11.2 in the uncompressed state. The packing characteristics and the dynamics involved in the formation and partial destruction of the crystallites can be understood in terms of interaction between the hydrophilic ionic head groups of the monolayer and, if present, the attached molecules or ions (water, K^+ or Cl^-). Additional support for the packing arrangements proposed at high, neutral, and low pH was obtained from studies of the oriented growth of sodium chloride under PFA monolayers.

1. Introduction

Our understanding of the mechanisms of crystal nucleation and growth on a molecular level is still at a rudimentary stage. Direct observation of three-dimensional (3-D) nucleation processes in solution is extremely difficult. Earlier work carried out on the oriented growth of α-glycine[1] crystals at interfaces from aqueous solutions in the presence of dissolved short-chain hydrophobic α-amino acids,[2] indicates that the α-amino acids form structured

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(1) Glycine is known to crystallize in three different forms α, β, and γ-glycine. The α form is the most common one, which we refer to as "glycine" throughout the paper.

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