# Helical Aggregates of Chiral *N*-(2-Hydroxydodecyl) Amino Acids

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L-*N*-(2-Hydroxydodecyl)valine forms fibrous aggregates with a right-handed helicity whilst those of the D-derivative have a left-handed twist; chiral *N*-(2-hydroxydodecyl)tryptophan forms rodlike aggregates with no helicity.

It is well established that aggregates of chiral 12-hydroxyoctadecanoic acid and its soaps with metal ions appear twisted when observed under the electron microscope. The direction of twist depends on both the chirality and the type of metal soap as reported by Tachibana *et al.*[1] Aggregates of the D-form of chiral poly(γ-benzyl glutamate) have a right-handed twist (with a left-handed twist for the α-helix), but those of L-form have a left-handed helicity (with a right-handed twist for the α-helix).[2] The reason for the formation of helical configurations in these molecular aggregates of chiral amphiphilic compounds has not been clarified.

We have published a series of studies on amphoteric surfactants containing hydroxy groups.[3] Some of these compounds which contain a 2-hydroxyalkyl group formed by the addition of epoxyalkane to the starting amino acids, exhibit thermotropic liquid crystalline properties.[4]

In this paper, we first establish that an amphiphilic compound containing a hydroxy group and an asymmetric carbon atom exists in fibrous helical aggregates. These chiral *N*-(2-hydroxydodecyl) amino acids were synthesized as follows:[5] the carboxy group of the amino acid (0.1 mol) was protected by adding an equivalent amount of triethylamine to 300 ml of an aqueous ethanol solution (65 wt% ethanol). Sodium hydroxide was not used as the masking agent as the chiral amino acid would be subject to racemization during the reaction. To the solution of the protected amino acid was added 0.1 mol of 1,2-epoxydodecane and the mixture was stirred at 50 °C for 8 h to avoid racemization. This was followed by evaporation of the triethylamine and ethanol to leave a crude product of *N*-(2-hydroxydodecyl) amino acid in *ca.* 40% yield. The *N*-(2-hydroxydodecyl) amino acid was purified by recrystallization from dioxane, ethanol, acetone, or water. The amino acids used were the L and D forms of valine (Val), leucine (Leu), α-alanine (α-Ala), and tryptophan (Try). Hereon the following abbreviation is used, *e.g.* L-$C_{12}$-Val for the L-form of *N*-(2-hydroxydodecyl)valine.

I.r. spectra of L- and D-$C_{12}$-Val were typical and showed principal bands at 3400 (−OH), 2930 (alkyl), 1620—1540 ($-CO_2^-\cdots NH_2^+-$), 2300—2700 ($-NH_2^+-$), and 1380 $cm^{-1}$ ($-CO_2^-$). The $^1H$ n.m.r. spectrum of $C_{12}$-Val in $D_2O$ solution was also typical with signals at δ 0.7 (terminal $-CH_3$ of alkyl chain), 0.93 [$(CH_3)_2C-$ of Val], 1.78 [$-C(OD)-CH_2-$], 2.46 [$Me_2CH-C(ND_2)$], 2.57 ($-CH-OD$), 2.86 [$ND-CH_2-C(OD)-$], and 3.96 [$-CH(NDR)-CO_2D$]. The elemental analyses for C, H, and N of all the substituted amino acids were within 2.0% of calculated values.

To confirm the chirality of the substituted valines, c.d. spectra were measured for 1 mM solutions of L- or D-$C_{12}$-Val in methanol–water mixtures (80:20, v/v) adjusted to pH 10.5 with NaOH. The c.d. spectrum for L-$C_{12}$-Val contained a positive peak; $[\theta]_{220} = +287 \times 10^4$. Since the L-valine used as the starting material had 99% optical purity and $[\theta]_{220} = +292 \times 10^4$, the L-$C_{12}$-Val has the same optical purity.

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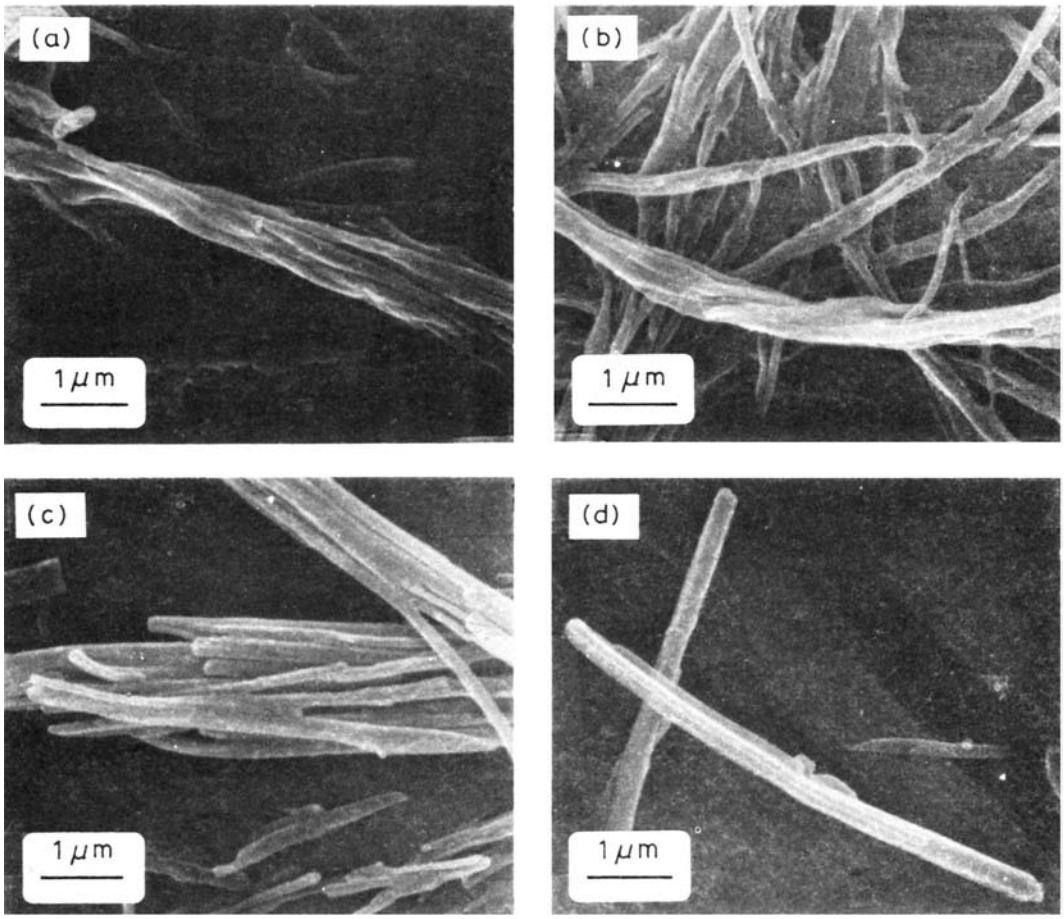
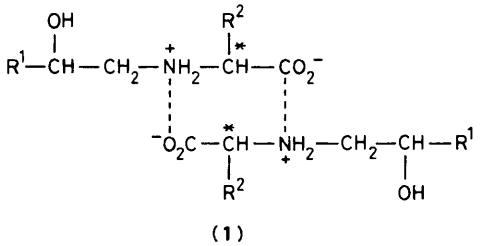



**Figure 1.** The sense of helicity in relation to absolute configuration in the fibrous aggregates of *N*-(2-hydroxydodecyl)valine: (a) L-form, right-handed twist; (b) D-form, left-handed twist, and in the rodlike aggregates of *N*-(2-hydroxydodecyl)tryptophan: (c) L-form, no twist; (d) D-form, no twist.

*viz.* 99%. In contrast, the spectrum for D-$C_{12}$-Val contained a negative peak, with $[\theta]_{220} = -318 \times 10^4$. The D-valine used has an optical purity of 98% and $[\theta]_{220} = -302 \times 10^4$, and hence the D-$C_{12}$-Val was similarly pure. Analogous tests of purity were performed for the other starting and derivatized amino acids.

To prepare specimens of the substituted amino acids suitable for the electron microscope, (JEOL-T 100), a small amount of each compound was suspended in an organic solvent such as diethyl ether or acetone.[6] A droplet of the solution was put on a piece of aluminium foil and solvent was evaporated *in vacuo*. The foil was then attached with a conductive adhesive to the sample stage of the scanning electron microscope. The specimens were shadowed with a Pt–Pd metal mixture. Polaroid photographs were then taken under direct magnification (30 000—20 000).

The photographs of the aggregates of $C_{12}$-Val are shown in Figures 1(a) and 1(b); they indicate that the direction of the twist in the L-form is right-handed, but that for the D-form is left-handed. The diameter of the fibrous aggregation for $C_{12}$-Val is *ca.* 0.1 μm. Similarly, the direction of twist in the aggregates of the L-forms of $C_{12}$-Leu and $C_{12}$-Ala is right-handed while that in their D-forms is left-handed. When the L- and D-form of each of the amino acids derivatives were mixed in equal amounts in an organic solvent, fibrous helical aggregates did not form and were replaced by leaflet-type crystalline aggregates. The chirality of an amphiphilic molecule then, has an influence on the direction of twist in its fibre at the level of the aggregation state. Figures 1(c) and 1(d) are the photographs for L- and D-$C_{12}$-Try, respectively. Both the L- and D-forms do not form twisted fibrous aggregates. The diameter of the fibres for $C_{12}$-Try is 0.1—0.2 μm. L (or D)-*N*-dodecyl valine with no hydroxy groups does not form fibrous aggregates but instead the leaflet-type crystalline aggregates.



(1)

It can be assumed that the direction of helical twist is affected by the –NH-, $-CO_2H$, and –OH groups in their ability readily to form intermolecular hydrogen bonds. Urea was added to $C_{12}$-Leu suspended in acetone to inhibit hydrogen bond formation but the direction of twists in the L- and D-forms remained unchanged. However, each entangled fibre was separated.

The i.r. assignments mentioned above for the substituted valines suggest the formation of the dimer unit (**1**). The ionic

attraction of the $-CO_2^-$ and $-NH_2^+-$ moieties occurs between bimolecules in the aggregates. Furthermore, intermolecular hydrogen bond formation is suggested by the i.r. absorption at 3400 $cm^{-1}$, which is attributed to vibrations in the hydroxy group in the alkyl chain. The dimer units then bind to each other through intermolecular hydrogen bonds to form the aggregated states. Since these molecules are arranged in fixed orientations, the aggregates can be thought of as twisted fibres.

As $C_{12}$-Try has a bulky group in the α-position, the formation of an intermolecular hydrogen bond is less probable due to steric hindrance. Thus, rodlike aggregates with no twist were formed.

In conclusion, for the helical aggregates to be formed at the molecular level in the substituted amino acids it is essential that they contain both an asymmetric carbon atom and hydroxy group in the attached alkyl chain.

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