Exceptional adhesive and gelling properties of fibrous nanoscopic tapes of self-assembled bipolar urethane amides of L-phenylalanine

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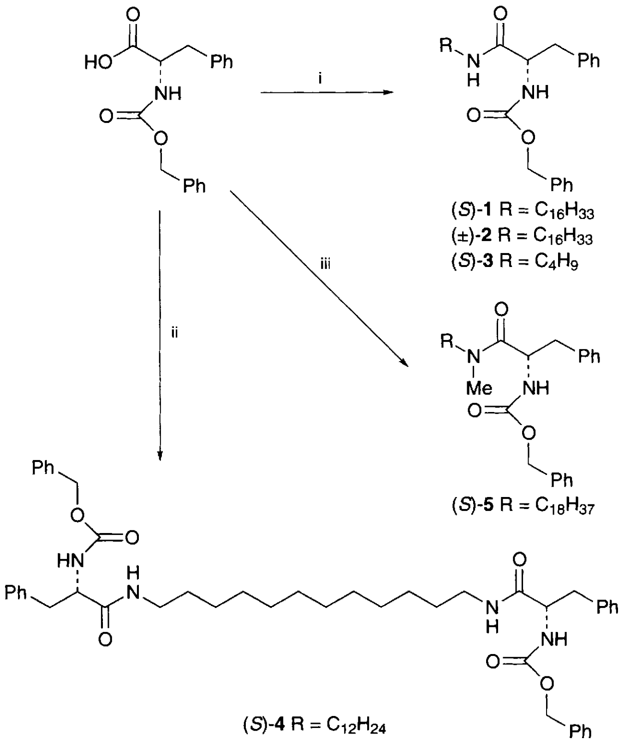
Seven L-phenylalanine based alkyl (monopolar) and alkanediyl (bipolar) derivatives are synthesized; while the bipolar urethane amides form gels and show strong adhesive properties, the monopolar analogues form fibrous nanoscopic cloth-like tapes.

Some organic molecules when dissolved in specific solvents produce widespread microstructures determined by the molecule, the solvent, the concentration and the temperature.[1] These systems are interesting as at each level of morphological complexity, new properties emerge.[2] However, it is often difficult to extrapolate the properties of the resulting systems on the basis of the individual molecular structures.[3] The lack of obvious correlation in these structure–property relationship makes the goal of predictable design of systems with high-value properties quite difficult.[3] Towards this end, supramolecularly organized matrices such as tapes, tubules or fibres of a submicron or nanoscopic scale are attracting a lot of attention[4] in various applications, *e.g.* in coating hard-discs or layering the inner walls of an artificial blood vessel. Similar uses for composite materials could also be imagined. The materials that produce gels upon solubilization in organic solvents have potential in other applications as hardeners of spilled toxic solvents or in environmental clean-up.

Although numerous systems that aggregate and form gels have been designed,[5] examples are rare in which vastly different material properties could be produced by small variation of the molecular structures or conditions. Owing to our continuing interest in supramolecular assemblies[6] we sought to design systems that would produce different macroscopic properties by subtle variation of their molecular architectures or by variation of organic solvents. Here we report novel types of mono- and bis-(amino acid)-based urethane amide derivatives some of which not only formed sub-micron fibres but also possessed strong gelling and unusual adhesive properties.

Compounds **1–5** were designed to contain selected structural subunits and synthesized‡ as described in Scheme 1. As a first step toward the exploitation of such systems for diverse material applications, we first examined their aggregation behaviour in various non-aqueous solvents. Notably, a solution of hexadecylamide of *N*-benzyloxycarbonyl-L-phenyl alanine (BCPA) **1** in hexane–EtOAc (3:2) formed *ca.* 10 cm long cloth-like sheets (width *ca.* 1 cm) upon standing at ambient temperature. Optical microscopy of this revealed the existence of hair-like fibrous microstructures [Fig. 1(*a*)]. Scanning electron microscopy (SEM) (Cambridge stereoscan S-360 SEM) of these aggregates further showed the presence of highly intertwined, rod-like fibres arranged in a network [Fig. 1(*b*)]. These fibrous assemblies were found to be considerably resistant to mechanical stress. In solvents such as in MeOH or DMF no such aggregate could, however, be detected even upon long standing. It was also realized that only optically pure BCPA derivatives had the ability to produce such cloth-like substances. Thus when the corresponding racemic BCPA derivative **2** was used under comparable conditions, only microcrystalline flakes were seen. To decipher the role of the long chains in such self-assembly motifs, we then examined the aggregation behaviour of a related chiral molecule with a butyl chain **3**. Compound **3** produced densely entangled network of fibrous tapes [Fig. 1(*c*)]. However, the tapes from **3** were quite 'fragile' compared to the ones formed from **1**. This suggests that it is the length of the alkyl chain which determines the mechanical strength in such aggregates. Next we examined the properties of the corresponding bipolar analogue **4**, which contained BCPA units at both



Scheme 1 *Reagents and conditions*: i, RNH_2, DCC, DMAP, dry $CHCl_3$, stir 12 h, room temp.; 82% for **1** and **2**, 85% for **3**; ii, H_2NRNH_2, DCC, DMAP, dry $CHCl_3$, stir 20 h, room temp., 74%; iii, $C_{18}H_{37}NHMe$, DCC, DMAP, dry $CHCl_3$, stir 24 h, room temp., 68%

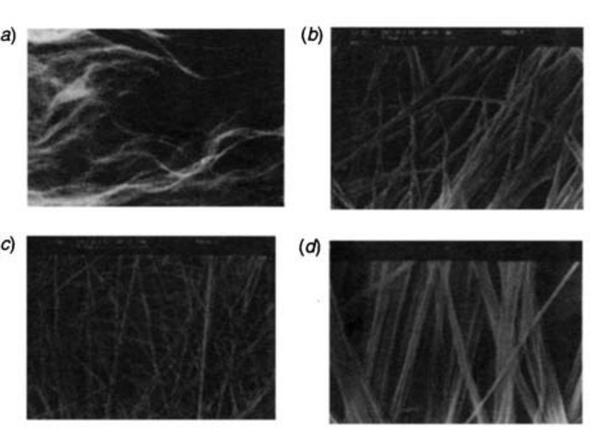


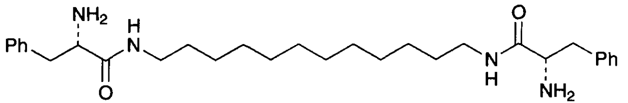
Fig. 1 (*a*) Optical micrographs of **1** from EtOAc–hexane; SEM images of (*b*) **1**, (*c*) **3** and (*d*) **4** in the same solvent mixture

ends of a $C_{12}H_{24}$ chain through amide linkages. From a solution of **4** in hexane–EtOAc, bundles of braided tapes were gradually formed as revealed under SEM [Fig. 1(*d*)]. The fibres from **4** were however found to be thinner and brittle. Fibre formation from **4** was also slower than that of their monopolar counterparts under comparable conditions. To verify the role of primary amides (HNC=O) in such molecular assemblies, we examined the aggregation of **5** (which had a secondary amide linker, *i.e.* MeNC=O between the $C_{18}H_{37}$ chain and the BCPA unit) in the same solvent mixture. Remarkably, **5** gave only platelets devoid of any microstructure. Thus it appears that the presence of the NH of the amide connectors between the hydrocarbon chain and the BCPA unit is crucial for the formation of such nanoscopic aggregates. Assembly of such molecules is presumably driven by a combination of hydrogen bonding between the NH and the C=O groups of both the urethane and the amide bonds and van der Waals interactions through hydrophobic segments (see below). To probe the role of urethane units in such aggregates, we also synthesized enantiomerically pure **6** and **7** from **4** and **1**, respectively. Both **6** and **7** gave solids devoid of microstructural features irrespective of the solvents as seen under SEM.

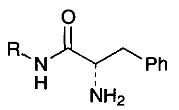
When we dissolved any of **1**–**7** in MeOH, no microstructures were seen. But a solution of **4** in $CHCl_3$ spontaneously transformed into a high viscous gel. In a typical gelation experiment, an excess of $CHCl_3$ was added to a weighed amount of **4** in a test tube and the resulting solution was kept at ambient temperature. A transparent, viscoelastic gel was formed when the tube was allowed to remain undisturbed for sometime. The excess solvent could be decanted away from the gel by mere inversion of the tube. A 100 mg sample of **4** (MW 763) gelated 2.21 g of $CHCl_3$. In other words, one molecule of **4** could bind *ca.* 140 molecules of $CHCl_3$. The gels could be kept for several months in a stoppered tube. Only under high vacuum with concomitant warming was a dry fibrous solid regenerated. When a thin layer of the gel was coated on a glass plate and is brought into contact with another pre-cleaned plate they stuck together in such a manner that the adhered plates could not be separated without physically breaking them. Such adhesive properties were however not seen with the corresponding monopolar systems.

The thermal stabilities of the solid aggregates produced from different solvents were also examined by differential scanning calorimetry (DSC 2 Perkin Elmer). Solids of **1** generated from a solution in MeOH melted at *ca.* 98 °C, while the fibres of **1** (from EtOAc–hexane) gave an endothermic, quasi-reversible transition at *ca.* 123 °C. Similarly, while the solid **3** formed from MeOH melted at *ca.* 92 °C, the fibres shown in Fig. 1(*c*) melted at *ca.* 146 °C. Similar differences were also noticed with **4**. Such variations in the thermal stabilities of the solids produced from the same molecule from different solvents suggest that their organization in the solid state must be different.§

FTIR studies of the fibres of **1** in KBr and in $CHCl_3$ gel confirm that the presence of both amide and urethane units are essential for the formation of such supramolecular arrays through intermolecular hydrogen bonding. Bands at 3300 (NH), 1720 (C=O), 1659 (amide-I) and 1511 (amide-II) cm^{-1} indicate manifestation of intermolecular hydrogen bonding in assemblies of **1**. Similar bands were also seen in samples that formed gels.



(*S*)-**6** R = $C_{12}H_{24}$



(*S*)-**7** R = $C_{16}H_{33}$

To create a plan that might help explain the aggregation behaviour of the compounds studied here, we minimized the conformation of representative urethane amides using the INSIGHT and DISCOVER programmes provided by BIOSYM. The energy minima were chosen by computing the energy of each assembly obtained from a dynamic simulation. Hydrogen bonding (N–H···O=C) and interaromatic stacks between L-Phe units as well as benzylcarbonyl units reinforce such assemblies. The presence of chirality makes the sheet curl as indicated in the CPK model in such supramolecular arrays (figure not shown). In contrast, assemblies of racemic **2** gave planar states devoid of any stacking interactions.

To our knowledge, this case represents the first example of a chiral, non-polymeric system which when present in a monopolar form gave fibrous tapes but when the corresponding bipolar analogue was used, adhesion and gelling properties were observed. Thus by making small changes in these molecules, we have been able to identify the importance of various parts of the molecule for the macroscopic properties of the systems.

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Footnotes

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‡ Compounds **1**–**7** were fully characterized by spectroscopy (IR, NMR) and elemental analysis.

§ This was indeed confirmed from the differences in their wide angle X-ray diffraction patterns (STOE/STADI-P powder X-ray diffractometer) of the solid **1** produced from MeOH or $CHCl_3$ or from the hexane–EtOAc mixture.

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