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# Birefringent physical gels of *N*-(4-*n*-alkyloxybenzoyl)-L-alanine amphiphiles in organic solvents: The role of hydrogen-bonding

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ABSTRACT

A new class of amphiphiles, *N*-(4-*n*-alkyloxybenzoyl)-L-alanine was designed and synthesized. These amphiphiles have been shown to form thermoreversible gels in organic solvents such as aromatic hydrocarbons, cyclohexane, and chlorinated hydrocarbons at room temperature. The effects of amide functionality, chain length of the hydrocarbon tail, and the chirality of the head group of the amphiphiles on the ability to promote gelation in organic solvents have been studied. The *n*-tetradecyl derivative showed the best gelation ability, whereas the amphiphile with DL-alanine as the head group formed weak organogels. The 4-dodecyloxybenzoic-1-carboxyethyl ester derivative in which the amide group is replaced by an ester group also formed weak organogels at a slightly lower temperature (293 K). The gelation number and the gel melting temperature of the gelators in different solvents were determined. The rheological measurements suggested that the organogels of *n*-tetradecyl derivatives are stronger than those of amphiphiles containing *n*-dodecyl chains. Also the organogels of the amphiphiles, except the one with an ester group, were found to have gel-to-sol transition temperatures, $T_{gs}$, higher than room temperature (~303 K), which increased with the increase of chain length and total concentration of the gelator. SEM pictures of the gels show fibrous structures. Small-angle XRD and optical microscopy were also employed to characterize the gels. The organogels of alanine derivatives, except that of 4-dodecyloxybenzoic-1-carboxyethyl ester, showed optical birefringence. The mechanism of gelation was studied using $^1$H NMR and FTIR spectroscopy. Hydrogen-bonding between $-CO_2H$ groups as well as π–π interactions were found to be important for the gelation process.

## 1. Introduction

Low-molecular-weight organogelators (LMOGs) that are used to harden organic liquids are of growing interest in the area of academic research in chemistry because of their potential for creating new soft materials, which may find applications in the environment, industry, and medicine [1–9]. Organogels are of great significance particularly for their potential uses as templates for material synthesis, drug delivery, cosmetics, separations, sensors, and biomimetics [10]. The gelator molecules organize themselves into supramolecular aggregates within the organic solvent, resulting in a three-dimensional structure, which causes the gelation. The three-dimensional (3-D) networks responsible for gelation are built by the noncovalent interactions among gelator molecules, such as hydrogen-bonding (H-bonding), hydrophobic interactions, van der Waals forces, π–π interactions, electrostatic interactions, and metal ion coordination [11–13]. It is also widely accepted that the ability to form gels is often associated with the presence of stereogenic centers in the molecular structures of LMOGs [14]. Indeed chirality plays critical roles in assembling processes taking place on surfaces and interfaces, in the liquid crystal phase, and in the formation of supramolecular polymers and gels [4,15]. In other words, the impact of chirality on assembled systems can be profound.

During the past 20 years a great deal of effort has been made to develop new types of LMOGs to understand the links between the properties and the structures of LMOGs and their organogels [16]. The LMOGs can be divided into two major groups—hydrogen bond-based gelators and non-hydrogen bond-based gelators. In amide compounds, such as amino acids [17–21] and urea [22–24], hydroxyl compounds, such as sugars [25–28], H-bonding is responsible for gelation. On the other hand, anthracene, cholesterol, and tropone derivatives [29–33] are non-hydrogen bond-based gelators. Amino acid–based gelators are mostly found to be biocompatible and biodegradable in nature. Recently, organogels of L-alanine derivatives have been shown to have potential applications in drug delivery [34,35]. It has been reported that *N*-acyl-L-alanine amphiphiles can gelate a number of hydrocarbon solvents, fuels [9,36,37], and sunflower oil [34]. Bhattacharya and co-workers [36] reported that the presence of both $-CO_2H$ and secondary amide (–NH–(=O)) groups is essential for the self-association of the amino acid-derived amphiphiles to form fibers, a necessary prerequisite for the

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building of 3-D networks of organogels. On the other hand, the work of Motulsky et al. demonstrated the gelation of sunflower oil by methyl esters of *N*-acyl-L-alanine amphiphiles [34]. This means that only the amide H-bonding is important for gelation.

In order to further understand the nature of driving forces that self-assemble the amphiphiles to form fibers thus leading to gelation of organic solvents, we have designed and synthesized five new *N*-(4-*n*-alkyloxybenzoyl)-alanine amphiphiles, **1**–**5** (see Chart 1 for structures), and studied their gelling behaviors in different organic solvents. To examine the importance of the secondary amide group, we have also synthesized a structurally similar amphiphile, **6**, in which the amide group is replaced by an ester group. These amphiphiles contain a phenyl group in their alkyl chain, which can have either positive or negative effects on gelation. The present investigation was therefore undertaken to examine the role of a stereogenic center, and H-bonding and π–π interactions on the gelation ability of this class of amphiphilic molecules. We have employed a number of techniques, such as electron microscopy, polarizing optical microscopy, rheology, and XRD to characterize the organogels. $^1$H NMR and FTIR spectroscopic techniques were used to study the nature of driving forces of gelation.

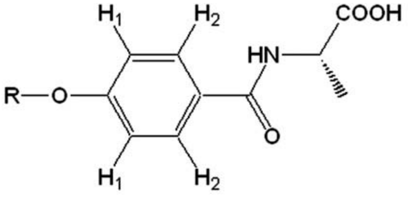
## 2. Materials and methods

### 2.1. Materials

Anhydrous potassium carbonate, sodium bicarbonate, 4-hydroxybenzoic acid, 1-bromododecane, 1-bromodecane, 1-bromooctane, *N*-hydroxysuccinimide (NHS), 1,3-dicyclohexylcarbodiimide (DCC), L-alanine, DL-alanine, and L-lactic acid were purchased from SRL, Mumbai, India, and were used without further purification. Tetrabutylammonium fluoride hydrate (TBAF), 1-bromohexadecane, and 1-bromotetradecane were obtained from Aldrich. All the organic solvents were of highest purity available and were dried and distilled fresh before use. The amphiphiles employed in this study were synthesized in the laboratory as described below.

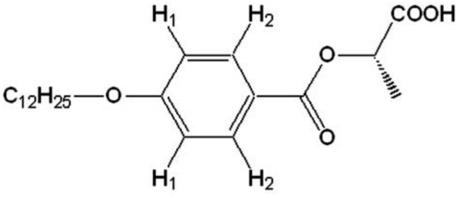
### 2.2. Synthesis

The syntheses of *N*-[4-*n*-alkyloxybenzoyl]-L-alanine, -DL-alanine, and -L-lactic acid ester were carried out according to the procedure described elsewhere [38,39]. Briefly, 4-*n*-alkyloxybenzoic acid was first synthesized from 4-hydroxybenzoic acid and 1-bromoalkane and purified according to the reported procedure [40]. The coupling of L-alanine, DL-alanine, or L-lactic acid ester and 4-*n*-alkyloxybenzoic acid was made via the formation of NHS ester in the presence of DCC. Finally, the compound was purified by column chromatography using silica gel (60–120 mesh) as the column packing material. Chloroform was used to elute the impurities and ethyl acetate was used at the end to elute pure compound. Chemical identification of all the compounds was performed by use of $^1$H NMR, elemental analysis, and FTIR spectroscopy (see ESI).



**N-(4-n-alkyloxybenzoyl)-L-alanine**

**R = $C_8H_{17}$ [1], $C_{10}H_{21}$ [2], $C_{12}H_{25}$ [3a, 3b], $C_{14}H_{29}$ [4], $C_{16}H_{33}$ [5]; L-alanine derivative, 1-5, DL-alanine derivative, 3b**



**4-Dodecyloxy-benzoic acid 1-carboxy-ethyl ester [6]**

**Chart 1.** Chemical structures of amphiphiles **1–6**.

### 2.3. Methods and instrumentation

FTIR spectra were measured with a Perkin–Elmer (Model Spectrum Rx I) spectrometer. $^1$H NMR spectra were recorded on a Bruker 400 MHz instrument in $CDCl_3$ solvent with TMS as a standard. Melting point measurements were done using Instind (Kolkata) melting point apparatus with open capillaries. The measurements of optical rotations were performed with a JASCO (Model P-1020) digital polarimeter. The circular dichroism (CD) spectra were measured with a JASCO J-810 spectropolarimeter using a quartz cell with a path length of 1 mm. All measurements were done at room temperature (~303 K) unless otherwise noted.

The hot sample solution was placed on the aluminum or copper foil to make thin film and was left to cool and air dry at room temperature. The specimen after further overnight drying in desiccators was coated with gold particles to make a conducting surface and finally transferred into the field emission scanning electron microscope (FE-SEM, Zeiss, Supra-40) operating at 5–10 kV to obtain the micrographs. The polarizing optical light micrographs for the samples were obtained from a Leica-DM4500 optical microscope by transmitted light under crossed Nicol. The samples for optical microscopy contained gelators at a concentration less than the corresponding critical gelation concentration. A drop of the liquid was placed on the microscope slide and covered with a coverslip.

Wide-angle XRD (WAXRD) at a lower angular range was taken for all the air-dried gel samples (cast film on a glass slide) at room temperature. The experiment was performed on a Pan Analytica XPert Pro X-ray diffractometer using Cu target (Cu Kα) and Ni filter at a scanning rate of 0.001 $s^{-1}$ between 2° and 10°, operating at a voltage of 40 kV, current 30 mA.

For all gels, rheological measurements in oscillatory mode were carried out on a Bohlin CVO D 100 controlled-stress rheometer using 20 mm diameter parallel plate geometry with a constant tool gap of 300 μm. The rheometer is fitted with a solvent trap and a peltier device that controls temperature within ±0.1 K. An equilibration time of 30 min was allowed before measurements were taken for each sample. All measurements were taken on matured gels after 10 h of cooling. Oscillatory stress sweeps from 0.1 to 1000 Pa (or 0.1 to 100 Pa) were measured at a constant frequency of 1 Hz to obtain storage modulus (G′) and loss modulus (G″). Prior to this a preliminary frequency sweep from 0.1 to 100 Hz was performed to determine the linear viscoelastic (LVE) regime. The shear strain ($\gamma$), phase angle ($\delta$), dynamic viscosity ($\eta^*$), G′, and G″ were recorded as a function of time at a constant stress of 0.5 Pa that resulted in small strains (<0.2%).

## 3. Results and discussion

### 3.1. Gelation behavior of amphiphiles

The gelation of the amphiphiles **1**–**6** was tested in a variety of organic solvents including aliphatic hydrocarbons of varying chain length, chlorinated hydrocarbons, and aromatic hydrocarbons. All