A new organogelator based on an enantiopure C_2 symmetric pyrrolidine†

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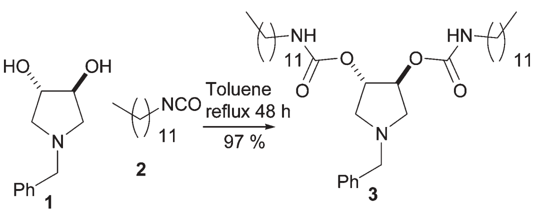
The synthesis and the properties of a new chiral organogelator based on a C_2 symmetric pyrrolidine, are described together with its use for the synthesis of other functionalised organogelators.

The increasing interest attracted by organogels[1] is due to a combination of their potential useful application[2] and the challenge posed by the full rationalization of the mechanisms responsible for this supramolecular assembly.[1] Although most organogelators have been discovered serendipitously, the increasing number of known gelators allowed some successful efforts to design efficient organogelators.[2a,3] Some of these compounds are characterized by long aliphatic chains bearing functional groups acting as hydrogen-bond donors and acceptors, such as amides,[4] carbamates[5] and ureas.[6] In such compounds the van der Waals forces and the hydrogen-bond interactions cooperate to build up fibers.[7]

Here, we describe the synthesis of a new C_2 symmetric enantiopure organogelator, **3**, the properties of its gels and the possibility to obtain derivatives with different substituents with the aim to obtain new gels with added properties. Compound **3** can be easily obtained by reaction of (3*S*,4*S*)-*N*-benzyl-3,4-dihydroxypyrrolidine (**1**) with dodecylisocyanate (**2**) (Scheme 1).

Both compounds **1** and **2** are commercially available, although compound **1** can be conveniently obtained from tartaric acid.[8] Compound **3** forms gels in several solvents (isopropanol (critical conc. (w/v) = 2.0%), hexane (1.0%), cyclohexane (0.2%), acetonitrile (0.3%)) while solutions are obtained in toluene and dichloromethane. The gels obtained in isopropanol and in hexane do not appear very stable and are opaque, while the gels in cyclohexane and acetonitrile, especially at low concentration, are almost transparent and stable for weeks. Since the most stable gel was obtained in cyclohexane, this solvent was chosen for a more detailed study of its properties.



Scheme 1

A DSC study demonstrated an exponential dependence of the gel–sol transition temperature on the concentration, while the enthalpy of the same transition showed a linear dependence as evidenced in Fig. 1 as commonly encountered for LMOG (low molecular weight organogelators).[9] An FT-IR study suggested that the organogel is based on the formation of a hydrogen-bonded network. A comparison of the IR spectrum of a CH_2Cl_2 solution of **3** with that of the cyclohexane gel of **3** revealed for the latter a shift of 130 cm^{-1} towards lower wavenumbers of the NH stretching band (3445 (CH_2Cl_2) *vs.* 3315 cm^{-1} (cyclohexane)). The same effect, although limited to 40 cm^{-1} was evidenced for the C=O stretching band. More meaningful is the variation of the IR spectrum of a cyclohexane gel of **3** induced by a temperature increase (Fig. 2). While at 25 °C only the band at 1690 cm^{-1} (νC=O involved in H bond) was visible, with an temperature increase the band at 1735 (free νC=O) grew in intensity becoming the main signal 68 °C. In this case the behaviour of νN–H was less diagnostic since the band at 3445 cm^{-1} simply became broader and broader with increasing temperature and almost disappeared at 68 °C.

An attempt to study the organogel by NMR techniques revealed unfruitful since the gel was completely NMR silent at room temperature.[1f] The organogel was also characterized by TEM. Fig. 3 shows a representative image of the 10 mg ml^{-1}

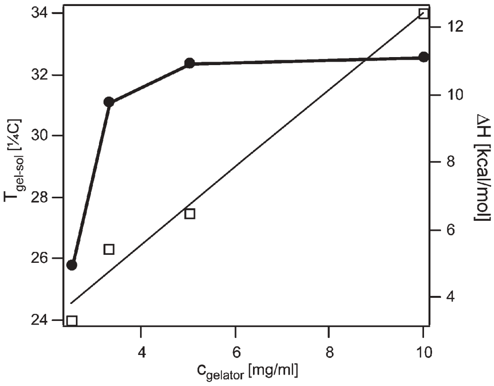


Fig. 1 Gel phase boundary (left) and transition enthalpies (right) as a function of the gelator concentration in cyclohexane.

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† Electronic supplementary information (ESI) available: Experimental procedure and full characterization of compounds **3–7**, experimental procedure for DSC, SAXS and cryo-TEM measurements. See DOI: 10.1039/b614311c

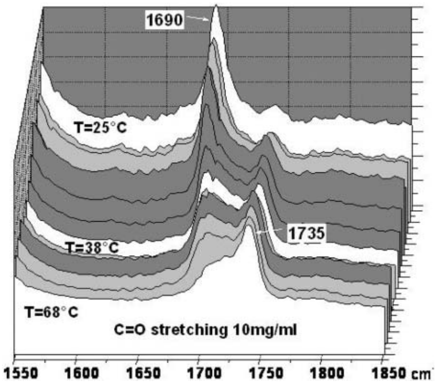


Fig. 2 FT-IR spectra of the C=O stretching region at different temperatures.

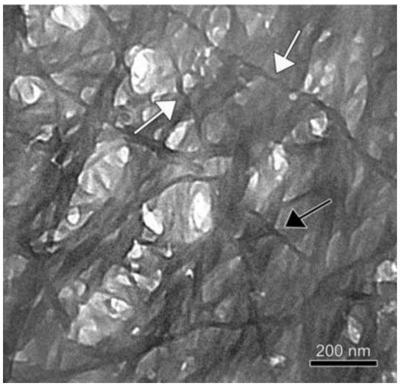


Fig. 3 Cryo-TEM image of the 10 mg ml^{-1} sample in cyclohexane. The black arrow indicates thin threads that form twisted objects, the white arrows indicate the presence of twisted structures formed by intertwining of thinner threads.

sample, showing the morphologic characteristics of this gel. Small angle X-ray scattering has also been performed as a function of concentration and temperature. Fig. 4 shows the temperature dependence for the 5 mg ml^{-1} sample. Below the gel phase boundary a definite scattering pattern with a q^{-1} scaling scattering law highlights the presence of locally cylindrical aggregates, whose cross sectional radius can be estimated, according to a Guinier asymptotic behavior,[10] to be around 27 Å. As the temperature is raised above the sol transition the scattering curves reduces to a flat background confirming the dissolution of the mesoscopic self-assemblies.

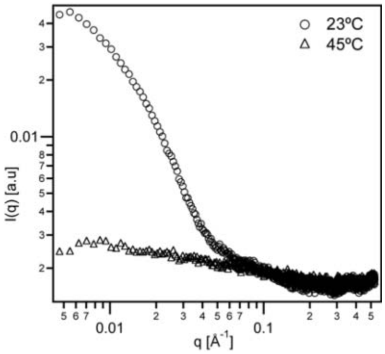


Fig. 4 SAXS curves of the gel obtained for the 5 mg ml^{-1} sample as a function of temperature.

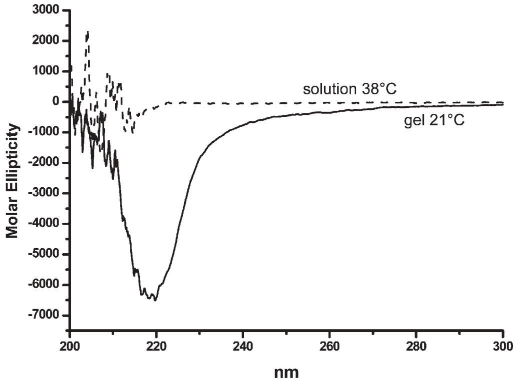


Fig. 5 CD spectra registered below and above the sol–gel transition temperatures (10 mg ml^{-1}).

It is known that the formation of supramolecular aggregates of chiral molecules often induces strong circular dichroism effects.[1g] For compound **3**, the CD spectrum registered at 38 °C (above the gel–sol transition temperature) was almost silent. Cooling the solution to room temperature induced the formation of the gel and a strong CD effect appeared (Fig. 5), suggesting the formation of an ordered supramolecular aggregate.

In several aspects compound **3** appears similar to known organogelators such as derivatives of *trans*-cyclohexane-1,2-diamine which are also enantiopure C_2 symmetric molecules, whose behaviour as gelators has been rationalised using largely accepted models.[11] However, the models proposed for organogels obtained with amide and urea derivatives of *trans*-cyclohexane-1,2-diamine[11] or benzene-1,2-diamine[12] cannot be directly applied to **3**, a dicarbamate derivative. Since the X-ray diffraction analysis of crystals of cyclohexanediamine derivatives have found application for the development of a model of the corresponding organogel,[3c,4e,6a] we decided to follow a similar approach for compound **3**. Since the crystals obtained revealed unsuitable for a crystallographic analysis, we synthesised other derivatives. Compound **3b**, bearing two octyl chains, obtained from **1** and octyl isocyanate gave crystals suitable for an X-ray analysis and the structure, showing the conformation of the carbamate groups and the relative configuration of the two stereocenters, is shown in Fig. 6.[13] The pyrrolidine nuclei are arranged to form long sequences held together by hydrogen-bonding interactions as highlighted in Fig. 6. The two carbamate functional groups showed antiparallel carbonyl groups so that they act as hydrogen-bond acceptor groups with different molecules. This antiparallel conformation of the two carbamate group is an energy minimum

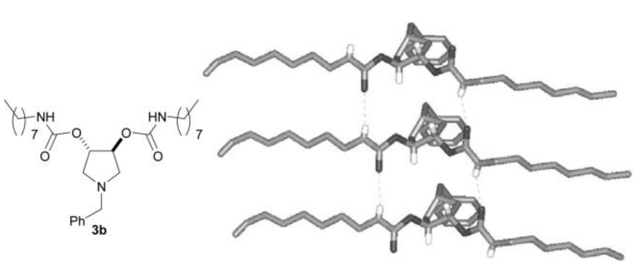
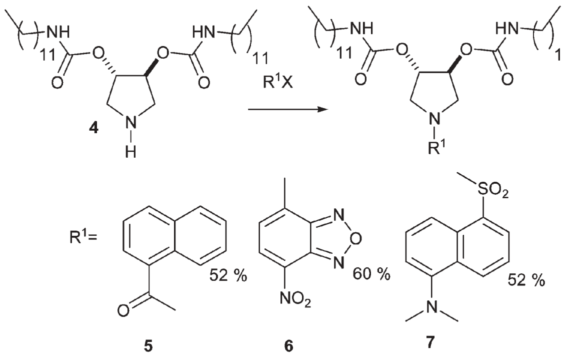


Fig. 6 X-Ray crystal structure of **3b**.



Scheme 2

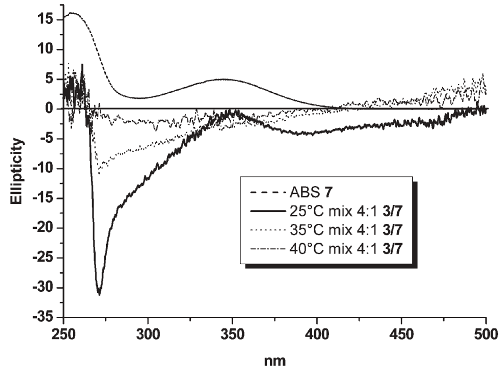


Fig. 7 UV spectrum of compound **7** (top) and CD spectra of a 4 : 1 mixture of compounds **3** and **7** at different temperatures.

for compound **3**, as shown by simple molecular mechanics analysis, while the corresponding dimer was more stable than the monomers by 20 kcal mol^{-1}.[14]

A second notable characteristic of compound **3** is the presence of a tertiary *N*-benzylamine that can be easily deprotected by hydrogenolysis to afford pyrrolidine **4**. The secondary nitrogen atom of **4** is a good point for anchoring new substituents and obtaining new core-functionalised organogelators. The feasibility of this application was demonstrated by the synthesis of the three new derivatives **5**–**7** (Scheme 2).

Compounds **5**–**7** are characterized by the presence of fluorescent groups so demonstrating the ability to confer new properties to the original gel formed by **3**.

Compounds **5** and **6** preserved the ability to form organogels in cyclohexane (2 and 0.2% for **5** and **6**, respectively) and showed enhanced CD effects when in the gel phase. Compound **7** was not able to produce gels in any of the tested solvents even at higher concentration. However, a mixture of compounds **3** and **7** in a 4 : 1 ratio were able to gelate cyclohexane (overall 10 mg mL^{-1}). The incorporation of compound **7** into the gel produced by **3** was demonstrated by a CD spectrum showing a large CD effect in the absorption region of the dansyl group (Fig. 7).

This result appears promising concerning the use of compound **4** as a gelating scaffold which can be decorated with different molecular fragments. Our effort is aimed to exploit this ability producing new organogels with different properties.

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13 $C_{29}H_{49}N_3O_4$; $M_r = 503.72$, monoclinic, space group $P2_1$, $a = 5.020(1)$, $b = 16.571(1)$, $c = 18.400(1)$ Å, $\beta = 93.370(2)°$, $V = 1528.0(3)$ Å^3, $Z = 2$, $T = 293(2)$ K; $F(000) = 552$, $\mu = 0.573$ mm^{-1}; no. reflections measured = 5945; no. independent reflections = 3680; $R_{\text{int}} = 0.0221$. Final R value = 0.0568; R(all data) = 0.0975. CCDC 627714. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b614311c.

14 Spartan '04 suite, Monte Carlo conformational search (molecular mechanics, MMFF94).