CHEMISTRY
A EUROPEAN JOURNAL

FULL PAPER

DOI: 10.1002/chem.201200707

Self-Assembly Studies of a Chiral Bisurea-Based Superhydrogelator

Francisco Rodríguez-Llansola,[a] Daniel Hermida-Merino,[d] Belén Nieto-Ortega,[c] Francisco J. Ramírez,[c] Juan T. López Navarrete,[c] Juan Casado,[c] Ian W. Hamley,[b] Beatriu Escuder,*[a] Wayne Hayes,*[b] and Juan F. Miravet*[a]

In memory of Purificación Escribano

Abstract: A chiral bisurea-based superhydrogelator that is capable of forming supramolecular hydrogels at concentrations as low as 0.2 mm is reported. This soft material has been characterized by thermal studies, rheology, X-ray diffraction analysis, transmission electron microscopy (TEM), and by various spectroscopic techniques (electronic and vibrational circular dichroism and by FTIR and Raman spectroscopy). The expression of chirality on the molecular and supramolecular levels has been studied and a clear amplification of its chirality into the achiral analogue has been observed. Furthermore, thermal analysis showed that the hydrogelation of compound **1** has a high response to temperature, which corresponds to an enthalpy-driven self-assembly process. These particular thermal characteristics make these materials easy to handle for soft-application technologies.

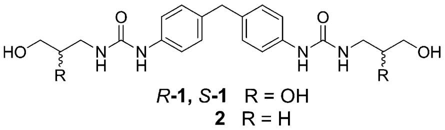
Keywords: chirality · hydrogels · self-assembly · soft materials · supramolecular chemistry

Introduction

The study of soft materials that are formed by low-molecular-weight compounds has attracted great attention over the last years.[1] Functional materials can be constructed from simple building blocks that spontaneously self-assemble, thereby translating their inherent molecular properties onto the supramolecular level. Of particular interest are compounds, which are not necessarily peptidic in nature,[2] that are able to form molecular hydrogels with properties that are suited to applications such as regenerative medicine or organocatalysis.[3]

Within this context, the expression of molecular chirality through aggregation processes that lead to the formation of hydrogel networks is of great interest. Examples have been reported in which molecular chirality is translated onto the mesoscopic level through the formation of helicoidal fibers.[4] Moreover, chirality may also be expressed into a stereoselective transformation or recognition process that takes place within the hydrogel fibers.[5]

Herein, based upon previous studies within our group,[6] we report an interesting example of a simple chiral bisurea compound (**1**) that is able to form hydrogels at very low concentrations (Scheme 1). The urea functionality has been used widely in low-molecular-weight organogelators because it provides a convenient 1D directionality and strong intermolecular hydrogen-bonding interactions.[7] However, aggregation in water is predominantly governed by hydrophobic interactions. In this sense, it is well known that molecules that contain a defined hydrophobic core and peripheral polar groups allow for their self-assembly into stable columnar aggregates.[8] Furthermore, the effects of the chirality of the peripheral hydroxy groups on the hydrogelation characteristics of compound **1**, as well as of achiral bisurea **2**, have



Scheme 1. Structures of bisurea-based compounds.

---

[a] Dr. F. Rodríguez-Llansola, Dr. B. Escuder, Dr. J. F. Miravet
Departament de Química Inorgànica i Orgànica
Universitat Jaume I
12071, Castelló (Spain)
Fax: (+34) 964728214
E-mail: escuder@uji.es
miravet@uji.es

[b] Prof. I. W. Hamley, Dr. W. Hayes
Department of Chemistry
University of Reading
Whiteknights, Reading, RG6 6AD (UK)
E-mail: w.c.hayes@reading.ac.uk

[c] B. Nieto-Ortega, Dr. F. J. Ramírez, Prof. J. T. L. Navarrete,
Prof. J. Casado
Department of Physical Chemistry
University of Málaga
Campus de Teatinos s/n, 29071 Málaga (Spain)

[d] Dr. D. Hermida-Merino
DUBBLE beamline at the ESRF
6 rue Jules Horowitz
BP 220, 38043
CEDEX 9, Grenoble (France)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201200707.

also been analyzed at the macroscopic (rheology), microscopic (TEM), and molecular levels (CD, VCD, IR, Raman, WAXD) and the results from these studies are reported.

Results and Discussion

Gelation studies: Bisureas **1** and **2** were obtained in high yield by the direct addition of their corresponding amino alcohol to 4,4′-methylene diphenyldiisocyanate without the need to protect the hydroxy groups; these compounds were subsequently exhaustively characterized (see the Supporting Information). Compound **1** (*R* and *S*) formed transparent hydrogels at room temperature at concentrations as low as 0.2 mᴍ and it can be considered as a supergelator with one of the lowest minimum gel concentrations reported in the literature.[9] In contrast, bisurea **2** was not able to form hydrogels, thereby revealing the paramount importance of the local structural on the self-assembly process.[10]

The thermal stability of the gels was studied by using the "vial inversion" method (Figure 1). The onset temperature for gel disassembly (T_{gel}) shows a typical dependence on concentration, with a plateau at 60 °C above 6 mᴍ. The relatively high response of this hydrogel to temperature is typical of enthalpy-driven gels, where weak interactions are broken by increasing temperature, in contrast to entropy-driven hydrogelation where the hydrophobicity of the molecule drives the self-assembly process and the hydrogel remains stable over a wide range of temperatures.[11] DSC measurements of the hydrogels (10 mᴍ) revealed a smooth second-order transition in the range 60–70 °C, which is typical of hierarchically assembled molecular gels (see the Supporting Information).[12a] Notably, this gel-to-sol transition can be explained by the progressive dissolution of the gelator network into the solvent upon increasing the temperature.[12b]

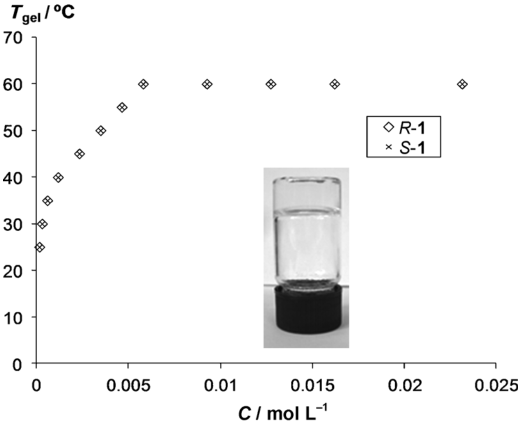


Figure 1. Thermal stability of bisureas *R*-**1** and *S*-**1**.

Rheological studies were also performed for hydrogel *S*-**1**. As evident in Figure 2 A, a 2 mᴍ hydrogel exhibited elastic (G′) and viscous moduli (G″) that were virtually independent of the oscillation frequency. The G′ values were one order of magnitude larger than those of G″, thereby demonstrating the dominant elastic behavior that is typical of gel systems. In addition, studies of G′ and G″ versus the concentration of the hydrogelator revealed (Figure 2 B) an increase in the values of both moduli up to a certain concentration (about 20 mᴍ), after which the rheological properties decreased and the values of G′ and G″ converged. This behavior can be ascribed to precipitation phenomena that are associated with a high concentration of the hydrogelator.

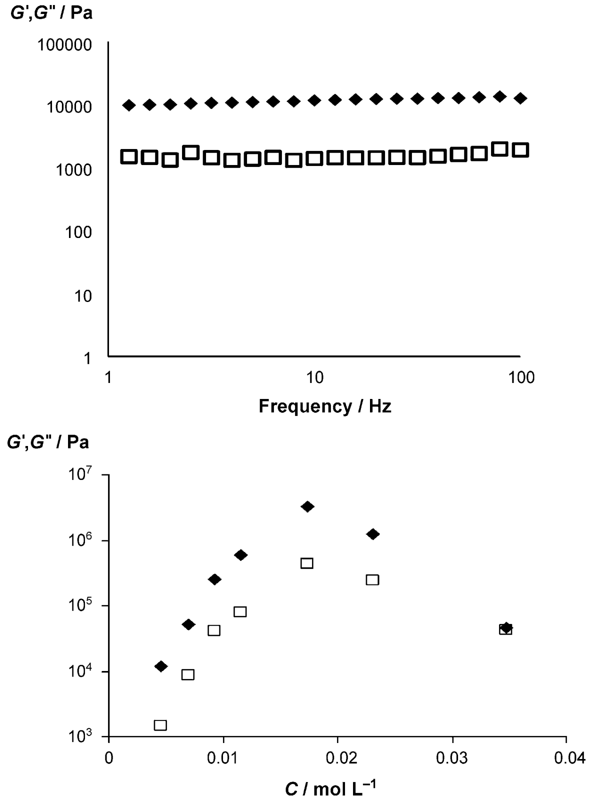


Figure 2. Rheological studies of compound *S*-**1**. Top: Plot of oscillation frequencies for a 2 mᴍ hydrogel; bottom: plot of moduli versus concentration (◆ *G*′, □ *G*″).

Spectroscopic studies: The transmission of chiral information from the molecular level into the supramolecular level is an issue of great interest.[13] In some cases, intermolecular interactions force the molecules to adopt helicoidal arrangements in the assemblies and, if the molecule has chiral centers, such an arrangement may lead to a preferred supramolecular handedness.[14] To investigate this possibility, electronic and vibrational circular dichroism spectroscopy (CD and VCD, respectively) were used. As shown in Figure 3, enantiomeric hydrogels *R*-**1** and *S*-**1** gave CD bands of opposite sign. Furthermore, we observed that nonaggregated solutions of these compounds (Figure 4 and Figure 5) did not exhibit dichroic bands, thus suggesting that the observed effects corresponded to the appearance of supramolecular chirality. Indeed, following the evolution of aggregation with

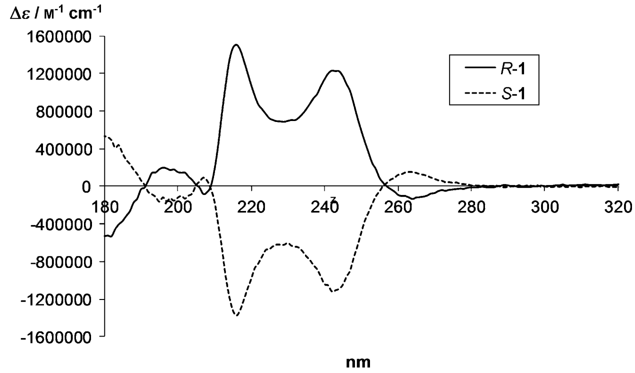


Figure 3. CD spectra for hydrogels (2 mM) of enantiomers *R*-**1** (solid line) and *S*-**1** (dotted line).

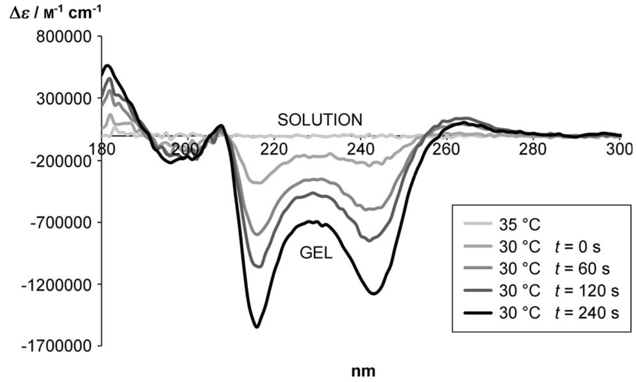


Figure 4. Time-dependent aggregation of hydrogelator *S*-**1** (2 mM), monitored by CD spectroscopy.

time (Figure 4), an increase in the intensity of the bands could be observed together with hydrogel formation.

Furthermore, concentration-dependent experiments (Figure 5, *R*-**1**) revealed a boost in the CD effect close to the minimum gel concentration. For both enantiomers, the spectra showed several zero-crossing points that were coincident with the maxima in the absorption spectra (205, 210, and 260 nm). From the shape of the band that was centered at 205 nm, a relative *P* configuration of the chromophores in the aggregates could be assigned for the *R*-**1** enantiomer and, consequently, an *M* configuration was assigned to the *S*-**1** enantiomer.

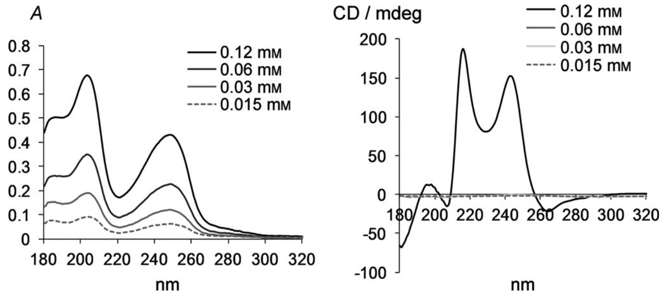


Figure 5. Concentration-dependent UV and CD spectra of compound *R*-**1**.

Whilst CD spectroscopy has been widely employed to study chiral supramolecular assemblies, VCD spectroscopy[15] is less-frequently utilized.[16] Given that most of these molecules have 3*N*−6 vibrational modes, where *N* is the number of atoms, significant vibrational data can be gained from VCD measurements,[17] in contrast with the restricted information (in terms of electronic bands) that is provided by CD spectroscopy. In addition, VCD spectra can be interpreted in terms of structural parameters, which is also advantageous for structure elucidation. Combined VCD, IR, and Raman analysis affords a detailed insight into the involvement of specific molecular parts or fragments during the formation of supramolecular assemblies. However, these advantages of VCD come at the expense of 1) a smaller magnitude of the VCD signals, which require longer data collection; 2) the need for higher concentrations of the sample; and 3) the requirement for short path-length cells (and high sample concentrations) because water exhibits strong IR absorptions at around 1650 cm^{-1}.[18] Accordingly, the VCD measurements were performed on compound **1** at a concentration of 70 mM. To test that this high concentration level did not modify the structure of the gel, a gel that formed at a concentration of 7 mM was studied, which revealed that the IR and VCD patterns were similar to those recorded at 70 mM (see the Supporting Information).

To obtain further details about the different steps in the self-assembly process of *S*-**1**, IR and VCD spectra were recorded at room temperature in solution with different D_2O/[D_6]DMSO mixtures (Figure 6) and the spectroscopic region between 1800 and 1300 cm^{-1} was analyzed.

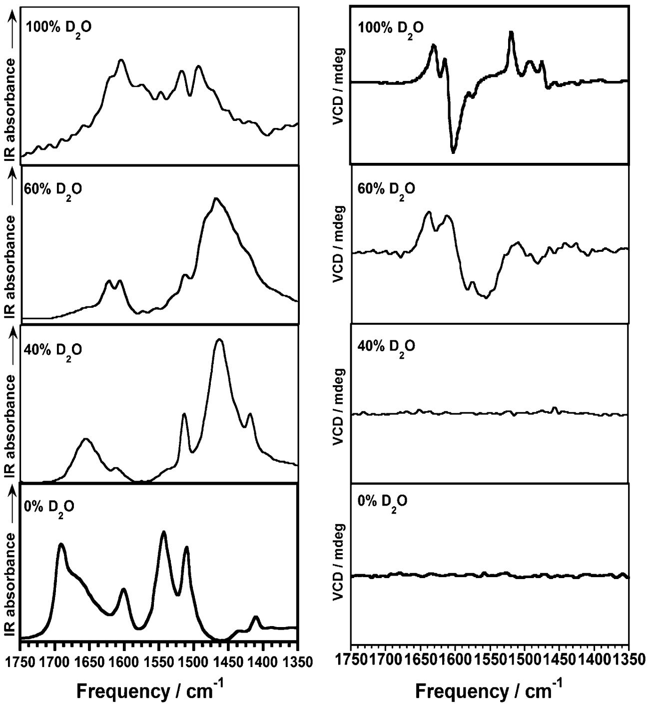


Figure 6. IR (left) and VCD spectra (right) of compound *S*-**1** in various mixtures of D_2O/[D_6]DMSO.

Significant differences were found when comparing the IR and VCD behavior with incremental increases in the D_2O concentration. Below 40 % D_2O, no VCD signals were evident, thus inferring that chiral aggregates were not formed. In contrast, noticeable changes were observed in the IR spectrum. The ν(C=O) vibration band of *S*-**1** (commonly called the amide I vibrational mode) appeared at 1691 cm^{-1} with a shoulder at 1669 cm^{-1} in pure DMSO. In the presence of 40 % D_2O, the most-intense band was measured at 1656 cm^{-1}. Two main phenomena could account for this shift in wavenumber: 1) H/D exchange of the acidic hydrogen atoms and 2) the establishment of hydrogen bonds with the carbonyl oxygen atom (note: these two phenomena are absent in pure [D$_6$]DMSO). It is quite reasonable to assign the displacement in the IR spectrum (1691 to 1656 cm^{-1}) to partial deuteration of the sample in D_2O, which provides a clear explanation for the absence of VCD-signal amplification. To support this explanation, an IR spectrum in [D$_6$]DMSO was recorded after lyophilization from D_2O (see the Supporting Information), in which the effect of deuteration on the IR frequencies could be evaluated in the absence of hydrogen-bonding interactions. In this IR spectrum, the amide I band appeared at 1661 cm^{-1}. The vibrational absorption band of *S*-**1** at 1543 cm^{-1} in [D$_6$]DMSO was assigned to a bending mode of the NH bonds on the amide group, mixed (to a certain extent) with the δ(C−H) vibrations of the aromatic moiety (δ(N−H), also called amide II). Given the nature of this IR band, its frequency will be shifted in D_2O given the H/D exchange. Indeed, this band disappeared in D_2O in the region 1600–1300 cm^{-1}.

A further increase in the D_2O concentration to 60 % is accompanied by the net detection of a VCD signal between 1550 and 1650 cm^{-1}, with an accompanying further downfield shift of the amide I band to 1621 cm^{-1}. Extensive formation of a hydrogen-bonding network in the gel can be rationalized, which serves to explain the further shift in the frequency of the amide I band and the amplification in the intensity of the VCD peak.

To investigate the structure of the gel in more detail, Raman spectroscopy was carried out on the same samples (Figure 7). Raman spectroscopy is a complementary technique to IR spectroscopy because it is sensitive to changes in molecular polarizability that are especially accentuated in the vibrational modes of aromatic groups, in particular the C=C stretches of the benzene moieties at around 1600 cm^{-1}. The Raman spectrum of the nonaggregated form (concentrations below 40 %) revealed a band at 1615 cm^{-1}, which shifted to high frequencies (1626 cm^{-1}) with the formation of the gel. This upshift in wavenumber can be ascribed to intermolecular aromatic π–π-stacking interactions.

Taking all of these spectroscopic data together, we conclude that the amplification of the VCD signal at high percentages of D_2O is a consequence of the chiral aggregates that are generated by the formation of a network of hydrogen bonds. The stability of the gel is also improved by the formation of hydrophobic interactions between benzene rings that are co-facially placed in the aggregates and interact through aromatic π–π-stacking forces, which cause the shifts in the Raman spectra. These findings exemplify the cooperative involvement of hydrophobic and hydrophilic groups to thermodynamically stabilize the structure of the gel. Our results also indicate that complementary electronic (CD) and vibrational spectroscopy (VCD, IR, Raman) provide experimental evidence and structural elucidation of the effects behind these phenomena.

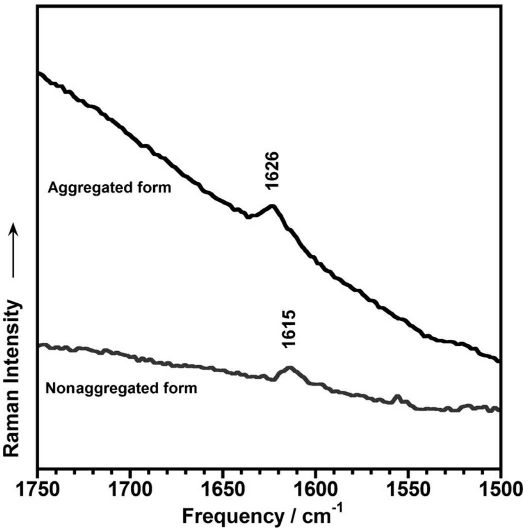


Figure 7. Raman spectra (excitation: 532 nm) of compound *S*-**1** at 40 % (bottom line) and 60 % D_2O (top line) with respect to [D$_6$]DMSO in solution.

X-ray diffraction: The structure of a dried hydrogel (xerogel) of bisurea **1** (*R* and *S*) was investigated by wide-angle X-ray powder diffraction (WAXD). For compound *R*-**1** (Figure 8), the xerogel showed a high degree of crystallinity. Sharp peaks were obtained with a periodicity of d, d/2, d/3, and d/4 (21, 10.6, 7.1, and 5.3 Å, respectively), thus suggesting a lamellar organization. The low-angle peak corresponds to the extended molecular dimension and a model with the packing shown in Figure 9 can be proposed in which chiral columnar stacks are packed into a layered structure. Similar

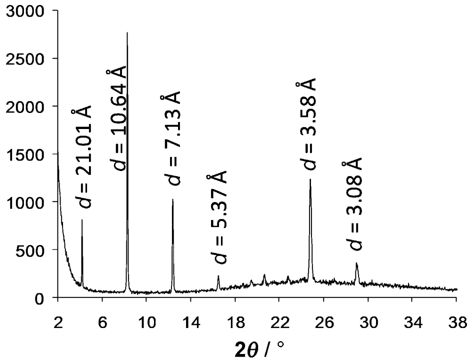


Figure 8. WAXD of the xerogels of bisurea *R*-**1**.

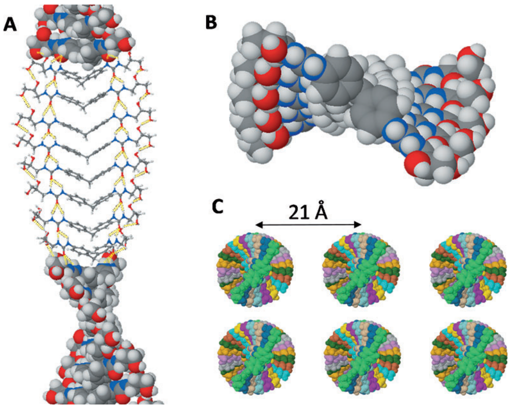


Figure 9. Model of the proposed self-assembly process for hydrogelator **1** (C: inter-columnar packing).

results were found for enantiomer *S*-**1** (see the Supporting Information). Notably, the crystallinity of the xerogel is indirect but strong evidence for the presence of microcrystalline fibers in the wet gel. For example, several cases of noncrystalline xerogels that were obtained from hydrogels have been reported.[11]

Electron microscopy: The expression of supramolecular chirality was also observed by TEM (Figure 10). Hydrogels of *S*-**1** at the minimum gel concentration (0.2 mM) exhibited the presence of left-handed helicoidal tapes (width: about 10 nm) that further coiled into longer fibers with no expression of chirality on the mesoscale.

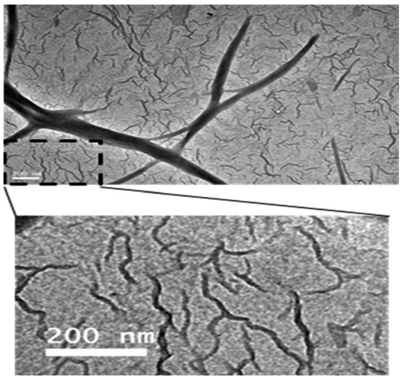


Figure 10. TEM images of hydrogel *S*-**1** (Pt-shadowing).

Amplification of chirality: The amplification of chirality by self-assembly, that is, the transmission of chiral information between chiral molecules and enantiomeric or achiral analogues has been a topic of great interest over the last few years. Several examples, including polymers,[19] liquid crystals,[20] and gels,[21] have been reported. Following on from the seminal studies on polyisocyanates reported by Green et al.,[22] studies that were specifically directed towards dynamic supramolecular systems have been reported by Meijer and co-workers, as well as by other groups.[23] In general, the two main amplification effects have been referred as the "sergeants-and-soldiers" and "majority-rules" principles. In the first effect, a few chiral molecules (sergeants) are able to induce supramolecular chirality in a large number of achiral molecules (soldiers).

In the case of the majority-rules principle, a slight excess of one enantiomer provokes a bias in the supramolecular chirality of the quasi-racemic mixture. In this context, we studied the transmission of chiral information in mixtures of two enantiomers of hydrogelator **1** (majority-rules experiments) and mixtures of *S*-**1** with compound **2** (sergeants-and-soldiers experiments).

In the majority-rules experiment, different ratios of *R*-**1** and *S*-**1** were mixed at a total concentration of 2 mM (10 times higher than the minimum gel concentration). As shown in Figure 11, an enantiomeric purity of at least 80% was required to obtain a stable hydrogel. Below this threshold, the minor enantiomer interfered with the aggregation of the major one. Indeed, WAXD of the solid racemate revealed a higher amorphous character than the enantiomerically pure xerogel (see the Supporting Information).

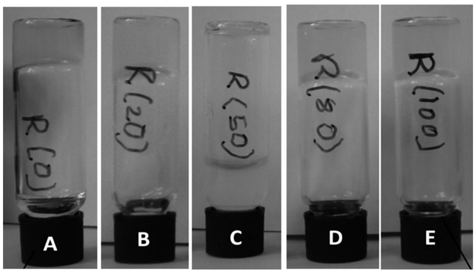


Figure 11. Hydrogelation study of mixtures of bisureas *S*-**1** and *R*-**1**: A) pure *S*-**1**, B) 20% *R*-**1**, C) racemic mixture, D) 80% *R*-**1**, and E) pure *R*-**1**.

In the sergeants-and-soldiers experiments, different mixtures of compound *R*-**1** (0.5 mg) and achiral compound **2** were prepared and both hydrogelation-ability (Table 1) and CD spectroscopic features were observed (Figure 12). The mixtures formed hydrogels up to a ratio of 1:0.6 and further addition of the achiral compound resulted in precipitation of the mixture. CD spectra confirmed a clear cooperative effect after the addition of 0.4 equivalents of bisurea **2**.

Table 1. Hydrogelation ability of different mixtures of bisureas *R*-**1** and **2**.

Entry	**2** [equiv]	Appearance[a]
1	0.2	G
2	0.4	G
3	0.6	WG
4	0.8	P

[a] G: gel, WG: weak gel, P: precipitate.

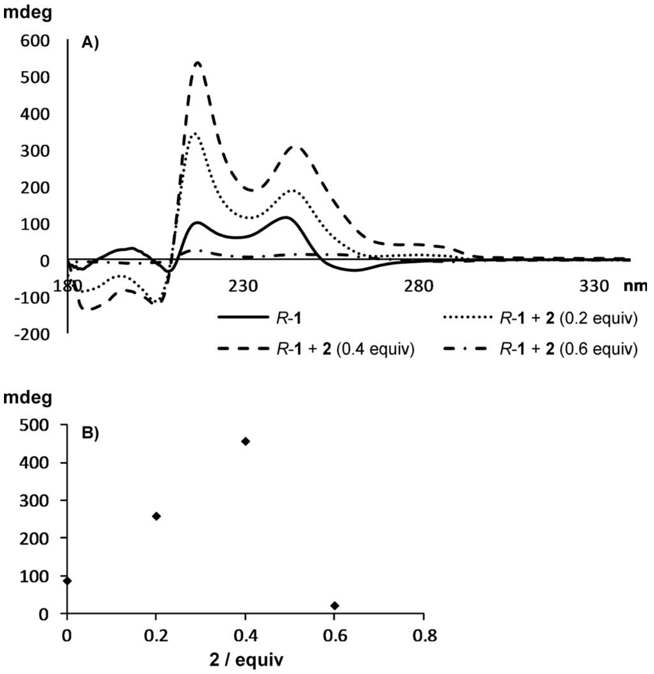


Figure 12. A) CD spectra of mixtures of compounds *R*-**1** and **2**; B) plot of ellipticity at 220 nm versus the amount of achiral compound **2**.

However, the addition of another 0.2 equivalents of compound **2** resulted in a notable decrease in this effect, as well as a weakening of the hydrogel.

In summary, hydrogel fibers that contain 40% of achiral "soldier" compound **2** remain stable and express the chirality of "sergeant" compound *R*-**1**. The main structural difference between compounds **1** and **2** is the chiral secondary hydroxy group, whilst the rest of the molecule is identical, which, in turn, permits stacking of the aromatic unit, as well as complementary hydrogen bonding between the urea functions. Presumably, after the inclusion of a high amount of a compound that lacks hydroxy groups, the peripheral hydrogen bonding network becomes disrupted and, as a consequence, the material precipitates out. The role of the secondary hydroxy group seems to be critical for the hydrogelation process to occur. In summary, molecular chirality plays a fundamental role in hydrogelation and expression at the supramolecular level.

Conclusion

In conclusion, we have described a potent hydrogelator with a very low minimum gel concentration and interesting thermal properties. For instance, the low thermal stability of this hydrogel and its high temperature-response could be attractive for its application as an injectable material. For example, it is very easy to handle and permits the preparation of hydrogels with alternated layers of *R*-**1** and *S*-**1**, thus yielding materials with potentially interesting chiroptical properties (Figure 13).

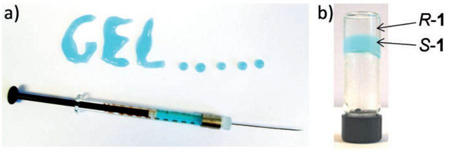


Figure 13. Demonstration of the application of chiral hydrogels of compound **1** as an injectable material. a) A solution of the gelator is charged into the syringe at 50 °C and a gel forms quickly after depositing the solution onto a surface at room temperature. b) Gels of compounds *R*-**1** and *S*-**1** can be easily prepared in the same vial by the consecutive addition of warm solutions of the gelator into the vial at room temperature. The blue color is due to the addition of methylene blue.

Furthermore, the investigation of the chiral self-assembly process by using a combination of spectroscopic techniques and X-ray powder diffraction has provided new information on the nature of these supramolecular assemblies. In fact, it has been established that these assemblies are formed by the cooperative effects of π–π stacking of the aromatic core and a hydrogen-bond network that involves the peripheral polar groups (urea, hydroxy). Remarkably, the final supramolecular structure of compound **1** (*R* and *S*) shows a strong enhancement of the chirality and its amplification in mixtures with achiral partners. Altogether, these features make the hydrogels of compound **1** of practical use as chiral gel media.

Experimental Section

Gelation tests: A given amount of the compound to be studied was weighed into a screw-capped vial (diameter: 20 mm) and suspended in water (1 mL). The temperature of the mixture was then increased until the solid had completely dissolved and the solution was left to cool to RT. A gel (G) was considered to have formed when gravitational flux was not observed upon inversion of the vial.

Thermal-stability measurements: Gel samples of different concentrations were placed in a thermostated bath and the temperature was gradually raised in 5 °C steps with 10 min of stabilization in between the temperature changes.

Circular dichroism (CD): Spectra were collected on a JASCO J-810 spectrometer. The samples were prepared in a quartz cuvette (thickness: 1 mm) prior to gelation. The samples were allowed to stabilize for 10 min at the desired temperature.

Vibrational circular dichroism (VCD) and IR and Raman Spectroscopy: Samples of *S*-**1** and *R*-**1** in D_2O and [D_6]DMSO at a concentration of 70 mM (about 30 mg mL^{-1}) were prepared for the vibrational spectroscopic measurements. After thermal treatment, the samples were placed at RT in a demountable cell A145 (Bruker, Germany) that was supplied with CaF_2 windows. A 25 μm Teflon spacer was used to optimize the vibrational signals. IR and VCD spectra were recorded on a Vertex 70 spectrometer that was equipped with a PMA 50 photoelastic modulator (Bruker, Germany). VCD spectra were obtained by adding 500 scans at a spectroscopic resolution of 4 cm^{-1}, which is equivalent to signal accumulation for 15 min; this is an unusually short time, because the standard accumulation time to obtain a suitable VCD spectrum is around 8 h. To ensure the absence of linear dichroism interference, which is caused by preferential orientation within the gels,[24] spectra on different aliquots of these compounds were recorded at different angles without observing any appreciable deviation. As a proof of the quality of the recorded data, the spectra from pure enantiomeric samples resulted in mirror images (see the Supporting Information). Raman spectra were recorded on a

Senterra dispersive Raman microscope (Bruker, Germany) with laser excitation at 532 nm and a power of 5 mW.

Transmission electron microscopy (TEM): Transmission electron micrographs were taken on a JEOL 2100 microscope. Samples of the hydrogels were prepared by dipping a copper grid that was coated with a formvar carbon support film into the gels and shadowing with Pt.

Powder X-ray diffraction: Data collection was performed at room temperature on a Bruker D4 Endeavor X-ray powder diffractometer by using Cu Kα radiation. Samples of the powdered xerogels were placed on a sample holder and data were collected for 2θ values between 2° and 40° with a step size of 0.03° and a step time of 10 s.

Rheology: The rheological properties of the systems were determined on a controlled stress AR-2000 rheometer (TA Instruments). A cone-and-plate geometry (diameter: 10 mm, gap: 26 µm) was used for all of the samples. Frequency sweeps were performed in the angular-frequency range 0.1–100 rad s^{-1} with the instrument in oscillatory mode at 25 °C. To ensure that the moduli were independent of strain, preliminary strain sweeps were performed for each sample.

Acknowledgements

We thank the Spanish Ministry of Science and Innovation (grants no. CTQ2009–13961 and CTQ2009–10098), the Junta of Andalucía (grant no. P09–FQM–4708) and the Universitat Jaume I-Bancaixa (grant no. P1·1B2009–42) for financial support. F.R.-L. thanks the Generalitat Valenciana for a FPI fellowship. We thank Henkel Adhesives Ltd for a PhD studentship to D.H.-M.

---

[1] a) *Molecular Gels: Materials with Self-Assembled Fibrillar Networks* (Eds.: R. G. Weiss, P. Terech), Springer, **2005**; b) *Low Molecular Mass Gelators* (Ed.: F. Fages), Springer, **2005**; c) P. Terech, R. G. Weiss, *Chem. Rev.* **1997**, *97*, 3133; d) D. J. Abdallah, R. G. Weiss, *Adv. Mater.* **2000**, *12*, 1237; e) J. H. van Esch, B. L. Feringa, *Angew. Chem. Int. Ed.* **2000**, *39*, 2263; f) O. Gronwald, E. Snip, S. Shinkai, *Curr. Opin. Colloid Interface Sci. Curr. Opin. Colloid In.* **2002**, *7*, 148; g) A. R. Hirst, D. K. Smith, *Chem. Eur. J.* **2005**, *11*, 5496; h) A. Ajayaghosh, V. K. Praveen, *Acc. Chem. Res.* **2007**, *40*, 644; i) P. Dastidar, *Chem. Soc. Rev.* **2008**, *37*, 2699; j) A. Dawn, T. Shiraki, S. Haraguchi, S.-I. Tamaru, S. Shinkai, *Chem. Asian J.* **2011**, *6*, 266; k) J. W. Steed, *Chem. Commun.* **2011**, *47*, 1379.

[2] a) F. Rodríguez-Llansola, B. Escuder, J. F. Miravet, D. Hermida-Merino, I. W. Hamley, C. J. Cardin, W. Hayes, *Chem. Commun.* **2010**, *46*, 7960; b) D. M. Wood, B. W. Greenland, F. Rodríguez-Llansola, C. Murray, C. J. Cardin, J. F. Miravet, B. Escuder, I. W. Hamley, W. Hayes, *Chem. Eur. J.* **2012**, *18*, 2692.

[3] a) N. M. Sangeetha, U. Maitra, *Chem. Soc. Rev.* **2005**, *34*, 821; b) A. R. Hirst, B. Escuder, J. F. Miravet, D. K. Smith, *Angew. Chem.* **2008**, *120*, 8122; *Angew. Chem. Int. Ed.* **2008**, *47*, 8002; c) S. Banerjee, R. K. Das, U. Maitra, *J. Mater. Chem.* **2009**, *19*, 6649.

[4] a) A. Brizard, R. Oda, I. Huc in *Chirality Effects in Self-assembled Fibrillar Networks, in Low Molecular Mass Gelators* (Ed.: F. Fages), Springer, **2005**; b) V. K. Praveen, S. S. Babu, C. Vijayakumar, R. Varghese, A. Ajayaghosh, *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1196; c) D. K. Smith, *Chem. Soc. Rev.* **2009**, *38*, 684.

[5] a) F. Rodríguez-Llansola, J. F. Miravet, B. Escuder, *Chem. Commun.* **2009**, 7303; b) A. Dawn, T. Shirali, S. Haraguchi, H. Sato, K. Sada, S. Shinkai, *Chem. Eur. J.* **2010**, *16*, 3676; c) X. Chen, Z. Huang, S.-Y. Chen, K. Li, X.-Q. Yu, L. Pu, *J. Am. Chem. Soc.* **2010**, *132*, 7297.

[6] P. Woodward, A. Clarke, B. W. Greenland, D. Hermida-Merino, L. Yates, A. T. Slark, J. F. Miravet, W. Hayes, *Soft Matter* **2009**, *5*, 2000.

[7] For example, see: a) F. Fages, F. Vögtle, M. Zinic, *Top. Curr. Chem.* **2005**, *256*, 77; b) J. W. Steed, *Chem. Soc. Rev.* **2010**, *39*, 3686 and the references cited therein.

[8] P. Besenius, K. P. van den Hout, H. M. H. G. Albers, T. F. A. de Greef, L. L. C. Olijve, T. M. Hermans, B. F. M. de Waal, P. H. H. Bomans, N. A. J. M. Sommerdijk, G. Portale, A. R. A. Palmans, M. H. P. van Genderen, J. A. J. M. Vekemans, E. W. Meijer, *Chem. Eur. J.* **2011**, *17*, 5193.

[9] O. Gronwald, S. Shinkai, *Chem. Eur. J.* **2001**, *7*, 4328.

[10] A. R. A. Palmans, J. A. J. M. Vekemans, H. Fischer, R. A. Hikmet, E. W. Meijer, *Chem. Eur. J.* **1997**, *3*, 300.

[11] V. J. Nebot, J. Armengol, J. Smets, S. Fernández Prieto, B. Escuder, J. F. Miravet, *Chem. Eur. J.* **2012**, *18*, 4063.

[12] a) S. R. Raghavan, B. H. Cipriano in *Gel Formation: Phase Diagrams Using Tabletop Rheology and Calorimetry, in Molecular Gels: Materials with Self-Assembled Fibrillar Networks*, (Eds.: R. G. Weiss, P. Terech), Springer, **2005**; b) A. R. Hirst, I. A. Coates, T. R. Boucheteau, J. F. Miravet, B. Escuder, V. Castelletto, I. W. Hamley, D. K. Smith, *J. Am. Chem. Soc.* **2008**, *130*, 9113.

[13] D. B. Amabilino, *Chirality at the Nanoscale*; Wiley-VCH, Weinheim, **2009**.

[14] T. Gulik-Krzywicki, T. Fouquey, J. M. Lehn, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 163.

[15] G. Gottarelli, G. P. Spada in *Circular Dichroism: Principles and Applications*, 2nd ed. (Eds.: N. Berova, K Nakanishi, R. W. Woody), Wiley, New York, **2000**, pp. 547.

[16] H. Sato, T. Yajima, A. Yamagishi, *Chem. Commun.* **2011**, *47*, 3736.

[17] L. P. Prasad in *Determination of Molecular Stereochemistry Using Optical Rotator Dispersion, Vibrational Circular Dichroism and Vibrational Raman Optical Activity in Chiral Analysis* (Eds.: K. W. Busch, M. A. Busch), Elsevier, **2006**, pp. 461.

[18] L. P. Prasad, C. Zhao, *Fresenius' J. Anal. Chem.* **2000**, *366*, 727.

[19] K. Maeda, E. Yashima, *Top. Curr. Chem.* **2006**, *265*, 47.

[20] R. P. Lemieux, *Chem. Soc. Rev.* **2007**, *36*, 2033.

[21] a) S. J. George, A. Ajayaghosh, P. Jonkheijm, A. P. H. J. Chenning, E. W. Meijer, *Angew. Chem.* **2004**, *116*, 3504; *Angew. Chem. Int. Ed.* **2004**, *43*, 3422; b) A. Ajayaghosh, R. Varghese, S. J. George, C. Vijayakumar, *Angew. Chem.* **2006**, *118*, 1159; *Angew. Chem. Int. Ed.* **2006**, *45*, 1141; c) A. Ajayaghosh, R. Varghese, S. Mahesh, V. K. Praveen, *Angew. Chem.* **2006**, *118*, 7893; *Angew. Chem. Int. Ed.* **2006**, *45*, 7729.

[22] M. M. Green in *A Model for How Polymers Amplify Chirality in Circular Dichroism: Principles and Applications*, 2nd ed. (Eds.: N. Berova, K. Nakanishi, R. W. Woody), Wiley, New York, **2000**, pp. 491.

[23] A. R. A. Palmans, E. W. Meijer, *Angew. Chem.* **2007**, *119*, 9106; *Angew. Chem. Int. Ed.* **2007**, *46*, 8948.

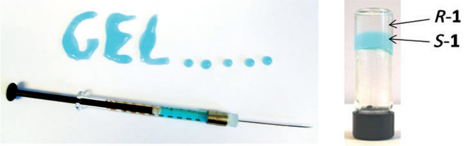
[24] A. Brizard, D. Berthier, C. Aime, T. Buffeteau, D. Cavagnat, L. Ducasse, I. Huc, R. Oda, *Chirality* **2009**, *21*, E153.

Received: March 2, 2012
Revised: July 9, 2012

Chiral Hydrogels

F. Rodríguez-Llansola, D. Hermida-Merino, B. Nieto-Ortega, F. J. Ramírez, J. T. L. Navarrete, J. Casado, I. W. Hamley, B. Escuder, W. Hayes,* J. F. Miravet** . . . ▮▮▮▮–▮▮▮▮

Self-Assembly Studies of a Chiral Bisurea-Based Superhydrogelator



Supergelator with a twist: A chiral bisurea-based compound is capable of forming supramolecular hydrogels at concentrations as low as 0.2 mM (see figure). Molecular chirality is manifested on the supramolecular level and the soft material is easy to handle.