

# Diastereoselective Self-Sorting

# Biphenyl Bis(amino alcohol) Oxalamide Gelators: Complex Gelation Involving Coupled Equilibria, Central-to-Axial Chirality Transfer, Diastereoisomer Interconversion, and Self-Sorting

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**Abstract:** Chiral gelators **3** and **4**, with two valinol- or leucinoloxalamido arms attached to the 2,2'-positions of the proatropisomeric biphenyl group, were prepared, and their gels were studied. Compound (R,R)-**3** in the solution and gel states forms a mixture of major [(R,aR,R)-**3**] and minor [(R,aS,R)-**3**] diastereomers due to central-to-axial chirality transfer. <sup>1</sup>H NMR studies of its toluene gel provide evidence of diastereomer interconversion and self-sorting, which results in exclusive incorporation of (R,aR,R)-**3** into the gel network. Gels formed in the

# $10^{-3}$ M concentration range show an irregular $T_{\rm g}$ /concentration dependence, which is in contrast to those formed in the $10^{-2}$ M concentration range. The peculiar properties of the former gels may be explained by kinetic effects due to the presence of coupled equilibria comprising diastereomer interconversion and (*R*,*aR*,*R*)-**3** self-assembly where the rate of gelation becomes dependent on the rate of formation of the gelling (*R*,*aR*,*R*)-**3** from the nongelling (*R*,*aS*,*R*)-**3**.

# Introduction

The supramolecular chemistry of low-molecular-weight organoand hydrogelators is a highly active field of research. Gels formed by the self-assembly of small organic molecules are of wide interest as dynamic soft materials with numerous possible applications, especially in biomedicine and nanotechnology. Such gels are used as cell scaffolds or supports for functional and responsive biomaterials, biosensors, and nanowires.<sup>[1]</sup> On the other hand, they also represent an excellent experimental system that enables in depth studies of self-assembly, a general phenomenon of the highest importance in biology and contemporary materials science.<sup>[2]</sup> Chiral information encoded in the structure of gelators has been found to have a profound influence on both their self-assembly and gelation properties.<sup>[3]</sup> For example, the racemic forms are generally weaker gelators than the corresponding pure enantiomers, although exceptions are known.<sup>[4]</sup> Importantly, it has been shown that in gels, as well as in other kinds of supramolecular polymers, efficient chirality transfer from the molecular to the supramolecular level may occur through the self-assembly of chiral monomers into helical

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aggregates following a multistep hierarchical pathway.<sup>[2d,2e]</sup> The majority of chiral gelators studied to date have central chirality; axially chiral gelators are very rare.<sup>[5,6]</sup> Recently, we reported the design and properties of chiral gelators combining central and axial chirality in the same molecule. Such gelators contain a conformationally flexible proatropisomeric 2,2'-dioxybiphenyl unit and amino acid chiral centres located in the 2,2'-biphenyl arms (Figure 1, I).<sup>[7]</sup> We have shown that in contrast to related molecular systems, here an efficient central-to-axial chirality transfer occurs through the intermolecular interactions in the gelator assemblies.<sup>[8]</sup> Such intermolecularly induced axial chirality, being the consequence of a specific gelator self-assembly motif, may be denoted as transient since it disappears and reappears during the thermoreversible sol-to-gel transitions. This may be of interest for the design of dynamic chirality-controlled supramolecular systems and devices. To further explore the potential of such systems, we have prepared a series of new gelat-



Figure 1. Structures of proatropisomeric 2,2'-biphenyl-containing di(amino acid oxalamide) I and di(amino alcohol oxalamide) II gelators.



ors of type **II**, which differ from **I** by their constitution, the rigidity of their 2,2'-biphenyl arms, and the shorter distance from the chiral centre to the proatropisomeric biphenyl unit.

In this paper, we report the synthesis and gelling properties of selected type II gelators, and characterization the of gel and solid-state assemblies formed by these gelators by FTIR and NMR spectroscopy, circular dichroism (CD), differential scanning calorimetry (DSC), X-ray crystallography, and transmission electron microscopy (TEM). These studies reveal their dramatically different properties compared to type I gelators.<sup>[7]</sup> We provide the evidence that in lipophilic solvents as well as in gels, centrally chiral gelator (R,R)-**3** forms a mixture of major [(R,aR,R)-**3**] and minor [(R,aS,R)-3] diastereomers due to induced axial (aR and aS) chirality in the biphenyl unit, and that by diastereoselective self-sorting only the major diastereomer is self-assembled into the gel network. We also present evidence that at lower ( $10^{-3}$  M) concentrations of (*R*,*R*)-**3** in toluene, long-lived nonequilibrium aggregate systems are formed that need prolonged ageing (up to 216 h at +4 °C) to transform into gels. In contrast, (R,R)-3 at  $10^{-2}$  M concentrations forms stable toluene gels that form instantaneously by the cooling of hot samples. The formation of nonequilibrium systems in the 10<sup>-3</sup> M concentration range is explained by kinetic effects under coupled equilibria conditions comprising diastereomer interconversion and (R,aR,R)-3 network-assembly/disassembly where the overall gelation rate becomes determined by slow formation of the gelling (R,aR,R)-3 from the nongelling (R,aS,R)-3 diastereomer.

## **Results and Discussion**

#### Synthesis

Hydrogenation of 2,2'-dinitrobiphenyl in ethanol using a Pd/C catalyst gave 2,2'-diaminobiphenyl in quantitative yield (Scheme 1).<sup>[9]</sup> Reaction of diaminobiphenyl with ethyl chloroformate in dichloromethane in the presence of triethylamine gave 1 (85 % yield). Diester 1 was treated with selected amino alcohols in dichloromethane to give biphenyldioxalamide derivatives **3** and **4**. The reaction of **1** with *rac*-valinol gave a mixture

of *rac*- and *meso*-**3**, which were separated by column chromatography. Detailed synthetic procedures and structural characterization data are provided in the Exp. Sect. provided as Supporting Information.

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#### **Gelling Properties and TEM Studies**

Optically active valinol and leucinol oxalamides (R,R)-**3** and (R,R)-**4**, respectively, showed moderate gelation ability towards toluene, *o*-xylene, *m*-xylene, tetraline, and decalin, while with the other tested solvents of various polarities the gelation failed. The two gelators showed different gelation efficiencies towards very similar solvents such as *o*-, *m*-, and *p*-xylene. *o*-Xylene is the best at forming gels; the *m* and *p* isomers form gels much less efficiently, or crystallization was observed. In highly polar solvents such as MeOH, EtOH, acetone, and DMSO, the compounds are soluble. They are also soluble in solvents of low or medium polarity such as dichloromethane, 2-octanol, THF, and dioxane. The gelators are insoluble in water, cyclohexane, and diethyl ether.

The gelation testing was carried out by consecutive additions of small measured volumes of the tested solvent, followed by heating and cooling of the sample until a weak gel was formed. We observed that some dilute samples showed rather slow gelation rates that needed 10–24 h of ageing at room temperature.

It is well documented that optically pure gelators are more efficient that the corresponding racemates, which tend to crystallize; however, exceptions to this rule are known.<sup>[10]</sup> Compound *rac-3* showed only very slow gelation of small volumes of toluene and *o*-xylene, and almost instantaneous gelation of tetraline. Compound *meso-3*, as has been reported for other types of gelators with internal symmetry, was found to lack any gelation ability, and in most cases tended to crystallize.

TEM investigation of the (R,R)-**3** toluene gel and the unstable partial gel of *rac*-**3** revealed clear differences between the two systems (Figure 2, a and b). In the first gel, very long fibres showing *P* helicity and with diameters in the 10 nm range were observed. This shows that molecular chirality is successfully transferred into supramolecular chirality of the toluene gel ag-



Scheme 1. Synthesis of biphenyldioxalamide derivatives 3 and 4, yields are given in parentheses.





gregates. In contrast, the image of the unstable *rac*-**3** toluene gel (Figure 2, b) shows the presence of short fibre bundles and crystals.



Figure 2. TEM images of (a) (R,R)-**3**, and (b) *rac*-**3** toluene gels. In (a), very tiny (d = 10 nm) and long fibres with P helicity can be observed. In (b), short fibre bundles are present together with crystals.



Figure 4. Hydrogen-bonded chains in the crystal packing of rac-**3** extend in the direction [101]. Symmetry operators i: -x, y, 3/2 - z; ii: 1/2 - x, 1/2 - y, 2 - z.

#### X-ray Molecular and Crystal Structure of rac-3

Crystals of *rac*-**3** suitable for X-ray analysis were obtained from  $[D_8]$ toluene. The molecule of *rac*-**3** is  $C_2$ -symmetric, with the midpoint of the C-1–C-1<sup>i</sup> (symmetry operator i: –*x*, *y*, 3/2 – *z*) bond located on the crystallographic twofold axis. Therefore, the two stereogenic centres (atoms C-9 and C-9<sup>i</sup>) are related by a rotation of 180° (Figure 3, a). The axially chiral conformation of the molecule is stabilized by a pair of intramolecular hydrogen bonds between the N-2 amine nitrogen and the hydroxyl group (Figure 3, b and Table S1, Supporting Information).



Figure 3. View of the (*R*,*aR*,*R*) enantiomer of *rac*-**3** showing: (a)  $C_2$  symmetry (position of the crystallographic twofold axis is indicated by a black ellipse), and (b) conformation of the molecule stabilized by a pair of symmetry-related intramolecular hydrogen bonds. Symmetry operator i: -x, *y*, 3/2 - z.

The molecules link to their inversion-related neighbours by a pair of inversion-related hydrogen bonds between the hydroxyl group and the O-2 carbonyl oxygen, thus forming hydrogenbonded chains running in the direction [101] (Figure 4, Table S1 in Supporting Information). The chains consist of alternating (R,aR,R) and (S,aS,S) enantiomers.

#### **CD** Investigation

As shown in Table 1, both, (R,R)-3 and (R,R)-4 are capable of gelling decalin at minimal gelation concentrations (mgc) of  $1.8 \times 10^{-2}$  and  $1.54 \times 10^{-2}$  M, respectively. The electronic absorption and circular dichroism (CD) spectra of enantiomeric gelators (R,R)-3 and (S,S)-3 were recorded in decalin at  $4.07 \times 10^{-3}$  M concentrations, which is below the minimal gelation concentration (mgc) (Figure 5, a and b). The CD spectra of the enantiomers have a mirror image relationship, with bands at 291, 261, and 231 nm. In the electronic absorption spectra, the biphenyl absorptions appear at 271 nm, the shoulder at around 240 nm, and a weak band at 212 nm (Figure 5, a). The absorption at 240 nm could be ascribed to the biphenyl A band appearing between 240 and 250 nm.<sup>[11]</sup> It is well documented that the sign of the Cotton effect corresponding to the biphenyl A band is related to the twist of the biphenyl system: a positive Cotton effect corresponds to an M-twist, and a negative Cotton effect to a P-twist of the biphenyl system.[12,13] Also, a recent experimental and theoretical study of chiral 2,2'-(2-butoxy)biphenyls showed the appearance of a positive-negative-positive sequence of Cotton effects at around 280, 240, and 210 nm, respectively, for the P (aS) biphenyl atropisomer, and the opposite sequence for the M (aR) isomer.<sup>[14]</sup> In the CD spectra of (R,R)-3 and (S,S)-3, the corresponding biphenyl bands are slightly redshifted due to 2,2'-carboxamide instead of 2,2'-butoxy biphenyl substitution and partial aggregation (vide infra).

Nevertheless, the appearance of a negative-positive-negative sequence of Cotton effects in the CD spectrum of (R,R)-**3**, and the opposite sequence in the spectrum of (S,S)-**3**, suggests an *M*-twist of the biphenyl in the former and a *P*-twist in the latter, corresponding to their (R,aR,R) and (S,aS,S) configurations, respectively. As described in the next section, NMR spectroscopic studies of (R,R)-**3** in  $[D_8]$ toluene and CDCl<sub>3</sub>, at room temperature showed that an equilibrium mixture of (R,aR,R)-**3** and (R,aS,R)-**3** diastereomers in a ratio close to 5:1 is present in those solvents.



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Table 1. Gelation efficiency of (*R*,*R*)-, *rac*-, and *meso*-**3** and (*R*,*R*)-**4** towards selected solvents expressed as the maximum solvent volume ( $V_{max}$  [mL]) gelled by 10 mg of gelator.<sup>[a]</sup>

Solvent	(R,R)- <b>3</b>	rac- <b>3</b>	meso- <b>3</b>	(R,R)- <b>4</b>
CH <sub>2</sub> Cl <sub>2</sub>	sol.	sol.	sol.	sol.
Cyclohexane	ins.	ins.	ins.	ins.
Acetone	sol.	sol.	sol.	sol.
MeOH	sol.	sol.	ins.	sol.
EtOH				sol.
Water	ins.	ins.	ins.	ins.
DMSO	sol.	sol.	sol.	sol.
Toluene	1.8	1.4**	cryst.	0.5**
o-Xylene	2.0	1.6**	cryst.	2.3
<i>m</i> -Xylene	0.7	cryst.	cryst.	1.1**
<i>p</i> -Xylene	cryst.	cryst.	cryst.	0.7**
Tetraline	1.4	1.0	cryst.	0.7**
Decalin	1.1*	cryst.	cryst.	1.3*
Octan-2-ol	sol.	sol.	cryst.	sol.
Diethyl ether	ins.	ins.	ins.	ins.
<i>i</i> Pr <sub>2</sub> O				Ins.
THF	sol.	sol.	sol.	sol.
Dioxane	sol.	sol.	sol.	sol.

[a] Gelation tests were carried out in test tubes. Abbrevations: sol.: soluble; ins.: insoluble; cryst.: crystallization; \*: crystallization by ageing; \*\*: very slow gelation that needs 10–24 h at room temp.



Figure 5. (a) Electronic absorption and (b) mirror image CD spectra of (*R*,*R*)-**3** and (*S*,*S*)-**3**, dissolved in decalin ( $c = 4.07 \times 10^{-3}$  m): (*R*,*aR*,*R*)-**3** (black curve) and (*S*,*aS*,*S*)-**3** (red curve); (c) (*R*,*R*)-**3** concentration-dependent CD spectra in decalin:  $c = 2.3 \times 10^{-2}$  m, black;  $1.1 \times 10^{-2}$  m, red;  $5.7 \times 10^{-3}$  m, green;  $2.5 \times 10^{-3}$  m, blue;  $1.1 \times 10^{-3}$  m, cyan;  $3.7 \times 10^{-3}$  m, magenta; and (d) (*R*,*R*)-**3** temperature-dependent CD spectra in decalin ( $c = 4.17 \times 10^{-3}$  m; temp. range 20 °C, black, to 100 °C, dark blue) showing decrease of signal intensities as indicated by the arrows, followed by slight blueshifts of the maxima.

Hence, also in the lipophilic decalin, the observed CD spectrum of (R,R)-**3** may in fact correspond to a mixture of the predominating (R,aR,R)-**3** and the less abundant (R,aS,R)-**3** diastereomer [and similarly for (S,S)-**3**, a mixture of the corresponding (S,aS,S) and (S,aR,S) diastereomers], possibly in a ratio higher than that observed in [D<sub>8</sub>]toluene. The CD-determined axial chirality of the biphenyls induced by the (R) and (S) centres of **3** is consistent with the (aR)- and (aS)-biphenyl configurations of the enantiomers found in the crystal structure of rac-**3** (Figure 3). Hence, in solution as well as in the solid state, the (R) centres

in **3** induce axial (*aR*) chirality in the biphenyl fragment, and the (*S*) centres induce (*aS*) chirality.

The concentration-dependent CD spectra of (R,R)-3 in decalin are shown in Figure 5 (c). At the highest concentration of the gel sample ( $2.3 \times 10^{-2}$  M), a strong negative Cotton effect appears at 303 nm; its intensity decreases with a decrease of the concentration, followed by a blueshift from 303 nm to 295 nm at  $1.1 \times 10^{-3}$  M concentration, the latter corresponding to a weak gel (Figure 5, c, red curve), and to 291 nm at  $5.7 \times 10^{-3}$  M (sol, green curve). Further decrease of the concentration does not affect the position of the maximum at 291 nm. At the same time, the positive Cotton effect at 261 nm and the negative one at 231 nm have their lowest intensities at the highest concentration in the gel state, and both increase in intensity for lower gelator concentrations. The CD spectra in the gel state are dominated by the presence of highly aggregated gelator molecules, which is reflected in the appearance of a strong redshifted CD band at 303 nm. A circular differential scattering effect may also contribute to the intensity of the latter band under high aggregation conditions. Such an effect is known to appear in the CD spectra of macromolecules with sizes larger than  $\lambda/20$  nm, and it has also been observed in the CD spectra of gels formed by other types of oxalamide gelators.<sup>[15,7]</sup> In such cases, the negative differential scattering band may diminish the intensity of the positive Cotton band at 261 nm, and enhance the intensity of the negative 291 nm band. The observation that decreasing the gelator concentration to  $5.7 \times 10^{-3}$  M to give a much less aggregated sol phase (green curve in Figure 5, c) results in a strong decrease in intensity and a blueshift of the 303 nm band, and an increase in intensity of the 261 nm band reinforces the above conclusion. For this concentration and also lower gelator concentrations, the expected bisignate CD spectra originating from coupled biphenyl excitons were observed.

The changes in the temperature-dependent CD spectra of (R,R)-3 (Figure 5, d) taken at a sample concentration below the mgc ( $c = 2.62 \times 10^{-3}$  M; mgc =  $1.8 \times 10^{-2}$  M), and hence containing less of the aggregated gelator, should also reflect the variations in the (R,aR,R)-3/(R,aS,R)-3 equilibrium at different temperatures. Increasing the temperature from 20 to 100 °C induces a steady decrease in intensity of both the negative 291 and the positive 263 nm maxima, together with their slight blueshifts to 289.8 and 256 nm, respectively. The observed changes could be explained by the combined effects of disaggregation and decrease of the (R,aR,R)-3/(R,aS,R)-3 ratio due to the interconversion of the more stable former diastereomer into the less stable latter diastereomer with the opposite (aS)-biphenyl configuration. The fact that even at 100 °C, where the degree of aggregation should be much smaller, a strong CD spectrum could still be observed reinforces the conclusion about its origin from the intrinsic chirality of the dissolved diastereomers.

#### FTIR and NMR Spectroscopic Studies

An FTIR spectroscopic study of the (R,R)-**3** toluene gel revealed the presence of bands at 3425, 3323, and 3274 cm<sup>-1</sup>, corresponding to hydrogen-bonded and free OH and NH vibrations.



In the amide I region, bands were observed at 1682 and 1650 cm<sup>-1</sup>, corresponding to free and hydrogen-bonded amide groups, respectively. The temperature-dependent FTIR spectra (Figure S1, Supporting Information) show that increasing the sample temperature results in a decrease in intensity of the 3323, 3274, and 1650 cm<sup>-1</sup> bands, and an increase in intensity of the 3425 and 1682 cm<sup>-1</sup> bands, as a result of the breakage of hydrogen bonds. In the amide I region, a new strong band at 1691 cm<sup>-1</sup> appears at the highest sample temperature. These observations indicate that both OH and amide groups participate in hydrogen bonding in the aggregates.

<sup>1</sup>H NMR spectra of (*R*,*R*)-**3** were recorded in  $[D_8]$ toluene as a gelling solvent, and in CDCl<sub>3</sub> and [D<sub>6</sub>]DMSO representing nongelling solvents. The spectra in the lipophilic [D<sub>8</sub>]toluene [viscous solution; concentration of (R,R)-3 slightly below mgc] and CDCl<sub>3</sub> are shown in Figure 6 (a and b, respectively). The [D<sub>8</sub>]toluene spectrum shows two singlets corresponding to the biphenyl NH ( $\delta$  = 9.53 and 9.68 ppm; integral ratio 5:1), and two doublets corresponding to the C\*-NH protons ( $\delta$  = 8.56 and 7.69 ppm; integral ratio 5:1). In the CDCl<sub>3</sub> spectrum, the corresponding singlets appear at  $\delta$  = 8.91 and 9.19 ppm (integral ratio 3.8:1), and doublets at  $\delta$  = 7.87 and 7.51 ppm (integral ratio: 3.8:1). In both spectra, also the two doublets of the biphenyl C-3 hydrogens appear in the range  $\delta = 8.0-9.0$  ppm with intensity ratios corresponding to those measured for the NH signals. In the spectrum recorded in [D<sub>6</sub>]DMSO (Figure 6, c), also two biphenyl NH singlets ( $\delta$  = 9.66 and 9.58 ppm), two C\*-NH doublets ( $\delta$  = 8.39 and 8.32 ppm), and two biphenyl C-3-H doublets ( $\delta$  = 8.0–8.1 ppm) were observed, with intensity ratios of 1.15:1. These observations are consistent with a diastereomeric equilibrium containing 83 and 80 % of the predominating diastereomer in [D<sub>8</sub>]toluene and CDCl<sub>3</sub>, respectively, while in [D<sub>6</sub>]DMSO practically a 1:1 mixture of diastereomers was observed. The results clearly show that in both lipophilic solvents favouring formation of hydrogen bonds, the gelling [D<sub>8</sub>]toluene and the nongelling CDCl<sub>3</sub>, one diastereomer predominates, whereas in the hydrogen-bond-competitive [D<sub>6</sub>]DMSO solution, practically a 1:1 mixture of diastereomers is formed.

The X-ray molecular and crystal structures of rac-3 (Figures 3 and 4) show the presence of two intramolecular NH---OH hydrogen bonds and four intermolecular OH---O=C< hydrogen bonds, respectively. Since (R,R)-3 is capable of forming a gel with toluene, the <sup>1</sup>H NMR spectra of the gel sample were analysed to find out whether intra- and intermolecular hydrogenbonding motifs similar to those observed in the crystal structure could also stabilize the gel aggregates. The NH-temperature coefficients ( $\Delta \delta_{\rm NH} / \Delta T$  [ppm/K]) calculated from the temperature-dependent spectra (Figure S2, Supporting Information) show that with a temperature increase, the biphenyl NH of the major and minor diastereomer, and the C\*-NH of the minor diastereomer are only weakly shifted upfield ( $\Delta \delta_{\rm NH} / \Delta T =$  $3.3 \times 10^{-3}$ ;  $2.7 \times 10^{-3}$  and  $2.1 \times 10^{-3}$  ppm/K, respectively) compared to the strong upfield shift of the doublet due to the C\*-NH of the major diastereoizomer ( $\Delta \delta_{\text{NH}} / \Delta T = 11.1 \times 10^{-3} \text{ ppm} / 10^{$ K). This confirms the involvement of the C\*-NH of the major diastereomer in the intramolecular hydrogen bonding, and the lack of such hydrogen bonding in the less abundant dia-





Figure 6. <sup>1</sup>H NMR amide-NH proton regions of (R,R)-**3** in a) [D<sub>8</sub>]toluene; b) CDCl<sub>3</sub>; and c) [D<sub>6</sub>]DMSO.

stereomer. The results of an NH/D exchange experiment with a sample of (R,R)-3 in CDCl<sub>3</sub> solution support the above conclusion (Figure S3, Supporting Information). Both biphenyl NH singlets, as well as the lower intensity C\*-NH doublet, disappeared within 24 h after the addition of D<sub>2</sub>O. This indicates that these NH are free or only slightly involved in hydrogen bonding. In contrast, the H/D exchange of the higher intensity C\*-NH protons was found to be much slower, and the signal was still observable after 7 d. Since (R,R)-3 should be much less aggregated in the CDCl<sub>3</sub> solution than in the toluene gel sample, the observed very slow NH/D exchange rate of the C\*-NH protons of the predominating diastereomer can be best explained by their involvement in strong intramolecular hydrogen bonding. These results also suggest that the structure of the predominating diastereomer closely resembles that of the intramolecularly hydrogen bonded (R,aR,R)-3 enantiomer found in the crystal structure of rac-3 (Figure 3), and that the less abundant diastereomer [i.e., (R,aS,R)-3] lacks the intramolecular C\*-NH---HO bonds. As additional support for the above conclusion, in the intramolecularly hydrogen bonded structure the biphenyl NH are located close to the biphenyl and oxalamide carbonyl  $\pi$ systems (Figure S4, Supporting Information), and should be more shielded (observed  $\delta$  = 9.53 ppm) than the biphenyl NH of the less abundant diastereomer (observed  $\delta$  = 9.68 ppm, Figure 6, a).

To find out whether both, or exclusively one of the two diastereomers (*R*,*aR*,*R*)- and (*R*,*aS*,*R*)-**3** is assembled in the [D<sub>8</sub>]toluene gel aggregates, a variable-temperature <sup>1</sup>H NMR investigation was carried out in the presence of tetrachloroethane as an internal standard. When the temperature was increased, the intensity of all the gelator signals increased due to disassembly of NMR-silent gel network into smaller NMR-observable aggregates.<sup>[16,17]</sup> In the <sup>1</sup>H NMR spectrum of the [D<sub>8</sub>]toluene gel sample ( $c = 1.48 \times 10^{-2}$  M) recorded at room temperature, signals of the dissolved major and minor diastereomer could be observed (Figure S5, Supporting Information). The variations of the rela-



tive concentrations of the dissolved major (R,aR,R)- $\mathbf{3}_{diss}$  and minor (R,aS,R)<sub>diss</sub>, diastereomers, as well as that of the assembled diastereomer, that occur with an increase in temperature were calculated based on the intensity changes of the biphenyl NH, C\*-NH and biphenyl C-3-H signals relative to the intensity of the internal standard (Figure 7, a).



Figure 7. (a) Variation of relative concentrations of (R,aR,R)- $\mathbf{3}_{diss}$  ( $\blacksquare$ ), (R,aS,R)- $\mathbf{3}_{diss}$  ( $\blacksquare$ ), and (R,aR,R)- $\mathbf{3}_{ass}$  ( $\blacktriangle$ ) in the temperature-dependent <sup>1</sup>H NMR spectra of (R)- $\mathbf{3}$  [D<sub>8</sub>]toluene gel; (b) variation of (R,aR,R)- $\mathbf{3}_{diss}/(R,aS,R)$ - $\mathbf{3}_{diss}$  ratio with temperature increase.

The concentrations of the assembled gelator were calculated from the known total concentration of (R,R)-3 and the NMRdetermined concentrations of the dissolved diastereomers. The concentration of (R,aR,R)-3<sub>diss</sub> shows a sharp increase between 35 and 50 °C, corresponding to the gel melting interval (independently determined  $T_{\rm q}$  = 54 °C). The concentration of minor diastereomer (R,aS,R)-3<sub>diss</sub> shows a slow and steady increase between 25-90 °C (Figure 7, a). The concentration curve of the assembled gelator shows a sharp decrease in the same temperature range (Figure 7, a, green curve), and is clearly related to the (R,aR,R)-3<sub>diss</sub> concentration curve. This result shows that exclusively the (R,aR,R) diastereomer is assembled into the gel network the due to a diastereoselective self-sorting process.<sup>[3a,18]</sup> The variation of the (R,aR,R)-3<sub>diss</sub>/(R,aS,R)<sub>diss</sub>-3 diastereomeric ratio (Figure 7, b) shows that it changes from approximately 2.5:1 in the sol at 90 °C to 8.5:1 in the gel state at 20-40 °C.

NOESY experiments with (R,R)-**3** [D<sub>8</sub>]toluene gel and [D<sub>6</sub>]DMSO solution samples were run to get additional information on the gelator conformations in both systems, and to identify intermolecular NOEs, which could provide information on the primary organization of gelator molecules in the aggregates (Figure S6, Supporting Information). As was recently shown, in the gel phase smaller aggregates dissolved in the entrapped solvent can be observed by NMR spectroscopy, and these have



organization similar to that in the gel fibres.<sup>[17]</sup> The NOE interactions observed for the major diastereomer and identified as intramolecular (H/H distances in the molecular model below 5 Å; red dotted arrows) or intermolecular (H/H distances exceeding 5 Å; blue arrows) are shown in Figure 8. The intramolecular NOEs correspond nicely to the distances between the respective protons measured from the intramolecularly hydrogenbonded crystal-structure conformation (Figure 3, a). The intramolecular NOEs found in the [D<sub>6</sub>]DMSO solution sample were similar, except for additional NH/HO and iPr-CH/HO interactions (black arrows), which were not identified in the NOESY spectrum of the gel due to the uncertain position of the OH signal. The latter observations suggest that the conformation of the amino alcohol/oxalamide arm is similar in the gel aggregates and in the DMSO solution. This could be explained by taking into account the conformations of the amino acid and the amino alcohol/oxalamide fragments found earlier in the X-ray structures of various bis(amino acid or amino alcohol) oxalamide gelators; those conformations as well as the crystal structure conformation of 3 (Figure 3, a) are characterized by the syn-periplanar positions of the C\*-H and the oxalamide carbonyl group (Figure 8, b, partial Newman projection of the C\*-NH bond).<sup>[19]</sup> Such a conformation is apparently the most stable one due to the lowest steric hindrance between the C\*-H (with H corresponding to the small group, S) and the oxalamide carbonyl group, compared to larger hindrance in the other possible conformations with the M or L group close to the carbonyl group. Consequently, the two larger CH\*-substituents (iPr as L, and hydroxymethylene as M in the case of 3) are located above and below the oxalamide plane, resulting in a rigid conformation with little rotational freedom around the C\*H-NH bond.



Figure 8. (a) NOE effects observed in (*R*,*R*)-**3** [D<sub>8</sub>]toluene gel and [D<sub>6</sub>]DMSO solution samples. Intramolecular NOEs observed in both [D<sub>8</sub>]toluene gel and [D<sub>6</sub>]DMSO solution samples (red dotted arrows) and NOEs observed only in the [D<sub>6</sub>]DMSO solution sample (black dotted arrows). Proton–proton distances in Å units measured from the extended molecular model (SYBYL package) with *syn*-periplanar C\*-H/carbonyl position are given above the arrows. The blue arrows connect protons at distances exceeding 5 Å, thus indicating intermolecular NOEs observed only in the [D<sub>8</sub>]toluene gel sample. (b) Partial Newman projection of valinol-oxalamide fragment showing *syn*-periplanar arrangement of C\*-H (small group, S)/oxalamide carbonyl, and positions of CH<sub>2</sub>OH (medium group, M) and *i*Pr (large group, L).

Hence, similar conformations of the amino alcohol/oxalamide arms in **3** can be expected to appear in the gel aggregates, in solution, and in solid-state aggregates.

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NOE interactions of the biphenyl C-3-H with the *i*Pr methyl and methyne protons were observed in the toluene gel spectrum, despite the fact that their intramolecular distance exceeds 6 Å. This points towards an intermolecular origin for these NOEs. To observe such NOEs, the *i*Pr and biphenyl groups should be located in close proximity in the aggregates, similar to the packing arrangement of the enantiomers in the crystal structure of *rac*-**3** (Figure 3, b). The intermolecular distances between the biphenyl C-3-H and the *i*Pr-CH and the methyl protons in the crystal structure of *rac*-**3** are 2.3 and 3.5 Å, respectively. These distances would allow the observation of intermolecular NOEs. This fact suggests that a similar arrangement of (*R*,*aR*,*R*)-**3** with a consecutive up and down orientation of biphenyl groups could be expected in the gel assemblies.

The observed central (*R*) and (*S*) to axial (*aR*) and (*aS*) chirality transfer, respectively, appears to be the consequence of intramolecular hydrogen bonding. The intramolecular C\*-NH---OH bonding in the case of the (*R*) centres is possible for the axially chiral (*aR*) conformation of the biphenyl system without violating the *syn*-periplanar arrangement of the C\*-H and the neighbouring oxalamide carbonyl group (Figure 9, a). However, such hydrogen bonding is not possible for the (*R*) centres and the (*aS*) configuration of the biphenyl system (Figure 9, b). In a molecular model of the latter conformation, the C\*-NH and CH<sub>2</sub>OH groups of neighbouring arms are over 7 Å apart, and may come within the hydrogen-bonding distance by rotation around the C\*H–NH bond, and by violation of the energetically most stable C\*-H/>C=O *syn*-periplanar arrangement.



Figure 9. Conformations of (a) intramolecularly hydrogen bonded (R,aR,R)-**3** and (b) non-hydrogen bonded (R,aS,R)-**3** generated by molecular modelling (SYBYL of TRIPOS Inc. software).

# Concentration-Dependent Formation of Equilibrium and Nonequilibrium Gel States

The properties of (R,R)-**3** toluene gels were assessed by constructing phase diagrams showing the dependence of gel melting temperatures ( $T_g$  [°C], determined by tube inversion method) on gelator concentration. In the preliminary experiments, highly peculiar behaviour of gels prepared with (R,R)-**3** concentrations in the 10<sup>-3</sup> M range was observed. In some cases, gels were formed at lower concentrations, and failed to form at higher concentrations, and  $T_g$  values showed highly irregular dependence on the gelator concentrations. Also, when the heating/cooling procedure was repeated with the same sample, the  $T_g$  values obtained were found to differ considerably. In contrast, gels formed in the  $10^{-2}$  M range formed immediately by cooling to room temperature, and showed the common  $T_g$  increase with increasing gelator concentration. Only slight variations of the  $T_g$  values within an ageing time range of 24–216 h were observed (Table 2), showing that the gels were at thermodynamic equilibrium.

Table 2.  $T_g$  [°C] values determined after specified ageing intervals [h] of the (*R*,*R*)-**3** toluene gel samples<sup>[a]</sup> in the 10<sup>-2</sup>  $\,$  concentration range.

<i>с</i> [10 <sup>-2</sup> м]	Ageing interval [h]					
	24	48	72	144	216	
3.12	65	62	63	63	64	
2.35	61	59	61	62	60	
1.56	56	53	54	54	54	

[a] Gels were prepared in NMR tubes.

The determination of the  $T_g$  values of the gels formed in the lower concentration range was carefully repeated in a way that for each specified concentration five gel samples were prepared by the heating/cooling procedure, and each sample of the specified concentration was aged from 24 up to 216 h at +4 °C before the  $T_g$  was determined. In this way, each sample was subjected to a single heating/cooling step before the determination of the  $T_g$ . For the gel samples with 2.4, 3.6, 4.8, 6.0, and  $7.2 \times 10^{-3}$  M concentrations aged for 24, 48, 72, and 144 h (Figure 10, a–d) a highly irregular variation of the  $T_g$  values with both increasing gelator concentration and ageing time was observed. For the 24 h aged sample (Figure 10, a) the  $T_g$  values increased from 33 to 47 °C for concentrations of 2.4, 3.6, 4.8, and  $6.0 \times 10^{-3}$  M, while for the highest concentration of



Figure 10. Dependence of (*R*)-**3** toluene gel melting temperatures ( $T_{g}$  [°C]) on gelator concentration (c = 2.4, 3.6, 4.8, 6.0, and  $7.2 \times 10^{-3}$  M) for gel samples aged for (a) 24, (b) 48, (c) 72, (d) 144, and (e) 216 h.





 $7.2 \times 10^{-3}$  m, only a weak gel with partial fluidity was obtained ( $T_{q}$  denoted as 25 °C). Surprisingly, all of the 48 h aged samples gave partially fluid weak gels (Figure 10, b). The samples aged for 72 and 144 h (Figure 10, c and d) showed irregular meltingtemperature changes with increasing concentrations. Only the 216 h aged samples (Figure 10, e) showed the expected  $T_{\rm q}$  increase with increasing gelator concentration, revealing that ageing between 144 and 216 h is needed for each sample of specified concentration to reach thermodynamic equilibrium. The variation of the  $T_{q}$  values did not change when the ageing time at +4 °C was lengthened for any of the tested concentrations; the  $T_{\alpha}$  values of more aged samples were often found to be lower than those of less aged samples (Figure S7, Supporting Information). These results imply that the low self-assembly rate may not be the major factor causing the irregular  $T_{\alpha}$ /ageing time relationship, since in that case, the  $T_{\alpha}$  values should increase with prolonged ageing, due to a higher degree of aggregation. The results presented in Figure 10 (a-e) clearly show that in the  $10^{-3}$  M concentration range, nonequilibrium gel states are formed that need up to 216 h of ageing at +4 °C to reach thermodynamic equilibrium.

DSC measurements support the above conclusions. For the gel formed at a concentration of  $7.2 \times 10^{-3}$  M, only weak transitions were seen. One or two endothermic transitions, and in some cases also exothermic transitions appearing at different temperatures could be observed. The transitions observed indicate the formation of different kinds of assemblies. The thermograms obtained are different for each ageing time, and the gel melting temperatures vary irregularly with increasing ageing times (Figure 11, a and Table S2, Supporting Information).



0 °C (4.3 and 2.1 kJ/mol). This indicates a low level of aggregation that becomes higher for the sample aged for 2 d at +4 °C (15.9 kJ/mol). The highest enthalpy change of 23.9 kJ/mol (sum of two transitions) was measured for the sample aged for 8 d at room temp., which indicates that a higher extent of aggregation results from ageing at a higher temperature. In contrast, for the 7.2 × 10<sup>-2</sup> M gel, a much stronger single endothermic transition was observed for the sample aged for just 30 min at 0 °C ( $\Delta H = 14.4$  kJ/mol; Table S2, Supporting Information). This gel also gave a much higher gel melting temperature ( $T_g = 69.1$  °C). These two values are only slightly different for the samples aged for 2 and 14 d at +4 °C, which is consistent with a gel state at thermodynamic equilibrium (Figure 11, b and Table S2, Supporting Information).

The gel formation/melting diagrams for the (*R*,*R*)-**3** toluene gel determined by <sup>1</sup>H NMR spectroscopy (Figure 7, a and b) clearly show that the (*R*,*aR*,*R*)<sub>diss</sub>-**3**/(*R*,*aS*,*S*)<sub>diss</sub>-**3** diastereomeric ratio varies from 2.5:1 in the sol state at 90 °C to 19:1 [sum of the network-assembled and dissolved gelator; (*R*,*aR*,*R*)-**3**<sub>ass</sub> + (*R*,*aR*,*R*)-**3**<sub>diss</sub>] in the gel state at 20 °C (Figure 7, a). Hence, in the gelation process starting from hot sol, at least two coupled equilibria are involved, that of the nongelling (*R*,*aS*,*R*)-**3** to gelling (*R*,*aR*,*R*)-**3** diastereomer interconversion, and that of the (*R*,*aR*,*R*)-**3** assembly/disassembly equilibrium. The formation of nonequilibrium gel states at the lower concentration could be explained by kinetic effects as a result of the slow nongellingto-gelling diastereomer interconversion step becoming the rate-determining step in the gelation.

We have also found that the formation of gels from  $10^{-3}$  M samples could be greatly accelerated by using ultrasound. The application of sonication is reported to increase gelling ability in some cases through local temperature increases, which induce disassembly of the nonproductive gelator aggregates and enable productive assembly into fibrous aggregates that can entangle and form gels.<sup>[20]</sup> The observed effect of sonication in our case could be explained both by an increased interconversion rate of the nongelling (R,aS,R)-3 into the gelling (R,aR,R)-3 diastereomer as a result of temperature increase, and by sonication-induced disassembly of nonproductive (R,aR,R)-3 or (R,aS,R)-3 aggregates indicated by appearance of two transitions in DSC experiments. In conclusion, all the experimental results taken together suggest that the peculiar behaviour of gels formed in the 10<sup>-3</sup> M concentration range may be best explained by the involvement of multiple coupled equilibria, as shown in Figure 12.



Figure 11. DCS heating diagrams of (*R*,*R*)-**3** toluene gels at: a)  $7.2 \times 10^{-3}$  m concentration, ageing time: 1 min at 0 °C (black), 2 d at +4 °C (red), 4 d at +4 °C (blue); 8 d at +4 °C (gray); and b)  $7.2 \times 10^{-2}$  m concentration, ageing time: 30 min at 0 °C (black), 1 d at +4 °C (red), and 14 d at +4 °C (blue); for the corresponding cooling diagram, see Figure S8 in the Supporting Information.

The sums of the enthalpy changes determined for both transitions are very low for the samples with short ageing times at

Figure 12. Multiple equilibria involved in gelation: dissolved (R,aR,R)- $\mathbf{3}_{diss}/(R,aS,R)$ - $\mathbf{3}_{diss}$  diastereomer interconversion, coupled with (R,aR,R)- $\mathbf{3}_{diss}$  productive aggregation (self-assembly) into gel network [(R,aR,R)- $\mathbf{3}_{Pagg}$ ], and diastereomer nonproductive (NPagg) aggregations in the sol phase.



# Conclusions

Chiral 2,2'-biphenyl-substituted amino alcohol oxalamide gelators **3** and **4** were prepared and studied as rare examples of proatropisomeric chiral gelators, having both central and axial chirality (Figure 1). The results show that type I and type II gelators have dramatically different properties. With type I gelators, central-to-axial chirality transfer was found to occur only upon self-aggregation.<sup>[7]</sup> In contrast, the crystal structure of rac-3, together with the results of the concentration- and temperature-dependent CD and <sup>1</sup>H NMR studies, revealed that in gelled toluene and nongelled chloroform and DMSO, a mixture of (R,aR,R)-3 and (R,aS,R)-3 diastereomers is formed due to centralto-axial chirality transfer. Crystallographic and spectroscopic (<sup>1</sup>H NMR, CD) evidence supports an intramolecularly C\*-NH--OH hydrogen-bonded structure for the major (R,aR,R)-3 diastereomer, and a structure for the minor (R,aS,R) diastereomer lacking such hydrogen bonding (Figure 9). The temperaturedependent NMR study of the (R,R)-3 solution samples  $(CDCl_3)$ and [D<sub>6</sub>]DMSO) and of the [D<sub>8</sub>]toluene gel revealed the occurrence of thermally induced diastereomer interconversion and diastereomer self-sorting processes, the latter resulting in the self-assembly into the gel network exclusively of the major (R,aR,R)-3 diastereomer.

The experimental results described for the (R,R)-3 toluene gel show that coupled equilibria comprising network-assembly/ dissolution of (R,aR,R)-3 and diastereomer interconversion are involved, giving gels with dramatically different properties in different (10<sup>-2</sup> and 10<sup>-3</sup> M) concentration ranges. At lower concentrations, gelation is very slow, and needs 9 d of ageing at +4 °C to reach equilibrium (Figure 10). The formation such longlived nonequilibrium states could be explained by kinetic effects, due to a slow nongelling-to-gelling diastereomer interconversion step becoming the rate-determining step at certain concentrations. It was also found that gelation could be greatly accelerated by sonication. This, together with the DSC results, which indicate the formation of two kinds of aggregates, suggest the formation of nonproductive assemblies of gel-forming (R,aR,R)-3 or nongelling (R,aS,R)-3 diastereomers. The described gelation of toluene by (R,R)-3 represents a highly complex and unique gelation system comprising central-to-axial chirality transfer, diastereomer interconversion, diastereoselective selfsorting, and multiple coupled equilibria. It gives equilibrated and long-lived nonequilibrium gel systems, depending on the gelator concentration. A detailed understanding of such dynamic systems of higher complexity could be of the utmost interest for the future design of soft materials and systems for advanced applications.

**Supporting Information** (see footnote on the first page of this article): Equipment, procedures, and experimental conditions; temperature-dependent FTIR spectra, DSC spectra, NOESY spectra of gel samples, NMR spectra of synthesized compounds.

## Acknowledgments

This work was supported by the Croatian Ministry of Science, Education and Sports (project number 098-0982904-2912) and



the Croatian Science Foundation (HrZZ) (project number IP-11-2013-7387).

**Keywords:** Supramolecular chemistry · Self-assembly · Chirality transfer · Sol-gel processes · Gels

- [1] For some recent reviews on low-molecular-weight gelators, see: a) K. Hanabusa, M. Suzuki, Polym. J. 2014, 46, 776–782; b) Z. F. Sun, Q. Y. Huang, T. He, Z. Y. Li, Y. Zhang, L. Z. Yi, ChemPhysChem 2014, 15, 2421–2430; c) X. D. Yu, L. M. Chen, M. M. Zhang, T. Yi, Chem. Soc. Rev. 2014, 43, 5346–5371; d) Q. i. Zhenhui, C. A. Schalley, Acc. Chem. Res. 2014, 47, 2222–2233; e) P. F. Duan, H. Cao, L. Zhang, M. H. Liu, Soft Matter 2014, 10, 5428–5448; f) C. Tomasini, N. Castellucci, Chem. Soc. Rev. 2013, 42, 156–172; g) J. W. Steed, Chem. Commun. 2011, 47, 1379–1383; h) J. W. Steed, Chem. Soc. Rev. 2010, 39, 3686–3699; i) A. Ayaghosh, V. K. Praveen, C. Vijayakumar, Chem. Soc. Rev. 2008, 37, 109–122; j) P. Dastidar, Chem. Soc. Rev. 2008, 37, 2699–2715; k) M. Sada, N. Takeuchi, M. Fujita, M. Numata, S. Shinkai, Chem. Soc. Rev. 2007, 36, 415–435; l) M. George, R. G. Weiss, Acc. Chem. Res. 2006, 39, 489–497; m) J. van Esch, B. L. Feringa, Angew. Chem. Int. Ed. 2000, 39, 2263–2266; Angew. Chem. 2000, 112, 2351–2354.
- [2] a) K. K. Diehn, O. H. Hyuntaek, R. Hashemipour, R. G. Weiss, S. R. Raghavan, *Soft Matter* **2014**, *10*, 2632–2640; b) A. R. Hirst, S. Roy, M. Arora, A. K. Das, N. Hodson, P. Murray, S. Marshall, N. Javid, J. Sefcik, J. Boekhoven, J. H. van Esch, S. Santabarbara, N. T. Hunt, R. V. Ulijn, *Nature Chemistry* **2010**, *2*, 1089–1094; c) A. R. A. Palmans, E. W. Meijer, *Angew. Chem. Int. Ed.* **2007**, *46*, 8948–8968; *Angew. Chem.* **2007**, *119*, 9106–9126; d) J. J. D. de Jong, T. D. Tiemersma Wegman, J. H. van Esch, B. L. Feringa, J. Am. Chem. Soc. **2005**, *127*, 13804–13805; e) A. Aggeli, I. A. Nyrkova, M. Bell, R. Harding, L. Carrick, T. C. B. McLeish, A. N. Semenov, N. Boden, *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 11857–11862; f) P. Jonkheijm, P. van der Schoot, A. P. H. J. Schenning, E. W. Meijer, *Science* **2006**, *313*, 80–83.
- [3] a) D. K. Smith, Chem. Soc. Rev. 2009, 38, 684–694; b) A. Brizard, R. Oda, I. Huc, Top. Curr. Chem. 2005, 256, 167–218.
- [4] a) M. Liu, L. Zhang, T. Wang, Chem. Rev. 2015, 115, 7304–7397; b) Z. Shen, T. Wang, M. Liu, Langmuir 2014, 30, 10772–10778; c) X. Luo, B. Liu, Y. Liang, Chem. Commun. 2001, 1556–1557; d) J. Makarević, M. Jokić, Z. Raza, Z. Štefanić, B. Kojić-Prodić, M. Žinić, Chem. Eur. J. 2003, 9, 5567– 5580; e) V. Čaplar, M. Žinić, J.-L. Pozzo, F. Fages, G. Mieden-Gundert, F. Vögtle, Eur. J. Org. Chem. 2004, 19, 4048–4059.
- [5] C. Wang, D. Zhang, D. Zhu, Langmuir 2007, 23, 1478–1482.
- [6] B. Escuder, M. LLusar, J. F. Miravet, J. Org. Chem. 2006, 71, 7747-7752.
- [7] J. Makarević, Z. Štefanić, L. Horvat, M. Žinić, Chem. Commun. 2012, 48, 7407–7409.
- [8] a) S. Superchi, R. Bisaccia, D. Casarini, A. Laurita, C. Rosini, *J. Am. Chem. Soc.* 2006, *128*, 6893–6902; b) E. Manna, A. Montero, M. A. Maestro, B. Herradon, *Helv. Chim. Acta* 2002, *85*, 3624–3638; c) B. Herradon, A. Montero, E. Manna, M. A. Maestro, *CrystEngComm* 2004, *6*, 512–521.
- [9] R. E. Moore, A. Furst, J. Org. Chem. 1958, 23, 1504-1506.
- [10] a) X. Luo, B. Liu, Y. Liang, *Chem. Commun.* **2001**, 1556–1557; b) J. Makarević, M. Jokić, Z. Raza, Z. Štefanić, B. Kojić-Prodić, M. Žinić, *Chem. Eur. J.* **2003**, *9*, 5567–5580; c) V. Čaplar, M. Žinić, J.-L. Pozzo, F. Fages, G. Mieden-Gundert, F. Vögtle, *Eur. J. Org. Chem.* **2004**, 4048–4059.
- [11] H. Suzuki, Electronic Absorption Spectra and Geometry of Organic Molecules, Academic Press, New York, 1967, p. 262 and 272.
- [12] K. Mislow, E. Bunnenberg, R. Records, K. Wellman, C. Djerassi, J. Am. Chem. Soc. 1963, 85, 1342–1349.
- [13] J.-P. Mazaleyrat, K. Wright, A. Gaucher, N. Toulemonde, M. Wakselman, S. Oancea, C. Peggion, F. Formaggio, V. Setnicka, T. A. Keiderling, C. Toniolo, J. Am. Chem. Soc. 2004, 126, 12874–12879.
- [14] T. Mori, Y. Inoue, S. Grimme, J. Phys. Chem. A 2007, 111, 4222-4234.
- [15] C. Bustamante, I. Tinolo Jr., M. F. Maestreo, Proc. Natl. Acad. Sci. USA 1983, 80, 3568–3572.
- [16] a) J. Makarević, M. Jokić, B. Perić, V. Tomišić, B. Kojić-Prodić, M. Žinić, *Chem. Eur. J.* **2001**, *7*, 3328–3341; b) B. Escuder, M. Llusar, J. F. Miravet, J. Org. Chem. **2006**, *71*, 7747–7752; c) 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*, 9113–9121.





- [17] S. Bouguet-Bounnet, M. Yemloul, D. Canet, J. Am. Chem. Soc. 2012, 134, 10621–10627.
- [18] a) M. M. Safont-Sempere, G. Fernandez, F. Wurthner, Chem. Rev. 2011, 111, 5784–5814; b) K. Osowska, O. Š. Miljanić, Synlett 2011, 1643–1648.
- [19] L. Frkanec, M. Žinić, Chem. Commun. **2010**, 46, 522–537.
- [20] a) D. Bardelang, Soft Matter 2009, 5, 1969–1971; b) J. Wu, T. Yi, T. Shu, M. Yu, Z. Zhou, M. Xu, Y. Zhou, H. Zhang, J. Han, F. Li, C. Huang, Angew. Chem. Int. Ed. 2008, 47, 1063–1067; Angew. Chem. 2008, 120, 1079–1083.

Received: October 1, 2015 Published Online: January 22, 2016