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Gelation Ability of Novel Oxamide-Based Derivatives Bearing a Stilbene as a Photo-Responsive Unit

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Oxamide-based derivatives containing one or two oxamide moieties coupled to the 4- or 4,4′-positions of *cis*- and *trans*-stilbene have been synthesised. In order to modulate the solvent gelation tendencies, a series of derivatives with modified terminal functions were prepared from them. The *trans*-stilbene dioxamide-based derivatives were found to be sparingly soluble or insoluble in water and in organic solvents, whereas the *trans*-stilbene monooxamide-based derivatives are soluble in most organic solvents. Incorporation of a C_{12} alkyl chain in the structure of the latter compounds results in a decreased solubility but in an increased gelation tendency of the substances. The ethyl ester oxamide-based derivative *trans*-**3a** and the amino acid oxamide-based derivative *trans*-**3e** act as efficient gelators of various organic solvents. In contrast, *cis*-**3a** shows a poor gelation ability or none at all, owing to its good solubility. Considering the difference in gelation abilities of the compounds *trans*-**3a** and *cis*-**3a** and the photo-responsive conformational changes of the stilbene part of the molecule, a controlled gelation by light was achieved. FT-IR and ^{1}H NMR spectroscopic measurements support the view that hydrogen bonding between the oxamide fragments plays an important role in gel formation.

Introduction

Some low-molecular-weight organic molecules are capable of forming thermoreversible and stable gels with water[1] and with various organic solvents.[2] Owing to a successful design and synthesis of these small gelling molecules, the diversity of gelators has been steadily increasing. The preparation of substances with a gelation ability that can be affected by external stimuli such as heat, light, magnetic or electric field, pH, or by chemical reactions seems to be particularly attractive.[3] Apart from temperature, which is the most commonly used tool for stimulating a gelation process, the development of gelling systems controlled by light has attracted much attention. A promising approach towards such smart gels is the introduction of a photo-responsive unit into the structure of the gelator molecule. Photoinduced changes in the structure[4–8] or geometry[9–15] of the integrated photochromic moiety result in gel formation and dissolution, potentially reversibly. The most frequently exploited process involving interconversion of two different molecule forms is photoisomerisation.[9–15] Among gelators capable of photoreversible gelation based on the difference in the gelation ability of *cis*- and *trans*-isomers, the majority incorporate an azobenzene unit.[9–12] Owing to its unique photochemistry[16] and molecular structure, which is similar to that of azobenzene, stilbene is a molecule of choice for the synthesis of gelators that can form gels that are sensitive to light.

In light of the excellent gelation ability of molecules containing oxamide fragments,[17–19] and considering the well-known phenomenon of stilbene photoisomerisation[16] as well as the gelation tendency of stilbenoid compounds,[13,20,21] in this work we report the synthesis of new stilbene oxamide-based gelators. A variety of oxamide compounds bearing one or two oxamide moieties at the *para* position of *cis*- and *trans*-stilbenes has been prepared and the gelation behaviour of the synthesised substances tested in water and in various organic solvents. The photoinduced gelation of ethanol by the selected pair of isomers is also investigated.

Results and Discussion

Rational Design

Compounds containing an oxamide function as a self-complementary binding group have been found to form thermoreversible and stable gels with water and with various organic solvents.[17–19] It has also been demonstrated that intermolecular lipophilic interactions between alkyl substituents and intermolecular hydrogen bonding involving oxamide fragments stabilize the networks of a hydro- and organogel, respectively. In addition, an irreversible photoinduced gelation system on the principle of photo-

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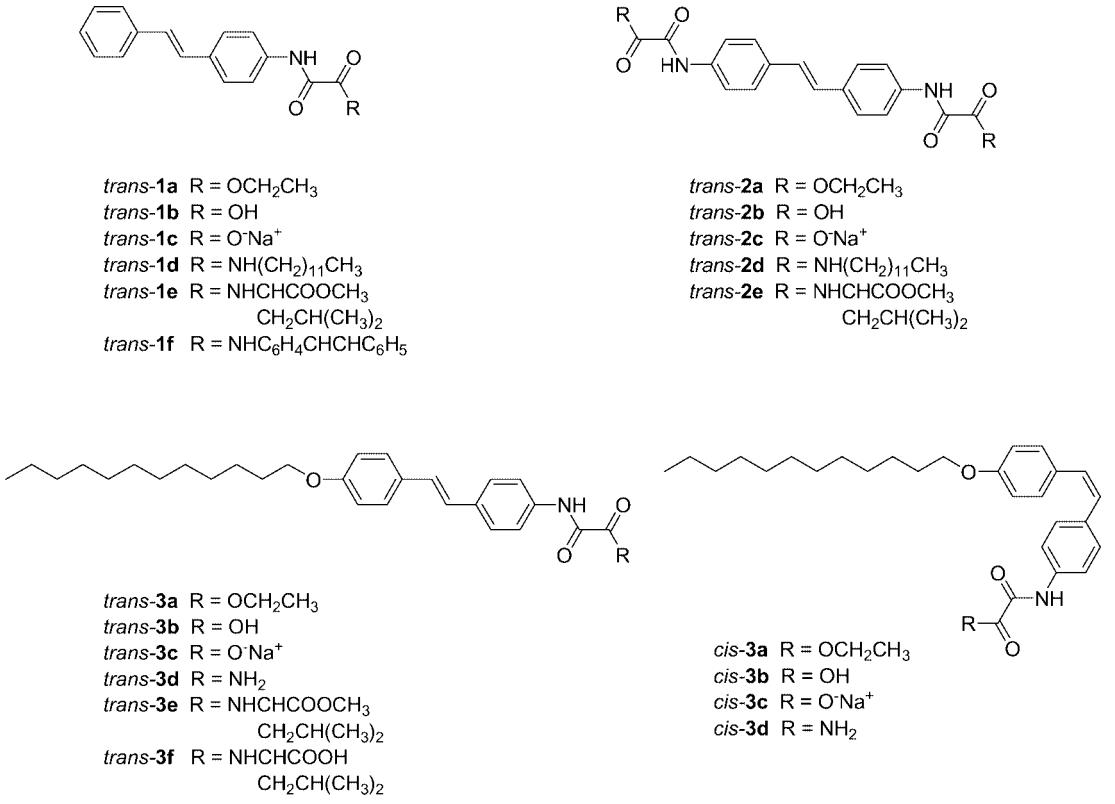


Scheme 1. Structures of stilbene oxamide-based compounds.

chemical isomerisation of non-gelling maleic acid amide to gelling fumaric acid amide has been prepared,[14] thereby indicating that incorporation of a photo-responsive unit in the structure of an oxamide-based gelator could lead to light-sensitive gels.

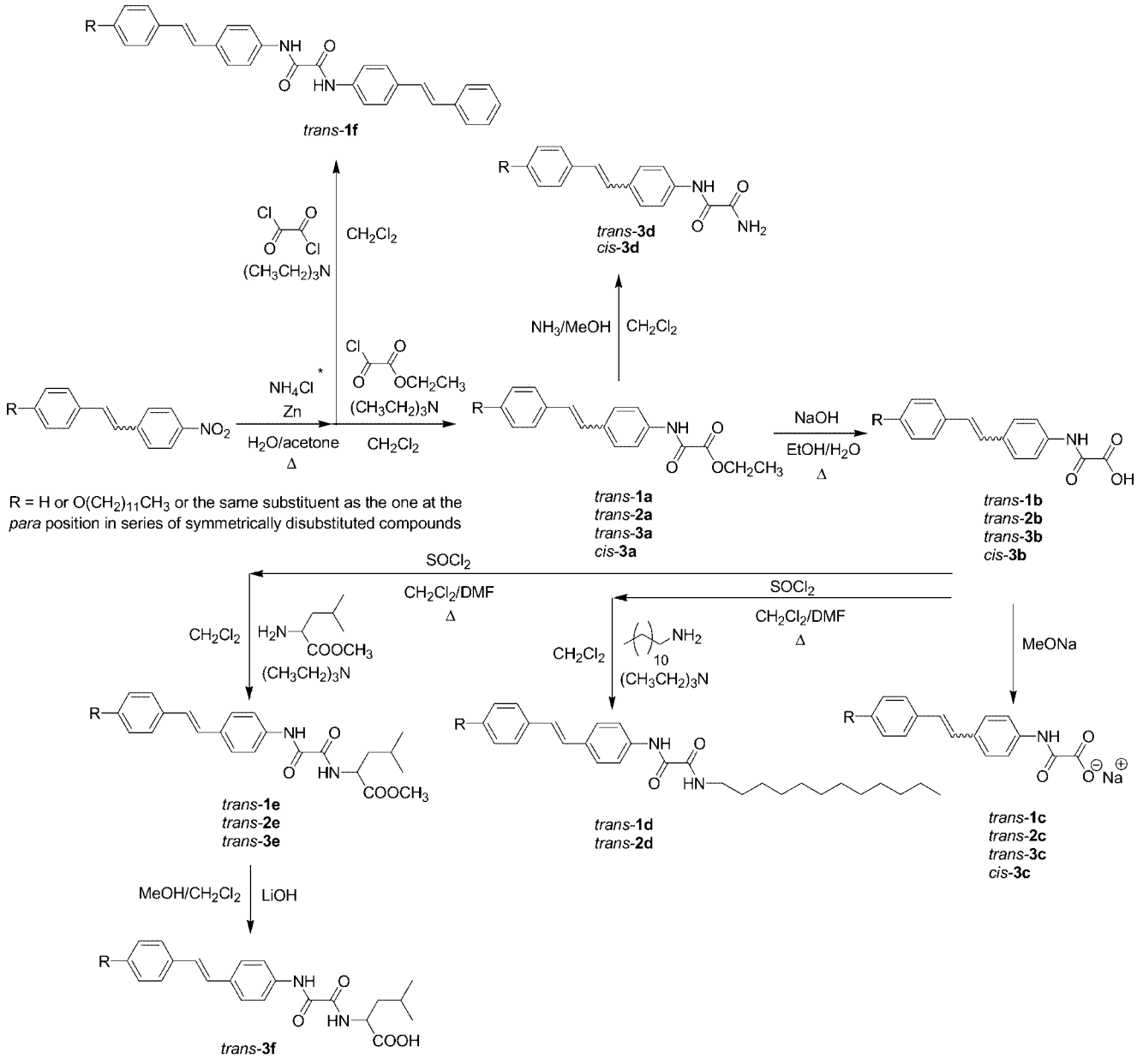
In light of the well-known *cis*/*trans* photoisomerisation of the stilbene molecule,[16] the stilbene skeleton was chosen to act as a photo-responsive unit, and stilbenoid compounds bearing one or two oxamide moieties at the *para* position of the stilbene molecule were synthesised (Scheme 1). In order to modulate the solvent gelation tendencies, a series of derivatives with modified terminal functions were prepared. Based on the strong stabilisation of gel aggregates observed in gelators possessing terminal sodium carboxylate groups,[22] the preparation of sodium salts of the corresponding carboxylic acids was carried out, and owing to the good gelation ability of monoalkyloxamide amphiphiles,[23] some derivatives containing a long lipophilic chain, (C_{12}) either bound directly to an oxamide fragment or as an oxyalkyl substituent on a stilbene unit, were also synthesised. Due to the fact that the stereogenic centre in the oxamide-based gelator molecule contributes to its gelation tendency,[17–19] an amino acid (L-leucine) was included in the structure of some derivatives.

With regard to the difference in solubility of the *cis* and *trans* isomers, it was assumed that the *trans* derivative would act as a better gelator than the corresponding *cis* isomer. For this reason, only the preparation of *trans* compounds with significant gelation properties was followed by synthesis of their *cis* isomers.

Synthesis

The Wittig reaction is a popular method for the preparation of stilbenes[24] as the availability of the starting materials and simple and mild reaction conditions override drawbacks such as separation of the product from triphenylphosphane oxide and the formation of a mixture of *cis* and *trans* isomers. Consequently, the arylmethyl bromide was treated with triphenylphosphane to give the arylmethyltriphosphonium bromide.[25] This phosphonium salt was deprotonated to the corresponding phosphorus ylide and then treated with an aryl aldehyde. One or both of the aryl reactants can be substituted by a nitro group depending on the final mono- or dioxamide-based compound required. This preparation of nitrostilbenes was followed by their reduction to aminostilbenes by treatment with zinc and ammonium chloride[26] or stannous chloride dehydrate.[27] The oxamide ethyl ester derivatives were obtained by reaction of the ethyl oxalyl chloride with the amino group of the stilbenes (Scheme 2). The resulting esters were saponified with sodium hydroxide to yield the neutral carboxylic forms after hydrolysis. The sodium salts were prepared by treatment of the carboxylic compounds with sodium methoxide, whereas dissolution of the ethyl ester derivatives in saturated ammonia/methanol solution gave the amides. Acyl chlorides were prepared in order to couple a C_{12} alkyl chain or L-leucine to the oxamide part of the molecule.[28]

Apart from the *trans* isomers of stilbene mono- and dioxamide derivatives, 4′-dodecyloxystilbene oxamide compounds were obtained in the *trans* as well as in the *cis* form,



* Reduction of 4,4'-dinitro-*trans*-stilbene with $SnCl_2$ in EtOH

Scheme 2. Synthesis of stilbene oxamide-based derivatives.

except for the amino acid derivative; in this case only a *trans* isomer was synthesised. The reaction via the acyl chloride, which was prepared from the starting *cis* carboxylic acid derivative, yielded the *trans* product, whereas the condensation reaction with dicyclohexylcarbodiimide (DCC) did not give the expected compound.[29] The synthesis of the *cis*-isomer failed, most likely due to the reaction conditions. We assume that traces of chlorine formed during the preparation of the acyl chloride induce isomerisation of the *cis* isomers into the energetically more favourable *trans* isomers. Upon peptide condensation, however, an adjacent carbonyl group could lower the reactivity of the target carbonyl group that should have reacted with the amino function of the amino acid.

Gelation Studies

The gelation behaviour of the prepared compounds was investigated in water and in various organic solvents. The ethyl ester derivative *trans*-**1a** and the carboxylic derivative *trans*-**1b** of *trans*-stilbene monooxamide compounds were found to be soluble in almost all of the organic solvents tested (Table 1). Introduction of a metal ion into the struc-

ture of *trans*-**1c** resulted in a poor solubility of this compound. The long-chain derivative *trans*-**1d** is insoluble in alcohols and precipitates from other organic solvents. In the series of derivatives investigated only compound *trans*-**1e**, which bears an amino acid, showed a significant gelation tendency. It is capable of forming a gel with methanol − a polar solvent − as well as with toluene and tetralin, which are non-polar solvents. We assume that in methanol the gelator molecules form a gel network due to aromatic π–π stacking of *trans*-stilbene units and lipophilic interactions between the amino acid parts of the molecules, whereas hydrogen bonding involving the oxamide fragments leads to self-assembly of the molecules in non-polar solvents. Weaker intermolecular interactions between the molecules of the symmetric derivative *trans*-**1f**, which contains two *trans*-stilbene units, cause the formation of a gelatinous precipitate. None of the compounds is soluble in water.

Table 1. Gelation properties of *trans*-stilbene monooxamide derivatives expressed as minimal gel concentration (10^{-3} M) of tested compound.[a]

Solvent	*trans*-**1a**	*trans*-**1b**	*trans*-**1c**	*trans*-**1d**	*trans*-**1e**	*trans*-**1f**
Water	I	I	I	I	I	I
MeOH	S	S	I	I	33.4	I
EtOH	S	P	I	I	GP	I
DMSO	S	S	P	S	S	S
EtOAc	S	S	I	P	S	GP
THF	S	S	I	P	S	P
Acetone	S	S	I	P	S	I
CH_2Cl_2	S	S	SS	I	S	GP
Toluene	S	P	I	P	110.3	GP
Tetralin	S	S	I	P	123.0	21.8

[a] Abbreviations: S, soluble; SS, slightly soluble; I, insoluble; P, precipitate; GP, gelatinous precipitate.

The *trans*-stilbene dioxamide compounds are sparingly soluble or insoluble in water and in the organic solvents tested (Table 2). Apart from the ethyl ester derivative *trans*-**2a**, which dissolves in dimethyl sulfoxide and tetrahydrofuran, the leucine derivative *trans*-**2e** shows a gelation tendency towards aromatic non-polar solvents such as tetralin.

Table 2. Gelation properties of *trans*-stilbene dioxamide derivatives expressed as minimal gel concentration (10^{-3} M) of tested compound.[a]

Solvent	*trans*-**2a**	*trans*-**2b**	*trans*-**2c**	*trans*-**2d**	*trans*-**2e**
Water	I	I	I	I	I
MeOH	I	I	I	I	I
EtOH	I	I	I	I	I
DMSO	S	SS	SS	SS	S
EtOAc	I	I	I	I	I
THF	S	I	I	I	P
Acetone	I	I	I	I	I
CH_2Cl_2	I	I	I	I	I
Toluene	I	I	I	I	GP
Tetralin	P	I	I	I	6.1

[a] Abbreviations: S, soluble; SS, slightly soluble; I, insoluble; P, precipitate; GP, gelatinous precipitate.

A comparison of the gelation properties of the 4′-dodecyloxy-*trans*-stilbene oxamide derivatives (Table 3) and those of the corresponding compounds without an alkyloxy substituent on the stilbene part of the molecule (Table 1) indicated that the incorporation of a C_{12} chain into the structure simultaneously caused a decrease in solubility and an increase in the gelation tendency of some substances. The ethyl ester derivative *trans*-**3a** and amino acid derivative *trans*-**3e** act as efficient gelators of most of the tested organic solvents. They exhibit an excellent gelation tendency towards ethanol, which they can gelatinize at concentrations as low as 0.21 wt.-% (3.4 mM) and 0.45 wt.-% (6.2 mM), respectively. In general, they form thermoreversible gels with a turbid appearance. The gels formed from *trans*-**3a** are sensitive to mechanical agitation and the gelator tends to crystallise after about 24 hours. On the other hand, the gels of *trans*-**3e** are stable for weeks, thus indicating that a stereogenic centre in the gelator molecule contributes to the formation of a three-dimensional gel network.

The *cis* isomer of the ethyl ester derivative *cis*-**3a** cannot gelatinize most of the tested solvents owing to its good solubility. Although it is capable of forming a gel with ethanol (5.09 wt.-%; 82.4 mM), its gelation ability is greatly inferior to that of the corresponding *trans* isomer.

Intermolecular lipophilic interactions between long alkyl chains, aromatic π–π stacking of the stilbene moieties and

Table 3. Gelation properties of 4′-dodecyloxy-*trans*-stilbene and 4′-dodecyloxy-*cis*-stilbene oxamide derivatives expressed as minimal gel concentration (10^{-3} M) of tested compound.[a]

Solvent	*trans*-**3a**	*trans*-**3b**	*trans*-**3c**	*trans*-**3d**	*trans*-**3e**	*trans*-**3f**	*cis*-**3a**	*cis*-**3b**	*cis*-**3c**	*cis*-**3d**
Water	I	I	I	I	I	I	I	I	I	I
MeOH	10.9	I	I	I	GP	GP	P	I	I	GP
EtOH	3.4	I	I	I	6.2	GP	82.4	I	GP	GP
DMSO	S	121.8	38.7	122.1	19.0	19.5	S	S	S	P
EtOAc	46.9	I	I	I	19.4	I	S	I	I	S
THF	6.4	SS	GP	P	76.9	39.4	S	P	P	S
Acetone	41.2	I	I	I	11.4	I	S	I	I	P
CH_2Cl_2	137.6	I	I	I	57.0	I	S	I	I	S
Toluene	45.3	I	I	GP	18.8	I	S	I	I	48.3
Tetralin	50.6	SS	GP	21.5	41.9	42.9	S	S	S	53.8

[a] Abbreviations: S, soluble; SS, slightly soluble; I, insoluble; P, precipitate; GP, gelatinous precipitate.

hydrogen bonding involving oxamide fragments are the driving forces for the gelation of organic solvents by the *trans* isomer. We assume that the bent geometry of the *cis*-stilbene unit hinders an efficient unidirectional self-assembly of the *cis* isomers in the gel network, thereby increasing the solubility of the compounds.[10]

Photoinduced Gelation

In light of the different gelation abilities of *trans*-**3a** and *cis*-**3a** as well as the presence of the photo-isomerizing stilbene moiety in the molecule, gel formation stimulated by light was investigated.[30] Upon irradiation with a high-pressure mercury lamp (250 nm $< \lambda <$ 520 nm) at room temperature, the clear solution of *cis*-**3a** in ethanol (2.0×10^{-2} M) turned into an opaque gel. Prolonged irradiation of the gel does not affect its structure; however, the gelator crystallised from the system with time. Heating a gel or a crystalline precipitate and cooling the obtained solution resulted in repeated gel formation (Scheme 3).

FT-Raman spectra indicated that a fast conversion of the *cis* molecules into *trans* molecules occurs during irradiation, leading to self-assembly of the *trans* molecules in the gel network. The double bond stretching band at 1628 cm^{-1} and the aromatic ring vibration band at 1607 cm^{-1} of *cis*-**3a** in solution are shifted to 1632 cm^{-1} and 1603 cm^{-1}, respectively (Figure 1). The position of the vibrational bands in the spectrum after irradiation for one hour confirmed the organisation of the formed *trans* molecules in the gel structure (Table 4).

Although *trans*-**3e** acts as a versatile gelator, synthesis of its *cis* isomer was not possible, thus excluding the possibility of designing a similar photo-induced gelation system (see above).

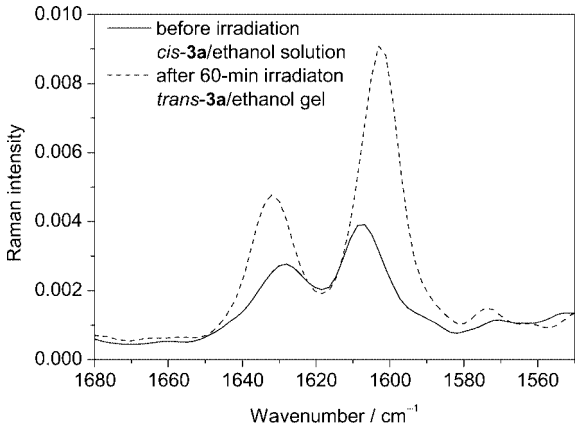


Figure 1. Raman spectra before and after 60-min irradiation of a *cis*-**3a**/ethanol solution.

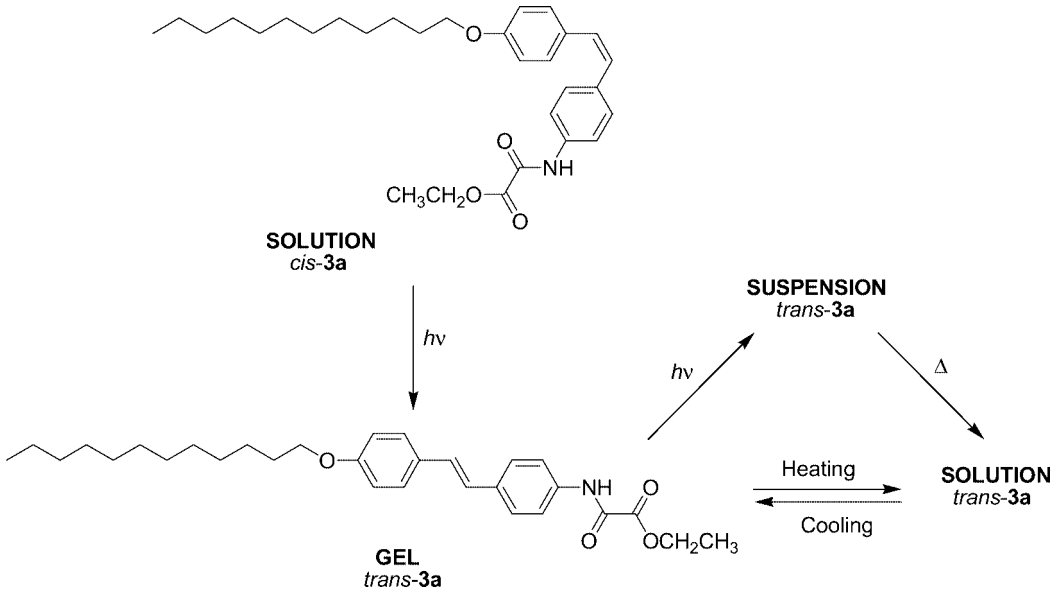
Table 4. Raman bands of C=C double bond stretching and aromatic ring vibration in the spectra of *trans*-**3a** and *cis*-**3a** in the solid state, solution and gel.

Sample	$\tilde{\nu}$ [cm^{-1}]	
	C=C	ArC–C
trans-**3a**[a]	1632	1601
cis-**3a**[a]	1621	1607
trans-**3a**/ethanol[b]	1636	1603
cis-**3a**/ethanol[b]	1628	1607
trans-**3a**/ethanol[c]	1633	1603
cis-**3a**/ethanol[c]	1622	1607

[a] Solid state. [b] Solution [*c*(*trans*-**3a**) = 0.020 M, 75 °C; *c*(*cis*-**3a**) = 0.020 M]. [c] Gel [*c*(*trans*-**3a**) = 0.020 M; *c*(*cis*-**3a**) = 0.100 M].

Investigation of Intermolecular Interactions by FT-IR and ^{1}H NMR Spectroscopy

Apart from the results of photoisomerisation and simultaneous gelation with compound **3a**, its spectroscopic data



Scheme 3. Photoirreversible and thermoreversible gelation of ethanol by oxamide-based stilbene compounds *cis*-**3a** and *trans*-**3a**.

implied that intermolecular oxamide–oxamide hydrogen bonding plays an important role in the formation of the *trans*-**3a**/ethanol gel.[30] The same interactions are also expected to be present in gels of the amino acid oxamide-based gelator *trans*-**3e**.

In the FT-IR spectrum of *trans*-**3e**/toluene gel (2.0×10^{-2} M), N–H and amide I (C=O) vibrational bands are observed at 3285 and 1661 cm^{-1}, respectively, and attributed to the hydrogen-bonded oxamide units. Upon increasing the temperature (25–70 °C) the gel dissolved, resulting in a reduction in intensity of these bands and the appearance of new bands at higher wavenumbers (Figure 2). In the FT-IR spectrum taken at 70 °C the band with maxima at 3364 and 3385 cm^{-1} is assigned to the free NH groups, close to the leucine and stilbene fragments of the molecule, whereas the band at 1691 cm^{-1} is assigned to the non-hydrogen-bonded carbonyl functionality. These results indicate that intermolecular hydrogen bonding between the oxamide parts of the gelator molecule plays a dominant role in the stabilisation of the organogel network.

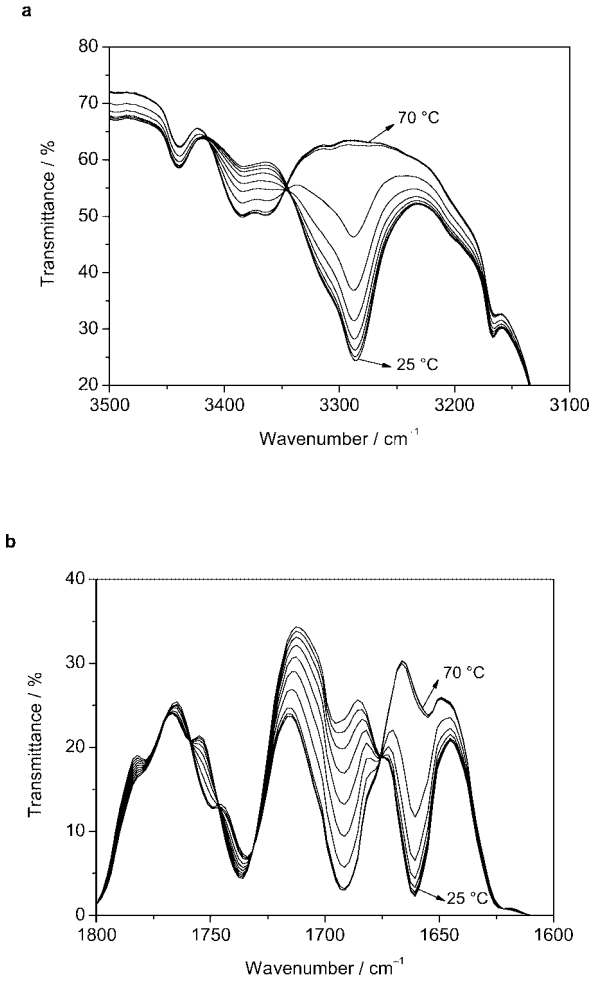


Figure 2. Temperature-dependent (25–70 °C) FT-IR spectra of *trans*-**3e** in toluene: (a) NH region; (b) carbonyl region.

The same argument was supported by the temperature-dependent ^{1}H NMR spectroscopic data. The amide NH protons, stilbene-NH and leucine-NH, are shifted upfield with increasing temperature (Figure 3). We assume that the NH protons participate in hydrogen bonding in gel aggregates and are therefore deshielded, whereas they become more shielded upon gel dissolution. In comparison to the non-linear temperature dependence of the NH proton shifts observed for the *trans*-**3e**/toluene gel, the linear relationship of the temperature-induced shifts of *trans*-**3e** NH protons in DMSO gel allowed evaluation of the temperature coefficients ($\Delta\delta_{NH}/\Delta T$) of 5.9×10^{-3} and 7.8×10^{-3} ppm K^{-1}. Moreover, higher temperature-induced shifts were obtained in the more polar solvent, which is capable of competing with intermolecular oxamide hydrogen bonding. Although a downfield shift of the aromatic protons, indicating intermolecular aromatic stacking interactions, was expected, a characteristic, temperature-dependent trend in the spectra of both gels was not obtained.

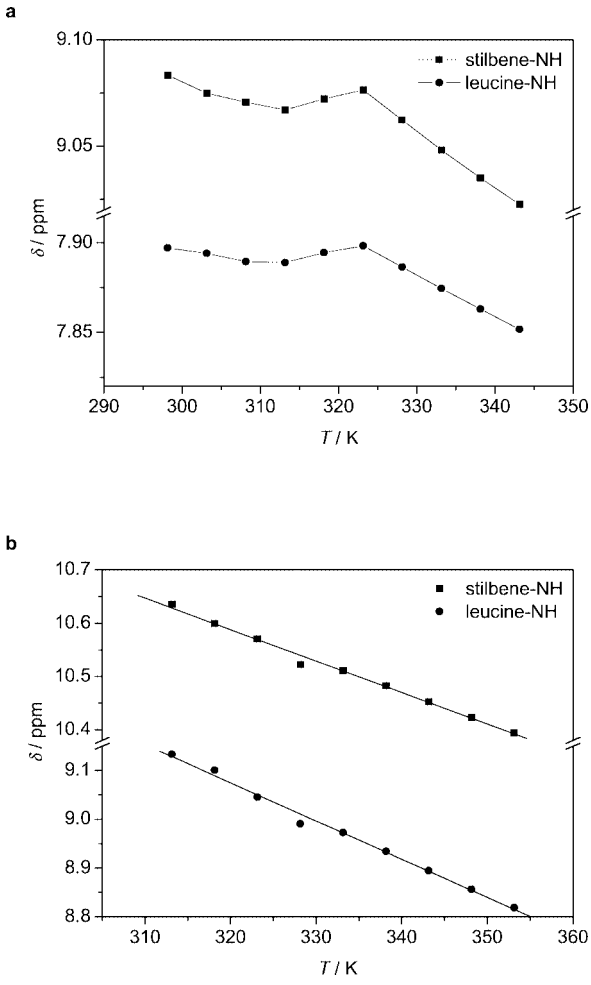


Figure 3. Temperature-induced chemical-shift changes of NH protons in the ^{1}H NMR spectra of a) *trans*-**3e**/toluene gel and b) *trans*-**3e**/DMSO gel.

Aside from the shifts of the proton signals, a temperature increase caused an increase in peak intensity, implying a collapse of the gel network, and, finally, dissolution of the fibrous aggregates. Using the internal standard 1,1,2,2-tetrachloroethane, the concentration of the dissolved gelator, c_d, was determined at each temperature, and the gelation

equilibrium constant $[K]_{gel}$, defined as $K_{gel} = 1/[c_d]$, was evaluated.[17] From the plot of $\ln K_{gel}$ vs. $1/T$ the gelation enthalpy (Figure 4), ΔH_{gel}, was estimated according to the equation $\ln K_{gel} = (-\Delta H_{gel}/R)1/T + C$. A linear dependence of $\ln K_{gel}$ on $1/T$ ($r^2 > 0.98$) was obtained for both gels, indicating that each gel network disintegrates into aggregates of similar size. For the *trans*-**3e**/toluene and *trans*-**3e**/DMSO gels, the ΔH_{gel} values obtained were –61 and –57 kJ mol^{-1}, respectively.

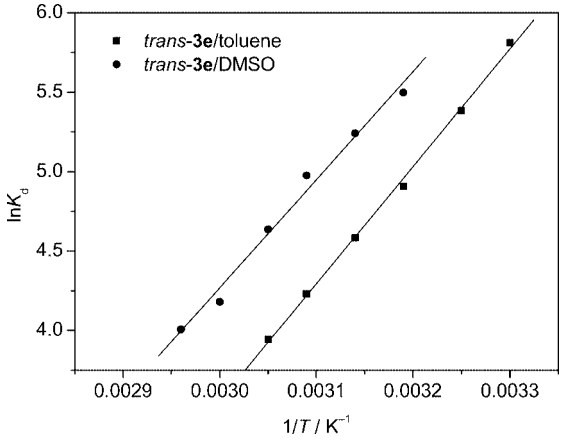


Figure 4. Linear dependence of $\ln K_{gel}$ vs. $1/T$ for *trans*-**3e**/toluene and *trans*-**3e**/DMSO gels used for the calculation of ΔH_{gel}.

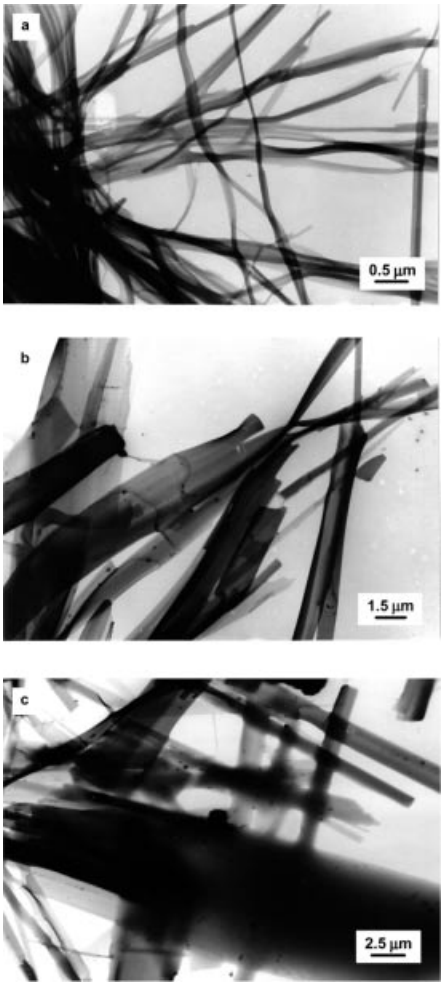


Figure 5. TEM images of ethanol gels of: a) *trans*-**3a** (0.02 M, magnification 25000×), b) *trans*-**3e** (0.02 M, magnification 7500×), c) *trans*-**3e** (0.02 M, magnification 5000×).

TEM Investigation

TEM images were obtained for ethanol gels formed from *trans*-**3a** and *trans*-**3e** (Figure 5). Both gelators form a typical three-dimensional network entangled by the self-assembled gel fibres. Molecules of *trans*-**3a** form rod-like fibres with a diameter of 150 nm, whereas *trans*-**3e** molecules aggregate in slightly twisted ribbons having a significantly larger diameter in the 1500–3000 nm range. The presence of an amino acid moiety in the structure of the latter compound implies that intermolecular interactions between chiral units in molecules lead to the formation of large microfibres.

Conclusions

The present study has demonstrated that the coupling of a photo-responsive unit to the fragment of a gelator molecule responsible for solvent gelation leads to the preparation of new gelators capable of forming smart gels. As gelation ability is not fully predictable by molecular design, a variety of oxamide-based derivatives bearing a stilbene as a photochromic moiety have been prepared and their gelation properties investigated. Depending only on the terminal functional group of the oxamide fragment, the substance either dissolved, precipitated or formed a gel with a solvent, thus indicating that, besides the self-complementary binding groups, the substituent plays an important role in the gel network formation. Introduction of an alkyl chain in the structure of the stilbene part of the molecule results in the preparation of amphiphilic molecules capable of forming stable self-assemblies. Owing to the different gelation abilities of stilbene isomers of long-chain oxamide-based ethyl ester derivatives, gelation controlled by light as an external stimulus has been achieved.

Experimental Section

General Information: Melting points were determined on a Kofler stage. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, with a Bruker Avance 300 spectrometer using tetramethylsilane as internal standard. FT-IR spectra were recorded with a Bruker Equinox 55 interferometer. A Micromass UK mass spectrometer (model Q-TOF Micro) was used for recording mass spectra. Thin-layer chromatography was performed on Merck 60 F_{254} coated silica plates, preparative thin-layer chromatography on silica gel Merck 60 coated glass plates, and preparative column chromatography using Merck 60 silica gel (0.063–0.200 mm). All chemicals were commercially available and were used without further purification. Solvents were purified and dried according to standard procedures.

(4-Nitrobenzyl)triphenylphosphonium Bromide: A mixture of 4-nitrobenzyl bromide (5.401 g, 25.0 mmol) and triphenylphosphane

(7.200 g, 27.5 mmol) in toluene (25 mL) was stirred at room temperature for 16 h.[25] The solvent was then removed by filtration to give a light-yellow solid (9.924 g, 83%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.87–7.73 (m, 11 H, Ar-CH), 7.59 (m, 6 H, Ar-CH), 7.48 (d, J = 8.81 Hz, 2 H, C2-H, C6-H), 6.03 (d, J = 15.81 Hz, 2 H, CH_2P) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 147.16 (C4), 135.69 (C1), 134.90, 134.86 (P-C1), 134.43, 134.30, 132.80, 132.73, 130.05, 129.88, 123.00, 122.96, 117.68, 116.54 (Ar-C), 29.78 (CH_2P) ppm. FT-IR (KBr) $\tilde{\nu}$ = 2919 cm^{-1}, 2852, 2771 (νC–H), 1597 ($\nu_{as}NO_2$), 1519 (νN=O), 1347 (ν_sNO_2), 1111 (δ_{ip}Ar-CH), 865 (δ_{oop}Ar-CH).

4-Nitro-*trans*-stilbene: (4-Nitrobenzyl)triphenylphosphonium bromide (4.783 g, 10.0 mmol), benzaldehyde (1.01 mL, 10.0 mmol) and a few crystals of dibenzo-18-crown-6 were added to a suspension of potassium carbonate (1.589 g, 11.5 mmol) in dichloromethane (80 mL). The red reaction mixture was stirred under argon at room temperature until it turned yellow. After 48 h stirring was stopped, the precipitate was removed by filtration and the filtrate was evaporated to dryness. The obtained solid was purified by column chromatography (silica gel; CH_2Cl_2) resulting in a mixture of isomers of 4-nitrostilbene. The isomer mixture (1.779 g, 79%) was dissolved in toluene (50 mL) and a catalytic amount of iodine was added.[31] The reaction mixture was stirred at room temperature for 24 h. The solvent was evaporated to a yellow solid. Recrystallisation from hot ethanol gave yellow crystals of the *trans* isomer (1.654 g, 93%; m.p. 158–159 °C).[32] ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.21 (d, J = 8.85 Hz, 2 H, C3-H, C5-H), 7.62 (d, J = 8.79 Hz, 2 H, C2-H, C6-H), 7.55 (d, J = 7.00 Hz, 2 H, C2′-H, C6′-H), 7.40 (t, J = 7.23 Hz, 2 H, C3′-H, C5′-H), 7.36–7.32 (m, 1 H, C4′-H), 7.20 (dd, 2 H, =CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 146.60 (C4), 143.70 (C1), 136.02 (C1′), 133.16 (C4′), 128.76, 128.71 (C3′, C5′), 126.88 (C2, C6), 126.71 (C2′, C6′), 126.12 (=CH), 124.00 (C3, C5) ppm. FT-IR (KBr) $\tilde{\nu}$ = 1631 (νArC–C), 1589 ($\nu_{as}NO_2$), 1509 (νN=O), 1344 (ν_sNO_2), 1189, 1109 (δ_{ip}ArC–H), 849 (δ_{oop}ArC–H), 695 (δNO_2).

***trans*-Stilbene Derivative *trans*-1a:** A solution of ammonium chloride (0.440 g, 8.2 mmol) in water (2 mL) was added to a solution of 4-nitro-*trans*-stilbene (1.000 g, 4.4 mmol) in acetone (11 mL).[26] After heating the mixture to boiling point the oil bath was removed and zinc (0.880 g, 13.5 mmol) was added in small portions. After the reaction subsided, an additional amount of zinc (0.440 g, 6.7 mmol) was added and the reaction mixture refluxed for two hours. The precipitate was filtered off while hot and the filtrate was evaporated until an aqueous solution remained. This was basified with 2 M NaOH until pH 10, followed by extraction of the suspension with dichloromethane. The organic phase was separated, dried (Na_2SO_4) and the solvent was evaporated to give an orange solid of 4-amino-*trans*-stilbene (0.653 g, 76%). The crude amine (0.615 g, 3.1 mmol) was dissolved in dichloromethane (30 mL) and triethylamine (0.48 mL, 3.4 mmol) was added.[28] The mixture was cooled (–10 °C) under argon. Ethyl oxalyl chloride (0.35 mL, 3.1 mmol) was added to the cooled mixture and stirring was continued at –10 °C and at room temperature for 30 min and for 20 h, respectively. The reaction mixture was washed with 2 M HCl, 2 M NaOH and with water. The organic phase was separated, dried (Na_2SO_4) and the solvent was evaporated to dryness. Addition of petroleum ether to a solution of the crude residue in dichloromethane gave *trans*-**1a** as a light brown precipitate (0.701 g, 77%; m.p. 158–160 °C). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.91 (s, 1 H, NH), 7.65 (d, J = 8.69 Hz, 2 H, C3-H, C5-H), 7.53 (d, J = 8.67 Hz, 2 H, C2′-H, C6′-H), 7.51 (d, J = 7.10 Hz, 2 H, C2-H, C6-H), 7.36 (t, J = 7.44 Hz, 2 H, C3′-H, C5′-H), 7.26 (t, J = 7.27 Hz, 1 H, C4′-H), 7.08 (s, 2 H, =CH), 4.43 (q, J = 7.15 Hz, 2 H, CH_2), 1.44 (t, J = 7.15 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 156.25 (COOEt), 148.98 (Ar-CONH), 132.41 (C4), 130.87 (C1′), 129.97 (C1), 123.97 (C3′, C5′), 122.98 (C4′), 122.92 (C2, C6), 122.54 (C2′, C6′), 121.76 (=CH), 115.22 (C3, C5), 59.05 (CH_2), 9.28 (CH_3) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3374 (νN–H), 2929 (νC–H), 1718 (νC=O, ester), 1707 (νC=O, amide I), 1587 (ArC–C), 1539 (ν_sN–C=O, amide II), 1509 (δNH), 1310 (νC–O), 1173 (δ_{ip}ArC–H), 971 (δ_{oop}=CH), 823 (δ_{oop}ArC–H). HRMS (ES+): calcd. for $C_{18}H_{18}NO_3$ [MH^+] 296.1287; found 296.1284.

***trans*-Stilbene Derivative *trans*-1b:** Compound *trans*-**1a** (0.670 g, 2.3 mmol) was suspended in a mixture of ethanol (55 mL) and water (30 mL), 2 M NaOH was added (11.50 mL, 23.0 mmol) and the reaction mixture was refluxed for 20 h. Stirring was then stopped and the ethanol was removed under reduced pressure. A 2 M HCl solution was added to this suspension until pH 2 and the product was then extracted with ethyl acetate. The organic phase was separated, dried (Na_2SO_4) and the solvents evaporated to dryness. Addition of petroleum ether to a solution of this crude residue in dichloromethane gave *trans*-**1b** as a light-brown precipitate (0.510 g, 83%; m.p. 163–165 °C). ^{1}H NMR (300 MHz, DMSO, 25 °C): δ = 10.78 (s, 1 H, NH), 7.80 (d, J = 8.71 Hz, 2 H, C3-H, C5-H), 7.59 (d, J = 8.80 Hz, 4 H, C2-H, C6-H, C2′-H, C6′-H), 7.38 (t, J = 7.49 Hz, 2 H, C3′-H, C5′-H), 7.26 (t, J = 7.29 Hz, 1 H, C4′-H), 7.22 (s, 2 H, =CH) ppm. ^{13}C NMR (75 MHz, DMSO, 25 °C): δ = 162.56 (COOH), 157.29 (Ar-CONH), 137.63 (C1′), 137.56 (C1), 133.79 (C4), 129.17 (C3′, C5′), 128.31 (C4′), 128.21 (=CH), 127.99 (=CH), 127.34 (C2, C6), 126.84 (C2′, C6′), 120.84 (C3, C5) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3309 (νN–H), 3250 (νCOOH), 2931 (νC–H), 1764 (νC=O, carboxylic acid), 1685 (νC=O, amide I), 1541 (ν_sN–C=O, amide II), 1509 (δNH), 1352 (νC–N), 1315 (νC–O), 965 (δ_{oop}=CH), 823 (δ_{oop}ArC–H).

***trans*-Stilbene Derivative *trans*-1c:** Compound *trans*-**1b** (0.045 g, 0.17 mmol) and a solution of sodium methoxide in methanol [7.1 mL, 0.17 mmol, c(Na) = 0.0236 M] were stirred together for 30 min. The solvent was then evaporated to give *trans*-**1c** as a yellow solid (0.048 g, 99%). ^{1}H NMR (300 MHz, DMSO, 25 °C): δ = 10.26 (s, 1 H, NH), 7.80 (d, J = 8.71 Hz, 2 H, C3-H, C5-H), 7.55 (m, 4 H, C2-H, C6-H, C2′-H, C6′-H), 7.37 (m, 2 H, C3′-H, C5′-H), 7.26 (m, 1 H, C4′-H), 7.18 (m, 2 H, =CH) ppm. ^{13}C NMR (75 MHz, DMSO, 25 °C): δ = 165.26 (COONa), 162.84 (Ar-CONH), 138.88 (C1′), 137.74 (C1), 132.39 (C4), 129.15 (C3′, C5′), 129.05 (C4′), 128.10 (=CH), 127.28 (=CH), 126.72 (C2, C6), 126.17 (C2′, C6′), 119.73 (C3, C5) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3334 (νN–H), 1671 (νC=O, amide I), 1644 (νC=O), 1532 (ν_sN–C=O, amide II), 1508 (δNH), 1396 (νC–N).

***trans*-Stilbene Derivative *trans*-1d:** Compound *trans*-**1b** (0.229 g, 0.9 mmol) was suspended in dichloromethane (25 mL) and thionyl chloride (0.63 mL, 9.0 mmol) and a drop of dimethylformamide were added. The reaction mixture was stirred at 40–50 °C for two hours. Evaporation of the solvent resulted in a yellow solid of the acyl chloride. This was suspended in dichloromethane (10 mL) and cooled (–10 °C) under argon.[28] Dodecylamine (0.159 g, 0.9 mmol) was dissolved in dichloromethane (10 mL) and triethylamine (0.13 mL, 1.0 mmol) was added. This solution of amines was added to the cooled suspension of the acyl chloride. The reaction mixture was stirred for 30 min at –10 °C and then for 20 h at room temperature. Filtration resulted in isolation of *trans*-**1d** as a light-yellow precipitate (0.257 g, 69%; m.p. 210–211 °C). ^{1}H NMR (300 MHz, DMSO, 80 °C): δ = 10.46 (s, 1 H, ar-NH), 8.74 (s, 1 H, dodecyl-NH), 7.82 (d, J = 7.50 Hz, 2 H, C3-H, C5-H), 7.58 (d, J = 7.36 Hz, 4 H, C2-H, C6-H, C2′-H, C6′-H), 7.37 (t, J = 7.03 Hz, 2 H, C3′-H, C5′-H), 7.26 (t, J = 7.81 Hz, 1 H, C4′-H), 7.19 (s, 2 H, =CH),

1.54–1.53 (m, 2 H, NHCH_2), 1.26 [s, 20 H, $(CH_2)_{10}$], 0.86 (t, 3 H, CH_3) ppm. Owing to the poor solubility of *trans*-**1d** its ^{13}C NMR spectrum was not recorded. FT-IR (KBr) $\tilde{\nu}$ = 3324 (νN–H), 3297 (νN–H), 3250 (νCOOH), 2919, 2850 (νC–H), 1652 (νC=O, amide I), 1587 (ArC–C), 1526 (ν_sN–C=O, amide II), 1507 (δNH), 1466 ($\delta_{as}CH_3$), 1414 (νC–N), 962 (δ_{oop}=CH), 819 (δ_{oop}ArC–H). HRMS (MALDI+): calcd. for $C_{28}H_{38}N_2O_2$ [M^+] 434.2933; found 434.2939.

***trans*-Stilbene Derivative *trans*-1e:** The acyl chloride of compound *trans*-**1b** (0.457 g, 1.6 mmol), which was prepared according to the procedure for the synthesis of the compound *trans*-**1d**, was suspended in dichloromethane (45 mL) and cooled to –10 °C under argon.[28] A solution of L-leucine methyl ester hydrochloride (0.292 g, 1.6 mmol) and triethylamine (0.49 mL, 3.5 mmol) in dichloromethane (10 mL) was added to this suspension and the reaction mixture was stirred in an ice bath for 30 min and then at room temperature for 22 h. The mixture was washed with 2 M HCl, 2 M NaOH and with water. The organic phase was separated, dried (Na_2SO_4) and evaporated to give a solid product. A light yellow solid of *trans*-**1e** was isolated by preparative thin-layer chromatography (silica gel; CH_2Cl_2) (0.146 g, 23%; m.p. 206–208 °C). ^1H NMR (300 MHz, DMSO, 25 °C): δ = 10.71 (s, 1 H, ar-NH), 9.23 (d, *J* = 8.27 Hz, 1 H, Leu-NH), 7.79 (d, *J* = 7.50 Hz, 2 H, C3-H, C5-H), 7.53 (d, *J* = 8.96 Hz, 2 H, C2′-H, C6′-H), 7.52 (d, *J* = 7.23 Hz, 2 H, C2-H, C6-H), 7.31 (t, *J* = 7.75 Hz, 2 H, C3′-H, C5′-H), 7.20 (t, *J* = 7.33 Hz, 1 H, C4′-H), 7.15 (s, 2 H, =CH), 4.38–4.34 (m, 1 H, $CH\alpha_{Leu}$), 3.59 (s, 3 H, OCH_3), 1.84–1.78 (m, 1 H, CH), 1.57–1.51 (m, 2 H, CH_2), 0.84 (d, *J* = 6.27 Hz, 3 H, CH_3), 0.81 (d, *J* = 6.11 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, DMSO, 25 °C): δ = 171.94 (COOMe), 160.25 (CONH-Leu), 158.01 (Ar-CONH), 137.12 (C1′), 137.01 (C1), 133.40 (C4), 128.72 (C3′, C5′), 127.86 (C4′), 127.81 (=CH), 127.54 (=CH), 126.87 (C2, C6), 126.38 (C2′, C6′), 120.53 (C3, C5), 52.13 ($C\alpha_{Leu}$), 50.78 (OCH_3), 24.33 (CH_2), 22.91 (CH), 21.03 [$(CH_3)_2$]. FT-IR (KBr) $\tilde{\nu}$ = 3294 (νN–H), 2957, 2927 (νC–H), 1750 (νC=O, ester), 1663 (νC=O, amide I), 1521 (ν_sN–C=O, amide II), 1507 (δNH), 1416 (νC–N), 1278 (νC–O), 963 (δ_{oop}=CH), 816 (δ_{oop}ArC–H). HRMS (ES+): calcd. for $C_{23}H_{27}N_2O_4$ [MH^+] 395.1971; found 395.1971.

Bis(*trans*-stilbene) Derivative *trans*-1f: 4-Amino-*trans*-stilbene (0.203 g, 1.0 mmol), which was prepared according to the procedure for the synthesis of compound *trans*-**1a**, was dissolved in toluene (20 mL) and the solution refluxed in a Dean–Stark apparatus for two hours. After cooling this solution to room temperature triethylamine (0.15 mL, 1.1 mmol) was added and the reaction mixture was stirred at –10 °C under argon. Ethyl oxalyl chloride (0.044 mL, 0.5 mmol) was added to the cooled mixture and stirring was continued for 20 h at room temperature. Filtration of the reaction mixture gave *trans*-**1f** as a light-yellow solid (0.207 g, 93%). ^1H NMR (300 MHz, DMSO, 25 °C): δ = 10.86 (s, 2 H, NH), 7.76 (d, *J* = 8.46 Hz, 4 H, C3-H, C5-H), 7.29–7.21 (m, 14 H, C2-H, C6-H, C2′-H, C3′-H, C4′-H, C5′-H, C6′-H), 6.62 (s, 4 H, =CH) ppm. ^{13}C NMR (75 MHz, DMSO, 25 °C): δ = 158.95 (CONH), 137.63, 137.51, 137.43, 137.11, 133.99, 133.59, 130.23, 130.00, 129.40, 129.14, 128.92 (=CH), 128.83 (=CH), 128.38, 127.71, 127.34, 126.85 (C2, C6), 121.07, 120.61 (C3, C5) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3344 (νN–H), 3299 (νN–H), 2927 (νC–H), 1675 (νC=O, amide I), 1661 (νC=O, amide I), 1585 (ArC–C), 1523 (ν_sN–C=O, amide II), 1416 (νC–N), 834 (δ_{oop}ArC–H). HRMS (ES+): calcd. for $C_{30}H_{24}N_2NaO_2$ [MNa^+] 467.1735; found 467.1729.

4,4′-Dinitro-*trans*-stilbene: Potassium carbonate (2.451 g, 17.7 mmol) was suspended in dichloromethane (125 mL) and (4-nitrobenzyl)triphenylphosphonium bromide (7.378 g, 15.4 mmol), 4-nitrobenzaldehyde (2.331 g, 15.4 mmol) and a catalytic amount of dibenzo-18-crown-6 were added. The orange reaction mixture was stirred at room temperature for four days until it turned yellow. The precipitate was filtered off and the filtrate was evaporated to give a yellow solid of a mixture of isomers of 4,4′-dinitrostilbene (3.121 g, 75%). Recrystallisation from hot ethanol gave the *trans*-isomer as yellow crystals (2.372 g, 57%).[33] ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.25 (d, *J* = 8.53 Hz, 4 H, C3-H, C5-H, C3′-H, C5′-H), 7.67 (d, *J* = 8.51 Hz, 4 H, C2-H, C6-H, C2′-H, C6′-H), 7.28 (s, 2 H, =CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 147.65 (C4, C4′), 142.47 (C1, C1′), 131.33 (=CH), 127.43 (C2, C6, C2′, C6′), 124.23 (C3, C5, C3′, C5′) ppm. FT-IR (KBr) $\tilde{\nu}$ = 1593 ($\nu_{as}NO_2$), 1506 (νN=O), 1339 ($\nu_s NO_2$), 1179, 1110 (δ_{ip}ArC–H), 853 (δ_{oop}ArC–H), 694 (δNO_2).

***trans*-Stilbene Derivative *trans*-2a:** 4,4′-Dinitro-*trans*-stilbene (2.585 g, 9.6 mmol) and stannous chloride dihydrate (21.595 g, 96.0 mmol) were suspended in ethanol (45 mL).[27] The reaction mixture was stirred and heated to 70 °C for two hours and then cooled to room temperature. The mixture was poured over ice and 5% aqueous sodium carbonate was added until pH 7–8. The product was extracted with ethyl acetate and the organic phase was washed with brine solution. The solution was treated with charcoal and dried (Na_2SO_4). The solvent was removed by filtration and evaporated to give a red-brown solid of 4,4′-diamino-*trans*-stilbene (1.469 g, 72%). A solution of this diamine (1.400 g, 6.7 mmol) and triethylamine (2.05 mL, 14.7 mmol) in dichloromethane (125 mL) was stirred at –10 °C under argon,[28] ethyl oxalyl chloride (1.51 mL, 13.6 mmol) was added, and stirring was continued in an ice bath for 30 min and at room temperature for 20 h. Filtration of the reaction mixture gave *trans*-**2a** as a yellow solid (1.732 g, 63%). ^1H NMR (300 MHz, DMSO, 25 °C): δ = 10.85 (s, 2 H, NH), 7.77 (d, *J* = 8.68 Hz, 4 H, C3-H, C5-H, C3′-H, C5′-H), 7.58 (d, *J* = 8.63 Hz, 4 H, C2-H, C6-H, C2′-H, C6′-H), 7.18 (s, 2 H, =CH), 4.31 (q, *J* = 7.09 Hz, 4 H, CH_2), 1.32 (t, *J* = 7.11 Hz, 6 H, CH_3) ppm. ^{13}C NMR (75 MHz, DMSO, 25 °C): δ = 161.09 (COOEt), 155.88 (Ar-CONH), 137.30 (C4, C4′), 134.07 (C1, C1′), 127.75 (=CH), 127.26 (C2, C6, C2′, C6′), 121.03 (C3, C5, C3′, C5′), 62.87 (CH_2), 14.32 (CH_3) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3333 (νN–H), 2997 (νC–H), 1730 (νC=O, ester), 1703 (νC=O, amide I), 1589 (ArC–C), 1533 (ν_sN–C=O, amide II), 1417 (νC–N), 1365 ($\delta_s CH_3$), 1291 (νC–O), 1184 (δ_{ip}ArC–H), 822 (δ_{oop}ArC–H). HRMS (ES+): calcd. for $C_{22}H_{23}N_2O_6$ [MH^+] 411.1556; found 411.1555.

***trans*-Stilbene Derivative *trans*-2b:** Compound *trans*-**2a** (1.630 g, 4.0 mmol) was suspended in a mixture of ethanol (100 mL) and water (50 mL) and 2 M NaOH was added (20.00 mL, 40.0 mmol). The reaction mixture was refluxed for 20 h. Stirring was stopped and ethanol was removed under reduced pressure. A 2 M HCl solution was added to this water suspension until pH 1, resulting in precipitation of *trans*-**2b** as a brown solid (1.092 g, 77%). ^1H NMR (300 MHz, DMSO, 25 °C): δ = 10.79 (s, 2 H, NH), 7.79 (d, *J* = 8.48 Hz, 4 H, C3-H, C5-H, C3′-H, C5′-H), 7.57 (d, *J* = 8.43 Hz, 4 H, C2-H, C6-H, C2′-H, C6′-H), 7.17 (s, 2 H, =CH) ppm. ^{13}C NMR (75 MHz, DMSO, 25 °C): δ = 161.84 (COOH), 156.81 (Ar-CONH), 136.82 (C4, C4′), 133.35 (C1, C1′), 127.12 (=CH), 126.55 (C2, C6, C2′, C6′), 120.29 (C3, C5, C3′, C5′) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3333 (νN–H), 2924, 2857 (νC–H), 1673 (νC=O, carboxylic acid), 1644 (νC=O, amide I), 1588 (ArC–C), 1533 (ν_sN–C=O, amide II), 1387 (νC–N), 1315 (νC–O), 818 (δ_{oop}ArC–H).

***trans*-Stilbene Derivative *trans*-2c:** This product was obtained by the same procedure as *trans*-**1c** but with *trans*-**2b** (0.073 g, 0.2 mmol) as starting material. *trans*-**2c** was isolated as a light-brown solid, (0.082 g, 100%). Due to its poor solubility ^1H and ^{13}C NMR spec-

tra were not recorded. FT-IR (KBr) $\tilde{\nu}$ = 3333 (νN–H), 2924, 2857 (νC–H), 1673 (νC=O), 1644 (νC=O, amide I), 1588 (ArC–C), 1560 (ν_sN–C=O, amide II), 1516 (δNH), 1388 (νC–N), 1315 (νC–O), 817 (δ_{oop}ArC–H).

***trans*-Stilbene Derivative *trans*-2d:** This product was prepared by the same procedure as *trans*-**1d** but with *trans*-**2b** (0.108 g, 0.3 mmol) as starting material. The precipitate was purified by suspension in 2 M HCl and in 2 M NaOH using an ultrasound bath, which gave *trans*-**2d** as a brown solid after filtration (0.060 g, 29%). ^{1}H NMR (300 MHz, DMSO, 25 °C): δ = 7.67 (d, J = 8.69 Hz, 4 H, C3-H, C5-H, C3′-H, C5′-H), 7.46 (d, J = 7.96 Hz, 4 H, C2-H, C6-H, C2′-H, C6′-H), 7.04 (s, 2 H, =CH), 1.27 [s, 44 H, $(CH_2)_{11}$], 0.86 (t, J = 6.75 Hz, 6 H, CH_3) ppm. Owing to the poor solubility of *trans*-**2d** its ^{13}C NMR spectrum was not recorded. FT-IR (KBr) $\tilde{\nu}$ = 3332 (νN–H), 2922, 2857 (νC–H), 1673 (νC=O, amide I), 1645 (νC=O, amide I), 1588 (ArC–C), 1532 (ν_sN–C=O, amide II), 1387 (νC–N), 1315 (νC–O), 1193 (δ_{ip}ArC–H), 817 (δ_{oop}ArC–H).

***trans*-Stilbene Derivative *trans*-2e:** This product was prepared by the same procedure as *trans*-**1e** but with *trans*-**2b** (0.196 g, 0.5 mmol) as starting material. Filtration of the reaction mixture gave *trans*-**2e** as a light-brown solid (0.112 g, 38%). ^{1}H NMR (300 MHz, DMSO, 25 °C): δ = 10.78 (s, 2 H, Ar-NH), 9.30 (d, J = 8.22 Hz, 2 H, Leu-NH), 7.85 (d, J = 8.46 Hz, 4 H, C3-H, C5-H, C3′-H, C5′-H), 7.58 (d, J = 8.42 Hz, 4 H, C2-H, C6-H, C2′-H, C6′-H), 7.18 (s, 2 H, =CH), 4.45–4.40 (m, 2 H, $CH\alpha_{Leu}$), 3.65 (s, 6 H, OCH_3), 1.91–1.84 (m, 2 H, CH), 1.60–1.58 (m, 4 H, CH_2), 0.90 (d, J = 6.29 Hz, 6 H, CH_3), 0.88 (d, J = 5.54 Hz, 6 H, CH_3) ppm. Owing to a poor solubility of *trans*-**2e** its ^{13}C NMR spectrum was not recorded. FT-IR (KBr) $\tilde{\nu}$ = 3294 (νN–H), 2957, 2927, 2877 (νC–H), 1740 (νC=O, ester), 1662 (νC=O, amide I), 1589 (ArC–C), 1522 (ν_sN–C=O, amide II), 1512 (δNH), 1418 (νC–N), 1321 (νC–O), 829 (δ_{oop}ArC–H). HRMS (MALDI+): calcd. for $C_{32}H_{40}N_4O_8$ [M^+] 608.2846; found 608.2840.

***trans*-Stilbene Derivative *trans*-3a:** This substance was prepared according to ref.[30]

***cis*-Stilbene Derivative *cis*-3a:** This substance was prepared according to ref.[30]

***trans*-Stilbene Derivative *trans*-3b:** This product was obtained by the same procedure as *trans*-**2b** but with *trans*-**3a** (0.290 g, 0.6 mmol) as starting material. *trans*-**3b** was isolated as a light-brown solid (0.255 g, 94%; m.p. 201–203 °C). ^{1}H NMR (300 MHz, DMSO, 80 °C): δ = 10.75 (s, 1 H, NH), 7.77 (d, J = 8.63 Hz, 2 H, C3-H, C5-H), 7.55 (d, J = 8.73 Hz, 2 H, C2-H, C6-H), 7.50 (d, J = 8.80 Hz, 2 H, C2′-H, C6′-H), 7.09 (dd, 2 H, =CH), 6.92 (d, J = 8.68 Hz, 2 H, C3′-H, C5′-H), 3.98 (t, J = 6.36 Hz, 2 H, OCH_2CH_2), 1.73–1.66 (m, 2 H, OCH_2CH_2), 1.24 [s, 18 H, $(CH_2)_9$], 0.85 (t, J = 6.64 Hz, 3 H, $CH_2CH_2CH_3$) ppm. ^{13}C NMR (75 MHz, DMSO, 80 °C): δ = 162.04 (COOH), 158.31 (C4′), 156.66 (Ar-CONH), 136.65 (C4), 133.72 (C1), 129.57 (C1′), 127.0 (C2′, C6′), 127.43 (=CH), 126.61 (C2, C6), 125.42 (=CH), 120.34 (C3, C5), 114.62 (C3′, C5′), 67.43 (OCH_2), 31.24 ($CH_2CH_2CH_3$), 28.93, 28.70, 28.64 (CH_2), 25.44 (OCH_2CH_2), 22.03 ($CH_2CH_2CH_3$), 13.88 (CH_3) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3368 (νN–H), 3318 (νCOOH), 2918, 2850 (νC–H), 1683 (νC=O, amide I), 1609 (ArC–C), 1540 (ν_sN–C=O, amide II), 1521 (δNH), 1473 ($\delta_{as}CH_3$), 1361 (νC–N), 1303 (νC–O), 1257 (ν_{as}C–O–C), 1178 (δ_{ip}ArC–H), 1025 (ν_sC–O–C), 831 (δ_{oop}ArC–H).

***cis*-Stilbene Derivative *cis*-3b:** This product was obtained by the same procedure as *trans*-**2b** but with *cis*-**3a** (0.100 g, 0.2 mmol) as starting material. *cis*-**3b** was isolated as a light-yellow solid (0.080 g, 89%; m.p. 114–115 °C). ^{1}H NMR (300 MHz, DMSO, 25 °C): δ = 10.68 (s, 1 H, NH), 7.67 (d, J = 8.18 Hz, 2 H, C3-H, C5-H), 7.21 (d, J = 8.25 Hz, 2 H, C2-H, C6-H), 7.15 (d, J = 8.29 Hz, 2 H, C2′-H, C6′-H), 6.81 (d, J = 8.15 Hz, 2 H, C3′-H, C5′-H), 6.48 (dd, 2 H, =CH), 3.92 (t, J = 6.21 Hz, 2 H, OCH_2CH_2), 1.70–1.65 (m, 2 H, OCH_2CH_2), 1.24 [s, 18 H, $(CH_2)_9$], 0.83 (t, 3 H, $CH_2CH_2CH_3$) ppm. ^{13}C NMR (75 MHz, DMSO, 25 °C): δ = 162.01 (COOH), 157.84 (C4′), 156.74 (Ar-CONH), 136.49 (C4), 133.31 (C1), 129.73 (C2′, C6′), 129.29 (=CH), 128.85 (C1′), 128.75 (C2, C6), 127.70 (=CH), 119.95 (C3, C5), 114.19 (C3′, C5′), 67.32 (OCH_2), 31.23 ($CH_2CH_2CH_3$), 28.96, 28.94, 28.91, 28.69, 28.64, 28.61 (CH_2), 25.44 (OCH_2CH_2), 22.03 ($CH_2CH_2CH_3$), 13.87 (CH_3) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3369 (νN–H), 2920, 2851 (νC–H), 1734 (νC=O), 1685 (νC=O, amide I), 1607 (ArC–C), 1541 (ν_sN–C=O, amide II), 1508 (δNH), 1458 ($\delta_{as}CH_3$), 1248 (ν_{as}C–O–C), 1177 (δ_{ip}ArC–H), 1029 (ν_sC–O–C), 836 (δ_{oop}ArC–H).

***trans*-Stilbene Derivative *trans*-3c:** This product was obtained by the same procedure as *trans*-**1c** but with *trans*-**3b** (0.100 g, 0.2 mmol) as starting material. *trans*-**3c** was isolated as a yellow solid (0.103 g, 99%). Due to the poor solubility of this compound its ^{1}H and ^{13}C NMR spectra were not recorded. FT-IR (KBr) $\tilde{\nu}$ = 3341 (νN–H), 2918, 2850 (νC–H), 1672 (νC=O, amide I), 1636 (νC=O), 1609 (ArC–C), 1582 ($\nu_{as}COO^-$), 1540 (ν_sN–C=O, amide II), 1473 ($\delta_{as}CH_3$), 1419 (ν_sCOO^-), 1257 (ν_{as}C–O–C), 1179 (δ_{ip}ArC–H), 1025 (ν_sC–O–C), 830 (δ_{oop}ArC–H).

***cis*-Stilbene Derivative *cis*-3c:** This product was obtained by the same procedure as *trans*-**1c** but with *cis*-**3b** (0.060 g, 0.13 mmol) as starting material. *cis*-**3c** was isolated as a yellow solid, (0.061 g, 99%). ^{1}H NMR (300 MHz, DMSO, 25 °C): δ = 8.53 (s, 1 H, NH), 7.64 (d, J = 7.41 Hz, 2 H, C3-H, C5-H), 7.18–7.13 (m, 4 H, C2-H, C6-H, C2′-H, C6′-H), 6.81 (d, J = 8.70 Hz, 2 H, C3′-H, C5′-H), 6.44 (s, 2 H, =CH), 3.92 (t, J = 6.31 Hz, 2 H, OCH_2CH_2), 1.68–1.66 (m, 2 H, OCH_2CH_2), 1.24 [s, 18 H, $(CH_2)_9$], 0.85 (t, 3 H, $CH_2CH_2CH_3$) ppm. Due to the poor solubility of this compound its ^{13}C NMR spectrum was not recorded. FT-IR (KBr) $\tilde{\nu}$ = 3361 (νN–H), 2920, 2850 (νC–H), 1669 (νC=O, amide I), 1631 (νC=O), 1606 (ArC–C), 1559 ($\nu_{as}COO^-$), 1523 (ν_sN–C=O, amide II), 1508 (δNH), 1458 ($\delta_{as}CH_3$), 1388 (ν_sCOO^-), 1253 (ν_{as}C–O–C), 1179 (δ_{ip}ArC–H), 1025 (ν_sC–O–C), 846 (δ_{oop}ArC–H).

***trans*-Stilbene Derivative *trans*-3d:** Compound *trans*-**3a** (0.063 g, 0.1 mmol) was suspended in a mixture of saturated ammonia solution in methanol (25 mL) and dichloromethane (10 mL). The suspension was left to stand at 4 °C for seven days, after which time the solvent was evaporated to dryness. Addition of petroleum ether to a solution of the crude residue in ethyl acetate gave *trans*-**3d** as a light-brown precipitate (0.054 g, 92%). ^{1}H NMR (300 MHz, DMSO, 80 °C): δ = 10.42 (s, 1 H, ar-NH), 8.09 (s, 1 H, $CONH_2$), 7.80 (d, J = 7.60 Hz, 2 H, C3-H, C5-H), 7.72 (d, J = 7.69 Hz, 1 H, $CONH_2$), 7.53 (d, J = 8.98 Hz, 2 H, C2-H, C6-H), 7.46 (d, J = 8.57 Hz, 2 H, C2′-H, C6′-H), 7.07 (dd, 2 H, =CH), 6.92 (d, J = 6.27 Hz, 2 H, C3′-H, C5′-H), 3.99 (t, 2 H, OCH_2CH_2), 1.80–1.63 (m, 2 H, OCH_2CH_2), 1.27 [s, 18 H, $(CH_2)_9$], 0.87 (t, 3 H, $CH_2CH_2CH_3$) ppm. Due to the poor solubility of this compound its ^{13}C NMR spectrum was not recorded. FT-IR (KBr) $\tilde{\nu}$ = 3404 (NH_2), 3313 (νN–H), 2918, 2851 (νC–H), 1655 (νC=O, amide I), 1609 (ArC–C), 1529 (ν_sN–C=O, amide II), 1472 ($\delta_{as}CH_3$), 1397 (νC–N), 1257 (ν_{as}C–O–C), 1179, 1112 (δ_{ip}ArC–H), 1035 (ν_sC–O–C), 831 (δ_{oop}ArC–H).

***cis*-Stilbene Derivative *cis*-3d:** This product was obtained by the same procedure as *trans*-**3d** but with *cis*-**3a** (0.100 g, 0.2 mmol) as starting material. *cis*-**3d** was isolated as a light-brown solid, (0.075 g, 83%; m.p. 179–181 °C). ^{1}H NMR (300 MHz, DMSO, 25 °C): δ = 10.60 (s, 1 H, ar-NH), 8.29 (s, 1 H, $CONH_2$), 7.98 (s, 1 H, $CONH_2$), 7.72 (d, J = 8.59 Hz, 2 H, C3-H, C5-H), 7.21 (d, J

= 8.56 Hz, 2 H, C2-H, C6-H), 7.15 (d, *J* = 8.63 Hz, 2 H, C2′-H, C6′-H), 6.81 (d, *J* = 8.68 Hz, 2 H, C3′-H, C5′-H), 6.48 (dd, 2 H, =CH), 3.92 (t, *J* = 6.45 Hz, 2 H, O*CH*$_2$CH$_2$), 1.74–1.62 (m, 2 H, OCH$_2$*CH*$_2$), 1.24 [s, 18 H, (CH$_2$)$_9$], 0.85 (t, *J* = 6.15 Hz, 3 H, CH$_2$CH$_2$*CH*$_3$) ppm. ^{13}C NMR (75 MHz, DMSO, 25 °C): δ = 162.03 (CONH$_2$), 158.74 (Ar-CONH), 157.83 (C4′), 136.53 (C4), 133.14 (C1), 129.73 (C2′, C6′), 129.21 (=CH), 128.89 (C1′), 128.71 (C2, C6), 127.76 (=CH), 119.85 (C3, C5), 114.20 (C3′, C5′), 67.32 (O*CH*$_2$), 31.23 (*CH*$_2$CH$_2$CH$_3$), 28.96, 28.95, 28.91, 28.69, 28.64, 28.61 (CH$_2$), 25.44 (OCH$_2$*CH*$_2$), 22.03 (CH$_2$*CH*$_2$CH$_3$), 13.88 (CH$_3$) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3383 (NH$_2$), 3292 (νN–H), 2920, 2851 (νC–H), 1661 (νC=O, amide I), 1605 (ArC–C), 1527 (ν_sN–C=O, amide II), 1510 (δNH), 1468 (δ_{as}CH$_3$), 1395 (νC–N), 1252 (ν_{as}C–O–C), 1179, 1114 (δ_{ip}ArC–H), 832 (δ_{oop}ArC–H).

***trans*-Stilbene Derivative *trans*-3e:** This product was obtained by the same procedure as *trans*-**1e** but with *trans*-**3b** (0.098 g, 0.2 mmol) as starting material. *trans*-**3e** was isolated as a yellow solid, (0.110 g, 87%; m.p. 174–176 °C). ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): δ = 9.14 (s, 1 H, ar-NH), 7.78 (d, *J* = 8.97 Hz, 1 H, Leu-NH), 7.55 (d, *J* = 8.64 Hz, 2 H, C3-H, C5-H), 7.42 (d, *J* = 8.61 Hz, 2 H, C2-H, C6-H), 7.36 (d, *J* = 8.72 Hz, 2 H, C2′-H, C6′-H), 6.92 (dd, 2 H, =CH), 6.82 (d, *J* = 8.73 Hz, 2 H, C3′-H, C5′-H), 4.61–4.57 (m, 1 H, C*H), 3.90 (t, *J* = 6,52 Hz, 2 H, O*CH*$_2$CH$_2$), 3.71 (s, 3 H, OCH$_3$), 1.74–1.67 (m, 2 H, OCH$_2$*CH*$_2$), 1.67–1.60 (m, 2 H, CH$_2$), 1.41–1.37 (m, 1 H, CH), 1.20 [s, 18 H, (CH$_2$)$_9$], 0.96–0.89 [m, 6 H, (CH$_3$)$_2$], 0.81 (t, *J* = 7.03 Hz, 3 H, CH$_2$CH$_2$*CH*$_3$) ppm. Owing to the gelation of the solvent by *trans*-**3e** the ^{13}C NMR spectrum was not recorded. FT-IR (KBr) $\tilde{\nu}$ = 3291 (νN–H), 2920, 2849 (νC–H), 1749 (νC=O, ester), 1663 (νC=O, amide I), 1610 (ArC–C), 1521 (ν_sN–C=O, amide II), 1512 (δNH), 1473 (δ_{as}CH$_3$), 1414 (νC–N), 1258 (ν_{as}C–O–C), 1177 (δ_{ip}ArC–H), 1019 (ν_sC–O–C), 835 (δ_{oop}ArC–H). HRMS (MALDI+): calcd. for C$_{35}$H$_{50}$N$_2$O$_5$ [M$^+$] 578.3720; found 578.3718.

***trans*-Stilbene Derivative *trans*-3f:** A 1 M LiOH solution (0.19 mL, 0.2 mol) was added to a suspension of *trans*-**3e** (0.109 g, 0.2 mmol) in a mixture of methanol (5 mL) and dichloromethane (10 mL). The reaction mixture was stirred at room temperature for 20 h. The organic solvents were removed under reduced pressure and water (10 mL) was added to the remaining aqueous suspension. Dropwise addition of 2 M HCl until pH 1 precipitated *trans*-**3f** as a light-brown solid (0.070 g, 65%). ^{1}H NMR (300 MHz, DMSO, 25 °C): δ = 10.67 (s, 1 H, Ar-NH), 8.55 (d, *J* = 8.97 Hz, 1 H, Leu-NH), 7.83 (d, *J* = 8.71 Hz, 2 H, C3-H, C5-H), 7.54 (d, *J* = 8.75 Hz, 2 H, C2-H, C6-H), 7.50 (d, *J* = 8.80 Hz, 2 H, C2′-H, C6′-H), 7.09 (dd, 2 H, =CH), 6.92 (d, *J* = 8.73 Hz, 2 H, C3′-H, C5′-H), 3.97 (t, *J* = 6.52 Hz, 2 H, O*CH*$_2$CH$_2$), 3.82–3.79 (m, 1 H, C*H), 1.73–1.66 (m, 2 H, OCH$_2$*CH*$_2$), 1.64–1.55 (m, 2 H, CH$_2$), 1.41–1.36 (m, 1 H, CH), 1.25 [s, 18 H, (CH$_2$)$_9$], 0.91–0.86 [m, 6 H, (CH$_3$)$_2$], 0.86 (t, *J* = 7.08 Hz, 3 H, CH$_2$CH$_2$*CH*$_3$) ppm. ^{13}C NMR (75 MHz, DMSO, 80 °C): δ = 172.03 (COOH), 158.39 (CONH),158.19 (C4′), 136.34 (C4), 133.53 (C1), 129.55 (C1′), 127.35 (C2′, C6′), 126.16 (C2, C6), 125.43 (=CH), 120.22 (C3, C5), 114.58 (C3′, C5′), 67.44 (O*CH*$_2$), 52.77 (C*), 41.56 (Leu-CH$_2$), 30.93 (*CH*$_2$CH$_2$CH$_3$), 28.59, 28.39, 28.30 (CH$_2$), 25.16 (OCH$_2$*CH*$_2$), 24.39 (Leu-CH), 22.8 (Leu-CH$_3$), 22.00 (Leu-CH$_3$), 21.69 (CH$_2$*CH*$_2$CH$_3$), 13.49 (CH$_3$) ppm. FT-IR (KBr) $\tilde{\nu}$ = 3305 (νN–H), 2920, 2850 (νC–H), 1654 (νC=O, amide I), 1521 (ν_sN–C=O, amide II), 1512 (δNH), 1473 (δ_{as}CH$_3$), 1419 (νC–N), 1258 (ν_{as}C–O–C), 1179 (δ_{ip}ArC–H), 1021 (ν_sC–O–C), 831 (δ_{oop}ArC–H).

Gelation Experiments: A suspension of the gelator (5 mg) in a measured volume of solvent was heated in a sealed test tube to boiling and then cooled to room temperature. Depending on the solvent, a clear solution remained or a precipitate or a gel formed. The minimal gel concentration was estimated by adding 100-μL portions of the solvent to the suspension until a low-viscosity solution instead of a gel formed upon cooling the hot solution.

Photoinduced Gelation: FT-Raman spectra were recorded with a Bruker Equinox 55 interferometer equipped with an FRA 106/S module using a Nd-YAG laser excitation at 1064 nm. Spectra of the sample (*cis*-**3a**, 2.0×10^{-2} M in ethanol) in a quartz cell (10×10 mm^2) were recorded during one hour irradiation ($250 < \lambda < 520$ nm) by an Elektrokovina high-pressure mercury lamp (type Ballast DHM 520–250). To obtain a spectrum of *trans*-**3a** in solution (2.0×10^{-2} M in ethanol), the cell was thermostatted at 75 ± 1 °C by means of a Medingen Dresden thermostat (model U3). All FT-Raman spectra were corrected by subtracting the solvent spectrum.

Temperature-Dependent Measurements: Temperature-dependent FT-IR spectra of the gel (*trans*-**3e**/toluene, 2.0×10^{-2} M) were recorded with an ABB Bomen MB 102 FT-IR spectrometer, equipped with CsI optics, DTGS detector and Specac 3000 Series high stability temperature controller with a 21-20730 heating jacket. A sealed heatable liquid cell (Specac, type 2051, path length 0.05 mm, KBr windows) was used for handling the sample. Temperature-dependent ^{1}H NMR spectra of toluene and DMSO gels (*trans*-**3e**, 2.0×10^{-2} M) was recorded on a Bruker Avance 300 spectrometer using tetramethylsilane and 1,1,2,2-tetrachloroethane as internal standards.

TEM Investigation: Transmission electron micrographs were taken on an EM-10 Zeiss transmission electron microscope from a small amount of an unstained gel sample (*trans*-**3a**/ethanol or *trans*-**3e**/ethanol, 2.0×10^{-2} M) placed on a carbon-coated grid (copper, 100 mesh).

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