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Self-Assembly of Ureido-Pyrimidinone Dimers into One-Dimensional Stacks by Lateral Hydrogen Bonding

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Abstract: Ureido-pyrimidinone (UPy) dimers substituted with an additional urea functionality self-assemble into one-dimensional stacks in various solvents through lateral non-covalent interactions. ^{1}H NMR and DOSY studies in $CDCl_3$ suggest the formation of short stacks (<10), whereas temperature-dependent circular dichroism (CD) studies on chiral UPy dimers in heptane show the formation of much larger helical stacks. Analysis of the concentration-dependent evolution of chemical shift in $CDCl_3$ and the temperature-dependent CD effect in heptane suggest that this self-assembly process follows an isodesmic pathway in both solvents. The length of the aggregates is influenced by substituents attached to the urea functionality. In sharp contrast, UPy dimers carrying an additional urethane group do not self-assemble into ordered stacks, as is evident from the absence of a CD effect in heptane and the concentration-independent chemical shift of the alkylidene proton of the pyrimidinone ring in $CDCl_3$.

Keywords: hydrogen bonds · helical structures · self-assembly · stacking interactions · supramolecular chemistry

Introduction

The *N*,*N*′-disubstituted urea moiety is often used in the construction of hydrogen-bonded supramolecular polymers,[1] organogelators,[2] foldamers[3] and novel crystalline frameworks.[4] Urea groups are known to associate strongly through bifurcated hydrogen bonds,[5] the strength of which exceeds that of amide and urethane hydrogen bonds.[6] The aggregation of *N*,*N*′-disubstituted urea groups leads to the formation of linear chains in the solid state[7] and in solution.[7] FTIR measurements in CCl_4 have shown that the self-assembly of *N*,*N*′-dialkyl-substituted urea groups into linear chains in solution is a cooperative process[8] as a result of polarization of the urea function during dimerization.[9]

Due to the aggregation of urea groups into linear chains, incorporation of these groups in covalent polymers has lead to the formation of thermoplastic elastomers in which cross-linking between the chains occurs through non-covalent interactions.[10] Due to the combination of strongly interacting segments alternating with weakly interacting segments, microphase-separated materials with a soft block/hard block morphology are obtained. When the hard blocks contain urethane and/or urea groups, strong and specific hydrogen-bonding interactions lead to useful properties, such as a high modulus for a given hard-block content.[6,11] In addition, these groups enable molecular recognition and allow for a modular approach in the development of functional (bio)-materials.[12]

Recently, Kautz et al. investigated the effect of a combination of lateral hydrogen bonding between polymeric chains induced by urea and urethane groups and chain extension due to strong end-to-end bonding by the quadruply hydrogen bonding 2-ureido-pyrimidinone (UPy) motif (see Figure 1).[13]

A series of telechelic UPy-, UPy-urea- and UPy-urethane-substituted poly(ethylene butylene) polymers was studied, and it was shown that directional lateral aggrega-

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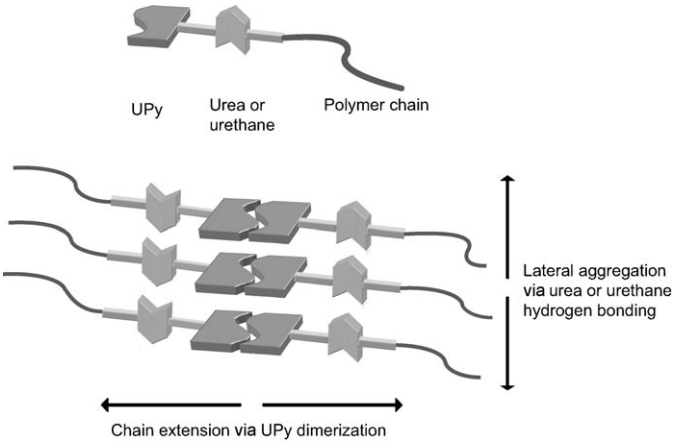
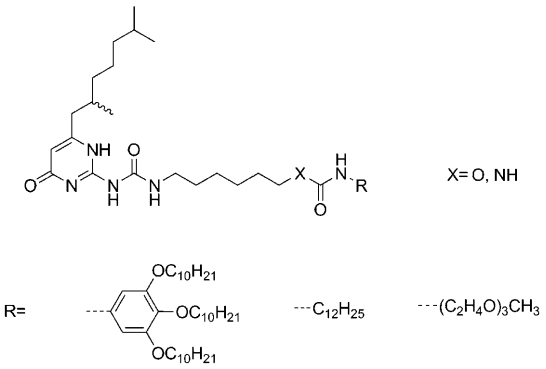


Figure 1. Chain extension and lateral aggregation in UPy-urea- and UPy-urethane-functionalized polymers.



Scheme 1. Design and structure of UPy monomers bearing additional laterally interacting urea or urethane substituents.

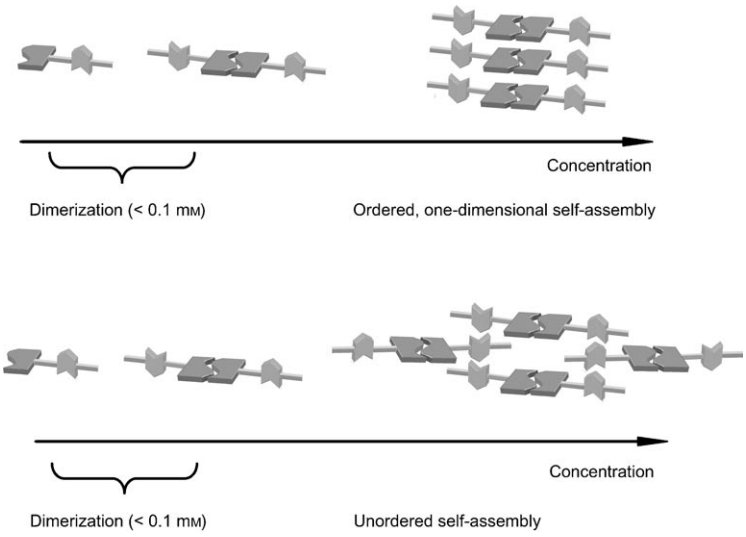


Figure 2. One-dimensional self-assembly and network formation of UPy-urea and UPy-urethane dimers.

tion in these supramolecular polymers results in one-dimensional aggregation of the dimerized UPy end groups into long fibres. Atomic force microscopy (AFM) on these polymers revealed marked differences between the urea- and urethane-substituted UPy polymers. Whereas lateral hydrogen bonding through the urea moiety resulted in the formation of micrometre-long fibres, lateral hydrogen bonding through the urethane moiety resulted in a much smaller and less densely packed morphology compared to the urea-substituted polymers indicating that aggregation is not complete. Furthermore, tensile testing showed that the material properties of these polymers are superior to those of the same supramolecular polymer lacking additional lateral hydrogen bonding. Interestingly, differential scanning calorimetry (DSC) showed that the fibres display a first-order melting transition at high temperatures, while temperature-dependent FTIR measurements have shown that this first-order phase transition is directly associated with the breakup of the UPy-urea aggregates.[13]

Here we aim to further elucidate the aggregation behaviour of UPy-urea and UPy-urethane aggregates. The synthesis of several discrete UPy monomers bearing urea and urethane groups, and their self-assembly in solution, studied by concentration-dependent ^{1}H NMR and temperature-dependent circular dichroism spectroscopy, will be discussed. The design of the UPy monomers is shown in Scheme 1.

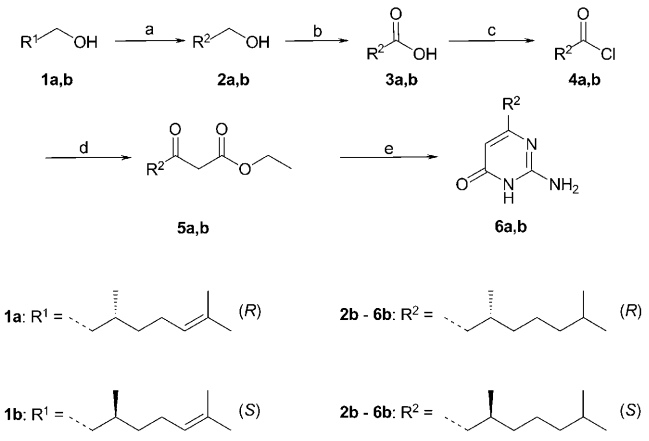
Each UPy monomer consists of the following parts:

1) A UPy group capable of quadruple hydrogen bonding: By dimerization of the two pyrimidinone rings ($K_{dim} = 6 \times 10^7\,M^{-1}$ in $CHCl_3$),[14] a flat surface is created which enhances π–π interactions between two hydrogen-bonded dimers. Previous DFT calculations using an implicit solvent model have shown that π-stacking of the 4[1*H*]-pyrimidinone dimer is an energetically favourable process.[15] This additional interaction is important because it results in the preference for ordered one-dimensional self-assembly over unordered network formation of the UPy-urea dimers (see Figure 2). Furthermore, these calculations have shown that the UPy dimers stack in an offset fashion, inducing formation of a helical aggregate.
2) Chiral groups attached to the C_6 position of the pyrimidinone group: By attaching chiral groups to this position, possible formation of helical aggregates can be biased by perturbation of the equilibrium between *P*- and *M*-type helical aggregates.[16] As a result of this perturbation, the self-assembly of the UPy dimers into ordered aggregates can be conveniently followed by temperature-dependent circular dichroism (CD) spectroscopy.
3) A urea or urethane functionality to induce lateral hydrogen bonding between UPy dimers. Because hydrogen bonding through the urea group is much stronger than hydrogen bonding through the urethane group, variation at this position will greatly influence the lateral association of UPy dimers into one-dimensional aggregates.
4) Additional solubilizing groups attached to urea or urethane moiety: By variation of the R substituent, the self-assembly of UPy dimers equipped with lateral interacting groups can be studied in a wide range of solvents.

Moreover, by introducing an electron-withdrawing aromatic substituent at this position the intermolecular association between the urea groups is expected to strengthen.[17]

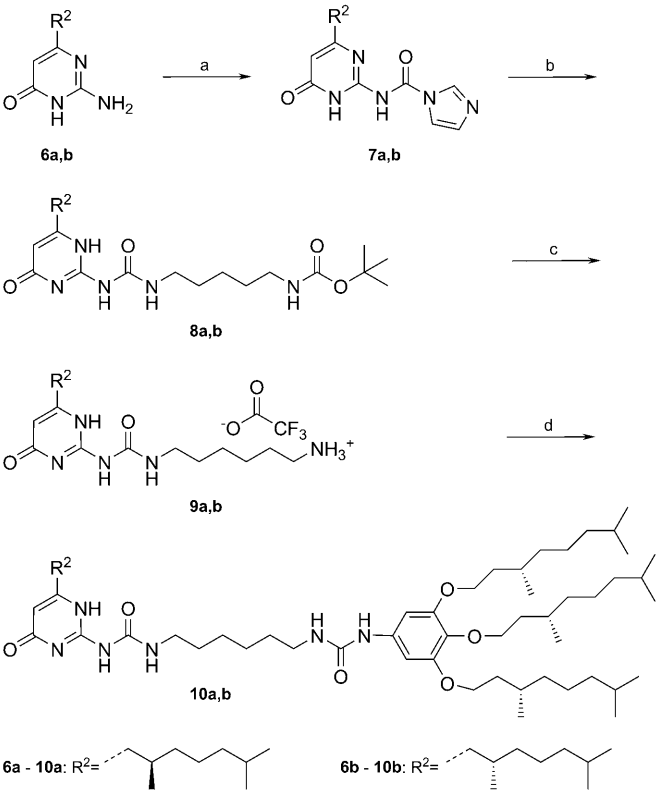
Results and Discussion

The synthesis of chiral isocytosines **6a** and **6b** is depicted in Scheme 2. The synthetic route towards isocytosines **6a** and **6b** was adapted from a previously established route for converting acyl chlorides to isocytosines.[18] The corresponding chiral acyl chlorides were synthesized from commercially available[19] (*R*)-3,7-dimethyl-6-octen-1-ol (**1a**, 100% *ee*) and (*S*)-3,7-dimethyl-6-octen-1-ol (**1b**, 98.4% *ee*) by reduction of the double bond with Pd/C and hydrogen and subsequent oxidation of alcohols **2a** and **2b** in the presence of periodic acid and a catalytic amount of pyridinium chlorochromate[20] to the corresponding carboxylic acids **3a** and **3b**, which were then converted to acyl chlorides **4a** and **4b** with oxalyl chloride.



Scheme 2. Synthetic route towards chiral isocytosines **6a** and **6b**. a) Pd/C, H_2, ethyl acetate, 24 h, RT, 98%; b) periodic acid, 2% pyridinium chlorochromate, acetonitrile, 3 h, 0–25 °C, 81%; c) oxalyl chloride, dimethylformamide (cat.), dichloromethane, 3–12 h, 0-25 °C, 90%; d) ethyl potassium malonate, $MgCl_2$, triethylamine, acetonitrile, 25 h, 0–25 °C, 61%; e) guanidinium carbonate, potassium *tert*-butoxide, ethanol, 43–65 h, reflux, 70%.

Isocytosines **6a** and **6b** were activated with 1,1′-carbonyldiimidazole[21] and further treated with mono-Boc-protected 1,6-hexanediamine in $CHCl_3$. Removal of the Boc group with trifluoroacetic acid resulted in chiral ammonium salts **9a** and **9b** (Scheme 3). Chiral synthons **9a** and **9b** serve as convenient intermediates in the synthesis of various chiral UPy-urea monomers. A chiral 3,4,5-tris[3(*S*),7-dimethyloctyloxy]phenyl group was introduced at this position to ensure solubility in apolar solvents. By introduction of this substituent, two different diastereomers were created: (*R*,*S*,*S*,*S*)-**10a** and (*S*,*S*,*S*,*S*)-**10b**.

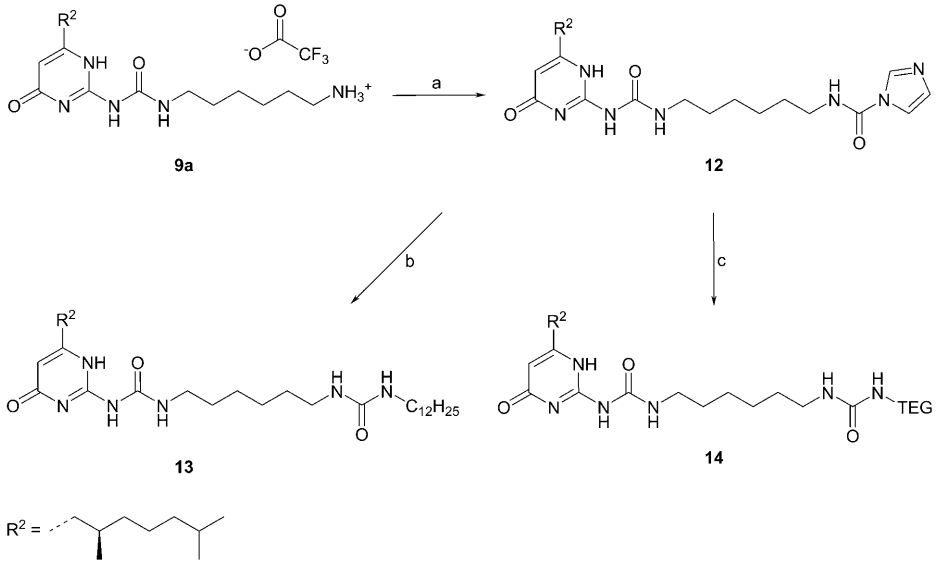


Scheme 3. Synthetic route towards chiral UPy-urea monomers **10a** and **10b** bearing a chiral gallic wedge at the urea functionality. a) 1,1′-Carbonyldiimidazole, $CHCl_3$, 4–12 h, 50 °C; b) mono-Boc-protected 1,6-hexanediamine, $CHCl_3$, 17 h, 50 °C; c) trifluoroacetic acid, dichloromethane, 4–13 h, RT; d) 3,4,5-tris[3(*S*),7-dimethyloctyloxy]phenyl isocyanate (**11**), triethylamine, $CHCl_3$, 48 h, 50 °C. Boc = *tert*-butoxycarbonyl.

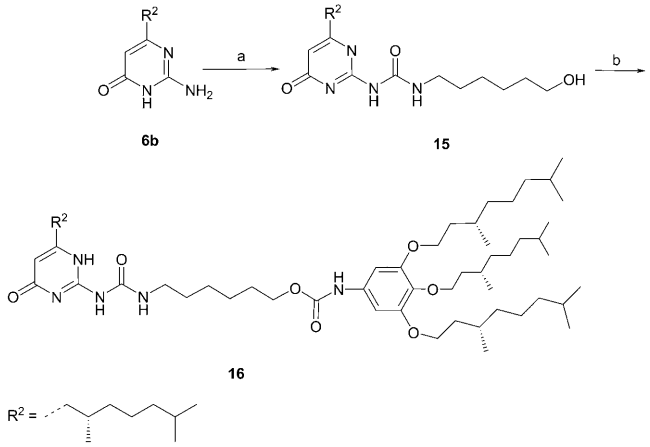
R-Chiral UPy-urea monomer **13** bearing an aliphatic substituent was synthesized in two steps from **9a** (Scheme 4). The solubility of **13** in apolar solvents such as heptane and cyclohexane is extremely low, but in $CDCl_3$ chiral UPy-urea **13** was found to be soluble up to a concentration of 20 mM. A more soluble UPy-urea **14** carrying a triethylene glycol substituent at the urea position was also synthesized in two steps from **9a**.

Finally, (*S*,*S*,*S*,*S*)-chiral UPy-urethane **16** was synthesized in two steps from isocytosine **6b** (Scheme 5) by reaction with 6-isocyanato-1-hexanol at elevated temperatures in dimethyl formamide. Reaction of UPy **15** with 3,4,5-tris[3(*S*),7-dimethyloctyloxy]phenyl isocyanate resulted in chiral UPy-urethane **16**.

Concentration-dependent ^{1}H NMR studies: Concentration-dependent ^{1}H NMR measurements in $CDCl_3$ were performed on UPy-urea **10a** in the concentration range of 0–100 mM, in which all **10a** is present as dimers.[22] These measurements show a downfield shift of both urea NH protons at higher concentrations (Figure 3) accompanied by an upfield shift of the alkylidene proton located at the pyrimidinone ring and significant line broadening. The upfield shift of the proton located on the pyrimidinone ring is typical for self-



Scheme 4. Synthetic route towards *R*-chiral UPy-urea monomer **13** bearing an aliphatic substituent and **14** bearing a triethylene glycol (TEG) substituent at the urea functionality. a) 1,1′-Carbonyldiimidazole, $CHCl_3$, 4 h, 50 °C, 95 %; b) *n*-dodecylamine, $CHCl_3$, 48 h, 55 °C, 73 %; c) 2-[2-(2-methoxyethoxy)ethoxy]ethyl amine, $CHCl_3$, 48 h, 55 °C, 83 %.



Scheme 5. Synthetic route towards *S*-chiral UPy-urethane monomer **16** bearing a chiral gallic wedge at the urethane functionality: a) Di-*tert*-butyl tricarbonate, 6-amino-1-hexanol, dichloromethane, 0.5 h, RT followed by **6b**, dimethylformamide, 4.5 h, 90 °C, 56 %; b) tris[3(*S*),7-dimethyloctyloxy]phenyl isocyanate **11**, dibutyltin dilaurate, $CHCl_3$, 48 h, 60 °C, 34 %.

assembled structures resulting from close contact of aromatics.[23]

Calculations on stacked cytosine assemblies have shown that ring-current effects due to intermolecular interactions result in a small upfield shift (between 0.1 and 0.3 ppm).[24] Moreover, the downfield shift of both urea NH protons indicate that these protons are involved in hydrogen bonds[25] at higher concentrations. The downfield shift of both NH protons and the concomitant upfield shift of the alkylidene proton suggest formation of a larger aggregate in which both urea NH protons involved in hydrogen bonds and the pyrimidinone rings of two UPy dimers are in close contact.

To gain further proof for the aggregation of these molecules, concentration-dependent DOSY measurements were performed on solutions of **10a** in $CDCl_3$ (Figure 4). They show that the viscosity-corrected[26] diffusion constant becomes smaller at higher concentrations, indicative of the formation of an aggregate consisting of multiple dimers of **10a**. The concentration-dependent chemical shift of all protons was subjected to a nonlinear least-squares analysis according to a three-parameter isodesmic (equal *K*) self-association model[27] (see the Supporting Information) using the Levenberg–Marquardt algorithm to gain additional insight into the self-assembly process of UPy-urea dimer **10a·10a**. In this way, the isodesmic equilibrium constant *K*, the chemical shift of protons in the non-aggregated UPy-urea dimer and the limiting value of the chemical shift of the protons within the stack were obtained.

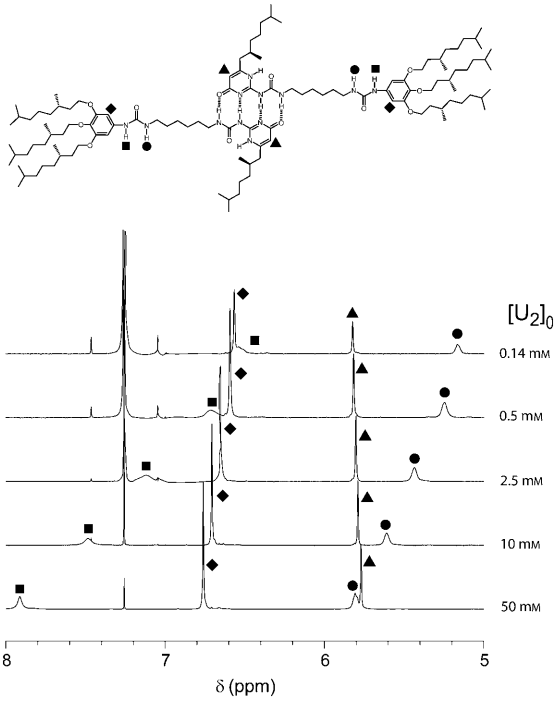


Figure 3. Concentration-dependent ^{1}H NMR spectra of UPy-urea dimer **10a·10a** in $CDCl_3$ at 25 °C.

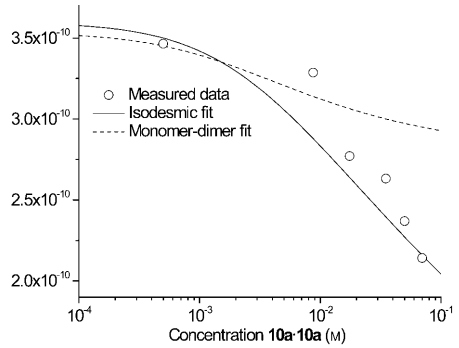


Figure 4. Concentration dependence of the viscosity-corrected[26] average diffusion constant for **10a·10a** in $CDCl_3$ at 25 °C, calculated from the measured diffusion constants of the signals depicted in Figure 3. The solid line represents the best fit of the data to the isodesmic model of indefinite association.

Figure 5 displays concentration-dependent chemical shift data of UPy-urea dimer **10a·10a** as well as the best-fit curves according to the isodesmic indefinite self-assembly model. As can be observed from Figure 5a, the concentration-dependent chemical shift evolution of the urea NH proton (●) is accurately described by the indefinite isodesmic self-assembly model. Fitting of the concentration-dependent chemical shift evolution of the second urea NH proton (■) and the aromatic proton located on the gallic wedge (◆) to the same isodesmic self-assembly model showed that the chemical shift evolution of these protons is also well described by this model. The isodesmic equilibrium constants K of these three protons, as determined by nonlinear least-square fitting, are in the range of 322–387 M^{-1} (Table 1). However, fitting of the concentration-dependent chemical shift evolution of the alkylidene proton (Figure 5b) shows that the isodesmic self-assembly model is inappropriate to describe the experimental data, especially in the high concentration regime. The isodesmic equilibrium constant of this proton was determined to be 254 M^{-1}.

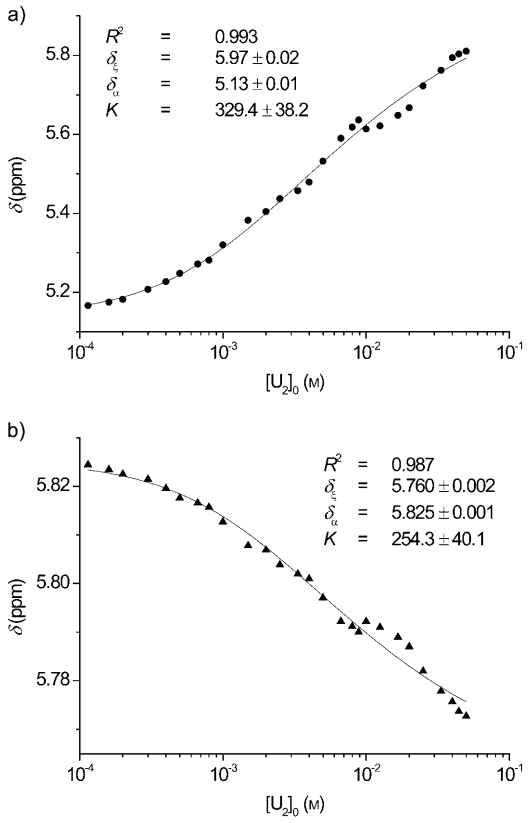


Figure 5. Concentration-dependent chemical shift of UPy-urea dimer **10a·10a**: a) Concentration-dependent chemical shift of the urea NH proton (■); b) concentration-dependent chemical shift of the alkylidene proton (▲). The curves represent the best fit of the data to the isodesmic model of indefinite association.

Table 1. Isodesmic equilibrium constants determined by ^1H NMR spectroscopy with dilution from 10^{-1} to 10^{-4} M in $CDCl_3$ at 25 °C for UPy-urea dimers **10a·10a**, **13·13** and **14·14** and for UPy-urethane dimer **16·16**. The protons are marked according to the symbols used in Figure 3.

UPy dimer	NH ●	NH ■	Gallic aryl	Alkylidene ▲
10a·10a	329 ± 40	322 ± 38	387 ± 41	254 ± 40
13·13[a]	14.9 ± 1.3	14.6 ± 1.9	–[b]	5.1 ± 2.1
14·14	2.4 ± 1.3	2.5 ± 0.5	–[c]	–[c]
16·16	–[a]	4.2 ± 0.5	–[b]	–[c]

[a] Compound **13** precipitates at a concentration of 30 mM. Dilution experiments were carried out between 30 mM and 0.1 mM. [b] Signal not present. [c] The observed changes in chemical shift were too small to be fitted in a reliable way.

The differences between the isodesmic equilibrium constants of the urea NH protons and the alkylidene proton can be attributed to one of the two following effects. Firstly, the error in the determination of the exact chemical shift is much higher for the alkylidene proton than for the urea NH protons, as the former only shifts by 0.1 ppm but the latter by almost 1 ppm. Secondly, the difference in isodesmic equilibrium constant between the two protons can be the result of the fact that self-assembly of UPy-urea dimer **10a·10a** is hierarchical: At low concentrations, hydrogen bonding of the urea NH protons results in formation of a hydrogen-bonded aggregate in which the pyrimidinone rings are not stacked on top of each other. Only at higher concentrations does additional stabilization of the aggregate due to π–π interactions occur.

Nevertheless, the equations that describe the concentration-dependent evolution of chemical shift as a result of dimerization and isodesmic aggregation are algebraically identical apart from a factor of two.[27] Therefore, the quality of the fits alone cannot be used to distinguish between the two mechanisms. It has been shown that either the osmotic coefficient or the concentration dependence of the diffusion coefficient can be used to distinguish between the two possible mechanisms.[28] Fitting of the concentration-dependent diffusion data of UPy-urea dimer **10a·10a**, obtained by PGSE NMR, to a monomer–dimer model and assuming spherical aggregates clearly shows that this model is inappropriate to describe the concentration dependence of the diffusion con-

stant, whereas the isodesmic self-assembly model does show good correspondence (see the Supporting Information).

Dilution of UPy-urea dimer **13·13**, bearing linear aliphatic substituents, resulted in concentration-dependent chemical shifts of both urea NH protons and the alkylidene proton (see the Supporting Information) in $CDCl_3$. Fitting of the concentration-dependent data to a three-parameter isodesmic self-assembly model resulted in isodesmic equilibrium constants for all three protons (Table 1) The average isodesmic equilibrium constant of **13·13** is an order of a magnitude lower than that value of UPy dimer **10a·10a**. As already mentioned, this lower value is most probably the result of decreased acidity of the urea NH protons in **13** compared to those in **10a**, or possibly due to the absence of attractive π–π interactions between aromatic rings at the urea group. In the case of UPy-urea dimer **13·13**, the isodesmic equilibrium constant obtained from the concentration-dependent chemical shifts of the alkylidene proton was also found to be lower than that found for the urea NH protons. Even weaker association was observed for UPy-urea dimer **14·14**, substituted with triethylene glycol chains at the urea positions (Table 1). This decrease, compared to the association constant that was found for UPy-urea dimer **13·13**, is most probably caused by competitive hydrogen bonding from the oxygen atoms in the ethylene glycol chain with the urea NH protons.[29,1c]

Finally, dilution studies were performed on UPy-urethane dimer **16·16** in $CDCl_3$. In sharp contrast to the urea-functionalized ureido-pyrimidinones, no concentration-dependent chemical shift was observed for the alkylidene proton, that is, aromatic stacking interactions are absent even at high concentrations. Fitting of the concentration-dependent chemical shift of the urethane NH proton to a four-parameter[30] indefinite isodesmic self-assembly model resulted in an isodesmic equilibrium constant of only $4.2\,\text{M}^{-1}$.

Temperature-dependent circular dichroism studies: Because UPy-urea dimers **10a·10a** and **10b·10b** are chiral, their self-assembly could be studied by circular dichroism (CD). Indeed, CD spectroscopy performed on solutions of **10a** and **10b** at a concentration of $3.5\times10^{-5}\,\text{M}$ (corresponding to a UPy-dimer concentration of $1.75\times10^{-5}\,\text{M}$) in heptane at room temperature showed the appearance of a Cotton effect indicating formation of an aggregate with supramolecular chirality (Figure 6a and b).[31] The reversibility of the aggregation process was further elucidated by temperature-dependent CD spectroscopy. At high temperatures, disappearance of the Cotton effect indicated formation of non-ag-

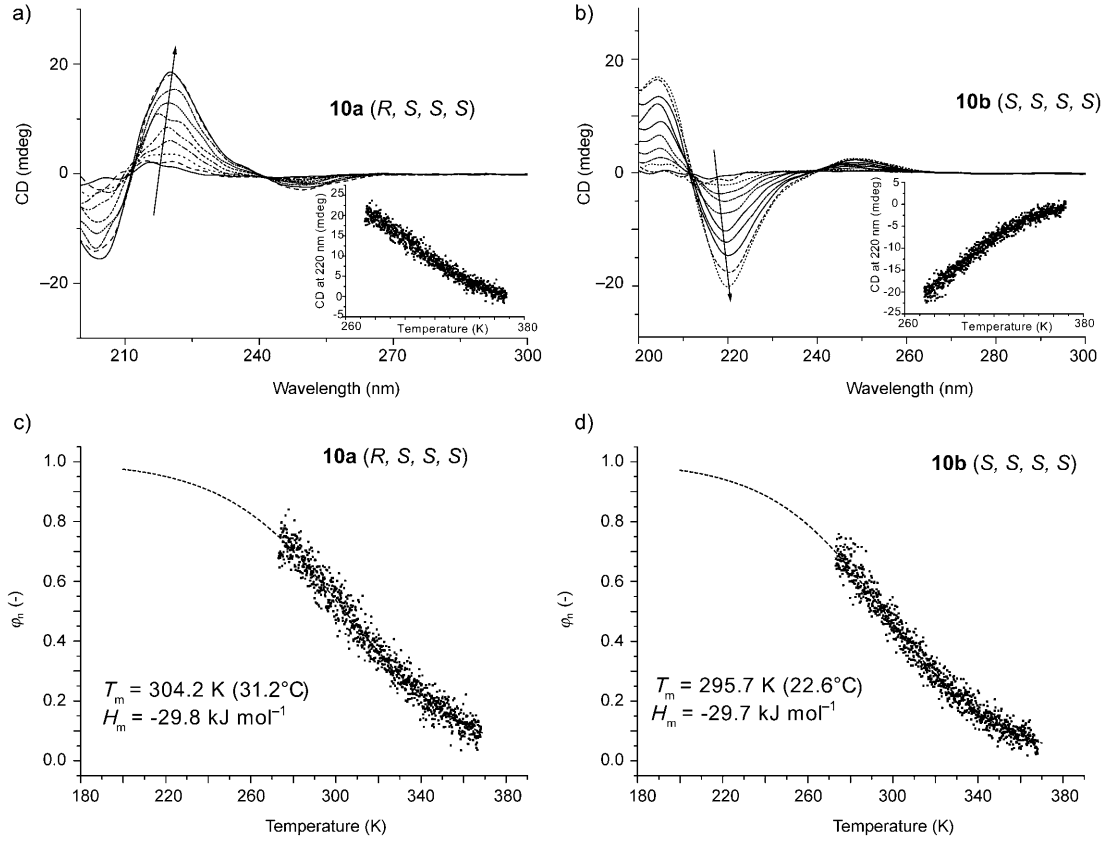


Figure 6. CD spectra of **10a** (a) and **10b** (b) in heptane ($3.5\times10^{-5}\,\text{M}$) at temperatures between 0 and 90 °C with 10 °C intervals (arrow indicates decreasing temperature). Insets show the molar ellipticity at 220 nm as a function of temperature for the same solution. Normalized degree of aggregation (ϕ_n) for **10a** (c) and **10b** (d). The solid lines in c) and d) are the best-fit curves for a temperature-dependent isodesmic self-assembly model.

gregated UPy-urea monomers or dimers, while the Cotton effect reappeared at lower temperatures. At 20 °C, the Cotton effects of **10a** and **10b** at 220 nm are opposite in sign, while the absolute value of the Cotton effects are 15.35 mdeg for UPy-urea **10a** (*R*,*S*,*S*,*S*) and 14.63 mdeg for UPy-urea **10b** (*S*,*S*,*S*,*S*). As this small difference can be explained by the chiral purity[19] of the starting material, it can be concluded that the chirality of the aliphatic chain directly attached to the pyrimidinone ring determines the helicity of the aggregates formed by UPy-urea dimers **10a·10a** and **10b·10b**.

The cooling curves obtained from the temperature-dependent changes of the Cotton effect at 220 nm for UPy-urea **10a** and **10b** are clearly sigmoidal (Figure 6a and b, insets), that is, the self-assembly of the UPy-urea dimers into helical aggregates occurs by an isodesmic (equal *K*) self-assembly mechanism. Fitting of the normalized degree of aggregation ϕ_n by using a temperature-dependent isodesmic self-assembly model[32] showed good correlation with the experimental data (Figure 6c and d). This model was used to obtain the "melting" temperature of the stack (defined as the temperature at which $\phi_n = 0.5$) and the molecular enthalpy release due to noncovalent interactions ΔH_m. From the calculated fraction of aggregated material, an isodesmic equilibrium constant of $4.5 \times 10^5\,\text{M}^{-1}$ at $T = 25\,°\text{C}$ for UPy-urea dimer **10a·10a** in heptane was calculated (see the Supporting Information).

In contrast with the behaviour observed in heptane, a solution of **10a** in the more polar solvent 2-propanol with the same concentration at which a solution of **10a** in heptane showed the appearence of a Cotton effect did not show a Cotton effect, that is, an ordered aggregate is not present in this solvent. As 2-propanol can be expected to compete with the intermolecular hydrogen bonds between UPy-urea dimers, it can be concluded that intermolecular hydrogen bonding of the urea functionality plays an important role in stabilization of the helical aggregate formed by UPy-urea dimer **10a·10a**.

This notion was further confirmed by temperature-dependent CD measurements on UPy-urethane dimer **16·16** in heptane at an analytical concentration of **16** (*S*,*S*,*S*,*S*) of $2.5 \times 10^{-5}\,\text{M}$. For UPy-urethane dimer **16·16**, a Cotton effect was absent, while UPy-urea dimer **10a·10a** does display a Cotton effect at approximately the same concentration. This clearly shows the necessity of strong intermolecular hydrogen bonding for formation of ordered aggregates consisting of stacked UPy dimers.

The isodesmic self-assembly of UPy-urea aggregates in solution raises an interesting question regarding the melting behaviour of UPy-urea-substituted polymers in the bulk. In the bulk, a first-order melting transition has been measured at high temperatures, and it has been shown that this first-order phase transition is directly associated with the breakdown of the UPy-urea aggregates.[12] How is it then possible that a non-cooperative growth process in dilute solution results in a first-order phase transition in the bulk? Recent Monte Carlo simulations on isodesmic supramolecular polymers reveal that a nucleated first-order phase transition is possible when a single supramolecular polymer condenses into a fibril consisting of multiple polymeric chains.[33] Hence, the first-order melting transition of UPy-urea-substituted polymers in the bulk is most probably the result of melting of fibres consisting of multiple UPy-urea aggregates associating through weak interactions, whereas initial formation of the one-dimensional aggregates is a non-cooperative process.

Conclusions

The self-assembly of UPy dimers substituted with additional urea and urethane functionality has been studied in various solvents. ^{1}H NMR dilution experiments on UPy-urea dimer **10a·10a** in $CDCl_3$ showed concentration-dependent chemical shifts for both urea protons and the alkylidene proton on the pyrimidinone ring. At high concentrations, the chemical shift of the two NH protons of the urea functionality shifts downfield, indicative of formation of a hydrogen-bonded aggregate, while that of the alkylidene proton shifts upfield, indicative of close contact between aromatic surfaces at high concentrations. The concentration dependence of the chemical shifts and the diffusion coefficient showed good correspondence with an isodesmic self-assembly model. Based on these observations, it can be concluded that self-assembly of the UPy-urea dimer **10a·10a** occurs by an isodesmic mechanism.

This notion is further confirmed by CD measurements in the less polar solvent heptane. In heptane, **10a** displays a temperature-dependent Cotton effect, indicative of formation of an ordered helical aggregate. From the temperature dependence of the Cotton effect, the fraction of aggregated material at each temperature could be determined, and the isodesmic equilibrium constant at room temperature calculated ($4.5 \times 10^5\,\text{M}^{-1}$). Good agreement between the temperature-dependent isodesmic self-assembly model and the fraction of aggregated molecules was found, that is, also in heptane the self-assembly of UPy-urea dimer **10a·10a** occurs in a stepwise manner.

The isodesmic equilibrium constant in heptane is more than three orders of magnitude higher than in $CDCl_3$, as a result of stronger hydrogen bonds and stronger π–π interactions. In contrast to $CDCl_3$, heptane is unable to disrupt the proposed one-dimensional hydrogen-bond array formed by the urea protons of aggregated **10a·10a**.[34] Furthermore, aromatic–aromatic interactions between UPy-urea dimers **10a·10a** are stronger in apolar solvents than in halogenated solvents such as chloroform, as these compete with the π electrons of the aromatic group.[35]

In contrast to the urea-substituted UPy dimers, urethane-substituted UPy dimer **16·16** displays only a small downfield shift of the NH proton and no upfield shift of the alkylidene proton in $CDCl_3$. This behaviour is translated to the more apolar solvent heptane, as no Cotton effect is observed for **16·16** even at the lowest temperature. The lack of a Cotton

effect for UPy-urethane dimer **16·16** in heptane shows that strong lateral hydrogen bonding between the UPy dimers is necessary to form an ordered aggregate consisting of several UPy dimers.

Experimental Section

General: All chemicals were purchased from Aldrich or Acros and were used as received unless otherwise noted. Dichloromethane was distilled over P_2O_5. Triethylamine was dried over KOH. Tetrahydrofuran was distilled over molecular sieves. $CDCl_3$ and ethyl acetate were dried over 4 Å molecular sieves for at least two days. All reactions were carried out under a protective atmosphere of nitrogen or argon and were followed by thin-layer chromatography (precoated 0.25 mm silica gel plates from Merck), and column chromatography was carried out with silica gel 60 (70–230 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on 400 MHz (Varian Mercury, 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR), 300 MHz (Varian Gemini, 300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR) or 500 MHz NMR spectrometers (Varian Unity Inova, 500 MHZ for ^{1}H NMR and 125 MHZ for ^{13}C NMR). Proton chemical shifts are reported in parts per million downfield from TMS. Carbon chemical shifts are reported downfield from TMS by using the resonance of the deuterated solvent as the internal standard. FTIR spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer with a Universal ATR sampling accessory. Matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectra were obtained on a PerSeptive Biosystems Voyager-DE PRO spectrometer by using an acidic [α-cyano-hydroxycinnamic acid (CHCA)] or a neutral 2-[(2*E*)-3-(4-*tert*-butylphenyl)-2-methylprop-2-enylidene]malononitrile (DCTB)] matrix. Elemental analysis was performed on a Perkin-Elmer 2400 series II CHNS/O Analyzer. Melting points were determined on a Büchi Melting Point B-540 apparatus. Optical rotations were measured on a Jasco DIP-370 digital polarimeter at a wavelength of 589 nm (Na D line) and a temperature of 25 °C. 3(*S*),7-dimethyloctanol (**2b**) was prepared as reported by Schouten et al.[36] 2-[2-(2-methoxyethoxy)ethoxy]ethyl amine was prepared as reported by Scherman et al.[37] 3,4,5-Tris[(*S*)-3,7-dimethyloctyloxy]aniline was prepared as reported by Van Gorp et al.[3a]

^{1}H NMR titrations: ^{1}H NMR dilution experiments on **10a** in $CDCl_3$ were performed on a 500 MHz Varian Unity Inova equipped with a 5 mm ^{1}H/X inverse detection probe with gradient capability at 25 °C. Typical procedure: Compound **10a** (56.9 mg) was dissolved in $CDCl_3$ (1 mL) to give a 100 mM solution, of which 0.6 mL was injected into an NMR tube. This was then diluted to a final concentration of 0.1 mM.

DOSY-NMR titrations: Compound **10a** (135 mg) was dissolved in dry $CDCl_3$ (1.0 mL) to give a 140 mM solution (70 mM in **10a·10a**). This was then diluted to a final concentration of 0.5 mM. At each concentration, a 2D DOSY spectrum was recorded using the DOSY bipolar pulse pair stimulated echo with convection compensation[38] (*Dbppste_cc* in the Varian DOSY package) sequence for the determination of the self-diffusion of the different components at a temperature of 25 °C. The self-diffusion constant was calculated as the average of the values obtained for the signals of the protons located on the gallic wedge, the alkylidene proton and the OCH_2 protons of the citronellyl chains attached to the gallic wedge and were corrected for changes in the viscosity.[26]

CD spectroscopy: CD measurements were performed on a Jasco J-815 spectropolarimeter at appropriate sensitivity, time constant and scan rate. Corresponding temperature-dependent measurements were performed with a PFD-425S/15 Peltier-type temperature controller with a temperature range of 263–383 K and adjustable temperature slope.

Synthesis: The synthesis of compounds **3b**–**10b** (*S* enantiomers) is to a large extent similar to that of the corresponding *R* enantiomers **3a**–**10a**. Synthesis and characterization of the former is described in the Supporting Information.

3(*R*),7-dimethyloctanol (2a): 3(*R*),7-Dimethyl-6-octen-1-ol (**1a**; 10.40 g, 66.6 mmol) was dissolved in ethyl acetate (75 mL) and argon bubbled through the solution for 15 min. Pd/C (0.5 g) was added, the solution was catalytically hydrogenated in a Parr apparatus and after 24 h no more H_2 was taken up. The suspension was filtered over Celite and washed with ethyl acetate (20 mL). After evaporation in vacuo pure **2a** was obtained as an colourless oil (9.71 g, 61.43 mmol, 92 %). ^{1}H NMR ($CDCl_3$): $\delta =$ 3.67–3.58 (m, 2H, C*H*$_2$OH), 1.62–1.47 (m, 3H, CH_2, $(CH_2)_2CHCH_3$), 1.39–1.06 (m, 7H, CH_2, $(CH_2)_2CH(CH_3)_2$), 0.89 (d, 3H, CHC*H*$_3$), 0.87 ppm (d, 6H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): $\delta = 60.0$ (COH), 39.9, 39.2, 37.3, 29.5, 27.9, 24.6, 22.6 (CH_2), 22.5 (CH*C*H$_3$), 19.6 ppm (CH-(*C*H$_3$)$_2$); IR (ATR): $\tilde{\nu} =$ 3324, 2954, 2926, 2870, 1464, 1383, 1366, 1052, 1010, 966 cm^{-1}; $[\alpha]_D^{25} = +3.734$ (neat).

3(*R*),7-Dimethyloctanoic acid (3a): Periodic acid (31.15 g, 136.8 mmol) was dissolved in acetonitrile (500 mL) and the mixture was vigorously stirred at room temperature for 40 min. The solution was cooled on an ice bath and a solution of 3(*R*),7-dimethyloctanol (**2a**, 9.71 g, 61.3 mmol) and acetonitrile (125 mL) was added dropwise. Pyridinium chlorochromate (0.272 g, 1.27 mmol) was added and the solution was stirred for an additional 15 min. The reaction mixture was stirred for 3 h at room temperature, after which the acetonitrile was evaporated in vacuo, ethyl acetate (1000 mL) was added and the mixture extracted with H_2O:brine (1:1 v/v, 600 mL), saturated $NaHSO_3$ (1000 mL) and brine (1000 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo. Kugelrohr distillation (1 mbar, 120 °C) yielded the pure acid as yellow oil (8.54 g, 49.57 mmol, 81 %). $[\alpha]_D^{25} = +4.61$ (neat); ^{1}H NMR ($CDCl_3$): $\delta =$ 12.0 (s, 1H, COH), 2.36–2.31 (dd, 1H, C*H*$_2$COOH), 2.15–2.10 (dd, 1H, C*H*$_2$COOH), 1.97–1.93 (m, 1H, $(CH_2)_2CHCH_3$), 1.55–1.48 (m, 1H, $CH_2CH(CH_3)_2$), 1.31–1.12 (m, 6H, CH_2), 0.95 (d, 3H, CHC*H*$_3$), 0.86 ppm (d, 6H, CH(C*H*$_3$)$_2$; ^{13}C NMR ($CDCl_3$): $\delta =$ 180.3 (*C*OOH), 41.7 ((C=O)CH_2), 39.0, 36.9, 30.1, 27.9, 24.6, 22.6 (CH_2), 22.5 (CH*C*H$_3$), 19.6 ppm (CH(*C*H$_3$)$_2$); IR (ATR): $\tilde{\nu} =$ 2956, 2928, 2870, 2678, 1705, 1463, 1410, 1293, 1220, 936 cm^{-1}.

3(*R*),7-Dimethyloctanoic acid chloride (4a): Under an argon atmosphere 3(*R*),7-dimethyloctanoic acid (**3a**; 8.54 g, 49.51 mmol) was dissolved in distilled dichloromethane (100 mL). The solution was cooled on an ice bath and a drop of dimethylformamide was added. A solution of oxalyl chloride (5.3 mL, 59.41 mmol) in dry dichloromethane (60 mL) was added dropwise and the solution was stirred at room temperature overnight. Evaporation of the solvent and excess oxalyl chloride followed by flushing with toluene yielded the product as a yellow oil (8.50 g, 44.57 mmol, 90 %). ^{1}H NMR ($CDCl_3$): $\delta =$ 2.90–2.85 (dd, 1H, (COOH)C*H*$_2$), 2.70–2.64 (dd, 1H, (COOH)C*H*$_2$), 2.16–2.07 (m, 1H, $(CH_2)_2CHCH_3$), 1.56–1.50 (m, 1H, $CH_2CH(CH_3)_2$), 1.34–1.13 (m, 6H, CH_2), 0.98 (d, 3H, CHC*H*$_3$), 0.88 ppm ((d, 6H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): $\delta =$ 173.0 (*C*OOH), 54.2 ((COOH)CH_2), 38.8, 36.3, 30.7, 27.8, 24.5, 22.6 (CH_2), 22.5 (CH*C*H$_3$), 19.2 ppm (CH(*C*H$_3$)$_2$); IR (ATR): $\tilde{\nu} =$ 2957, 2930, 2871, 1798, 1464, 1385, 985, 967, 929, 724 cm^{-1}.

5(*R*),9-Dimethyl-3-oxodecanoic acid ethyl ester (5a): Potassium ethyl malonate (11.8 g, 66.8 mmol) and dry ethyl acetate (100 mL) were transferred to a round bottom flask. The mixture was cooled on an ice bath under an argon atmosphere. To this mixture triethylamine (12.1 g, 119.5 mmol) was added followed by dry $MgCl_2$ (5.46 g, 57.4 mmol). The mixture was heated at 35 °C for 6 h and subsequently cooled on an ice bath, and a solution of 3(*R*),7-dimethyloctanoic acid chloride (**4a**; 8.3 g, 43,5 mmol) in dry ethyl acetate (35 mL) was added dropwise. The mixture was allowed to stir at room temperature for 19 h and then cooled on an ice bath while adding 13 % HCl (120 mL) carefully while keeping the temperature below 25 °C. The aqueous layer was separated and then back-extracted with $CHCl_3$:ethyl acetate (1:1 v/v, 65 mL). The combined organic layers were washed with 13 % HCl (2×65 mL), followed by H_2O (70 mL), brine (70 mL) and 5 wt % $KHCO_3$ (150 mL). The organic layer was dried over sodium sulfate, filtered and evaporated in vacuo. Column chromatography (SiO_2, $CHCl_3$:methanol 100:0 to 98:2 v/v) yielded the pure product as a yellow oil (7.4 g, 30.53 mmol, 70 %). $[\alpha]_D^{25} = +2.332$ (neat); ^{1}H NMR ($CDCl_3$): $\delta =$ 4.22–4.16 (d, 2H, OC*H*$_2$CH$_3$), 3.41 (s, 2H, (C=O)C*H*$_2$(COOEt)), 2.54–2.49 (dd, 1H, C*H*$_2$(C=O)(COOEt)), 2.36–2.30 (dd, 1H, CH$_2$(C=O)(COOEt)), 2.02–1.81 (m, 1H, $(CH_2)_2CHCH_3$), 1.55–1.48 (m, 1H, $CH_2CH(CH_3)_2$), 1.33–1.10 (m, 6H, CH_2), 0.91–0.85 ppm (m, 12H, C*H*$_3$); ^{13}C NMR ($CDCl_3$): $\delta =$ 202.4 (COOH), 167.0 ((O=C)O),

61.1(OCH_2), 50.3 ((C=O)CH_2(COOEt)), 49.6 ((C=O)CH_2), 38.9, 36.9, 28.8, 27.8, 24.5, 22.5, 22.4, 19.6 (CH_2), 19.3 ($CHCH_3$), 14.0 ppm (CH(CH_3)$_2$); IR (ATR): $\tilde{\nu}$ = 2956, 2929, 2871, 1744, 1716, 1647, 1630, 1465, 1367, 1315, 1232, 1150, 1096, 1030 cm^{-1}.

2-Amino-6-(2(*R*),6-dimethylheptyl)-6[1*H*]-pyrimidinone (6a): 5(*R*),9-Dimethyl-3-oxodecanoic acid ethyl ester (**5a**; 7.4 g, 30.53 mmol), guanidinium carbonate (3.364 g, 40.30 mmol, 1.3 equiv) and potassium *tert*-butoxide (3.43 g, 30.53 mmol) were dissolved in ethanol (120 mL) and the solution was stirred at reflux for 65 h. The solvent was evaporated in vacuo and $CHCl_3$ (400 mL) was added. The organic layer was extracted with 10% citric acid (2×200 mL), saturated $KHCO_3$ (2×200 mL) and brine (2×200 mL). The organic layer was dried over sodium sulfate. The product was concentrated in vacuo and precipitated in pentane. Column chromatography (SiO_2, $CHCl_3$:EtOH 100:0 to 95:5 v/v) yielded the pure isocytosine (4.45 g, 18.73 mmol, 61%) as a slightly yellow solid. M.p. 201.9–208.7 °C; $[\alpha]_D^{25} = +0.031$ (0.02 g mL^{-1} in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 7.00 (br s, 3H, NH), 5.56 (s, 1H, C=CH), 2.42–2.37 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2), 2.14–2.09 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2)), 1.83 (m, 1H, (CH_2)$_2$C*H*CH_3), 1.53–1.46 (m, 1H, CH_2C*H*(CH_3)$_2$), 1.31–1.10 (m, 6H, CH_2), 0.89–0.84 ppm (m, 9H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 38.9, 36.8, 27.7, 24.5, 22.5 (CH_2), 22.3 ($CHCH_3$), 19.1 ppm (CH(CH_3)$_2$); IR (ATR): $\tilde{\nu}$ = 3320, 3104, 2953, 2926, 2869, 2742, 1645, 1612, 1520, 1467, 1384 cm^{-1}; MALDI-TOF MS: *m*/*z*: calcd: 237.18; found: 238.27 $[M+H]^+$; elemental analysis (%) calcd for $C_{13}H_{23}N_3O$: C 65.79, H 9.77, N 17.70; found: C 66.12, H 9.78, N 17.85.

2-(1-Imidazolylcarbonylamino)-6-[2(*R*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (7a): 2-Amino-6-(2(*R*),6-dimethylheptyl)-6[1*H*]-pyrimidinone (**6a**; 1.5 g, 6.31 mmol) and 1,1′-carbonyldiimidazole (1.24 g, 7.58 mmol) were dissolved in dry $CHCl_3$ (20 mL) under an argon atmosphere at 50 °C and the solution stirred overnight. $CHCl_3$ (50 mL) was added and the organic layer was extracted with H_2O (2×35 mL) and brine (2×35 mL). The organic layer was dried over magnesium sulfate and evaporated in vacuo. Trituration in diethyl ether (20 mL) yielded the product as a white solid (1.62 g, 4.89 mmol, 77%). ^{1}H NMR ($CDCl_3$): δ = 12.01–11.86 (br s, 2H, NH), 8.86 (s, 8.86, NCH=N), 7.64 (s, 1H, (C=O)NC*H*=CH), 7.02 (s, 1H, (C=O)NCH=C*H*), 5.79 (s, 1H, C=C*H*), 2.63–2.60 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2), 2.46–2.41 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2)), 1.97–2.00 (m, 1H, (CH_2)$_2$C*H*CH_3), 1.54–1.51 (m, 1H, CH_2C*H*(CH_3)$_2$), 1.44–1.15 (m, 6H, CH_2), 1.00–0.86 ppm (m, 9H, CH_3).

2-(6-[*tert*-Butoxycarbonylamino]hexylureido)-6-[2(*R*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (8a): 2-(1-Imidazolylcarbonylamino)-6-[2(*R*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (**7a**; 1.60 g, 4.83 mmol) and mono-Boc-protected 1,6-hexanediamine (1.25 g, 5.77 mmol) were dissolved in dry $CHCL_3$ (20 mL) under an argon atmosphere and the solution stirred at 50 °C for 17 h. $CHCl_3$ (100 mL) was added and the solution was extracted with 1 M HCl (60 mL), saturated $NaHCO_3$ (60 mL) and brine (60 mL). The organic layer was dried over magnesium sulfate, filtered and evaporated in vacuo to give the product as a white solid (2.17 g, 4.52 mmol, 94%). M.p. 122.0–123.1 °C; $[\alpha]_D^{25} = +0.48$ (50 mg mL^{-1} in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 13.18 (s, 1H, C=CNHC), 11.87 (s, 1H, CNH(C=O)), 10.17 (s, 1H, (C=O)N*H*-CH_2), 5.82 (s, 1H, C=C*H*), 4.64 (s, 1H, NHBoc), 3.32–3.19 (q, 2H, NHC$H_2$$CH_2$), 3.17–3.08 (q, 2H, CH_2CH_2NHBoc), 2.51–2.39 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2), 2.32–2.16 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2)), 1.82 (m, 1H, (CH_2)$_2$C*H*CH_3), 1.61 (m, 1H, CH_2C*H*(CH_3)$_2$), 1.60–1.03 (m, 23H, CH_2, CH_3), 0.99–0.65 ppm (m, 9H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 173.1, 156.6, 155.9, 154.7, 151.5, 106.8, 78.9 (O*C*(CH_3)$_3$), 40.4, 39.7, 38.9, 16.6, 31.9, 29.8, 29.3, 28.4, 27.8, 26.4, 26.2, 24.5, 22.6, 22.5, 19.2 ppm; IR (ATR): $\tilde{\nu}$ = 3217, 1954, 2929, 2868, 1698, 1659, 1585, 1525, 1462, 1390, 1365, 1251, 1172, 1140, 801 cm^{-1}; elemental analysis (%) calcd for $C_{25}H_{45}N_5O_4$: C 62.60, H 9.46, N 14.60; found: C 62.37, H 9.44, N 14.66; MALDI-TOF MS: *m*/*z*: calcd: 479.35; found: 480.22, 502.21 $[M+Na]^+$.

2-(6-Aminohexylureido)-6-[2(*R*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (9a): 2-(6-[*tert*-Butoxycarbonylamino]hexylureido)-6-[2(*R*),6-dimethylheptyl]-4[1*H*]-pyrimidinone **8a** (2.17 g, 4.52 mmol) was stirred in distilled dichloromethane (200 mL). Trifluoroacetic acid (TFA) (65 mL, 30 equiv) was added at room temperature and the mixture was stirred for 13 h. Afterwards, trifluoroacetic acid and dichloromethane were evaporated in vacuo and the remaining solid was flushed several times with toluene. Trituration with diethyl ether (25 mL) yielded the product as a white solid (1.96 g, 3.97 mmol, 88%). M.p. 123.4–130.3 °C; ^{1}H NMR ([D_6]DMSO): δ = 10.6–8.4 (br s, 2H, CNH(C=O), (C=O)N*H*CH_2), 7.73 (s, 1H, CH_2NH_3^+), 7.61 (s, 1H, C=CNHC), 5.76 (s, 1H, C=CH), 3.17–3.12 (q, 2H, NHC$H_2$$CH_2$), 2.80–2.75 (q, 2H, CH_2CH_2NH_3^+), 2.38–2.30 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2)), 2.17–2.12 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2)), 1.90–1.78 (m, 1H, (CH_2)$_2$C*H*CH_3), 1.55–1.44 (m, 1H, CH_2C*H*(CH_3)$_2$), 1.39–1.09 (m, 14H, CH_2), 0.87–0.79 ppm (m, 9H, CH_3); ^{13}C NMR ([D_6]DMSO): δ = 167.6, 162.7, 155.7, 152.5, 106.1, 44.9, 39.7, 39.5, 37.3, 32.4, 29.9, 28.3, 27.9, 26.7, 26.4, 25.1, 23.5, 23.4, 20.2 ppm; IR (ATR): $\tilde{\nu}$ = 2934, 2866, 1698, 1640, 1575, 1526, 1465, 1435, 1251, 1202, 1182, 1133, 835, 798, 722 cm^{-1}; MALDI-TOF MS: *m*/*z*: calcd: 379.29; found: 380.41, 402.40 $[M+Na]^+$; elemental analysis (%) calcd for $C_{22}H_{39}F_3N_5O_4$: C 53.54, H 7.76, N 14.19; found: C 52.50, H 7.40, N 13.75 (0.15 equiv TFA).

2-{6-(3,4,5-Tris[3(*S*),7-dimethyloctyloxy]phenylureido}hexylureido-6-[2(*R*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (10a): 2-(6-Aminohexylureido)-6-(2(*R*),6-dimethylheptyl)-4[1*H*]-pyrimidinone (**9a**; 0.50 g, 1.01 mmol) was dissolved in dry Et_3N (0.11 g, 1.11 mmol, 1.1 equiv) and distilled $CHCl_3$ (20 mL). 3,4,5-Tris[3(*S*),7-dimethyloctyloxy]phenyl isocyanate (**11**; 0.71 g, 1.22 mmol, 1.2 equiv) was added and the mixture stirred under argon atmosphere at 50 °C for 48 h. Afterwards, $CHCl_3$ (15 mL) was added and the organic layer was extracted with $NaHCO_3$ (25 mL), citric acid (25 mL, pH 3~4) and brine (25 mL). The organic layer was dried over magnesium sulfate and evaporated in vacuo. The pure product was obtained after column chromatography (SiO_2, $CHCl_3$:ethanol 98:2 to 95:5 v/v) and precipitation in cold acetonitrile (40 mL) as an off-white solid (0.43 g, 0.44 mmol, 45%). M.p. 99.8–102.9 °C; $[\alpha]_D^{25} = +1.32$ (25 mg mL^{-1} in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 13.32 (s, 1H, CNHC), 11.75 (s, 1H, CNHC=O), 10.03 (s, 1H, O=CN*H*CH_2), 7.74 (s, 1H, O=CNHC_{arom}), 6.74 (s, 2H, CH_{arom}), 5.78 (s, 1H, C=C*H*), 5.73 (s, 1H, CH_2N*H*C=O), 3.99–3.86 (m, 6H, OCH_2), 3.25–3.17 (m, 4H, HNC$H_2$$CH_2$), 2.51–2.45 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2), 2.25–2.19 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2)), 1.85–1.11 (m, 46H, alkyl H), 0.97–0.84 ppm (m, 36H, CH_3); ^{1}H NMR ([D_7]DMF): δ = 12.08–11.72 (br s, 1H, CNHC), 10.04–9.63 (br s, 1H, CNHC=O), 8.53 (s, 1H, O=CNHC_{arom}), 8.03–7.81 (br s, 1H, O=CN*H*CH_2), 7.07 (s, 2H, CH_{arom}), 6.35 (s, 1H, CH_2N*H*C=O), 5.96 (s, 1H, C=CH), 4.20–4.01 (m, 6H, OCH_2), 3.44–3.32 (m, 4H, HNC$H_2$$CH_2$), 2.61–2.57 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2), 2.37–2.32 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2)), 2.03–1.26 (m, 46H, alkyl H), 1.21–1.01 ppm (m, 36H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 173.5, 156.3, 156.2, 154.8, 153.3, 152.3, 135.5, 133.4, 106.4, 98.2, 71.8, 67.3, 40.4, 39.4, 39.4, 39.0, 37.6, 37.4, 37.3, 36.8, 36.4, 32.0, 29.8, 29.7, 29.4, 29.1, 28.0, 27.9, 25.8, 25.6, 24.7, 24.5, 22.7, 22.6, 22.6, 22.6, 22.5, 19.6, 19.5, 19.5, 19.2 ppm; IR (ATR): $\tilde{\nu}$ = 3333, 2954, 2927, 2869, 1656, 1583, 1504, 1464, 1423, 1250, 1227, 1114, 907 cm^{-1}; MALDI-TOF MS: *m*/*z*: calcd: 966.78; found: 967.72; elemental analysis (%) calcd for $C_{57}H_{102}N_6O_6$: C 70.76, H 10.63, N 8.69; found: 70.97, H 10.67, N 8.73.

3,4,5-Tris[3(*S*),7-dimethyloctyloxy]phenyl isocyanate (11): Under argon atmosphere, a solution of 3,4,5-tris(3(*S*),7-dimethyloctyloxy)aniline (0.69 g, 1.23 mmol) in distilled toluene (25 mL) was added to a solution of phosgene (20% w/w in toluene, 2.43 g, 12.9 mL, 24.56 mmol, 20 equiv) and the mixture stirred at room temperature. After 3 h the excess phosgene and solvent were evaporated in vacuo. This yielded the pure compound as a brown oil. (0.71 g, 1.21 mmol, 98%). ^{1}H NMR ($CDCl_3$): δ = 6.29 (s, 2H, C=CHC), 3.98–3.91 (m, 6H, OCH_2), 1.86–1.13 (m, 30H, alkyl H), 0.95–0.91 (d, 9H, CHCH_3), 0.88–0.86 ppm (d, 18H, CH(CH_3)$_2$); IR (ATR): $\tilde{\nu}$ = 2954, 2927, 2870, 2264, 1588, 1436, 1384, 1227, 1117 cm^{-1}; MALDI-TOF MS *m*/*z*: calcd: 587.49; found: 587.43 $[M]^{\cdot}$.

2-(6-[1-Imidazolylcarbonylamino]hexylureido-6-[2(*R*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (12): A mixture of **9a** (1.00 g, 2.0 mmol), 1,1′-carbonyldiimidazole (0.39 g, 2.4 mmol) and dry triethylamine (0.30 g, 3 mmol) in 5 mL of dry $CHCl_3$ was stirred for 4 h at 50 °C under an atmosphere of argon, until the mixture became clear. After evaporation of the solvent in vacuo, the residue was transferred to a glass filter with acetone (3×5 mL), filtered, rinsed with acetone (3×5 mL) and diethyl ether (5 mL) and dried in vacuo at 50 °C. The product was obtained as an off-white

powder (0.9 g, 1.9 mmol, 95%). ^{1}H NMR ($CDCl_3$): δ = 13.33 (s, 1H, NH), 11.85 (s, 1H, NH), 10.02 (s, 1H, NH), 8.20 (s, 1H, imidazole CH), 7.47 (s, 1H, imidazole CH), 7.05 (s, 1H, imidazole CH), 5.64 (s, 1H, O=CC*H*=CCH_2), 3.47–3.25 (m, 4H, NHCH_2CH_2), 2.46–2.36 (dd, 1H, CH=CCH_2CH(CH_3)CH_2), 2.24–2.13 (dd, 1H, CH=CCH_2CH(CH_3)CH_2), 1.69–1.11 (m, 17H, CH_2 and CH_2-C*H*-(CH_3)$_2$), 0.90 (d, 3H, CH_3), 0.86 ppm (d, 6H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 173.6, 156.4, 154.7, 152.3, 149.1, 136.0, 130.0, 116.1, 106.3, 40.4, 40.0, 38.9, 38.8, 36.6, 31.9, 29.1, 28.4, 27.8, 25.2, 25.1, 24.5, 22.6, 22.5, 19.1 ppm; IR (ATR): $\tilde{\nu}$ = 3219, 3029, 2929, 2867, 1743, 1698, 1656, 1581, 1523, 1479, 1466, 1381, 1365, 1315, 1284, 1249, 1138, 1101, 1062, 1017, 953, 913, 838, 735 cm^{-1}.

2-(6-[2-Dodecylureido]hexyl)ureido-6-[2(*R*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (13): Activated UPy **12** (0.20 g, 0.42 mmol) and *n*-dodecylamine (0.12 g, 0.65 mmol) were added to dry $CHCl_3$ (5 mL) and the mixture stirred at 55°C for 2 d under an atmosphere of argon. After the mixture had been cooled to room temperature, $CHCl_3$ (25 mL) was added, and the mixture was extracted with 0.1 M HCl (aq) (3×15 mL), neutralized with saturated $NaHCO_3$ (aq) (20 mL) and washed with brine (20 mL). After drying with $MgSO_4$ the solvent was removed by evaporation in vacuo to give the crude 2-ureido-pyrimidinone. Further purification by recrystallization from 2-propanol resulted in pure **13** as a white powder (0.18 g, 0.30 mmol, 73%). M.p. 155°C; ^{1}H NMR ($CDCl_3$): δ = 13.22 (s, 1H, NH), 11.85 (s, 1H, NH), 10.10 (s, 1H, NH), 5.82 (s, 1H, O=CC*H*=CCH_2), 4.64 (t, 1H, NH), 4.42 (t, 1H, NH), 3.25 (m, 2H, NHCH_2CH_2), 3.18–3.11 (m, 4H, NHCH_2CH_2), 2.50–2.45 (dd, 1H, CH=CCH_2CH(CH_3)CH_2), 2.27–2.21 (dd, 1H, CH=CCH_2CH(CH_3)CH_2), 1.83 (m, 1H, CH=CCH_2C*H*(CH_3)CH_2), 1.61–1.12 (m, 35H, CH_2 and CH_2C*H*-(CH_3)$_2$), 0.95–0.86 ppm (m, 12H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 173.3, 158.5, 156.5, 154.8, 151.8, 106.7, 40.54, 40.48, 40.1, 39.6, 39.0, 36.7, 32.0, 31.9, 30.3, 29.71–29.60 (m), 29.38, 29.34, 29.23, 27.9, 26.9, 26.2, 26.1, 24.5, 22.67, 22.66, 22.5, 19.2, 14.1 ppm; IR (ATR): $\tilde{\nu}$ = 3317, 3222, 2954, 2923, 2853, 1699, 1655, 1627, 1575, 1527, 1482, 1462, 1378, 1366, 1320, 1307, 1294, 1256, 1179, 1135, 1098, 1019, 941, 907, 892, 860, 801, 769, 742 cm^{-1}; MALDI-TOF MS: *m*/*z*: calcd: 590.49; found: 591.54, 613.50 $[M+Na]^+$, 629.47 $[M+K]^+$; elemental analysis (%) calcd for $C_{33}H_{62}N_6O_3$: C 67.08, H 10.58, N 14.22; found: C 66.45, H 10.87, N 14.05.

2-(6-[2-{2-(2-Methoxyethoxy)ethoxy}ethylureido]hexyl)ureido-6-[2(*R*),6-dimethylheptyl]-4[^{1}*H*]-pyrimidinone (14): Activated UPy **12** (0.20 g, 0.42 mmol) and 2-{2-[2-methoxyethoxy]ethoxy}ethyl amine (1.06 g, 0.65 mmol) were added to dry $CHCl_3$ (4 mL) and the mixture stirred at 55°C for 2 days under an atmosphere of argon. After the mixture had been cooled to room temperature, $CHCl_3$ (20 mL) was added, and the mixture was extracted with 0.1 M HCl (aq) (3×10 mL), neutralized with saturated $NaHCO_3$ (aq) (15 mL) and washed with brine (15 mL). After the mixture had been dried with $MgSO_4$ the solvent was removed by evaporation in vacuo to give the crude ureido-pyrimidinone. Further purification by recrystallization from 2-propanol resulted in pure **14** as a white powder (0.20 g, 0.35 mmol, 83%). M.p. 135.5°C; ^{1}H NMR ($CDCl_3$): δ = 13.18 (s, 1H; NH), 11.87 (s, 1H, NH), 10.16 (s, 1H, NH), 5.81 (s, 1H, O=CC*H*=CCH_2), 5.08 (t, 1H, NH), 4.98 (t, 1H, NH), 3.65–3.54 (m, 10H, OCH_2), 3.39–3.35 (m, 5H, OCH_3 and NHCH_2), 3.24 (m, 2H, NHCH_2CH_2), 3.14 (m, 2H, NHCH_2CH_2), 2.50–2.45 (dd, 1H, CH=CCH_2CH(CH_3)CH_2), 2.27–2.21 (dd, 1H, CH=CCH_2CH(CH_3)CH_2), 1.83 (m, 1H, CH=CCH_2C*H*(CH_3)CH_2), 1.61–1.12 (m, 15H, CH_2 and CH_2C*H*-(CH_3)$_2$), 0.94 (d, 3H, CH_3), 0.87 ppm (d, 6H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 173.1, 158.6, 156.5, 154.7, 151.6, 106.7, 71.9, 70.6, 70.3, 70.1, 58.8, 40.4, 40.1, 39.8, 38.9, 36.6, 31.9, 30.1, 29.4, 27.8, 26.5, 26.4, 24.5, 22.6, 22.5, 19.2 ppm; FTIR (ATR, solid state): $\tilde{\nu}$ = 3340, 3220, 2929, 2958, 1700, 1655, 1624, 1572, 1527, 1483, 1463, 1382, 1366, 1351, 1294, 1255, 120, 1200, 1183, 1110, 1028, 1005, 941, 854, 801, 769, 743 cm^{-1}; MALDI-TOF MS: *m*/*z*: calcd: 568.39; found: 569.46, 591.44 $[M+Na]^+$, 607.42 $[M+K]^+$; elemental analysis (%) calcd for $C_{28}H_{52}N_6O_6$: C 59.13, H 9.22, N 14.78; found: C 59.48, H 9.35, N 14.74.

2-(6-Hydroxyhexylureido)-6-[2(*S*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (15): A solution of 6-amino-1-hexanol (0.56 g, 4.81 mmol, 1.1 equiv) in distilled dichloromethane (15 mL) was added to a solution of di-*tert*-butyl carbonate (1.37 g, 5.25 mmol, 1.2 equiv) in dry dichloromethane (10 mL) at room temperature under argon atmosphere. The reaction mixture showed immediate gas evolution (CO_2) indicating formation of the isocyanate. Stirring was continued for 1 h. This reaction mixture was slowly added to a solution of 2-amino-6-[2(*S*)-dimethylheptyl]-4[1*H*]-pyrimidinone (**6b,** 1.04 g, 4.38 mmol) in dry dimethylformamide (20 mL) at 90°C under an argon atmosphere. The reaction mixture was stirred for 4.5 h, after which it was cooled. The solvent was evaporated in vacuo and the remaining solid was recrystallized from cold acetone (30 mL), filtered and washed with cold diethyl ether. Column chromatography (SiO_2, $CHCl_3$/ethanol 93:7 v/v), yielded the pure product as a white solid (0.94 g, 2.47 mmol, 56%). M.p. 99.9–101.7°C; ^{1}H NMR ($CDCl_3$): δ = 13.20 (s, 1H, C=CNHC), 11.86 (s, 1H, CNH(C=O)), 10.11 (s, 1H, (C=O)N*H*CH_2)), 5.84 (s, 1H, C=CH), 3.64–3.61 (q, 2H, CH_2CH_2OH), 3.30–3.25 (q, 2H, NHCH_2CH_2), 2.49–2.44 (dd, 1H, (CH=C)CH_2CH(CH_3)-(CH_2), 2.27–2.21 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2)), 1.78–1.67 (m, 1H, (CH_2)$_2$C*H*CH_3), 1.65–1.51 (m, 1H, CH_2C*H*(CH_3)$_2$), 1.48–1.11 (m, 14H, CH_2), 0.96–0.84 ppm (m, 9H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 173.4, 156.6, 154.7, 151.7, 106.8, 62.0, 40.4, 39.3, 39.0, 36.7, 32.5, 31.9, 29.3, 27.9, 25.8, 24.6, 24.5, 22.6 (CH(CH_3)$_2$)., 22.5 (CH(*C*H$_3$)$_2$), 19.2 (CH(CH_3)$_2$), 19.1 ppm (*C*HCH_3); IR (ATR): $\tilde{\nu}$ = 3021, 2955, 2929, 2855, 1702, 1655, 1562, 1527, 1463, 1251, 1055, 798, 750, 740 cm^{-1}; MALDI-TOF MS: *m*/*z*: calcd: 380.28; found: 381.13, 403.12 $[M+Na]^+$; elemental analysis (%) calcd for $C_{20}H_{36}N_4O_3$: C 63.13, H 9.54, N 14.72; found: C 62.97, H 9.56, N 14.52.

2-{6-(3,4,5-Tris(3(*S*),7-dimethyloctyloxy)-phenylurethane}hexylureido-6-[2(*S*),6-dimethylheptyl]-4[1*H*]-pyrimidinone (16): 2-(6-Hydroxyhexylureido)-6-(2(*S*),6-dimethylheptyl)-4[1*H*]-pyrimidinone (**15**; 0.50 g, 1.31 mmol) was dissolved in distilled $CHCl_3$ (20 mL). 3,4,5-Tris[3(*S*),7-dimethyloctyloxy]phenyl isocyanate (**11**, 0.93 g, 1.58 mmol, 1.2 equiv) and a drop of dibutyltin dilaurate (cat.) were added to the solution and the mixture stirred under argon atmosphere at 60°C for 48 h. $CHCl_3$ (20 mL) was added and the organic layer was extracted with $NaHCO_3$ (25 mL), citric acid (25 mL, pH 3–4) and brine (25 mL). The organic layer was dried over magnesium sulfate and evaporated in vacuo. The pure product was obtained after column chromatography (SiO_2, $CHCl_3$:ethanol 98:2 v/v) (SiO_2, ethyl acetate:heptane 4:6 v/v) and precipitation in cold acetonitrile (25 mL) as an off-white solid (0.42 g, 0.434 mmol, 34%). M.p. 79.9–82.0°C; ^{1}H NMR ($CDCl_3$): δ = 13.17 (s, 1H, CNHC), 11.88 (s, 1H, CNHC=O), 10.20 (s, 1H, O=CN*H*CH_2), 6.69 (s, 1H, O=CN*H*C_{arom}), 6.66 (s, 2H, CH_{arom}), 5.80 (s, 1H, C=CH), 4.15–4.12 (s, 2H, CH_2CH_2O), 4.00–3.88 (m, 6H, OCH_2), 3.28–3.23 (m, 4H, HNCH_2CH_2), 2.46–2.43 (dd, 1H, (CH=C)CH_2CH(CH_3)(CH_2), 2.25–2.23 (dd, 1H, (CH=C)CH_2CH(CH_3)-(CH_2)), 1.86–1.14 (m, 46H, alkyl-*H*), 0.93–0.84 ppm (m, 36H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 173.2, 156.6, 154.7, 153.7, 153.3, 151.6, 134.1, 133.7, 106.8, 97.6, 71.7, 67.3, 65.2, 40.4, 39.9, 39.4, 39.3, 39.0, 37.5, 37.4, 37.3, 36.7, 36.4, 31.9, 29.8, 29.7, 29.3, 28.6, 28.0, 27.9, 26.6, 25.6, 24.7, 24.5, 22.7, 22.6, 22.6, 22.6, 22.5, 19.6, 19.5, 19.2 ppm; IR (ATR): $\tilde{\nu}$ = 2954, 2927, 2869, 1699, 1657, 1581, 1525, 1506, 1463, 1428, 1247, 1216, 1116, 908, 730 cm^{-1}; elemental analysis (%) calcd for $C_{57}H_{101}N_5O_7$: C 70.69, H 10.51, N 7.23; found: C 70.90, H 10.75, N 6.78; MALDI-TOF MS: *m*/*z*: calcd: 967.77; found: 968.78.

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[1] a) F. Lortie, S. Boileau, L. Bouteiller, C. Chassenieux, B. Demé, G. Ducouret, M. Jalabert, F. Lauprêtre, P. Terech, *Langmuir* **2002**, *18*, 7218; b) S. Boileau, L. Bouteiller, F. Lauprêtre, F. Lortie, *New J. Chem.* **2000**, *24*, 845; c) E. Obert, M. Bellot, L. Bouteiller, F. Andrioletti, C. Lehen-Ferrenbach, F. Boué, *J. Am. Chem. Soc.* **2007**, *129*, 15601; d) V. Simic, L. Bouteiller, M. Jalabert, *J. Am. Chem. Soc.* **2003**, *125*, 13148; e) T. Shikata, T. Nishida, B. Isare, M. Linares, R. Lazzaroni, L. Bouteiller, *J. Phys. Chem. B* **2008**, *112*, 8459; f) J. J. van Gorp, J. A. J. Vekemans, E. W. Meijer, *J. Am. Chem. Soc.* **2002**,

124, 14759; g) L. S. Shimizu, M. D. Smith, A. D. Hughes, K. D. Shimizu, *Chem. Commun.* **2001**, 1592; h) Y. Liu, Y. Li, L. Jiang, H. Gan, H. Liu, Y. Li, J. Zhuang, F. Lu, D. Zhu, *J. Org. Chem.* **2004**, *69*, 9049.

[2] a) K. Hanabusa, K. Shimura, K. Hirose, M. Kimura, H. Shirai, *Chem. Lett.* **1996**, 885; b) M. de Loos, J. van Esch, R. M. Kellogg, B. L. Feringa, *Angew. Chem.* **2001**, *113*, 633; *Angew. Chem. Int. Ed.* **2001**, *40*, 613; c) J. van Esch, F. Schoonbeek, M. de Loos, H. Kooijman, A. L. Spek, R. M. Kellogg, B. L. Feringa, *Chem. Eur. J.* **1999**, *5*, 937; d) J. van Esch, S. de Feyter, R. M. Kellogg, F. de Schryver, B. L. Feringa, *Chem. Eur. J.* **1997**, *3*, 1238; e) M. de Loos, J. van Esch, R. M. Kellogg, B. L. Feringa, *Tetrahedron* **2007**, *63*, 7285; f) M. de Loos, A. Friggeri, J. van Esch, R. M. Kellogg, B. L. Feringa, *Org. Biomol. Chem.* **2005**, *3*, 1631; g) L. A. Estroff, A. D. Hamilton, *Angew. Chem.* **2000**, *112*, 3589; *Angew. Chem. Int. Ed.* **2000**, *39*, 3447; h) G. Wang, A. D. Hamilton, *Chem. Eur. J.* **2002**, *8*, 1954; i) K. Yabuuchi, E. Marfo-Owusu, T. Kato, *Org. Biomol. Chem.* **2003**, *1*, 3464; j) M. Piepenbrock, G. O. Lloyd, N. Clarke, J. W. Steed, *Chem. Commun.* **2008**, 2644; k) M. Ávalos, R. Babiano, P. Cintas, A. Gomez-Carretero, J. L. Jimenez, M. Lozano, A. L. Ortiz, J. C. Palacios, A. Pinazo, *Chem. Eur. J.* **2008**, *14*, 5656; l) C. Baddeley, Z. Yan, G. King, P. M. Woodward, J. D. Badjic, *J. Org. Chem.* **2007**, *72*, 7270.

[3] a) J. J. van Gorp, J. A. J. M. Vekemans, E. W. Meijer, *Chem. Commun.* **2004**, 60; b) A. M. Zhang, Y. H. Han, K. Yamato, X. C. Zeng, B. Gong, *Org. Lett.* **2006**, *8*, 803; c) J. M. Rodriguez, A. D. Hamilton, *Angew. Chem.* **2007**, *119*, 8768; *Angew. Chem. Int. Ed.* **2007**, *46*, 8614; d) P. S. Corbin, S. C. Zimmerman, P. A. Thiessen, N. A. Hawryluk, T. J. Murray, *J. Am. Chem. Soc.* **2001**, *123*, 10475; e) H. L. Ricks, L. S. Shimizu, M. D. Smith, U. H. F. Bunz, K. D. Shimizu, *Tetrahedron* **2004**, *60*, 3229.

[4] R. Custelcean, *Chem. Commun.* **2008**, 295, and references therein.

[5] M. C. Etter, Z. Urbanczyk-Lipkowska, M. Zia-Ebrahimi, T. W. Panunto, *J. Am. Chem. Soc.* **1990**, *112*, 8415.

[6] For a comparison between urea and urethane hydrogen bonding, see: E. Yilgör, E. Burgaz, E. Yurtsever, I. Yilgör, *Polymer* **2000**, *41*, 849.

[7] a) X. Zhao, Y. L. Chang, F. W. Fowler, J. W. Lauher, *J. Am. Chem. Soc.* **1990**, *112*, 6627; b) Y. L. Chang, M. A. West, F. W. Fowler, J. W. Lauher, *J. Am. Chem. Soc.* **1993**, *115*, 5991.

[8] a) J. Jadzyn, M. Stockhausen, B. Zywucki, *J. Phys. Chem.* **1987**, *91*, 754; b) S. G. Musselmann, T. M. Santosusso, J. D. Barnes, L. H. Sperling, *J. Polym. Sci. Part B Polym. Phys.* **1999**, *37*, 2586.

[9] A. Masunov, J. J. Dannenberg, *J. Phys. Chem. B* **2000**, *104*, 806.

[10] a) D. Heikens, A. Meijers, P. H. von Reth, *Polymer* **1968**, *9*, 15; b) S. G. Musselman, T. M. Santosusso, J. D. Barnes, L. H. Sperling, *J. Polym. Sci.* **1999**, *37*, 2586; c) R. A. Beck, R. W. Truss, *Polymer* **1999**, *40*, 307; d) H. Shirasaka, S. I. Inoue, K. Asai, H. Okamoto, *Macromolecules* **2000**, *33*, 2776; e) J. T. Garrett, C. A. Siedlecki, J. Runt, *Macromolecules* **2001**, *34*, 7066; f) J. T. Garrett, J. S. Lin, J. Runt, *Macromolecules* **2002**, *35*, 161; g) N. R. Legge, G. Holden, R. P. Quirk in *Thermoplastic Elastomers*, 2nd ed., Hanser Publishers, Munich, **1996**.

[11] a) D. B. Klinedinst, E. Yilgor, I. Yilgor, F. L. Beyer, G. L. Wilkes, *Polymer* **2005**, *46*, 10191; b) R. M. Versteegen, R. P. Sijbesma, E. W. Meijer, *Macromolecules* **2005**, *38*, 3176.

[12] E. Wisse, A. J. H. Spiering, E. N. M. van Leeuwen, R. A. E. Renken, P. Y. W. Dankers, L. A. Brouwer, M. J. A. van Luyn, M. C. Harmsen, N. A. J. M. Sommerdijk, E. W. Meijer, *Biomacromolecules* **2006**, *7*, 3385.

[13] H. Kautz, D. J. M. van Beek, R. P. Sijbesma, E. W. Meijer, *Macromolecules* **2006**, *39*, 4265.

[14] S. H. M. Söntjens, R. P. Sijbesma, M. H. P. van Genderen, E. W. Meijer, *J. Am. Chem. Soc.* **2000**, *122*, 7487.

[15] D. Guo, R. P. Sijbesma, H. Zuilhof, *Org. Lett.* **2004**, *6*, 3667.

[16] Examples: a) J. H. K. Hirschberg, L. Brunsveld, A. Ramzi, J. A. J. M. Vekemans, R. P. Sijbesma, E. W. Meijer, *Nature* **2000**, *407*, 167; b) P. Jonkheijm, P. van der Schoot, A. P. J. H. Schenning, E. W. Meijer, *Science* **2006**, *313*, 80; c) L. Brunsveld, A. P. H. J. Schenning, M. A. C. Broeren, H. M. Janssen, J. A. J. M. Vekemans, E. W. Meijer, *Chem. Lett.* **2000**, 292; d) M. M. Green, N. C. Peterson, T. Sato, A. Teramoto, R. Cook, S. Lifson, *Science* **1995**, *268*, 1860.

[17] T. V. Kozlova, V. Zharkov, *Zh. Prikl. Spektrosk.* **1981**, *35*, 303.

[18] J. H. K. K. Hirschberg, R. A. Koevoets, R. P. Sijbesma, E. W. Meijer, *Chem. Eur. J.* **2003**, *9*, 4222.

[19] (*R*)-3,7-Dimethyl-6-octen-1-ol (**1a**) and (*S*)-3,7-dimethyl-6-octen-1-ol (**1b**) were purchased from Sigma-Aldrich. The purity of these compounds was investigated by using chiral GC/MS. (*R*)-3,7-Dimethyl-6-octen-1-ol was found to contain no impurities, whereas (*S*)-3,7-dimethyl-6-octen-1-ol contained 1.5% of the *R* enantiomer.

[20] M. Hunsen, *Synthesis* **2005**, 2487.

[21] H. M. Keizer, R. P. Sijbesma, E. W. Meijer, *Eur. J. Org. Chem.* **2004**, 2553.

[22] Because the dimerization constant of 2-ureido-pyrimidinones is $>10^6\,\text{M}^{-1}$ in $CDCl_3$, the concentration of monomer is negligible even at the lowest concentrations at which the ^{1}H NMR measurements are performed.

[23] Examples: a) D. Zhao, J. S. Moore, *J. Org. Chem.* **2002**, *67*, 3548; b) A. Kraft, F. Osterod, R. Frohlich, *J. Org. Chem.* **1999**, *64*, 6425; c) H. Nakade, B. J. Jordan, H. Xu, G. Han, S. Srivastava, R. R. Arvizo, G. Cooke, V. M. Rotello, *J. Am. Chem. Soc.* **2006**, *128*, 14924.

[24] C. Giessnerprettre, B. Pullman, *J. Theor. Biol.* **1970**, *27*, 87.

[25] A downfield shift of both urea protons has also been observed for a bis-urea-based low molecular weight gelator under dilute conditions.[2i]

[26] The viscosity-corrected diffusion constants are determined by using the following formula: $D_{corr}=D_{meas}\times(D_{sol,pure}/D_{sol,meas})$ where D_{meas} and $D_{sol,meas}$ are the measured values for the solute and the residual solvent peak ($CHCl_3$) respectively and $D_{sol,pure}$ is the diffusion constant measured for the residual $CHCl_3$ in pure $CDCl_3$.

[27] R. B. Martin, *Chem. Rev.* **1996**, *96*, 3043.

[28] a) P. R. Stoesser, S. J. Gill, *J. Phys. Chem.* **1967**, *71*, 564; b) N. J. Buurma, I. Haq, *J. Mol. Biol.* **2008**, *381*, 607.

[29] Examples: a) I. Yoshikawa, J. Sawayama and K. Araki, *Angew. Chem.* **2008**, *120*, 1054; *Angew. Chem. Int. Ed.* **2008**, *47*, 1038; b) T. F. A. de Greef, M. M. L. Nieuwenhuizen, P. J. P. Stals, C. F. C. Fitié, A. R. A. Palmans, R. P. Sijbesma, E. W. Meijer, *Chem. Commun.* **2008**, 4306.

[30] Fitting of the concentration-dependent data to a three-parameter indefinite isodesmic self-assembly model resulted in an unrealistic value of δ_ξ. Therefore, the data were fitted to a four-parameter isodesmic self-assembly model (see Supporting Information).

[31] For at review on the use of CD spectroscopy in the study of chiral self-assemblies: G. Gottarelli, S. Lena, S. Masiero, S. Pieraccini, G. P. Spada, *Chirality* **2008**, *20*, 471.

[32] The temperature-dependent isodesmic self-assembly model has the following form: $\phi_n(T)=1/(1+\exp[-0.908\Delta H(T-T_m)/RT_m^2])$, in which R represents the universal gas constant ($8.3144\,\text{J}\,\text{K}^{-1}\,\text{mol}^{-1}$), ϕ_n the fraction of aggregated material, T_m the temperature at which $\phi_n=0.5$ and ΔH is the molecular enthalpy release [$\text{J}\,\text{mol}^{-1}$]. See: M. M. J. Smulders, M. M. L. Nieuwenhuizen, T. F. A. de Greef, P. P. A. M. van der Schoot, A. P. H. J. Schenning, E. W. Meijer, *Chem. Eur. J.* **2010**, *16*, 362.

[33] B. A. H. Huisman, P. G. Bolhuis, A. Fasolino, *Phys. Rev. Lett.* **2008**, *100*, 188301.

[34] Chloroform has good H-bond donor but relatively weak H-bond acceptor properties. On the other hand, heptane is neither a good H-bond donor nor a good H-bond acceptor. For a discussion on the competitive effect of solvents on hydrogen-bonded assemblies, see: C. A. Hunter, *Angew. Chem.* **2004**, *116*, 5424; *Angew. Chem. Int. Ed.* **2004**, *43*, 5310.

[35] Dissolution of benzene in chloroform is exothermic, as was first found by Tamres (M. Tamres, *J. Am. Chem. Soc.* **1952**, *74*, 3375). It is now generally believed that this is the result of a weak hydrogen bond between the CH proton of chloroform and the π electrons of the aromatic ring. Because of these solvent–solute interactions, the solute–solute interactions are weakened resulting and a lower equilibrium constant results.

[36] P. G. Schouten, J. F. van der Pol, J. W. Zwikker, W. Drenth, S. J. Picken, *Mol. Cryst. Liq. Cryst.* **1991**, *195*, 291.
[37] O. A. Scherman, G. B. W. L. Ligthart, H. Ohkawa, R. P. Sijbesma, E. W. Meijer, *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 11850.
[38] A. Jerschow, N. Müller, *J. Magn. Reson.* **1997**, *125*, 372.

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