Part One
Formation of Supramolecular Polymers

1
Multiple Hydrogen-Bonded Supramolecular Polymers

Wilco P.J. Appel, Marko M.L. Nieuwenhuizen, and E.W. Meijer

1.1
Introduction

1.1.1
Historical Background

Since the introduction of the first synthetic polymer more than a hundred years ago by Leo Hendrik Baekeland, covalent polymers have become indispensable in everyday life. The term 'polymeric' was first introduced in 1832 by Jöns Jacob Berzelius to describe a compound with a higher molecular weight than that of the normal compound but with an identical empirical formula as a result of the repetition of equal units [1]. In 1920, Hermann Staudinger defined polymers, which he called macromolecules, to be multiple covalently bound monomers. For this work he was awarded with the Nobel Prize in 1953 [2]. Today, our knowledge of organic synthesis and polymer chemistry allows the preparation of virtually any monomer and its associated polymer. In addition, an in-depth understanding of 'living' types of polymerization facilitates tuning of the molecular weight and molecular weight distribution, at the same time creating the possibility to synthesize a wide variety of copolymers [3].

The macroscopic properties of polymers are directly linked to their molecular structure. As a result, polymer chemists devised synthetic approaches to control the sequence architecture. More recently, the importance of introducing supramolecular interactions between macromolecular chains has become evident, and many new options have been introduced. The final step in this development would be to develop polymers entirely based on reversible, noncovalent interactions. Rather than linking the monomers in the desired arrangement via a series of polymerization reactions, the monomers are designed in such a way that they autonomously self-assemble into the desired structure. As with covalent polymers, a variety of structures of these so-called supramolecular polymers are possible. Block or graft copolymers, as well as polymer networks, can be created in this way.

The first reports on supramolecular polymers date back to the time when many scientists studied the mechanism by which aggregates of small molecules gave rise to

increased viscosities. To the best of our knowledge it was Louise Henry who proposed the idea of molecular polymerization by associative interactions in 1878, approximately at the same time that van der Waals proposed his famous equation of state, which took intermolecular interactions in liquids into account, and was only 50 years after Berzelius coined the term polymers. Stadler and coworkers were the first to recognize that hydrogen bonds can be used to bring polymers together [4]. Lehn and coworkers synthesized the first main-chain supramolecular polymer based on hydrogen bonding [5]. In our group, we introduced the self-complementary ureido-pyrimidinone (UPy) quadruple hydrogen-bonding motif that shows a high dimerization constant and a long lifetime. In this chapter, we review the field of supramolecular polymers based on multiple hydrogen bonds and discuss some general approaches to the creation of supramolecular materials based on multiple hydrogen-bonded supramolecular polymers.

1.1.2
Supramolecular Chemistry

Jean-Marie Lehn defined supramolecular chemistry as '. . . *a highly interdisciplinary field of science covering the chemical, physical, and biological features of chemical species of higher complexity, which are held together and organized by means of intermolecular (noncovalent) binding interactions* [5].' This exciting new field introduced the possibility of self-sorting of subunits during the self-assembly process. At the same time large, complex structures can be created by the assembly of small supramolecular building blocks, thereby allowing the elimination of elaborate synthetic procedures. Complex self-assembly processes are widely recognized to have played an important part in different elements of the origin of life. As a result, many researchers explored different aspects of the field of supramolecular chemistry, using noncovalent interactions to self-assemble molecules into well-defined structures. Noncovalent interactions can vary in type and strength, ranging from very weak dipole-dipole interactions to very strong metal-ligand or ion-ion interactions with binding energies that can approach that of covalent bonds [6]. The most obvious benefits of noncovalent interactions are their reversible nature and their response to external factors such as temperature, concentration, and the polarity of the medium. A subtle interplay between these external factors allows precise control of the self-assembly process. Due to their directionality and the possibility to tune the dynamics and lifetime, hydrogen bonds are among the most interesting assembly units for supramolecular polymers. Before focusing on hydrogen bonding, we shall first address the different mechanisms for the formation of supramolecular polymers.

1.1.3
Supramolecular Polymerization Mechanisms

The mechanism of noncovalent polymerization in supramolecular chemistry is highly dependent on the interactions that play their part in the self-assembly process.

Growing polymer
chains

(a) Isodesmic

Chains

(b) Ring-Chain

Rings

Growing polymer
chains

(c) Cooperative

Concentration
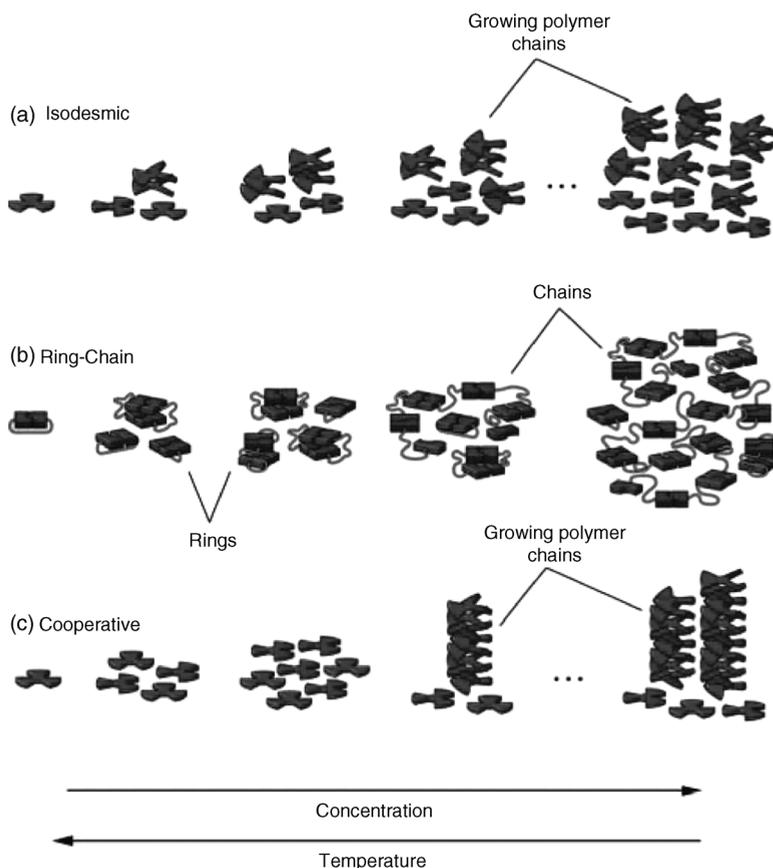
Temperature

Figure 1.1 Schematic representation of the major supramolecular polymerization mechanisms. Reprinted with permission from Nature Publishing Group [7].

In contrast to covalent bonds, noncovalent interactions depend on temperature and concentration, thereby affecting the degree of polymerization. The mechanisms of supramolecular polymerizations can be divided in three major classes, these being isodesmic, cooperative, or ring-chain equilibria (Figure 1.1) [7].

Isodesmic polymerizations occur when the strength of noncovalent interactions between monomers is unaffected by the length of the chain. Because each addition is equivalent, no critical temperature or concentration of monomers is required for the polymerization to occur. Instead, the length of the polymer chains rises as the concentration of monomers in the solution is increased, or as the temperature decreases.

The ring-chain mechanism is characterized by an equilibrium between closed rings and linear polymer chains. In this mechanism, below a certain monomer concentration the ends of any small polymer chain react with each other to generate closed rings. Above this critical concentration, linear chain formation becomes more

favored, and polymer growth is initiated. The degree of polymerization changes abruptly once the critical conditions are reached. The critical polymerization concentration is largely dependent on the length and rigidity of the monomers. Especially at low concentrations, the presence of cyclic oligomers can drastically influence the macroscopic properties.

Cooperative polymerizations occur in the growth of ordered supramolecular polymers in which there are additional interactions present besides the formation of linear polymers, such as those that form helices. This involves two distinct phases of self-assembly: a less favored nucleation phase followed by a favored polymerization phase. In this mechanism, the noncovalent bonds between monomers are weak, hindering the initial polymerization. After the formation of a nucleus of a certain size, the association constant is increased, and further monomer addition becomes more favored, at which point the polymer growth is initiated. Long polymer chains will form only above a minimum concentration of monomer and below a certain temperature, resulting in a sharp transition from a regime dominated by free monomers and small aggregates to a regime where almost all of the material is present as large polymers. For further details about supramolecular polymerization mechanisms we would refer the reader to a recent review by our group [7].

1.2
General Concepts of Hydrogen-Bonding Motifs

The existence of the hydrogen bond was first suggested by Moore and Winmill in 1912 [8], and it was defined in 1920 by Latimer and Rodebush as '*a hydrogen nucleus held between 2 octets, constituting a weak bond*' [9]. In that time the concept of hydrogen bonding was used to explain physical properties and chemical reactivities due to intramolecular and intermolecular hydrogen bonding. Nowadays, we interpret hydrogen bonds as highly directional electrostatic attractions between positive dipoles or charges on hydrogen and other electronegative atoms. In the field of supramolecular chemistry, hydrogen bonding is currently one of the most widely applied noncovalent interactions.

1.2.1
Arrays of Multiple Hydrogen Bonds

Hydrogen bonding is especially suitable as a noncovalent interaction because of the high directionality of the hydrogen bonds. In general, the strength of a single hydrogen bond depends on the strength of the hydrogen bond donor (D) and acceptor (A) involved, and can range from weak $CH - \pi$ interactions to very strong $FH - F^-$ interactions. When multiple hydrogen bonds are arrayed to create linear hydrogen-bonding motifs, both their strength and directionality are increased. However, the binding strength of the motif is dependent not only on the type and number of hydrogen bonds, but also on the order of the hydrogen bonds in the motif.
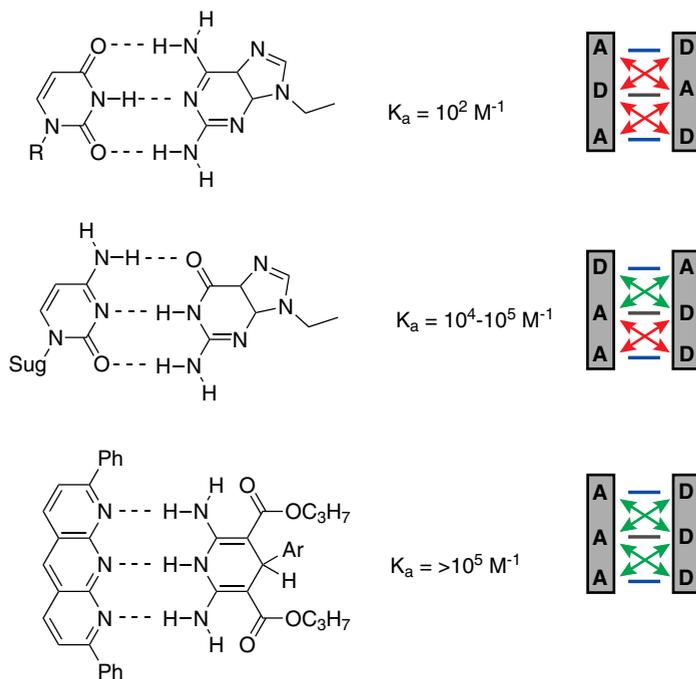
Figure 1.2 Influence of attractive and repulsive secondary interactions on the association constant of threefold hydrogen-bonding motifs [10, 11]. Reprinted with permission from The Royal Society of Chemistry [13].

This important aspect of linear hydrogen-bonding motifs was pointed out by Jorgensen *et al.,* who found a large variation in the association constants of threefold hydrogen-bonding motifs. Although the ADA – DAD and DAA – ADD arrays exhibit an equal amount of hydrogen bonds, the association constants of these motifs were significantly different. This was attributed to the different order of the hydrogen bonds [10]. Since the hydrogen bonds in the motifs are in close proximity, the distance of a hydrogen-bonding donor or acceptor to the neighbor of its counterpart is also relatively small, creating attractive or repulsive electrostatic secondary cross-inter-actions (Figure 1.2). This theory was later confirmed by Zimmerman *et al.*, who completed the series with the AAA – DDD array and indeed found a significantly higher dimerization constant due to the presence of solely attractive secondary interactions [11].

These so-called secondary interactions have a significant influence on the association constant of the corresponding motif, changing the association constant of the triple hydrogen-bonding motif by at least three orders of magnitude. Based on these results, Schneider *et al.* developed a method to calculate the free association energy for linear hydrogen-bonding motifs taking into account the secondary interactions, each contributing $2.9 \, \text{kJ mol}^{-1}$ to the binding energy, and expanded it to quadruple hydrogen-bonding motifs [12].
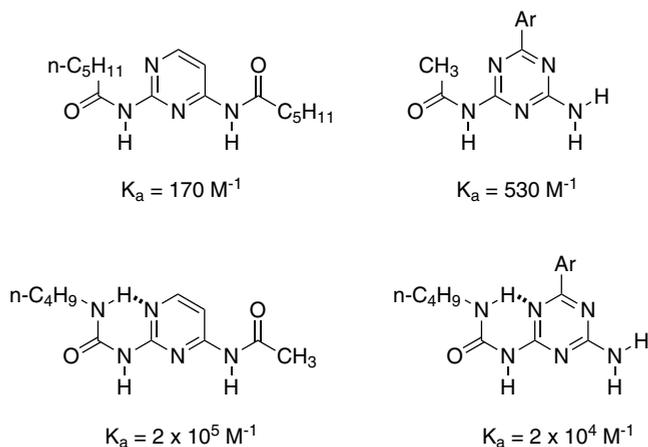
Figure 1.3 Quadruple hydrogen-bonding motifs with their corresponding dimerization constants, revealing the effect of the intramolecular hydrogen bond on the dimerization constant [14].

1.2.2
Preorganization through Intramolecular Hydrogen Bonding

Throughout the development of supramolecular chemistry, our knowledge of hydrogen-bonding motifs expanded rapidly. To attain high association constants, multiple hydrogen-bonding motifs were developed. Our group developed quadruple hydrogen-bonding motifs based on diaminotriazines and diaminopyrimidines in which a remarkably high dimerization constant was achieved when an amide moiety was replaced by a ureido moiety (Figure 1.3) [14]. A large deviation in the values of the experimentally determined dimerization constants of the ureido molecules was observed when compared to the calculations as proposed by Scheider *et al.* However, the experimental values for the amide molecules were in agreement with the calculated values. The large difference between the experimental and the predicted dimerization constants was attributed to the presence of an intramolecular hydrogen bond between the ureido NH and the nitrogen in the ring. This intramolecular hydrogen bond stabilizes the cis conformation of the ureido moiety and forces the carbonyl in plane with the aromatic ring. This causes prearrangement of the DADA hydrogen-bonding motif and results in an increase in the association constant by two or three orders of magnitude.

To reduce the number of repulsive secondary interactions, thereby increasing the association constant, our group introduced the self-complementary 2-ureido-4[1H]-pyrimidinone (UPy) quadruple hydrogen-bonding DDAA motif [15]. The intramolecular hydrogen bond prearranges the motif, resulting in a nearly planar DDAA motif (Figure 1.4) [16]. Due to the reduced number of repulsive secondary interactions and the intramolecular hydrogen bond, the dimerization constant was found to be $6 \times 10^7\,M^{-1}$ in chloroform, with a long lifetime of $0.1\,s$ [17].
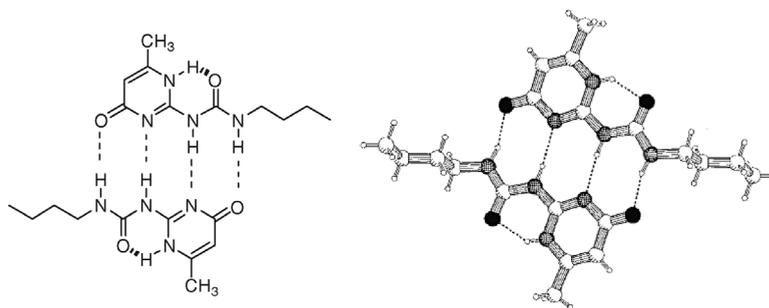
Figure 1.4 2-Ureido-4[1H]-pyrimidinone dimer and its corresponding single-crystal structure. Reprinted with permission from the American Chemical Society [16].

1.2.3
Tautomeric Equilibria

Although the UPy motif exhibits a high dimerization constant, the type of aggregate that is obtained during self-assembly is highly dependent on the substituent on the 6-position of the pyrimidinone ring, since different tautomeric forms can be present [16]. With electron-withdrawing or -donating substituents, the tautomeric equilibrium is shifted to the pyrimidin-4-ol tautomer, which is self-complementary as a DADA hydrogen-bonding motif (Figure 1.5). Due to more repulsive secondary
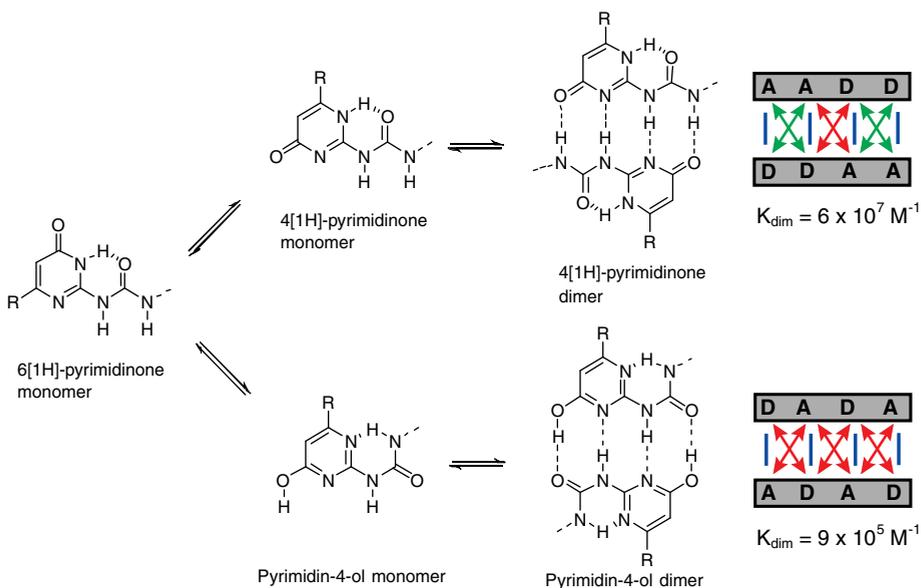
Figure 1.5 Tautomeric equilibria in the 2-ureido-pyrimidinone motif. Reprinted with permission from The Royal Society of Chemistry [13].

interactions, the dimerization constant of this DADA motif is lowered to $9 \times 10^5 \, M^{-1}$ in chloroform [18]. The tautomeric equilibrium showed a high dependence on the solvent, and also showed concentration dependence. This illustrates that understanding the tautomeric equilibria is crucial for predicting the properties of hydrogen-bonding motifs.

Nowadays, the synthesis of new hydrogen-bonding motifs is almost unrestricted. Current hydrogen-bonding motifs used in supramolecular chemistry are not only purely derived from organic chemistry, but are also derived from hydrogen bonding as found in nature, for example by using the hydrogen-bonding motifs found in DNA base pairs [19] or using peptide mimics (Figure 1.6) [20, 21]. Since the start of supramolecular chemistry, many different hydrogen-bonding motifs have been reported, ranging from monovalent up to dodecavalent hydrogen bonds [21], with dimerization constants up to $7 \times 10^9 \, M^{-1}$ [22]. However, it has to be noted that some of the reported hydrogen-bonding motifs require a multistep synthetic pathway, which lowers the overall yield tremendously, thereby making them less attractive to use.

1.3
Hydrogen-Bonded Main-Chain Supramolecular Polymers

1.3.1
The Establishment of Supramolecular Polymers

In macromolecular chemistry, the monomeric units are held together by covalent bonds. In 1990, Jean-Marie Lehn introduced a new area within the field of polymer chemistry by creating a polymer in which the monomeric units were held together by hydrogen bonds, resulting in a liquid crystalline supramolecular polymer (Figure 1.7) [23]. This initiated the field of supramolecular polymer chemistry, generating materials with reversible interactions, and thereby introducing the opportunity to produce materials with properties that otherwise would have been impossible or difficult to obtain.

Inspired by this work, Griffin *et al.* developed main-chain supramolecular polymers based on pyridine/benzoic acid hydrogen bonding, also obtaining liquid crystalline supramolecular polymers [24]. Our group introduced supramolecular polymers based on the ureido-pyrimidinone motif. Due to the high dimerization constant present in the UPy motif, supramolecular polymers were formed with a high degree of polymerization even *in semi-dilute solution* [15].

We have defined supramolecular polymers as '...*polymeric arrays of monomeric units that are brought together by reversible and highly directional secondary interactions, resulting in polymeric properties in dilute and concentrated solutions, as well as in the bulk. The monomeric units of the supramolecular polymers themselves do not possess a repetition of chemical fragments. The directionality and strength of the supramolecular bonding are important features of these systems, that can be regarded as polymers and behave according to well-established theories of polymer physics. In the past the term "living polymers" has been used for this type of polymer. However, to exclude confusion with the important field of*
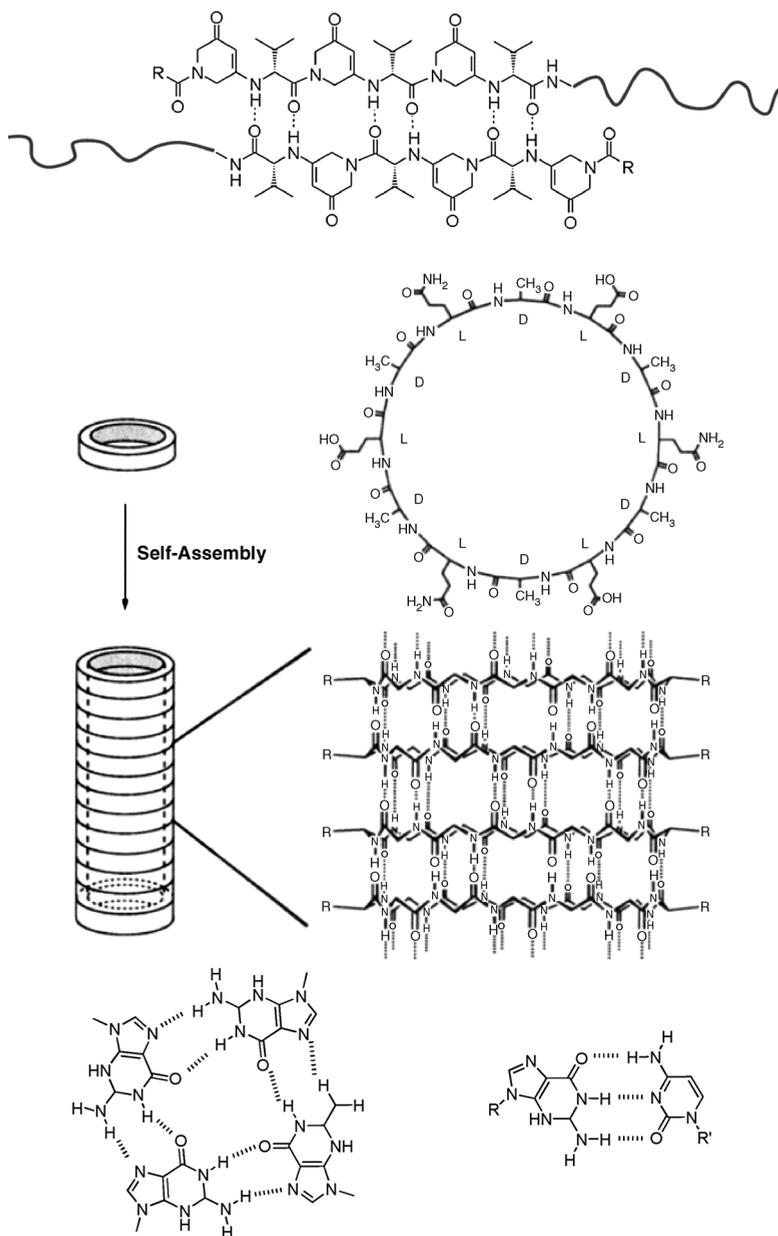
Figure 1.6 Hydrogen-bonding motifs inspired on self-assembly as found in nature. Reprinted with permission from the American Chemical Society [19–21].

living polymerizations, we prefer to use the term supramolecular polymers.' [25] The irony is that in the field of polymer science, Hermann Staudinger fought many scientific battles to prove that polymer molecules consist of covalently bonded monomers rather than noncovalent aggregates of small molecules. Almost a hundred years later,
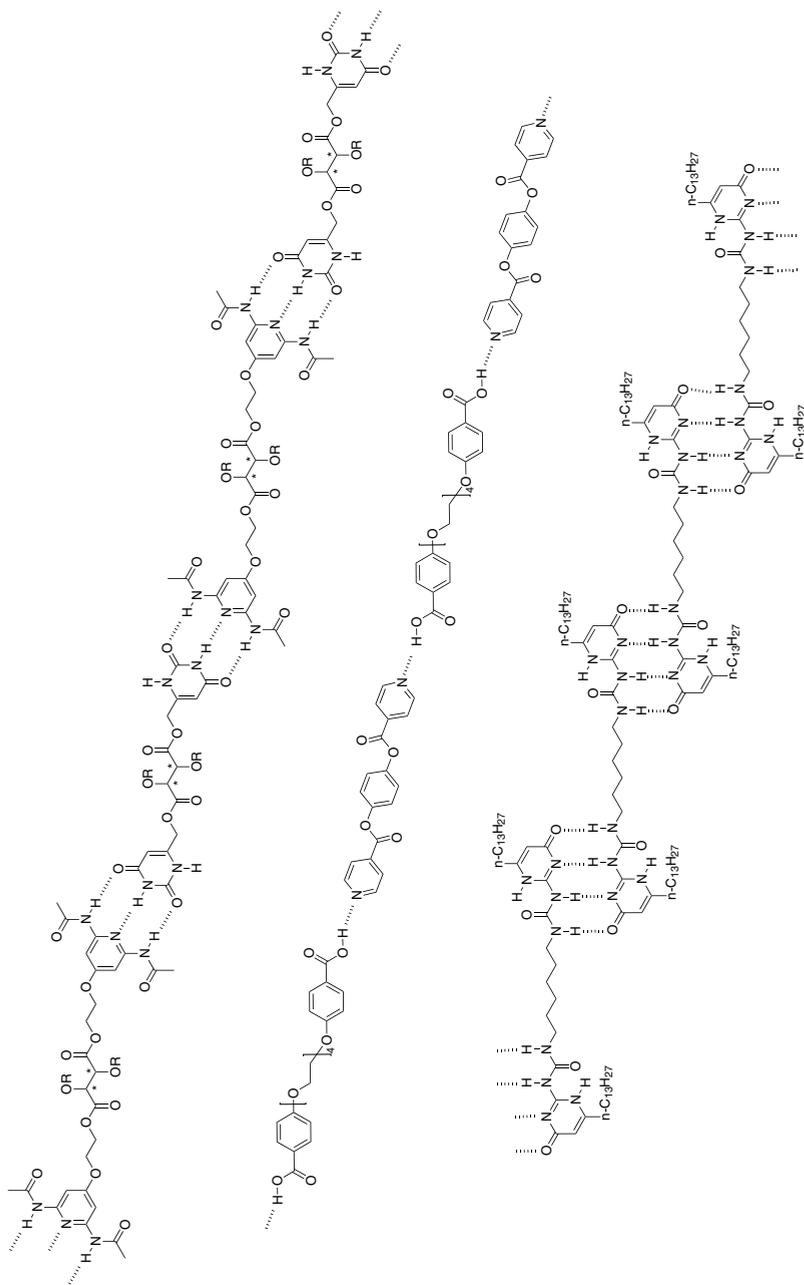
Figure 1.7 The formation of a supramolecular liquid crystalline polymer by hydrogen bonding as introduced by Lehn *et al.* (top), Griffith *et al.* (middle) and our group. (bottom).
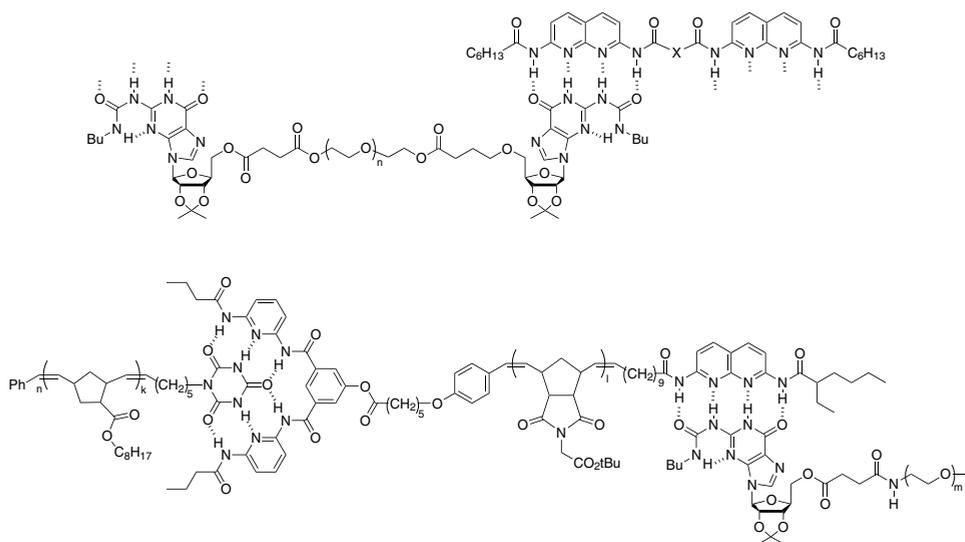
Figure 1.8 Alternating (top) and triblock (bottom) supramolecular copolymers created in solution by using the directionality of complementary hydrogen-bonding motifs [28b,29].

material properties typical of macromolecules can also be obtained by the non-covalent aggregation of small molecules.

In macromolecular chemistry, different types of polymers are distinguished, ranging from linear polymers and graft copolymers to networks. Soon after the introduction of supramolecular polymers, it was recognized that by replacing the covalent bonds between the monomeric units by hydrogen bonds, these polymers can be made in a supramolecular fashion, and one year *before* the introduction of the linear supramolecular polymer by Lehn the group of Fréchet introduced supra-molecular graft copolymers [26]. Using multiple hydrogen-bonding moieties attached to one molecule, one can also generate supramolecular polymer net-works [27]. With the development of new hydrogen-bonding motifs and a better understanding of the concept of supramolecular polymers, nowadays even alter-nating [28] or triblock [29] supramolecular hydrogen-bonding copolymers can be created using the high directionality of different hydrogen-bonding motifs (Figure 1.8).

1.3.2
Supramolecular Polymerizations

The polymerization of multivalent linear supramolecular polymers based solely on hydrogen bonding without any additional interactions will in general result in an isodesmic polymerization mechanism. As a consequence, the degree of polymer-ization (DP) that is obtained will be highly dependent on the dimerization constant and the concentration (Figure 1.9) [30]. Therefore, the obvious approach to increase
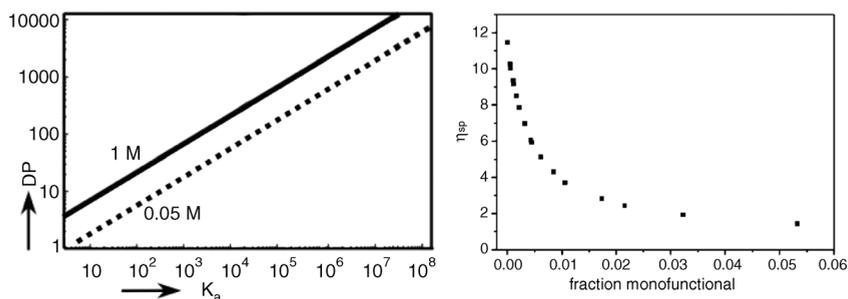
Figure 1.9 Theoretical dependence of the degree of polymerization as a function of association constant and concentration for an isodesmic polymerization mechanism (left) and the influence of monofunctional chainstopper on the polymerization (right). Reprinted with permission from the American Association for the Advancement of Science [15] and the American Chemical Society [25].

the degree of polymerization is to create hydrogen-bonding motifs with high dimerization constants. However, the synthetic accessibility of these motifs and their attachment to other molecules is highly important since incomplete functionalization or other monofunctional impurities present at less than one percent can act as a chainstopper. This has a huge effect on the degree of polymerization, as was demonstrated by viscosity measurements (Figure 1.9) [15, 31]. When one uses the AA-BB type of supramolecular polymers in which the hydrogen-bonding motifs are not self-complementary but need a complementary counterpart, this results in the need for perfect stoichiometry in order to attain high degrees of polymerization, since even a small excess of either one will act as a chainstopper [32]. To avoid this problem, when creating supramolecular polymers a self-complementary hydrogen-bonding motif is preferred.

An important factor that cannot be neglected when going from small molecules to supramolecular polymers is the influence of modifications of the molecular structure on the association constant of the hydrogen-bonding motif [33]. This can be caused by steric effects when attaching large molecules to the motif [34], and it is observed that the polarity of the attached molecule influences the association constant drastically [35]. This will therefore influence the degree of polymerization significantly.

1.3.3
Hydrophobic Compartmentalization

The isodesmic type of polymerization of main-chain hydrogen bonded supramolecular polymers results in a low degree of polymerization and results in the need for hydrogen-bonding motifs with a high dimerization constant in order to obtain long polymers in solution. To overcome this issue, several different strategies can be applied.
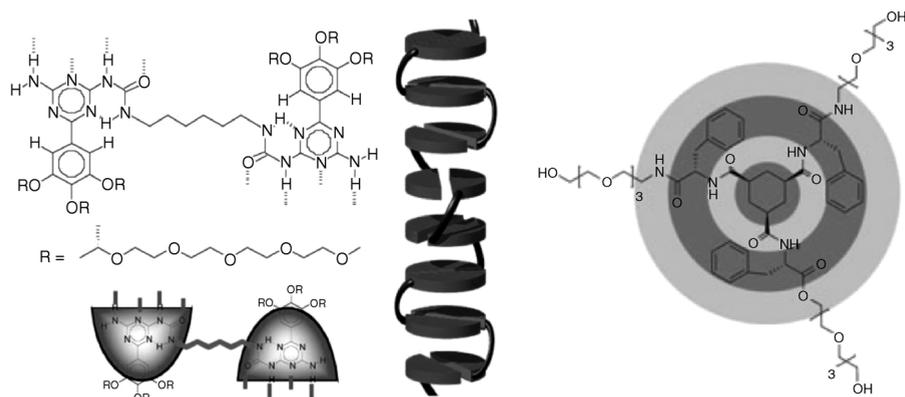
Figure 1.10 Helical supramolecular ureido-triazine polymer (left) and cyclohexane hydrogelator (right) in which the hydrogen-bonding motif is shielded from the solvent by hydrophobic interactions, creating aggregates in water. Reprinted with permission from the National Academy of Sciences [38b] and The Royal Society of Chemistry [39c].

It is widely believed that supramolecular polymers in water based on purely hydrogen bonding are not possible due to the competition of the intermolecular hydrogen bonds with hydrogen-bonding with water molecules [36]. However, hydrophobic compartmentalization is widely found in nature and can shield the hydrogen bonds from the aqueous environment. This decreases the competitive hydrogen bonding of water molecules with the desired intermolecular hydrogen bonds. At the same time this creates a more apolar local environment for the hydrogen-bonding motifs, which strengthens the hydrogen-bonding interactions. Due to their weak interaction energy, the hydrophobic interactions are highly dependent on the temperature and can be induced or eliminated depending on the solvent [37]. However, using hydrophobic compartmentalization to shield the hydrogen-bonding motif from the environment, it is possible to attain supramolecular hydrogen-bonding polymers [38] and hydrogels [39] in water (Figure 1.10).

Additional interactions can be introduced into hydrogen-bonding supramolecular polymers by using hydrophobic compartmentalization. As shown in Figure 1.10, π-π interactions occur between the aromatic cores, creating chiral columnar structures. An important result of these additional interactions is the change of polymerization mechanism from isodesmic to cooperative, creating supramolecular polymers with a high degree of polymerization. This circumvents the requirement for a high dimerization constant in order to obtain supramolecular polymers with a high degree of polymerization. Additional π-π interactions in hydrogen bonded supramolecular polymers are not uncommon and can be applied to obtain higher-order structures [40].

1.4
From Supramolecular Polymers to Supramolecular Materials

1.4.1
Thermoplastic Elastomers

The introduction of polyamides and polyurethanes as polymeric materials created the possibility of having elastomeric materials which are processable at higher temperatures. The intermolecular hydrogen bonding between the polymer chains generates noncovalent crosslinks that crystallize upon hydrogen bonding. The crosslinks are broken upon heating the material, resulting in a dramatic decrease in viscosity, giving it its thermoplastic elastomeric behavior [41]. These polymers could be classified as supramolecular polymers due to their noncovalent crosslinks. However, the entanglements of the high-molecular-weight polymer chain have a significant influence on the macroscopic properties, thereby disqualifying them as true supramolecular polymers.

Inspired by the outstanding mechanical properties and processability of polyamides and polyurethanes, new polymers have been developed in which the amide and urethane moiety were replaced by urea moieties. Ureas can form stronger bifurcated hydrogen bonds than those formed by amides and urethanes. Indeed, when reacting amine-functionalized oligomers with diisocyanates, bis-urea thermoplastic elastomers were obtained which showed a nanofiber morphology, as observed with atomic force microscopy (AFM) (Figure 1.11) [42]. The aggregation of the bis-urea is cooperative due to the synergistic aggregation of the second urea within the bis-urea motif and the less favorable formation of dimers due to alignment of dipole moments. In addition, the bis-urea motif bundles together and crystallizes into long nano-fibers that act as supramolecular crosslinks. This reinforces the material and gives it its good mechanical properties [43]. Using so-called supramolecular self-
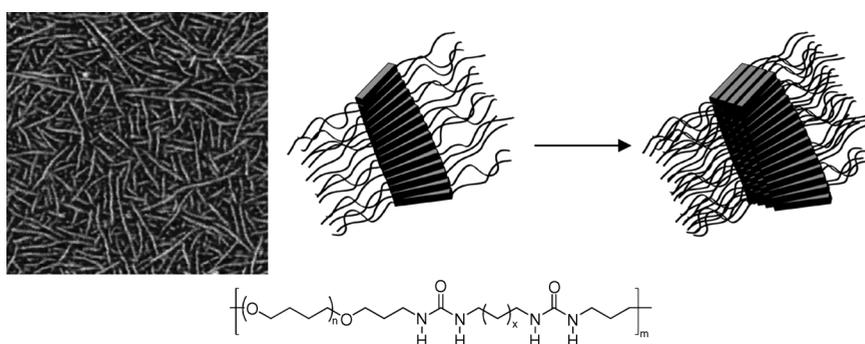
Figure 1.11 Atomic force microscopy phase image (500 × 500 nm) of nano-fibers as observed in thermoplastic elastomers based on the bis-urea motif (left) and the schematic aggregation of bis-urea stacks into the nano-fibers (right). Reprinted with permission from the American Chemical Society [43].

sorting, matching bis-urea molecules were selectively incorporated into the material [42a,d], and these were used to introduce, for example, bioactive molecules to bis-urea supramolecular biomaterials to improve cell adhesion and proliferation for tissue engineering [44]. Moreover, the incorporated bis-urea molecules were used to tune the mechanical properties of the bis-urea polymer [42c].

While the bis-urea crystallization results in favorable material properties, its high melting point severely reduces the mobility of the hydrogen-bonding moieties at room temperature. As a result, these supramolecular materials do not possess self-healing properties.

Leibler *et al.* introduced a system based on dimer fatty acids to synthesize amidoethyl imidazolidone, di(amidoethyl) urea, and diamido tetraethyl triurea oligomers (Figure 1.12) [45]. The system consists of a network of hydrogen bonds, which do not crystallize. At low temperatures the material is crosslinked by hydrogen bonds and behaves as a soft rubber, whereas at high temperatures the hydrogen bonds are broken and the material behaves like a viscoelastic liquid which can be molded, extruded, and reshaped. While the pure oligomer mixture exhibits a glass transition temperature of 28 °C, it can be plasticized with dodecane or water to lower the glass transition temperature. Due to the absence of crystallization and a glass transition temperature below room temperature, this material exhibits remarkable self-healing properties. The material is capable of regaining its mechanical properties after being macroscopically broken by simple mending at room temperature, although the re-establishment of the macroscopic properties and the hydrogen-bonding network takes time.

The examples discussed above show the potential of supramolecular polymers to create novel materials with new and advanced properties. The importance of thermal properties such as glass transition temperatures or melt temperatures dominates the macroscopic properties of the material. When the glass transition temperature is above room temperature, the mobility of the hydrogen-bonding moieties is limited.
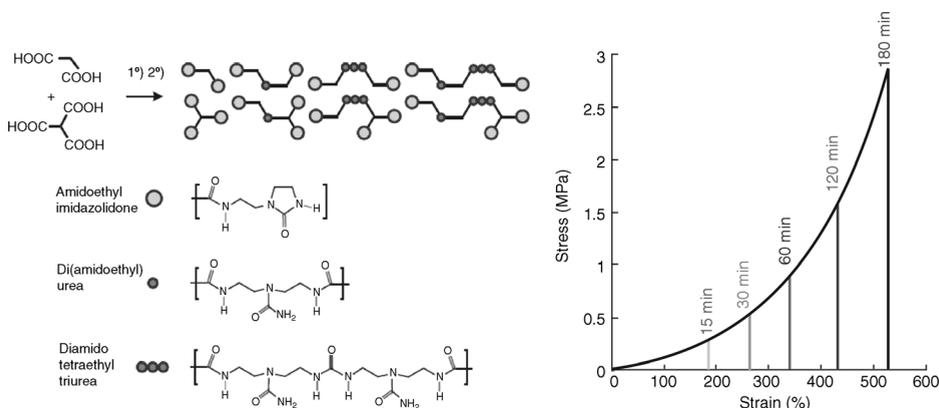
Figure 1.12 A supramolecular rubber based on hydrogen bonding generates a self-healing material at room temperature. The mechanical properties recover in time as the hydrogen-bonding network is restored. Reprinted with permission from Nature Publishing Group [45a].

This prevents the rearrangement of hydrogen bonds and results in a lack of self-healing properties. However, the presence of a glass transition temperature or a melt temperature above room temperature will improve the mechanical properties of the material by acting as crosslinks. The desired macroscopic properties of the material will therefore depend on its application.

1.4.2
Phase Separation and Additional Lateral Interactions in Supramolecular Polymers in the Solid State

Small molecule supramolecular systems as reported by Lehn form supramolecular polymers that show liquid crystalline behavior in bulk. However, these systems are rigid and give brittle materials with inferior mechanical properties at room temperature. To improve the mechanical properties, telechelic amorphous or semi-crystalline oligomers have been functionalized with hydrogen-bonding motifs [46, 47]. Upon functionalization of the oligomer with a hydrogen-bonding motif, materials with properties that resemble the covalent high-molecular-weight counterparts were obtained. However, due to the reversibility of the hydrogen bonds, at high temperatures the noncovalent interactions are broken, resulting in a material exhibiting the properties of the low-molecular-weight oligomers. This could be especially suitable for the synthesis of materials with improved processing properties at elevated temperatures. By using amorphous or semi-crystalline oligomers with multiple functionizable end groups, flexibility is introduced within the molecule and crystallinity is reduced. At the same time, the telechelic oligomer used influences the material properties of the supramolecular polymer.

Phase separation in block copolymers is well known and originates from the immiscibility of one block in the other block and vice versa. By adding hydrogen-bonding motifs to telechelic oligomers, a block copolymer-like molecule is obtained in which the hydrogen-bonding end groups can phase separate from the oligomer in the bulk, depending on their polarity difference and aggregation behavior. Examples illustrate that by using block copolymers with weak hydrogen-bonding blocks on the exterior, quasi-telechelic supramolecular polymers are obtained [48]. Chien *et al.* introduced telechelic supramolecular polymers based on poly(tetrahydrofuran) with benzoic acid end groups [46a]. The supramolecular polymers showed a tendency for micro-phase separation with a high-temperature melting point. This additional endotherm was attributed to the melting of hard segments which originate from the crystallization of benzoic acid end groups driven by benzoic acid dimerization. The hard segments are phase separated, creating physical crosslinks which increased the mechanical properties tremendously [46b]. Similar findings were obtained when using supramolecular polymers with benzoic acid hydrogen-bonding moieties in the side-chain [49]. Whether these self-assembly processes are driven by phase separation of the different blocks or by hydrogen bonding remains uncertain.

Hayes *et al.* investigated the influence of the strength of the hydrogen-bonding motif on the phase separation and mechanical properties of telechelic supramolec-
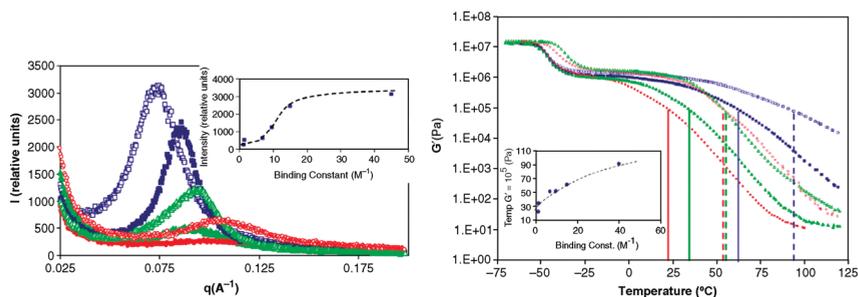
Figure 1.13 Influence of the binding constant of telechelic supramolecular polymers on phase separation as observed with SAXS and corresponding rheological analysis. Reprinted with permission from the American Chemical Society [50].

ular polymers. A clear influence of the dimerization constant on the phase separation was found, which coincides with a change in the mechanical properties as observed by rheological measurements (Figure 1.13) [50]. This clearly shows the influence of hydrogen bonding on the phase separation of telechelic supramolecular polymers and subsequent mechanical properties.

1.4.3
Supramolecular Thermoplastic Elastomers Based on Additional Lateral Interactions and Phase Separation

Phase separation is particularly interesting for supramolecular polymers based on weak hydrogen-bonding motifs, since the phase separation can increase the local concentration. This results in a higher degree of polymerization and a change in supramolecular polymerization mechanism from isodesmic to cooperative. This approach was demonstrated by Rowan *et al.* who synthesized supramolecular thermoplastic elastomers based on hydrogen-bonding telechelic poly(tetrahydrofuran) [51]. Although weak complementary nucleobase hydrogen-bonded motifs were used ($K_a = 21 \, \text{M}^{-1}$ in $CDCl_3$), the supramolecular polymer exhibits good mechanical properties. The formation of such a thermoplastic elastomer is not expected based on solely linear chain extension due to the weak hydrogen bonding and was shown to be related to the phase separation and π-π stacking of the hydrogen-bonding end groups within the soft oligomer matrix (Figure 1.14). The phase separation results in crystallization of the end groups with melting points at 108 °C and 135 °C. Detailed studies revealed that the nucleobase end groups aggregate on top of each other, creating supramolecular cross-links. In a similar system based on a poly(ε-caprolactone) oligomers, the hydrogen-bonding end groups were later visualized with AFM. In combination with X-ray diffraction studies, it was shown that the end groups were arranged in lamellae [52].

Phase separation of the hydrogen-bonding end groups can be induced by introducing additional lateral interactions when the end groups themselves do not exhibit lateral interactions. This was demonstrated by functionalizing telechelic poly(ethyl-
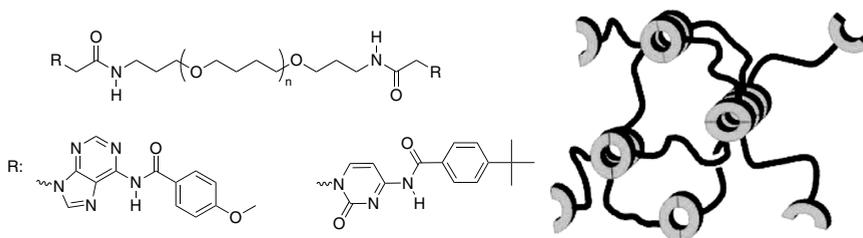
Figure 1.14 Nucleobase hydrogen-bonded supramolecular polymers and their schematic aggregation into phase-separated hard segments. Reprinted with permission from the American Chemical Society [51b].

ene-butylene) oligomers with the ureido-pyrimidinone (UPy) motif. The corresponding supramolecular polymer displays a remarkable increase in macroscopic properties, creating a supramolecular thermoplastic elastomer (Figure 1.15) [47b]. Although the UPy exhibits an extremely high dimerization constant, it was not expected to result in a thermoplastic elastomer upon isodesmic supramolecular polymerization of this molecule, since both the poly(ethylene-butylene) oligomer and its high-molecular-weight counterpart are amorphous, with a glass transition temperature well below room temperature.

The increase in macroscopic properties is a result of the aggregation of the end groups, not only polymerizing in a linear fashion, but also forming stacks of dimers due to the urethane moiety in the end groups that induces lateral aggregation (Figure 1.16) [53, 54]. Due to these lateral interactions, supramolecular crosslinks are obtained that crystallize into nanofibers which could be observed with AFM.
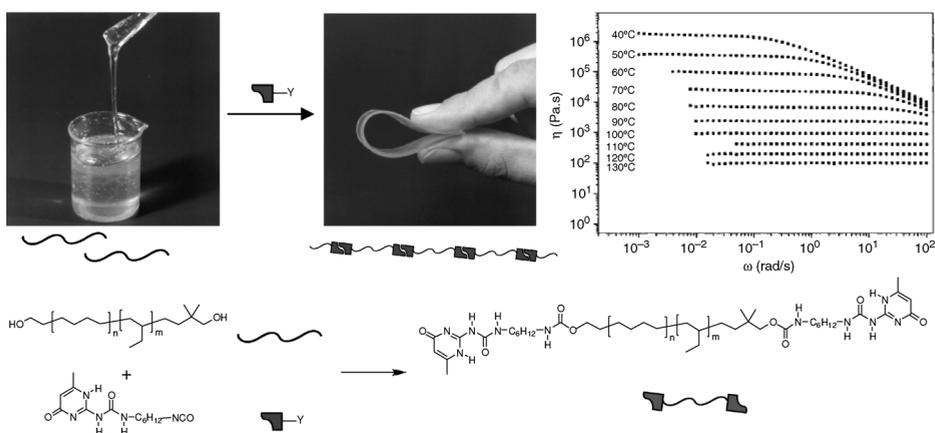
Figure 1.15 A supramolecular thermoplastic elastomer obtained by functionalization of a short telechelic poly(ethylene-butylene) oligomer with an ureido-pyrimidinone hydrogen-bonding moiety and its dynamic melt viscosity as a function of temperature. Reprinted with permission from Wiley-VCH [47b].
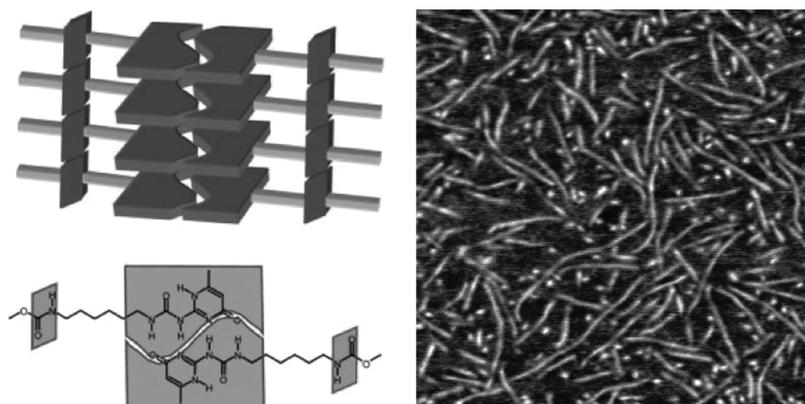
Figure 1.16 Schematic representation of the lateral interactions creating supramolecular crosslinks (left) and the nanofibers as visualized with AFM (500 × 500 nm phase image). Reprinted with permission from Wiley-VCH [54b].

A more detailed study of the influence of the lateral interactions in the end groups by eliminating or reinforcing the lateral interactions confirmed their importance [53]. The supramolecular polymer with no lateral interactions is a sticky gum and shows no distinct phase separation, rheology measurements confirming the presence of UPy-UPy hydrogen bonding (Figure 1.17). Upon introduction and reinforcement of the lateral interactions in the UPy urethane (UPy-T) and UPy urea (UPy-U) motifs respectively, the mechanical properties increase drastically, resulting in thermoplastic elastomers.

The influence of the strength of the lateral interactions is clearly visible, as the UPy-T nanofibers are ill-defined and display a melt at 69 °C, whereas the UPy-U nanofibers are well-defined with a melt at 129 °C (Figure 1.18). An important result of these lateral interactions is the change in polymerization mechanism. In solution,
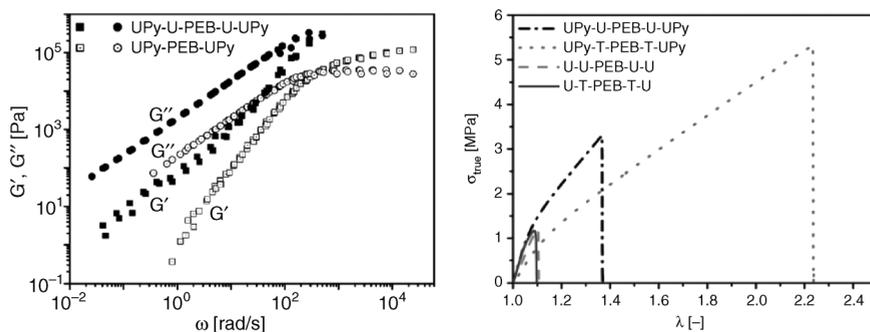
Figure 1.17 Rheological master curves (left) and tensile testing (right) of various telechelic supramolecular poly(ethylene-butylene) polymers. Reprinted with permission from the American Chemical Society [53].
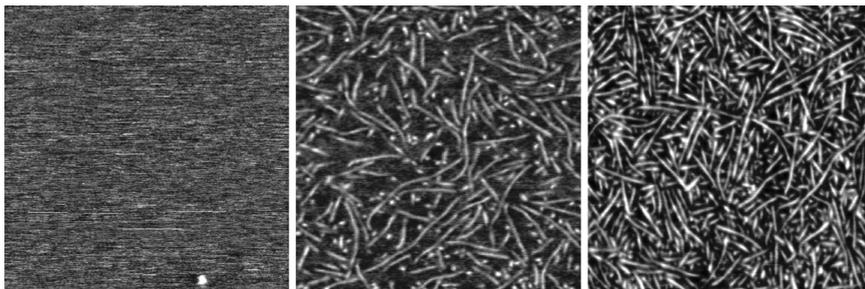
Figure 1.18 AFM phase images (500 × 500 nm) of UPy-PEB-UPy, UPy-T-PEB-T-UPy and UPy-U-PEB-U-UPy respectively.

UPy-urea model compounds reveal an isodesmic polymerization mechanism into stacks, with a lateral association constant of $3 \times 10^2 \, \mathrm{M}^{-1}$ in CDCl$_3$ [55]. However, in the bulk the polymerization mechanism becomes cooperative due to phase separation and results in the crystallization of long nanofibers.

The usability of these materials was exemplified by the creation of supramolecular biomaterials, in which telechelic poly(ε-caprolactone) was functionalized with UPy groups to generate a supramolecular biocompatible material. Using the noncovalent nature of the material, UPy-functionalized peptides can be incorporated in the material by simple mixing (Figure 1.19) [56]. The bioactive molecules are anchored into the supramolecular material via the UPy hydrogen-bonding units, establishing the possibility to obtain a dynamic biomaterial that closely resembles the extracellular matrix due to its noncovalent character.

Using this modular approach, materials with different bioactive molecules can easily be made without resynthesizing the whole construct. The incorporation of UPy-functionalized cell adhesion peptides into the supramolecular biomaterial increased cell adhesion, spreading, and proliferation compared to the bare construct, revealing the applicability of this approach. Due to the significant mechanical
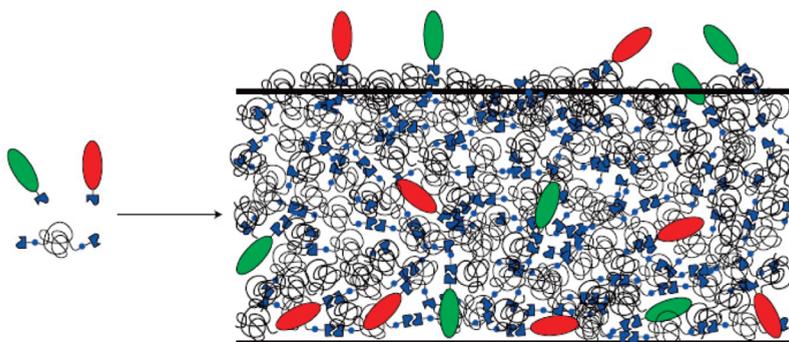
Figure 1.19 Modular approach to supramolecular biomaterials using the noncovalent interactions for the anchoring of bioactive molecules. Reprinted with permission from Nature Publishing Group [56a].
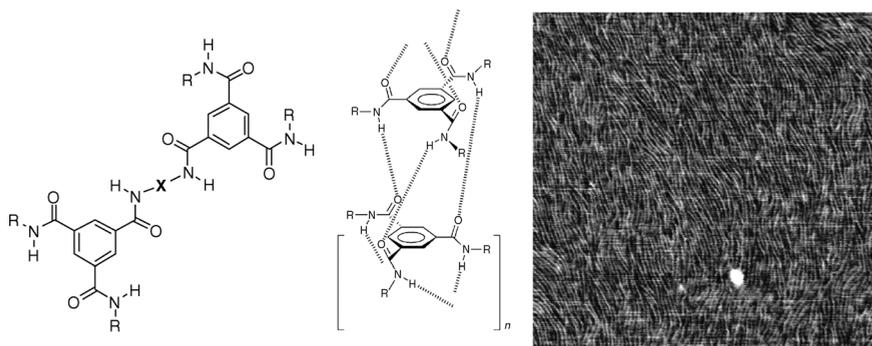
Figure 1.20 Supramolecular polymers based on the benzene-1,3,5-tricarboxamide motif (left) and the nano-fibers as observed with AFM (phase image, 450×450 nm, right). Reprinted with permission from the American Chemical Society [59].

properties of these materials, it is possible to electrospin fibrous membranes with diameters less than 1 µm [57].

The need to incorporate lateral interactions in supramolecular polymers could be circumvented by using hydrogen-bonding motifs that comprise the possibility to chain extend and simultaneously act as supramolecular crosslinks [58]. When telechelic poly(ethylene-butylene) was functionalized with the benzene-1,3,5-tricarboxamide (BTA) motif, a supramolecular thermoplastic elastomer was obtained [59]. The BTA motif is capable of chain extending by hydrogen bonding to neighboring BTA molecules. Due to the fact that one BTA motif exhibits two binding sites for other BTA molecules, being above and below the face of the BTA molecule, this results in chain extension as well as supramolecular cross-linking.

The polymerization mechanism is cooperative due to the unfavorable arrangement of the carbonyl groups in the initial aggregation steps and additional dipole-dipole interactions [60]. This results in nano-fibers with a transition to the isotropic phase around 200 °C (Figure 1.20). At room temperature, the material is liquid crystalline, giving it high elastomeric properties but results in a low toughness.

1.5
Future Perspectives

The developments within the fields of polymer chemistry and organic chemistry have enabled the synthesis of complex monomers and polymers. The state-of-the-art knowledge in the field of supramolecular chemistry gives increasing control over self-assembled systems and paves the way for the creation of supramolecular materials based on noncovalent interactions. In the past decades, the hydrogen bond has proven itself to be a most suitable candidate for applications where structuring interaction is required in supramolecular synthesis. With increasing

knowledge of hydrogen-bonding motifs and their self-assembly behavior in solution and in the solid state, the exploration of supramolecular synthesis of multi-component systems with different supramolecular motifs has started in recent years. Using purely hydrogen bonding, multi-component systems have shown promising results as, for example, supramolecular block copolymers and bioactive biomaterials.

It is now the time to acquire structures with a well-defined molecular as well as supramolecular structure by combining the vast knowledge on traditional polymer chemistry with the current knowledge on supramolecular chemistry. The next step in the development of hydrogen bonding in supramolecular polymer chemistry is to gain control over the self-assembly, possibly by the use of supramolecular protective groups or by turning 'on' or 'off' the supramolecular polymerizations by switchable hydrogen-bonding motifs. This would be a step toward materials with well-defined properties.

As an example, we have combined our knowledge of polymer chemistry and supramolecular chemistry to obtain supramolecular nano-particles based on hydrogen bonding (Figure 1.21) [61]. Using polymer chemistry, covalent polymers with a narrow molecular weight distribution were synthesized which bear a small fraction of covalently protected UPy groups on their side-chains. Upon deprotection with UV-light, the UPy motif was switched 'on' and supramolecular cross-linking via UPy hydrogen bonding was obtained. Using dilute conditions, single-chain supramolecular nanoparticles were obtained, which mimic the supramolecular folding of proteins. This could be a first step toward artificial proteins and enzymes, suggesting endless possibilities for supramolecular polymers. Moreover, when the temperature of a film of these nanoparticles is raised, intermolecular hydrogen bonds are formed
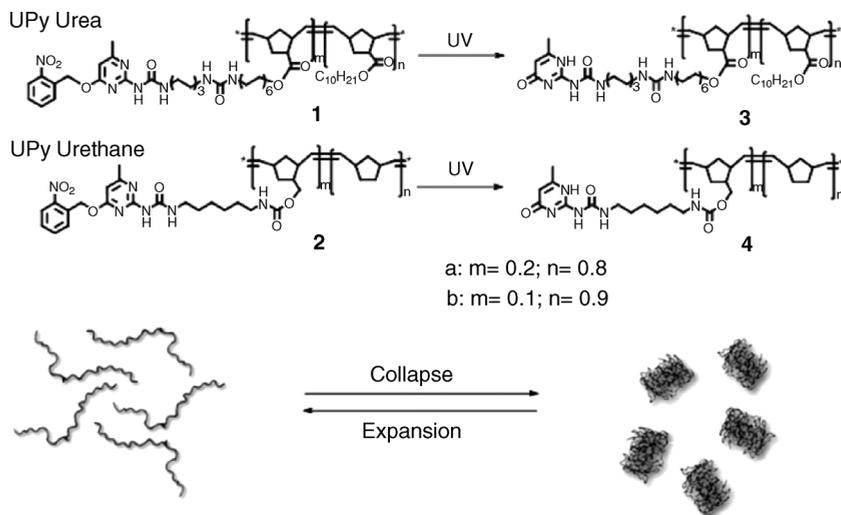
Figure 1.21 The creation of supramolecular nano-particles based on intramolecular cross-linking via hydrogen bonding. Reprinted with permission from the American Chemical Society [61a].

and the system is converted into a three-dimensional hydrogen-bonded network. Thus the full potential of reversible supramolecular interactions is applied in material processing.

References

1 Morawetz, H. (1985) *Polymers: The Origins and Growth of a Science*, John Wiley and Sons.

2 Staudinger, H. (1920) *Ber. Deut. Chem. Ges.*, **53** (6), 1073.

3 Thematic Issue of Chemical Reviews (2009) **109** (11), 4961–6540.

4 (a) Stadler, R. and Burgert, J. (1986) *Makromol. Chem.*, **187**, 1681–1690; (b) Stadler, R. and de Lucca Freitas, L. (1986) *Colloid Polym. Sci.*, **264**, 773; (c) de Lucca Freitas, L. and Stadler, R. (1987) *Macromolecules*, **20**, 2478.

5 (a) Lehn, J.-M. (1990) *Angew. Chem. Int. Ed.*, **26**, 1304–1319; (b) Lehn, J.-M. (1993) *Science*, **260**, 1762–1763.

6 Goshe, A.J., Steele, I.M., Ceccarelli, C., Rheingold, A.L., and Bosnich, B. (2002) *PNAS*, **99**, 4823–4829.

7 De Greef, T.F.A., Smulders, M.M.J., Wolffs, M., Schenning, A.P.H.J., Sijbesma, R.P., and Meijer, E.W. (2009) *Chem. Rev.*, **109**, 5687–5754.

8 Moore, T.S. and Winmill, T.F. (1912) *J. Chem. Soc. Trans.*, **101**, 1635–1676.

9 Latimer, W.M. and Rodebush, W.H. (1920) *J. Am. Chem. Soc.*, 1419–1433.

10 (a) Jorgensen, W.L. and Pranata, J. (1990) *J. Am. Chem. Soc.*, **112**, 2008–2010; (b) Pranata, J., Wierschke, S.G., and Jorgensen, W.L. (1991) *J. Am. Chem. Soc.*, **113**, 2810–2819.

11 Murray, T.J. and Zimmerman, S.C. (1992) *J. Am. Chem. Soc.*, **114**, 4010–4011.

12 Blight, B.A., Hunter, C.A., Leigh, D.A., McNab, H., Thomson, P.I.T. (2011) *Nature Chemistry*, **3**, 244–248.

13 Sijbesma, R.P. and Meijer, E.W. (2003) *Chem. Commun.*, 5–16.

14 Beijer, F.H., Kooijman, H., Spek, A.L., Sijbesma, R.P. and Meijer, E.W. (1998) *Angew. Chem. Int. Ed.*, **37** (1), 75–78.

15 Sijbesma, R.P., Beijer, F.H., Brunsveld, L., Folmer, B.J.B., Ky Hirschberg, J.H.K., Lange, R.F.M., Lowe, J.K.L., and Meijer, E.W. (1997) *Science*, **278**, 1601–1604.

16 Beijer, F.H., Sijbesma, R.P., Kooijman, H., Spek, A.L., and Meijer, E.W. (1998) *J. Am. Chem. Soc.*, **120**, 6761–6769.

17 Söntjens, S.H.M., Sijbesma, R.P., van Genderen, M.H.P., and Meijer, E.W. (2000) *J. Am. Chem. Soc.*, **122**, 7487–7493.

18 de Greef, T.F.A., Ercolani, G., Ligthart, G.B.W.L., Meijer, E.W. and Sijbesma, R.P. (2008) *J. Am. Chem. Soc.*, **130**, 13755–13764.

19 (a) Spada, G.P., Carcuro, A., Colonna, F.P., Garbesi, A. and Gottarelli, G. (1988) *Liquid Crystals*, **3** (5), 651–654; (b) Marlow, A.L., Mezzina, E., Spada, G.P., Masiero, S., Davis, J.T., and Gottarelli, G. (1999) *J. Org. Chem.*, **64**, 5116–5123; (c) Sivakova, S. and Rowan, S.J. (2005) *Chem. Soc. Rev.*, **34**, 9–21.

20 (a) Zeng, H., Yang, X., Flowers, R.A., and Gong, B. (2002) *J. Am. Chem. Soc.*, **124** (12), 2903–2910; (b) Jahnke, E., Lieberwirth, I., Severin, N., Rabe, J.P., and Frauenrath, H. (2006) *Angew. Chem. Int. Ed.*, **45**, 5383–5386; (c) Isimjan, T.T., de Bruyn, J.R., and Gillies, E.R. (2010) *Macromolecules*, **43**, 4453–4459; (d) Skrzeszewska, P.J., de Wolf, F.A., Cohen Stuart, M.A., and van der Gucht, J. (2010) *Soft Matter*, **6**, 416–422.

21 Khazanovich, N., Granja, J.R., McRee, D.E., Milligan, R.A. and Reza Ghadiri, M. (1994) *J. Am. Chem. Soc.*, **116**, 6011–6012.

22 Zeng, H., Yang, X., Brown, A.L., Martinovic, S., Smith, R.D., and Gong, B. (2003) *Chem. Commun.*, 1556–1557.

23 Fouquey, C., Lehn, J.-M., and Levelut, A.-M. (1990) *Adv. Mater.*, **5**, 254–257.

24 (a) Lee, C.-M., Jariwala, C.P. and Griffin, A.C. (1994) *Polymer*, **35** (21), 4550–4554; (b) St. Pourcain, C.B. and Griffin, A.C. (1995) *Macromolecules*, **28**, 4116–4121.

25 Brunsveld, L., Folmer, B.J.B., Meijer, E.W., and Sijbesma, R.P. (2001) *Chem. Rev.*, **101**, 4071–4097.

26 (a) Kato, T. and Fréchet, J.M.J. (1989) *Macromolecules*, **22**, 3819–3821; (b) Shandryuk, G.A., Kuptsov, S.A., Shatalova, A.M., Plate, N.A., and Talroze, R.V. (2003) *Macromolecules*, **36**, 3417–3423; (c) Burd, C. and Weck, M. (2005) *Macromolecules*, **38**, 7225–7230; (d) Pollino, J.M. and Weck, M. (2005) *Chem. Soc. Rev.*, **34**, 193–207; (e) Hammond, M.R. and Mezzenga, R. (2008) *Soft Matter*, **4**, 952–961.

27 (a) Hilger, C. and Stadler, R. (1990) *Macromolecules*, **23**, 2097–2100. (b) Hilger, C. and Stadler, R. (1992) *Macromolecules*, **25**, 6670–6680; (c) St. Pourcain, C.B. and Griffin, A.C. (1995) *Macromolecules*, **28**, 4116–4121; (d) Lange, R.F.M., van Gurp, M. and Meijer, E.W. (1999) *J. Polym. Sci, Part A*, **37** (19), 3657–3670; (e) Chino, K. and Ashiura F M. (2001) *Macromolecules*, **34**, 9201–9204; (f) Rieth, L.R., Eaton, R.F., and Coates, G.W. (2001) *Angew. Chem. Int. Ed.*, **40** (11), 2153–2156; (g) Berl, V., Schmutz, M., Krische, M.J., Khoury, R.G., and Lehn, J.-M. (2002) *Chem. Eur. J.*, **8** (5), 1227–1244.

28 (a) Park, T. and Zimmerman, S.C. (2006) *J. Am. Chem. Soc.*, **128**, 13986–13987; (b) Scherman, O.A., Ligthart, G.B.W.L., Ohkawa, H., Sijbesma, R.P., and Meijer, E.W., *PNAS* (2006) **103** (32), 11850–11855.

29 Yang, S.K., Ambade, A.V., and Weck, M. (2010) *J. Am. Chem. Soc.*, **132**, 1637–1645.

30 Tessa ten Cate, A. and Sijbesma, R.P. (2002) *Macromol. Rapid Commun.*, **23**, 1094–1112.

31 (a) Knoben, W., Besseling, N.A.M., and Cohen Stuart, M.A. (2007) *J. Chem. Phys.*, **126**, 024907; (b) van Beek, D.J.M., Spiering, A.J.H., Peters, G.W.M., te Nijenhuis, K., and Sijbesma, R.P. (2007) *Macromolecules*, **40**, 8464–8475.

32 Burke, K.A., Sivakova, S., McKenzie, B., Mather, P.T., and Rowan, S.J. (2006) *J. Polym. Sci, Part A*, **44**, 5049–5059.

33 Lortie, F., Boileau, S., and Bouteiller, L. (2003) *Chem. Eur. J.*, **9**, 3008–3014.

34 (a) Gillies, E.R. and Fréchet, J.M.J. (2004) *J. Org. Chem.*, **69**, 46–53; (b) Pensec, S., Nouvel, N., Guilleman, A., Creton, C., Boué, F., and Bouteiller, L., *Macromolecules* (2010) **43**, 2529–2534; (c) Feldman, K.E., Kade, M.J., Meijer, E.W., Hawker, C.J., and Kramer, E.J. (2010) *Macromolecules*, **43**, 5121–5127.

35 (a) de Greef, T.F.A., Nieuwenhuizen, M.M.L., Stals, P.J.M., Fitié, C.F.C., Palmans, A.R.A., Sijbesma, R.P., and Meijer, E.W. (2008) *Chem. Commun.*, 4306–4308; (b) Mes, T., Smulders, M.M.J., Palmans, A.R.A., and Meijer, E.W., *Macromolecules* (2010) **43**, 1981–1991; (c) de Greef, T.F.A., Nieuwenhuizen, M.M.L., Sijbesma, R.P., and Meijer, E.W., *J. Org. Chem.* (2010) **75**, 598–610.

36 Rehm, T. and Schmuck, C. (2008) *Chem. Commun.*, 801–813.

37 Obert, E., Bellot, M., Bouteiller, L., Andrioletti, F. Lehen-Ferrenbach, C., and Boué, F. (2007) *J. Am. Chem. Soc.*, **129**, 15601–15605.

38 (a) Ky Hirschberg, J.H.K., Brunsveld, L., Ramzi, A., Vekemans, J.A.J.M., Sijbesma, R.P., and Meijer, E.W. (2000) *Nature*, **407**, 167–170; (b) Brunsveld, L., Vekemans, J.A.J.M., Ky Hirschberg, J.H.K., Sijbesma, R.P., and Meijer, E.W. (2002) *PNAS*, **99** (8), 4977–4982; (c) Boekhoven, J., van Rijn, P., Brizard, A.M., Stuart, M.C.A., and van Esch, J.H. (2010) *Chem. Commun.*, **46**, 3490–3492.

39 (a) van Bommel, K.J.C., van der Pol, C., Muizebelt, I., Friggeri, A., Heeres, A., Meetsma, A., Feringa, B.L., and van Esch, J. (2004) *Angew. Chem. Int. Ed.*, **43**, 1663–1667; (b) Friggeri, A., van der Pol, C., van Bommel, K.J.C., Heeres, A., Stuart, M.C.A., Feringa, B.L., and van Esch, J. (2005) *Chem. Eur. J.*, **11**, 5353–5361; (c) Boekhoven, J., van Rijn, P., Brizard, A.M., Stuart, M.C.A., and van Esch, J.H. (2010) *Chem. Commun.*, **46**, 3490–3492.

40 (a) Barberá, J., Puig, L., Romero, P., Serrano, J.L., and Sierra, T. (2006) *J. Am. Chem. Soc.*, **128**, 4487–4492; (b) Kolomiets, E., Buhler, E., Candau, S.J., Lehn, J.-M. (2006) *Macromolecules*, **39**, 1173–1181; (c) Seki, T., Yagai, S., Karatsu, T., and Kitamura, A. (2008) *J. Org. Chem.*, **73**, 3328–3335.

41 Korshak, V.V. and Frunze, T.M. (1955) Bulletin of the Academy of Sciences of the USSR. *Div. Chem. Sci. (English Translation)*, **1**, 143–149.

42 (a) Koevoets, R.A., Versteegen, R.M., Kooijman, H., Spek, A.L., Sijbesma, R.P., and Meijer, E.W. (2005) *J. Am. Chem. Soc.*, **127**, 2999–3003; (b) Versteegen, R.M., Sijbesma, R.P., and Meijer, E.W. (2005) *Macromolecules*, **38**, 3176–3184; (c) Wisse, E., Govaert, L.E., Meijer, H.E.H., and Meijer, E.W. (2006) *Macromolecules*, **39**, 7425–7432; (d) Botterhuis, N.E., Karthikeyan, S., Veldman, D., Meskers, S.C.J., and Sijbesma, R.P. (2008) *Chem. Commun.*, 3915–3917; (e) Botterhuis, N.E., Karthikeyan, S., Spiering, A.J.H., and Sijbesma, R.P. (2010) *Macromolecules*, **43**, 745–751.

43 Wisse, E., Spiering, A.J.H., Pfeifer, F., Portale, G., Siesler, H.W., and Meijer, E.W. (2009) *Macromolecules*, **42**, 524–530.

44 Wisse, E., Spiering, A.J.H., van Leeuwen, E.N.M., Renken, R.A.E., Dankers, P.Y.W., Brouwer, L.A., van Luyn, M.J.A., Harmsen, M.C., Sommerdijk, N.A.J.M., and Meijer, E.W. (2006) *Biomacromolecules*, **7**, 3385–3395.

45 (a) Cordier, P., Tournilhac, F., Soulié-Ziakovic, C., and Leibler, L. (2008) *Nature*, **451**, 977–980; (b) Montarnal, D., Tournilhac, F., Hidalgo, M., Couturier, J.-L., and Leibler, L., *J. Am. Chem. Soc.* (2009) **131**, 7966–7967.

46 (a) Peter Lillya, C., Baker, R.J., Hütte, S., Henning Winter, H., Lin, Y.-G., Shi, J., Charles Dickinson, L., and Chien, J.C.W. (1992) *Macromolecules*, **25**, 2076–2080; (b) Duweltz, D., Lauprêtre, F., Abed, S., Bouteiller, L., and Boileau, S. (2003) *Polymer*, **44**, 2295–2302.

47 (a) Ky Hirschberg, J.H.K., Beijer, F.H., van Aert, H.A., Magusin, P.C.M.M., Sijbesma, R.P., and Meijer, E.W. (1999) *Macromolecules*, **32**, 2696–2705; (b) Folmer, B.J.B., Sijbesma, R.P., Versteegen, R.M., van der Rijt, J.A.J., and Meijer, E.W. (2000) *Adv. Mater.*, **12** (12), 874–878; (c) Rowan, S.J., Suwanmala, P., and Sivakova, S. (2003) *J. Polym. Sci, Part A*, **41** (22), 3589–3596; (d) Sivakova, S., Bohnsack, D.A., Mackay, M.E., Suwanmala, P., and Rowan, S.J. (2005) *J. Am. Chem. Soc.*, **127**, 18202–18211.

48 (a) Bohle, A., Brunklaus, G., Hansen, M.R., Schleuss, T.W., Kilbinger, A.F.M., Seltmann, J., and Spiess, H.W. (2010) *Macromolecules*, **43**, 4978–4985; (b) Ibarboure, E. and Rodríguez-Hernández, J. (2010) *Eur. Polym. J.*, **46**, 891–899.

49 (a) Hilger, C. and Stadler, R. (1990) *Makromol. Chem.*, **191**, 1347–1361; (b) Hilger, C. and Stadler, R. (1991) *Makromol. Chem.*, **192**, 805–817; (c) Schirle, M., Beckmann, J., and Stadler, R. (1992) *Angew. Makromol. Chem.*, 261–282.

50 Woodward, P.J., Merino, D.H., Greenland, B.W., Hamley, I.W., Light, Z., Slark, A.T., and Hayes, W. (2010) *Macromolecules*, **43**, 2512–2517.

51 (a) Rowan, S.J., Suwanmala, P., and Sivakova, S. (2003) *J. Polym. Sci, Part A*, **41**, 3589–3596; (b) Sivakova, S., Bohnsack, D.A., Mackay, M.E., Suwanmala, P., and Rowan, S.J. (2005) *J. Am. Chem. Soc.*, **127**, 18202–18211.

52 Lin, I.-H., Cheng, C.-C., Yen, Y.-C., and Chang, F.-C. (2010) *Macromolecules*, **43**, 1245–1252.

53 Kautz, H., van Beek, D.J.M., Sijbesma, R.P., and Meijer, E.W. (2006) *Macromolecules*, **39** (13), 4265–4267.

54 (a) van Beek, D.J.M., Spiering, A.J.H., Peters, G.W.M., te Nijenhuis, K., and Sijbesma, R.P. (2007) *Macromolecules*, **40**, 8464–8475; (b) Botterhuis, N.E., van Beek, D.J.M., van Gemert, G.M.L., Bosman, A.W., and Sijbesma, R.P. (2008) *J. Polym. Sci, Part A*, **46**, 3877–3885.

55 Nieuwenhuizen, M.M.L., de Greef, T.F.A., van der Bruggen, R.L.J., Paulusse, J.M.J., Appel, W.P.J., Smulders, M.M.J., Sijbesma, R.P., and Meijer, E.W. (2010) *Chem. Eur. J.*, **16**, 1601–1612.

56 (a) Dankers, P.Y.W., Harmsen, M.C., Brouwer, L.A., van Luyn, M.J.A., and Meijer, E.W. (2005) *Nature Mater.*, **4**, 568–574; (b) Dankers, P.Y.W., van Leeuwen, E.N.M., van Gemert, G.M.L., Spiering, A.J.H., Harmsen, M.C., Brouwer, L.A., Janssen, H.M., Bosman, A.W., van Luyn, M.J.A., and Meijer, E.W. (2006) *Biomaterials*, **27**, 5490–5501.

57 Dankers, P.Y.W., Boomker, J.M., Huizinga-van der Vlag, A., Smedts, F.M.M., Harmsen, M.C., and van Luyn, M.J.A. (2010) *Macromol. Biosci.*, **10**, 1345–1354.

58 (a) Lightfoot, M.P., Mair, F.S.,
Pritchard, R.G., and Warren, J.E. (1999)
Chem. Commun., 1945; (b) Smulders,
M.M.J., Schenning, A.P.H.J., and
Meijer, E.W. (2008) *J. Am. Chem. Soc.*, **130**,
606–611; (c) Fan, E., Yang, J., Geib, S.J.,
Stoner, T.C., Hopkins, M.D., and
Hamilton, A.D. (1995) *J. Chem. Soc.,
Chem. Commun.*, 1251–1252;
(d) Hanabusa, K., Kawakami, A., Kimura,
M., and Shirai, H. (1997) *Chem. Lett.*, **5**,
429–430; (e) van Bommel, K.J.C.,
van der Pol, C., Muizebelt, I.,
Friggerri, A., Heeres, A., Meetsma, A.,
Feringa, B.L., and van Esch, J.H. (2004)
Angew. Chem., Int. Ed., **43**,
1663–1667.

59 Roosma, J., Mes, T., Leclère, P., Palmans,
A.R.A., and Meijer, E.W. (2008) *J. Am.
Chem. Soc.*, **130**, 1120–1121.

60 (a) Stals, P.J.M., Everts, J.C., de Bruijn, R.,
Filot, I.A.W., Smulders, M.M.J.,
Martín-Rapún, R., Pidko, E.A., de Greef,
T.F.A., Palmans, A.R.A., and Meijer, E.W.
(2010) *Chem. Eur. J.*, **16**, 810–821; (b) Filot,
I.A.W., Palmans, A.R.A., Hilbers, P.A.J.,
van Santen, R.A., Pidko, E.A., and de
Greef, T.F.A. (2010) *J. Phys. Chem. B*, **114**,
13667–13674.

61 (a) Johan Foster, E., Berda, E.B., and
Meijer, E.W. (2009) *J. Am. Chem. Soc.*, **131**,
6964–6966; (b) Berda, E.B.,
Johan Foster, E., and Meijer, E.W. (2010)
Macromolecules, **43** (3), 1430–1437.