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Unconventional, Amphiphilic Polymers Based on Chiral Poly(ethylene oxide) Derivatives. 2. Ordering and Assembly

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ABSTRACT: The poly(ethylene oxide) derivatives 1–3 (Figure 1) are—in design—synthetic analogues of coiled-coil-forming peptides. A comparative optical rotatory dispersion (ORD) study and TEM measurements have been used to investigate the ordering and assembly processes that are involved in the aggregation of these amphiphilic polymers 1–3 in H2O. ORD measurements have shown that various ethylene oxide derivatives display an inversion of optical rotation upon complexation with KSCN, i.e., upon adoption of a helical conformation. This observation has led to the proposal that polymers 1–3 are helically ordered in H2O, since the methyl-substituted polymer 3 exhibits an inversion of optical rotation on going from apolar (THF) to polar (H2O) solvents; phase separation prohibits the detection of such an inversion for the isobutyl-substituted polymers 1 and 2. TEM studies on surfaces onto which polymers 1–3 were deposited from aqueous solutions revealed granular and threadlike aggregates. The formation of the threadlike higher structures requires a directionality in the assembly process. Such a directionality could be provided by the formation of coiled-coil tertiary structures. However, substantial evidence for the formation of coiled coils or other specific tertiary structures is lacking.

Introduction

Nature provides us with an almost infinite number of well-defined, functioning, supramolecular systems and therefore gives inspiration to chemists in their search for useful, new architectures. The construction of synthetic equivalents of structures found in nature is challenging and may eventually lead to new insights in the development of materials with unique and previously unattainable properties. The ongoing activity in the field of supramolecular chemistry has, for instance, led to the synthesis of an equivalent of the tobacco mosaic virus, in the sense that the spatial design of the virus has been copied in a synthetic system. An elegant supramolecular structure found in certain peptides is the so-called coiled coil: a structure of associated α-helices, which was modeled for the first time theoretically by Crick in 1952 and for which the first precise X-ray data were published almost 40 years later by O'Shea. In recent years, coiled-coil superstructures have received enormous attention. Not only naturally occurring proteins but also synthetically designed polypeptides have been investigated in order to distinguish between the different factors that are involved in the formation of coiled coils. It is now generally accepted that coiled coils are formed due to hydrophobic interactions between the α-helical parts; these parts have a 3,4 repeat (also called a 72-repeat) of apolar amino acids in a polar sequence of amino acids. As a result, the hydrophobic residues are directed in an apolar ribbon along the surface of the α-helix. At the right pH, the 'ribbon-type' of amphiphiles associate in H2O to bundles of superhelices.

The formation of well-defined, secondary or tertiary structures is not confined to (natural) peptides, since numerous synthetic polymers can form ordered structures, especially in the solid state (e.g., helical arrangements are quite common secondary structures for synthetic polymers; a few synthetic polymers form so-called stereocomplexes). However, to our knowl-

Figure 1. PEO-based polymers 1–3: analogues—in primary structure—of coiled-coil-forming peptides.
1–3 is used to perform a comparative study, using optical rotatory dispersion (ORD) spectroscopy. ORD spectra of polymers 1–3 in various solvents and under various conditions are related to each other and to ORD spectra of similar, oligomeric or polymeric reference components. The synthesis and characterization of these oligomeric and polymeric species are also described here. Additionally, polymers 1–3 are studied by microscopy techniques—mainly transmission electron microscopy (TEM)—to examine the aggregates that are formed in H$_2$O.

**Results and Discussion**

**Approach.** Coiled-coil superstructures can conveniently and in detail be examined by investigation of the X-ray data of crystals of coiled-coil-forming peptides. In solution, CD spectroscopy of $\alpha$-helical peptides is a simple and powerful technique to determine the formation of coiled-coil structures. In contrast to peptides, polymers 1–3 are not monodisperse, so the crystallization of these sticky oils would be even more laborious than that for peptides and is presumably not possible at all. Also, the extensive knowledge on the chiroptical behavior of $\alpha$-helical peptides cannot be used in a study of aqueous solutions of polymers 1–3 (because these polymers are constituted differently). The possibility of the formation of well-defined structures by polymers 1–3 in aqueous solutions can therefore be studied by (i) developing new characterization methods, (ii) screening existing characterization methods and testing whether these methods can be applied to the characterization of the systems under investigation, and (iii) using various microscopy methods to directly observe the structures or aggregates that are formed. Since option (i) is not connected to our field of research, this option was not investigated. Option (ii) has extensively been examined here—ORD spectroscopy has been screened—and results on (iii) are also reported in this work.

Optical activity is strongly dependent on conformational equilibria, and, therefore, circular dichroism (CD) and optical rotatory dispersion (ORD) spectroscopy are two techniques that can give telling information on the spatial arrangement of molecules in solution. ORD spectroscopy has been used in various studies on the conformational behavior of macromolecules. Coil–helix transitions in poly(amino acids) in general, and in poly($\gamma$-benzyl-$L$-glutamate), poly($\beta$-benzyl-$L$-aspartate), and poly($\beta$-glutamic acid) in particular, can be monitored by measuring the specific optical rotation at the Na D line. In several studies by Pino and others, synthetic polymers—including PPOs (poly(propylene oxides))—have been studied by ORD spectroscopy.

**Synthesis of the Molecular Components.** All oligomeric and polymeric species that have been used as reference components for polymers 1–3 are shown in Figure 2. The syntheses of polymers 1–3 and of compounds (SS)-4 and (SS)-8 have been reported in Part 1. O-Monobenzyl hexaethylene glycol has been described elsewhere.

Oligomer 5 was synthesized by protection of O-monobenzyl hexaethylene glycol with MEMCl in refluxing CH$_2$Cl$_2$, employing N(i-Pr)$_2$Et as HCl scavenger. Production of the quinoline-derivatized oligomer (SS)-6 was achieved by tosylation of the $\alpha$-$\omega$-diol (SS)-8 in CH$_2$Cl$_2$ using KOH as base and by coupling of the resulting tosylate (SS)-9 with 8-hydroxyquinoline (Scheme 1). Yields exceeding 85% could be obtained for both steps.

![Scheme 1. Synthesis of Oligomer (SS)-6](image)

**Scheme 2. Polymerization of 4(S)-Methyl-$\epsilon$-caprolactone Using SnOct$_2$ as Catalyst**

Poly(4(S)-methyl-$\epsilon$-caprolactone) (7) was prepared as reference polymer for polymer 3 (Scheme 2). The enantiomerically pure 4(S)-methyl-$\epsilon$-caprolactone was obtained in an enzymatically controlled Baeyer–Villiger oxidation of 4-methylcyclohexanone. Polymerization of the (S)-monomer was performed at 140 °C using stannous 2-ethylhexanoate (SnOct$_2$) as catalyst. Two monomer/catalyst molar ratios were applied: a ratio of 98/1 gave a sticky oil with a molecular weight ($M_n$) of 8.4 kg/mol and a dispersity of 2.3, whereas a ratio of 810/1 gave polymeric material with an increased molecular weight of $M_n = 29.7$ kg/mol and a decreased
dispersity of 1.4. The latter polymer was also a sticky oil.

Ordering Processes of Polymers 1–3 in Aqueous Solutions: An ORD Analysis. Polyethylene oxide derivatives 1–3 were studied by ORD spectroscopy in various solvents ranging from apolar EtOAc to polar aqueous solvents. The behavior of the polymers in aqueous solutions had our special interest, since in these solutions hydrophobic interactions can play a role. Reliable ORD spectra can only be recorded when the solutions under investigation are sufficiently concentrated, homogeneous, transparent, and not macroscopically ordered (not birefringent). In practice, ORD spectroscopy of materials without chromophores or large dipoles is performed at concentrations ranging from approximately 0.1 mg/mL to 30 mg/mL. However, in this concentration range, polymeric solutions of 1, 2, and 3, in pure H2O are stable turbid solutions or give macroscopic phase separation (solutions of 1, 2, and 3 in H2O become transparent at concentrations lower than ca. 0.1, 0.3, and 1.0 mg/mL, respectively).

The aggregation of polymer 3 in H2O at 20 °C was monitored by ORD spectroscopy. The methyl-substituted polymer 3 is the only polymer for which such a monitoring experiment is possible, since the critical association concentration (cac) of 3 is sufficiently high to allow ORD experiments (the cac of 3 is ca. 0.15 mg/mL). ORD spectra of 3 were recorded at concentrations as low as 0.12 mg/mL (at which the polymer is molecularly dissolved) to concentrations as high as 1.4 mg/mL (at which the aqueous solution is hardly turbid and at which the polymer is aggregated). No change in specific rotation was observed upon the increase of the polymer concentration; invariably a positive specific rotation of the same magnitude was found. It can therefore be concluded that association of polymer 3 does not have any effect on the measured optical rotation.

The next step in the ORD analysis of polymers 1–3 involved the chiroptical behavior of 1–3 in solvents of varying polarity. In contrast to the positive specific rotation of 3 in H2O, all polymers displayed a negative specific rotation in THF. In Figure 3, the results of the ORD measurements at 20 °C are depicted. All polymers showed the same trend: increasing the polarity of the solvent induced a less negative specific rotation. In particular for polymer 1, but also for polymer 2, no dramatic changes in specific rotation could be induced by changing the polarity of the solvent (plots A and B in figure 3), whereas—in contrast—polymer 3 displayed an inversion in optical rotation going from apolar to polar solvents, i.e., going from EtOAc or THF to MeOH or H2O (see plots C and D). This inversion is only caused by the change in polarity of the solvent and not by the aggregation of the polymer, as evidenced by the ORD data reported in the previous paragraph. To put these initial ORD spectroscopy results in perspective, several reference ORD spectra have been recorded.

Oligomer (SS)-4 and poly(4(S)-methyl-ε-caprolactone) (7) were selected as reference materials for polymers 1 and 2 and polymer 3, respectively. The oligomer and the polymer were dissolved in MeOH and dioxane, respectively. While H2O was added to both solutions, the specific rotation at 20 °C was monitored by recording ORD spectra. For both reference experiments, less negative rotations were observed upon increasing sol-
vent polarity, but no spectacular changes in specific rotation could be induced (see Figure 4; plots A and B). The combined experimental data of Figures 3 and 4 show that the chiroptical behavior of the methyl-substituted polymer 3 is anomalous: it is the only investigated material that shows an inversion in optical rotation upon increasing the polarity of the solvent. In the literature, such inversions of chiroptical rotation have seldom been described for polymers and have usually been related to ordering processes of the polymers involved.

We propose that the inversion in optical rotation of polymer 3 upon increasing the polarity of the solvent signifies a distinct conformational transition in this polymer. Presumably, polymer 3 has a random conformation in good solvents such as EtOAc and THF and is more ordered conformationally in polar solvents such as MeOH and particularly H2O. Possibly, also polymers 1 and 2 are more ordered conformationally in pure H2O. However, an inversion in optical rotation upon increasing water content cannot be measured for aqueous solutions of 1 and 2, since these polymers are not sufficiently soluble in H2O.

Finally, ORD spectra of polymer 3 at various temperatures have been recorded. From Figure 5A, it is apparent that the specific rotation of an aqueous solution of polymer 3 becomes less positive with temperature. Thus, an increase in temperature of an aqueous solution of 3 has a similar effect on the monitored specific rotation as a decrease in polarity of the solvent would have. In Figure 5B, it is shown that a temperature increase in more apolar solvents hardly changes the specific rotation of polymer 3. These results are in line with the previously mentioned hypothesis or proposal. A higher temperature enlarges the rotational freedom of polymer 3 in aqueous solution and will result in a less ordered conformation of this macromolecule (figure 5A). When the conformation of the polymer is already less ordered, as proposed for polymer 3 in apolar i-ProH/MeCN solutions, an increase in temperature can hardly result in a dramatic change in conformation (Figure 5B).

In the described ORD analysis, it has been argued that the conformation of polymers 1–3 is more ordered in polar solvents than in apolar solvents. Reference data of known and extensively studied ordering processes of ethylene oxide compounds can lead to a more defined hypothesis concerning the nature of the proposed conformational order in the ethylene oxide derivatives in polar solvents. The complexation of ethylene oxide compounds with alkali salts is such an extensively studied ordering process.

**Complexation of Chiral Ethylene Oxide Derivatives with Alkali Salts.** Crystal structures of a wide variety of complexes of ethylene oxide compounds with salts have been reported, including crown ether complexes and complexes of linear, oligomeric ethylene oxides with alkali salts. Especially the linear, oligomeric ethylene oxides are of relevance to this work, because these glycol derivatives are most related to the systems we are interested in. Vögtle and co-workers have shown that larger oligomeric species fold into helical conformations in complexes with alkali salts. As an example, the crystal structure of RbI with α,ω-O,O′-diquinolinyl-modified tetraethylene glycol is shown in Figure 6.

**Figure 4.** ORD spectra of oligomer (SS)-4 (plot A) and poly(4(S)-methyl-ε-caprolactone) (7) (plot B) in various solvents at 20 °C. Specific rotations [α]20 are plotted versus the wavelength λ. Concentrations of approximately 4 and 3 mg/mL have been used in plots A and B, respectively. Solvent–solvent ratios are denoted in v/v ratios. See Experimental Section for details.

**Figure 5.** ORD spectra of polymer 3 in THF/H2O (65/35) and in i-ProH/MeCN (62/38) at different temperatures. Specific rotations [α] are plotted versus the wavelength λ. Concentrations of 24.4 and 17.9 mg/mL are used in plots A and B, respectively. Solvent–solvent compositions are denoted in v/v ratios. See the Experimental for details.
In analogy to the work of Vögtle, the complexation of the ethylene oxide oligomers (SS)-4, 5, and (SS)-6 (all three pictured in Figure 2) with the alkali salts Rbl, NH₄PF₆, and—in most cases—KSCN was studied. Initially, cocrystallization of the oligomers with KSCN was attempted. Standard procedures for the synthesis of cocrystals of KSCN with either the diisobutyl-substituted (SS)-4 or the unsubstituted oligomer 5 failed. Vögtle has shown that the introduction of quinoline end groups increases the impetus of ethylene oxide derivatives toward cocrystallization with alkali salts. Therefore, it was attempted to obtain cocrystals of compound (SS)-6 with KSCN or Rbl. Again, all standard procedures failed. Apparently, the introduction of asymmetrical features in ethylene oxide compounds—alkyl side-chains—blocks the ability of these compounds to form cocrystals with alkali salts. Consequently, solid state data of the desired complexes could not be obtained and the study of these complexes was confined to the solution state.

1H NMR, 13C NMR, and ORD spectroscopy have been used to examine the complexation of the ethylene oxide oligomers (SS)-4, 5, and (SS)-6 with alkali salts in MeOH (again, KSCN was typically used). The titration of (SS)-4 with KSCN in CD₃OD at 20 °C was monitored by 13C NMR, and all carbon signals of (SS)-4 shifted upon addition of KSCN (Figure 7A). A Job plot was constructed to investigate the stoichiometry of the complex, and it was established that in CD₃OD a 1:1 complex is formed (Figure 7B). The induced shifts of the carbon signals were plotted against the KSCN-concentration, and fitting of the data gave an association constant (K) for the (SS)-4—KSCN complex of approximately 35 L/mol (Figure 7C). When the complexation at 25 °C was monitored by measuring the specific rotation at the Na D line (λ = 589 nm), a K value in the same range was found (K = 29 L/mol, Figure 7D).

The complexation of the quinolinyl-functionalized ethylene oxide (SS)-6 with KSCN was also studied. An association constant of 330 L/mol for the 1:1 complex was determined in CD₃OD at 20 °C by monitoring the 13C NMR spectra upon titration with KSCN. Thus, the effect observed by Vögtle confirmed: the introduction of quinoline end groups increases the stability of glycol—KSCN complexes. Compared to that of the (SS)-4—KSCN complex, the Gibbs free energy for complexation is ca. 5.5 kJ/mol lower for the (SS)-6—KSCN complex. The association constant of the complex of unsubstituted oligomer 5 with KSCN in CD₃OD at 20 °C was also determined employing 13C NMR and was found to be 25 L/mol. This value for the 1:1 complex is in the same order of magnitude as the K value of the (SS)-4—KSCN complex. Apparently, the introduction of isobutyl side chains to linear ethylene glycol compounds does not dramatically influence the stability of the complexes these compounds can form with alkali salts in solution.

The complex formation of oligomers (SS)-4 and (SS)-6 with KSCN in MeOH at 20 °C was monitored by ORD spectroscopy. The results of the titrations of (SS)-4 and (SS)-6 with KSCN are shown in Figure 8A and B, respectively. Similar results were obtained for both oligomers: complexation gave an inversion of specific optical rotation [α]₀. Analogous to the complexation of oligomeric species (SS)-4 and (SS)-6 with KSCN in MeOH, the complexation of polymers 1—3 with KSCN in MeOH was also monitored by ORD-spectroscopy. Polymers 1 and 2 displayed inversions of optical rotation, whereas polymer 3 gave an increasing specific optical rotation as complexation proceeded (polymer 3 without added KSCN already has a positive specific rotation in MeOH, see Figure 3C). We interpret these inversions as conformational changes from an approximately random conformation to a helical conformation, assuming a similar geometry of the ethylene oxides in solution and in the solid state (see Figure 6 for a helical conformation of a complexed ethylene oxide in the solid state).

When all ORD data (Figures 3—5 and 8) are combined, it can be imagined that in the studied ethylene oxide systems—i.e., polymers 1—3 and their oligomeric reference compounds—an inversion of optical rotation stems from a conformational transition from an approximately random arrangement to a more helically ordered arrangement. It is therefore proposed that polymer 3 and possibly polymers 1 and 2 are helically ordered in H₂O (the ORD data do not give definite proof, but all ORD data are in accordance with this for this proposition).

The described ORD measurements can give information on the conformational behavior of polymers 1—3 in aqueous solutions. However, a solid rationale concerning the probability of the formation of well-defined tertiary structures by these polymers in aqueous solutions cannot be inferred from the ORD-data available. The assembly of polymers 1—3 in H₂O can be studied in more detail applying various microscopy techniques. With these techniques the shapes of the formed aggregates can be examined.

Microscopy Studies on Polymers 1—3. Nanoscopic and microscopic structures formed by materials in solution can be studied by various microscopy techniques, such as atomic force microscopy (AFM), scanning tunneling microscopy (STM), and transmission electron microscopy (TEM). The only assumption that usually has to be made is that the observed structures on the substrate surfaces are representative for the structures that are formed in aqueous solutions.

TEM has been chosen to study the aggregation behavior of 1—3 in detail. Solutions of polymers 1—3 in H₂O, ranging from the dilute transparent solutions to the concentrated turbid solutions, were investigated. A range of sample preparation techniques was used, either carbon or polymer (formvar) surfaces were applied, and both uranyl acetate negative staining and Pt-
shading were employed to make detection of the formed structures possible. TEM pictures have been collected in Figure 9 to illustrate the observed structural features. On most grids, clusters of granular structures and clusters of threadlike structures were found (the threadlike structures were not found for the methyl-substituted polymer 3). The dimensions of the granules and the 'threads' were in the range 10–50 nm (see the Experimental Section for details). In addition to the granules and 'threads', vesicle-like structures were observed. However, these vesicle-like structures were only found on one grid.

In conclusion, macromolecules 1–3 aggregate in H₂O to diversely shaped higher structures; structures such as those generally observed for amphiphiles. Most strikingly, threadlike structures have been found for...
polymers 1 and 2: these structures require a directionality in the assembly process.

3. Conclusion

TEM microscopy studies on surfaces onto which poly-(ethylene oxide) amphiphiles 1–3 were deposited from aqueous solutions have revealed spherical (granular) and threadlike structures. Such structures are typically found for amphiphilic aggregates. However, in this case, the formation of the assemblies stems from amphiphiles with an unconventional design—i.e., amphiphiles with an unconventional primary structure. The formation of especially the threadlike structures can be regarded as surprising: for the formation of such higher structures, a directionality in the assembling process is necessary. A comparative ORD analysis on polymers 1–3 and on reference components has been performed to obtain indications for the origin of this directionality. Assuming that an inversion of optical rotation in the studied examples of chiral ethylene oxides stems from a transition from a random conformation to a helical conformation, it is proposed that polymer 3 and possibly polymers 1 and 2 adopt helical conformations in H$_2$O.

Summarized, ORD data indicate that polymers 1–3 form helically ordered secondary structures in H$_2$O, and TEM-pictures show the formation of higher structures that require a specific assembly process. However, there is no substantial evidence that the aggregation of 1–3 in H$_2$O is accompanied by the formation of the unique coiled-coil tertiary structure.

Experimental Section

General. Commercially available compounds employed in the syntheses were used without further purification, except stannous octanoate (SnOct$_2$), which was distilled in vacuo in a Kugelrohr apparatus (0.3 mbar, 200–220 °C) and stored in a glovebox. Solvents were dried and distilled if necessary, and reactions were routinely carried out under an inert atmosphere of dried argon or nitrogen. Details on the devices, materials, and methods are collected in the Experimental Section (General) of Part 1.

ORD Experiments. ORD spectra were recorded on a JASCO DIP 370 spectropolarimeter. Depending on the applied concentrations, sample holders of 1 cm or 1 dm were used.
Additional Data on Figure 3. For plots A, B, C, and D polymers 1, 2, 3, and again 3 were used, respectively. The polymer batches that were used correspond to entries B, G, J, and I from Table 1 in Part 1. Plot A: concentrations of 2.4, 1.8, 3.2 and 2.9 mg/mL were used in the solutions of THF, THF/H2O, EtOAc, and MeOH. Plot B: concentrations of 11.1, 9.5, 10.2, and 9.3 mg/mL were used in the solutions of THF, THF/H2O, MeCN, and MeOH/H2O. Plot C: concentrations of 13, 13, 26, and 22 mg/mL were applied, respectively. Polymer 7 prepared by procedure B (vide infra) has been used for plot B. Concentrations of 3.2, 3.1, and 2.7 mg/mL were used for the dioxane, dioxane/H2O, and EtOAc solutions.

Additional Data on Figure 4. In plot A, (SS)-4 was measured in aqueous solutions of MeOH containing 0%, 6%, and 21% H2O (v/v). Concentrations of 4.8, 4.5, and 3.8 mg/mL were applied, respectively. Polymer 7 prepared by procedure B (vide infra) has been used for plot B. Concentrations of 3.2, 3.1, and 2.7 mg/mL were used for the dioxane, dioxane/H2O, and EtOAc solutions.

Additional Data on Figure 5. Polymer 3 corresponding to entries H and K in Table 1 (see Part 1), respectively, has been used for plots A and B.

Additional Data on Figure 7. In plots A and C of Figure 7, a concentration of 0.34 mol/L of (SS)-4 has been used. In plot B the cumulative concentration of glycol and salt was kept constant (a requirement for J ob plots): [KSCN] + [(SS)-4] = 0.145 mol/L. In plot D a concentration of 0.0357 mol/L of (SS)-4 was applied (employed temperature: 25 °C). The diquinolinyl glycol (SS)-6 was titrated in CD2OD with KSCN at a concentration of 0.013 mol/L. The carbon shifts of the two carbons have been used to determine the K value. The titration of ether 5 with KSCN at a concentration of 0.30 mol/L was also monitored by 13C NMR. In this case, only one carbon signal was selected to obtain the K value. Errors in the obtained K values for the 1:1 complexes of KSCN with (SS)-4, 5 and (SS)-6 did not exceed 15%. Unless mentioned otherwise, the titrations were executed in MeOH or in CD2OD at 20 °C.

Additional Information on Figure 8. For plot A, (SS)-4 was dissolved in MeOH at a concentration of 0.3 mg/mL (0.0145 mg/mL was titrated with 0.1, 1.7, 4.0, 10.9, and 24.8 mol equiv of KSCN, respectively. For plot B, (SS)-6 was dissolved in MeOH at a concentration of 13.05 mg/mL (=0.020 mol/L) and was titrated with 0, 0.48, 0.97, 1.8, 4.5, and 8.9 mol equiv of KSCN, respectively.

Complexation Experiments. Attempts To Obtain Solid Complexes of Glycols (SS)-4, 5, and (SS)-6 with KSCN or RbI (in the Case of (SS)-6). Both the ethylene oxide and the salt were dissolved in MeCN or MeCN/ETOAc solvent mixtures and maintained at reflux overnight. Neither addition of petroleum ether nor cooling to 4 °C resulted in the crystallization of a complex.

Microscopy Measurements. All grids were studied with a Philips TEM 201 (60 kV). TEM samples were prepared by dissolving 1, 2, or 3 in a minimum amount of MeCN or MeCN and diluting the solutions with H2O to the desired concentrations (the amount of MeCN or MeCN in the aqueous solutions always was < 1%). Concentrations of the final solutions of 1, 2, and 3 varied from 2 × 10⁻⁴ to 8 × 10⁻⁴ mg/mL, from 5 × 10⁻⁵ to 0.3 mg/mL, and from 2 × 10⁻³ to 5 mg/mL, respectively. Droplets of these solutions were brought on Cu grids covered with carbon or polymer (formvar) surfaces. The droplets were either removed after 1 min or allowed to evaporate overnight, thus varying the deposition time of the polymeric material on the substrates substantially. The best results were obtained when dilute solutions of the polymer were used (concentrations in the range of 2 × 10⁻⁴ to 3 × 10⁻³ mg/mL) and when the droplets were allowed to evaporate overnight. Pt-shadowing, and sometimes negative staining, was used to make detection of the formed structures possible. Negative staining was performed by placing a droplet of a 2% (w/w) uranyl acetate (UO2(OOCCH3)2) aqueous solution onto the Cu grid and removing it after 15 s. Pt-shadowing was performed by placing the Cu grid in a Balzers sputter unit.

Granular (spherical) and threadlike structures were observed on most grids, and usually these structures were found in clusters. In one case, vesicle-like structures were found. The granular structures were found for polymers 1, 2, and 3. The diameters of the granules were typically in the order of 50 nm. The clusters of the granules had no specific appearance but had diameters in the order of 400 nm. The threadlike structures were only found for the isobutyl-substituted polymers 1 and 2. The clusters of the threadlike structures had diameters in the order of 1000 nm. The ‘threads’ varied in diameter from 8 to 50 nm and varied in length from 80 to 400 nm. Often, the clusters of the threads also contained the previously mentioned granules. Finally, ‘vesicles’ were found for polymer 2. Outer diameters and thicknesses of the bilayers of ca. 150 and 50 nm were observed, respectively. (Note None of the found structures were frequently spread over the surfaces of the grids.)

AFM samples were prepared by dissolving polymer 2 in MeCN and diluting the solution with H2O to concentrations of 3 × 10⁻³ and 2.5 × 10⁻⁴ mg/mL. Droplets of these solutions were brought on a Si wafer substrate and were allowed to evaporate. STM samples were prepared by dissolving polymer 1 and 2 in MeCO and diluting the solutions with H2O to concentrations of 4 × 10⁻³ and 5 × 10⁻⁴ mg/mL. The droplets were brought on a Si wafer substrate and then etched electrophoretically. The droplets were allowed to evaporate. The AFM/STM measurements were performed in an ultrahigh vacuum chamber (base pressure 10⁻¹⁰ mbar) with an Omicron apparatus. The AFM detection mechanism is based on the beam-deflection method. The normal and lateral forces experienced by the rectangular cantilever with the integrated silicon tip were calibrated.

1-(2-Methoxyethoxy)methylen-17-(benzoxyl)-3,6,9,12,15-pentaaxoheptadecane (SS)-6. A solution of (SS)-6 in EtOAc and MeOH was evaporated. Yield: 400 mg (68%). 1H NMR (CDCl3): δ 7.3 (5H, m, Ph), 4.7 (2H, s, OCH2), 4.6 (2H, s, OCH2Ph), 3.7–3.6 (26H, m), 3.5 (2H, m), 3.3 (3H, s).
Poly(4(S)-methylcaprolactone) (7). This polymer was obtained by polymerization of (4S)-4-methylcaprolactone. Purification of the monomer was achieved by silica column chromatography using CH2Cl2/CH3EtO (8/1) as eluent (Rf = 0.50). The (enantiomeric) purity of the lactone was checked on an analytical gelpermeation GC column, that was processed with 2% m-acetylated pullulan (PS) standards. No traces of contaminants were found. 1H NMR (CDCl3): δ 4.2 (1H, m), 4.1 (1H, m), 2.65 (2H, m), 1.90 (2H, m), 1.75 (1H, m), 1.45 (1H, m), 1.30 (1H, m), 0.95 (3H, d). 13C NMR (CDCl3): δ 176.0 (CO), 22.0 (CH2), 68.0 (OCH3) 37.1, 35.1, 33.1, 30.7. [α]D20 = -53.8 (c = 0.77, CH2Cl2). FTIR (cm⁻¹): ν = 2975, 2927, 2872, 1740, 1478, 1448, 1389, 1339, 1206, 1265, 1163, 1095, 1079, 1008, 935, 862, 796, 730, 711, 585, 522. GC-MS (FW = 128): 128 and 129 (with abundances of 4.2% and 0.5%, respectively).

Procedure A. (4S)-4-Methylcaprolactone (104 mg, 0.81 mmol) and 10 μL of a 0.10 M solution of SnCl4 in PhMe (monomer/catalyst ratio of 80/1) were mixed under an argon atmosphere at 140 °C in a silylated Schlenk flask. After 24 h the oily product was dissolved in CHCl3 and precipitated in MeOH. The polymer was collected as a sticky yellowish oil. Yield: 36 mg (35%). SEC: Mw = 29.7 kg/mol, D = 1.36 (data obtained with PS standards).

Procedure B. (4S)-4-Methylcaprolactone (56 mg, 0.44 mmol) and 9 μL of a 0.50 M solution of SnCl4 in PhMe (monomer/catalyst ratio of 98/1) were mixed under an argon atmosphere at 110 °C in a silylated Schlenk flask for 3 h. Further reaction at 140 °C for 24 h gave an oily product that was dissolved in CH2Cl2 and precipitated in hexane/ether (4/1). The polymer was collected as a sticky yellowish oil. Yield: 32 mg (57%). SEC: Mw = 8.4 kg/mol, D = 2.3 (data obtained with PS standards). This polymer was used for the QCM measurements in Figure 4. 1H NMR (CDCl3): δ 4.2 (2H, m), 2.30 (2H, m), 1.8–1.4 (5H, m), 0.95 (3H, d), 3.4 Hz. 13C NMR (CDCl3): δ 173.7 (CO), 19.0 (CH2), 62.6 (OCH3) 35.2, 31.9, 31.7, 29.5.

References and Notes

1. This is the second part of a back-to-back article sequence. Additionally, a previous communication has reported on the first results on this research topic: J. ansen, H. M.; Peeters, E.; van Zundert, M. F.; van Genderen, M. H. P.; Meier, V. Angew. Chem. 1997, 109, 152 (Angew. Chem., Int. Ed. Engl. 1997, 36, 122).


13. Recently, information has been published about synthetic phenylacylactone oligomers that fold into helical arrangements as a result of hydrophobic effects. Nelson, J. C.; Saven, J. S.; Moore, J. S.; Weinstock, S. 1976, 277, 1763.


(25) See Part 1 of this article sequence.

(26) Preliminary and brief AFM studies on polymer 2 as well as STM studies on polymers 1 and 2 did not reveal any well-defined structures. The size of peptide based coiled coils is in the order of 2 nm in diameter, 14 nm in pitch, and 150 nm in length, and therefore, these and other tertiary structures can in principle most ideally be studied by AFM or STM.

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(28) An aqueous 5% KI/I₂ solution was used as fixation liquid for the TLC plates.

(29) See Part 1 of this article sequence.