Self-Assembling Biomaterials: L-Lysine-Dendron-Substituted Cholesteryl-(L-lactic acid)$_{\bar{n}}$

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ABSTRACT: This report describes the synthesis and supramolecular organization of a novel class of linear−dendritic block copolymers. The molecules, which are termed rodcoil dendrons, consist of a cholesterol moiety that is attached to L-lysine dendrons of three different generations via a biodegradable oligo(L-lactic acid)$_{\bar{n}}$ spacer. Whereas the molecules exhibit very poor ordering in the dry state, different supramolecular morphologies were observed in the hydrated state. Cholesteryl-(L-lactic acid)$_{\overline{23}}$-(L-lysine)$_{G1}$ and cholesteryl-(L-lactic acid)$_{\overline{23}}$-(L-lysine)$_{G2}$ self-assemble into lamellar structures with periodicities that depend on degree of hydration. At low degrees of hydration, lamellar ordering was also observed for cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$. However, at 50 wt %, water steric hindrance in the highly hydrated L-lysine dendrons no longer allows lamellar ordering, and discrete nanosized aggregates are formed. Evidence for the formation of such nanoaggregates was obtained from dynamic light scattering, electron microscopy, and atomic force microscopy. These rodcoil dendron biomaterials could be of potential interest as temporary molecular scaffolds for cell and tissue engineering.

Introduction

Amphiphilic linear−dendritic block copolymers represent an interesting class of molecules, which has received increased attention over the past few years.[1−6] One of their unique features is that they combine the characteristics of low molar mass surfactants and high molecular weight amphiphilic block copolymers. On the one hand, amphiphilic linear−dendritic block copolymers can form aggregates in aqueous solution, which resemble those obtained by self-assembly of amphiphilic block copolymers with respect to size and stability. On the other hand, as it is well-known for low molecular weight surfactants,[7] the shape of aggregates formed by self-assembly of amphiphilic linear−dendritic block copolymers can be manipulated by varying the size (=generation) of the dendritic block. Depending on the relative sizes of the hydrophilic headgroup and the hydrophobic tail, low molecular weight surfactants can form micellar, vesicular, and bilayer type structures.[7] Most of the linear−dendritic block copolymers reported so far are based on poly(ethylene oxide)[1,2,5,6] or poly(styrene)[3] as the linear segment. The chemical composition of the dendritic segment has been varied to a greater extent. Typical examples include benzyl ether,[1] L-lysine,[2] propyleneimine,[3] amidoamine,[4,5] and carbosilane[6] dendritic segments.

We describe here the synthesis and characterization of a novel class of amphiphilic linear−dendritic block copolymers, which could be of potential interest as temporary molecular scaffolds for cell growth and tissue engineering applications. The molecules that will be discussed contain a cholesteryl moiety that is linked to a short chain of approximately 20 L-lactic acid residues. The hydroxyl terminus of this L-lactic acid chain is substituted with L-lysine dendrons of different generations. Because of their molecular architecture, we have termed these molecules rodcoil dendrons.

The different segments that constitute the rodcoil dendrons are not only structurally important, but also have functional relevance. Since the liquid crystalline character of certain cholesteryl esters has been known for a long time,[8] it was anticipated that the cholesteryl moiety could provide a driving force for the self-assembly of the rodcoil dendrons. Depending on generation number, the L-lysine dendrons can provide sterics that could prevent long-range ordering and direct the formation of nanostructures. In addition to these structural aspects, the rodcoil dendrons also possess a number of features that could make them of interest as molecular scaffolds for cell growth. Since the L-lactic acid segment is biodegradable, these scaffolds may be gradually replaced by natural tissue. Cholesterol has a high thermodynamic affinity for the cell membrane and has universally important function in all eukaryotic cells.[9,10] The positively charged L-lysine dendron can interact both with the negatively charged proteoglycans found in extracellular matrix and the negatively charged phospholipids of the cell membrane. In this way, the rodcoil dendrons could promote and simultaneously facilitate cell adhesion. This paper describes the synthesis, molecular characterization, and self-assembly of the rodcoil dendrons.

Results and Discussion

A molecular graphics representation of a cholesteryl-(L-lactic acid)$_{\bar{n}}$-(L-lysine)$_{Gx}$ rodcoil dendron is shown in Figure 1.[11] This particular molecule contains a cholesteryl moiety that is linked to an oligo(L-lactic acid)$_{\bar{n}}$ fragment consisting of 20 repeat units. The hydroxyl terminus of this cholesteryl-(L-lactic acid)$_{\overline{22}}$ molecule is substituted with a third-generation L-lysine dendron ((L-lysine)$_{G3}$).

The rodcoil dendrons are obtained by attaching the L-lysine dendron, which has a 4-aminobenzoic acid

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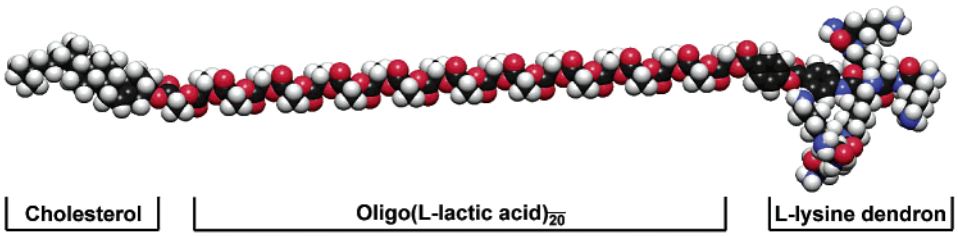
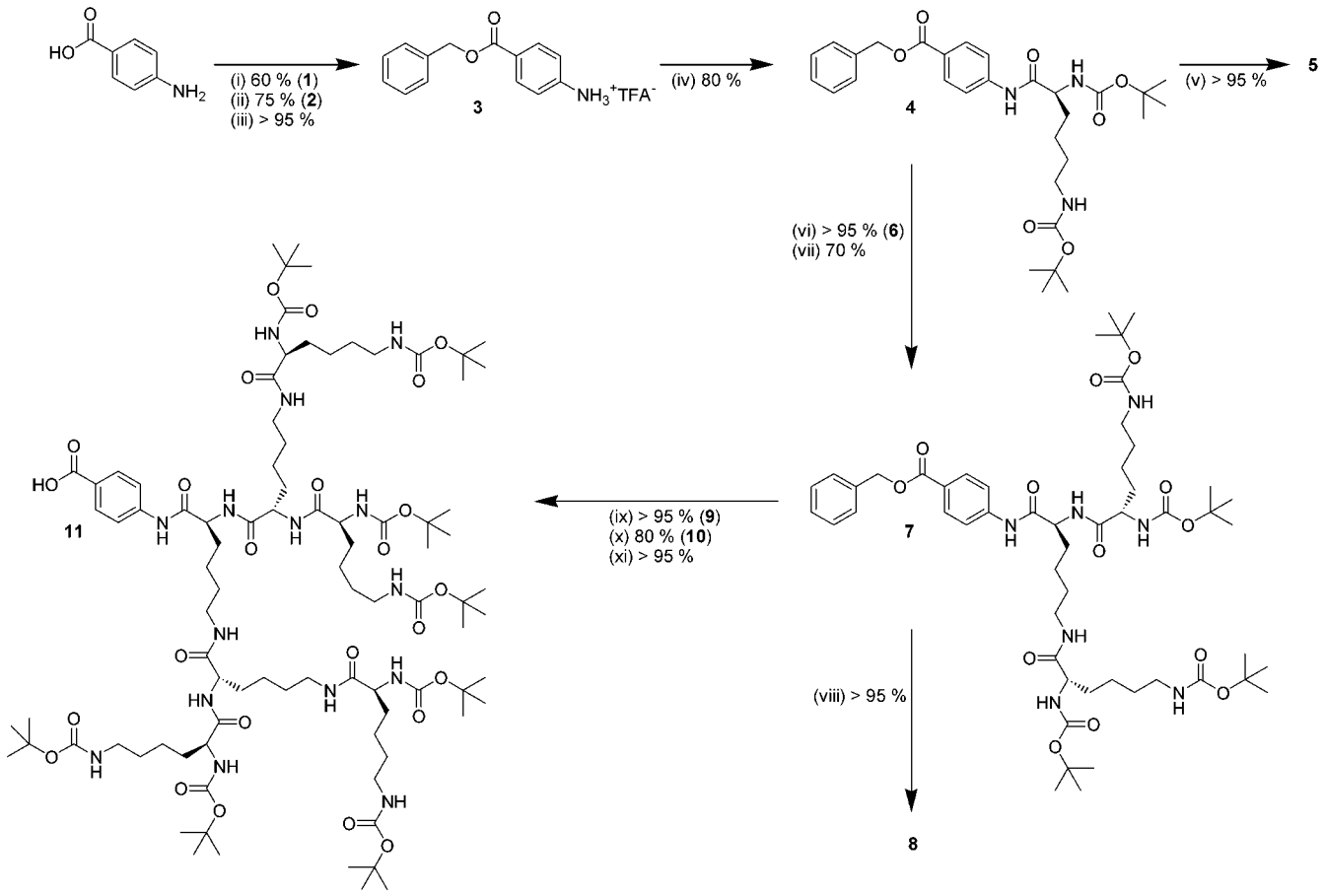


Figure 1. Molecular graphics representation of a cholesteryl-(L-lactic acid)$_{20}$-(L-lysine)$_{G3}$ molecule.

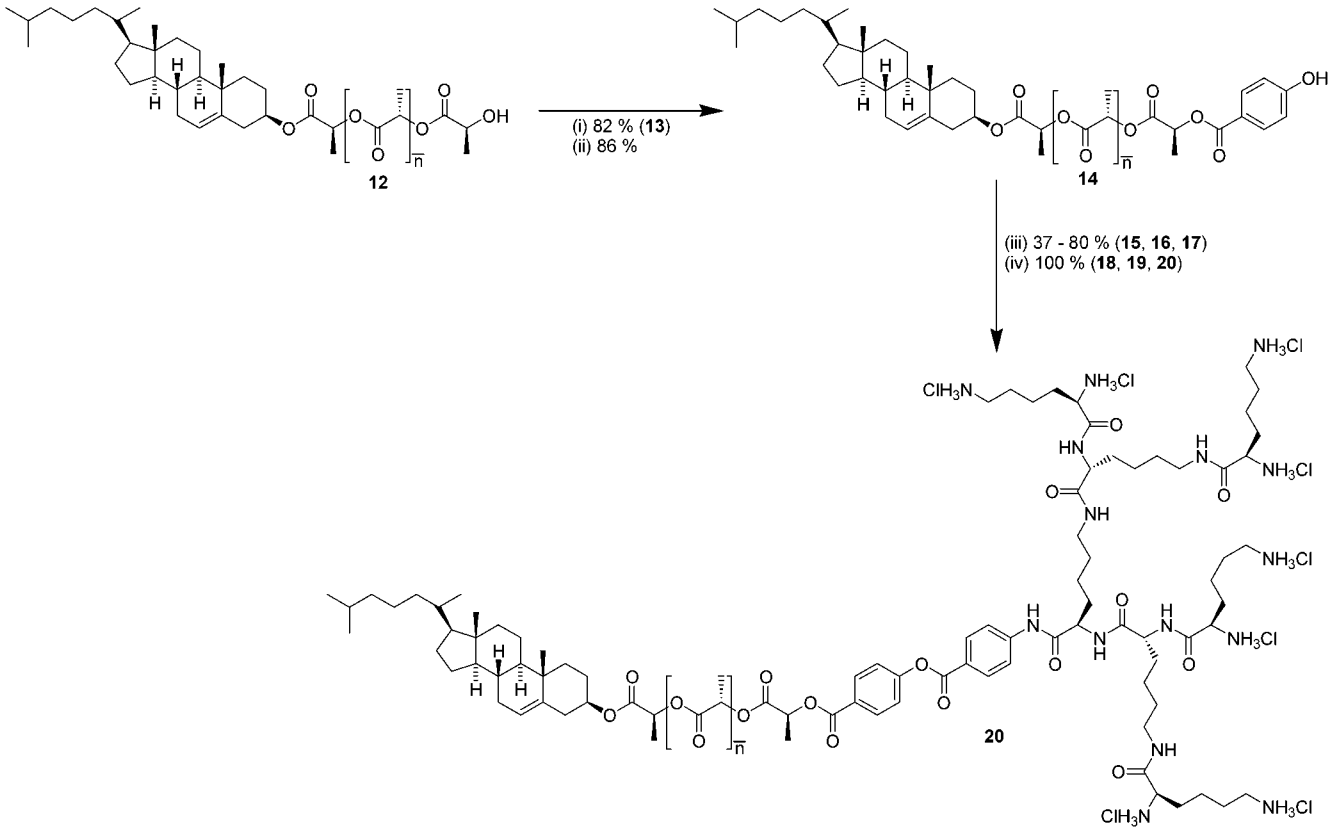
Scheme 1[a]



[a] Reagents and conditions: (i) $(BOC)_2O$, NaOH, H_2O/dioxane; (ii) BnOH, DIPC/DPTS, DMF; (iii) TFA, CH_2Cl_2; (iv) N^{α},N^{ϵ}-di-BOC-L-lysine, EDC/DMAP, CH_2Cl_2; (v) H_2, Pd−C, EtOH; (vi) TFA, CH_2Cl_2; (vii) N^{α},N^{ϵ}-di-BOC-L-lysine, BOP/TEA, CH_2Cl_2; (viii) H_2, Pd−C, EtOH; (ix) TFA, CH_2Cl_2; (x) N^{α},N^{ϵ}-di-BOC-L-lysine, BOP/TEA, CH_2Cl_2; (xi) H_2, Pd−C, EtOH.

moiety at its focal point, to the hydroxyl terminus of a 4-hydroxybenzoic acid modified cholesteryl-(L-lactic acid)$_{\bar{n}}$ oligomer.[12] The synthesis of the L-lysine dendrons and the subsequent linkage of these molecules to cholesteryl-(L-lactic acid)$_{\bar{n}}$ are shown in Schemes 1 and 2. As illustrated in Scheme 1, the L-lysine dendrons were prepared in divergent fashion from a benzyl-4-aminobenzoate core (**3**) by repetitive coupling and deprotection of N^{α},N^{ϵ}-di(*tert*-butoxycarbonyl)-L-lysine (N^{α},N^{ϵ}-di-BOC-L-lysine). The aromatic core, **3**, was readily prepared in three steps from 4-aminobenzoic acid, involving BOC protection of the amino-group,[13] esterification of 4-(N-BOC) aminobenzoic acid (**1**) with benzyl alcohol (BnOH) and subsequent removal of the amino protective group under the action of trifluoroacetic acid (TFA). Coupling of N^{α},N^{ϵ}-di-BOC-L-lysine to the deprotected first and second generation dendrons **6** and **9** proceeded smoothly under very mild conditions, using benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP) in the presence of triethylamine (TEA) as a coupling agent.[14] Presumably due to the lower reactivity of the aromatic amine, attempts to couple N^{α},N^{ϵ}-di-BOC-L-lysine to **3** under these conditions were unsuccessful. Compound **4**, however, could be prepared in good yields using 1-(3-(dimethylamino)-propyl)-3-ethylcarbodiimide hydrochloride (EDC) as a coupling agent[15] and 4-(dimethylamino)pyridine (DMAP) as an acylation catalyst.[16] The fully protected L-lysine dendrons **4**, **7**, and **10** could be easily purified employing standard silica gel chromatography techniques. Quantitative removal of the BOC protective groups from **4** and **7**, which is necessary for the preparation of each new generation, was achieved by treating the dendrons with a 2/1 (v/v) mixture of CH_2Cl_2 and TFA. Finally, hydrogenation of **4**, **7**, and **10** in EtOH in the presence of Pd−C afforded the desired BOC-protected L-lysine dendrons **5**, **8**, and **11**, which possess an aromatic acid functionality to allow coupling to the hydroxyl terminus

Scheme 2[a]



[a] Reagents and conditions: (i) 4-(*tert*-butoxy)benzoic acid, DIPC/DPTS, CH_2Cl_2; (ii) TFA, CH_2Cl_2; (iii) **5**, **8**, or **11**, DIPC/DPTS, CH_2Cl_2; (iv) 4 M HCl/dioxane.

of 4-hydroxybenzoic acid end-functionalized cholesteryl-(L-lactic acid)$_{\bar{n}}$.

Cholesteryl-(L-lactic acid)$_{\bar{n}}$ (**12**) was prepared via living ring-opening polymerization of L-lactide. Polymerizations were carried out at 80 °C in toluene, using the aluminumalkoxide obtained by the reaction between cholesterol and $Al(Et)_3$ as the initiator. The length of the L-lactic acid segment can be controlled by the ratio between the monomer and the initiator. The synthesis and properties of these cholesteryl-(L-lactic acid)$_{\bar{n}}$ oligomers have been reported in detail in previous publications.[17] End-modification of the original secondary alcohol terminus of cholesteryl-(L-lactic acid)$_{\bar{n}}$ by a phenolic hydroxyl group, which was necessary to facilitate coupling of the dendrons, was achieved by esterification of 4-(*tert*-butoxy)benzoic acid under mild diisopropylcarbodiimide/4-(dimethylaminopyridinium)-4-toluenesulfonate (DIPC/DPTS) conditions,[18] followed by removal of the *tert*-butyl ether protective group in CH_2Cl_2/TFA 2/1 (v/v). After end group modification of cholesteryl-(L-lactic acid)$_{\bar{n}}$, the BOC-protected dendrons **5**, **8**, and **11** could be attached in good yields using the DIPC/DPTS esterification method.[18] This is illustrated in Scheme 2 for the third generation dendron **11**, but the same methodology is applicable to the lower generation dendrons **5** and **8**, as well. In the final step, the BOC protective groups are removed under the action of a 4 M solution of HCl in dioxane, yielding rodcoil dendrons **18**, **19**, and **20**, which are functionalized with, respectively, first, second, and third generation L-lysine dendrons.

The molecular structure of rodcoil dendrons **18**−**20** was confirmed by ^{1}H NMR and MALDI−TOF mass-spectrometry. Figure 2 shows the MALDI−TOF mass-spectra of a 4-hydroxybenzoic acid modified cholesteryl-(L-lactic acid)$_{\overline{25}}$ oligomer (**14**) and of the corresponding rodcoil dendrons obtained by attachment of L-lysine-dendrons of different generation.[19] In some of the MALDI−TOF spectra, one or two additional homologous series of signals are present, which can be assigned as the Na^+ and K^+ labeled molecular ions. In Figure 2, the mass corresponding to a representative peak is indicated in the MALDI−TOF spectrum of each of the materials. Since the molecular weights of the cholesterol moiety, the L-lactic acid repeat units, the 4-hydroxybenzoic acid and 4-aminobenzoic acid linkers and of the different L-lysine dendrons are all known, the mass of each of the oligomers at a given degree of polymerization of the oligo(L-lactic acid)$_{\bar{n}}$ spacer can be calculated. The agreement between the selected peak in the spectrum and one of the possible molecules in the distribution proves the chemical composition of the molecules. The difference in mass between two neighboring peaks in the MALDI spectra in Figure 2 is 72 Da (which is the molar mass of L-lactic acid), even though the oligomers were prepared by ring-opening polymerization of L-lactide (M = 144 Da). In absence of any side reactions, the ring-opening polymerization of L-lactide would result in chains containing only an even number of L-lactic acid repeats. The observed difference in mass of 72 Da between two neighboring signals, however, indicates that both odd and even membered chains are present, which points to the occurrence of transesterification reactions during the polymerization of L-lactide.[20] Finally, the MALDI−TOF mass-spectra nicely illustrate the increase in the molecular weight with increasing

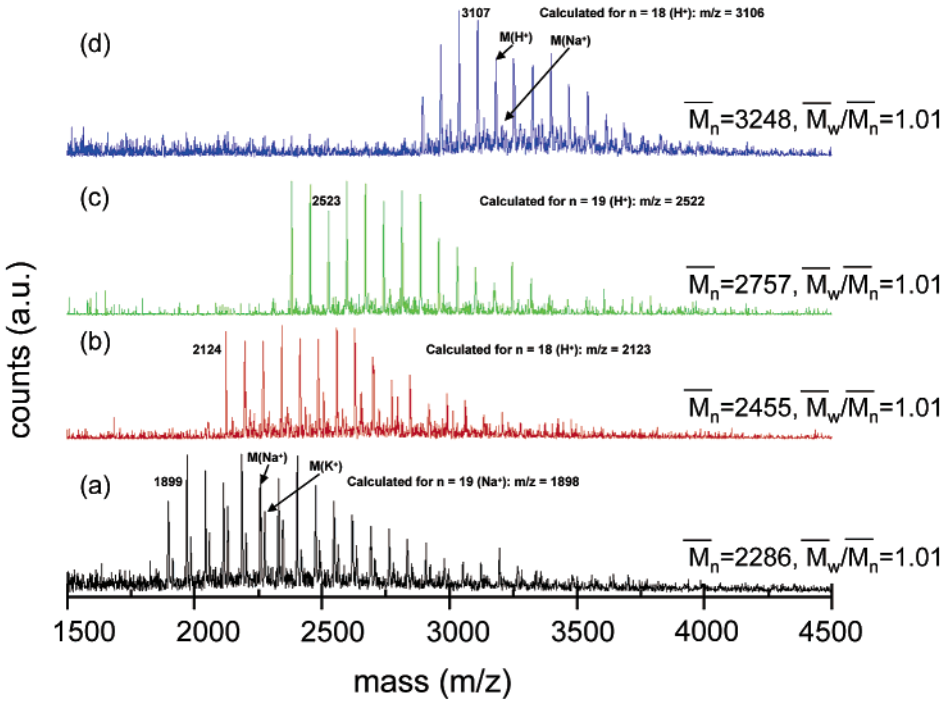


Figure 2. MALDI−TOF mass spectra of the 4-hydroxybenzoic acid functionalized cholesteryl-(L-lactic acid)$_{\overline{25}}$ oligomer **14** (a) and of the rodcoil dendron molecules cholesteryl-(L-lactic acid)$_{\overline{23}}$-(L-lysine)$_{G1}$ (b), cholesteryl-(L-lactic acid)$_{\overline{21}}$-(L-lysine)$_{G2}$ (c), and cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ (d).

Table 1. Average Estimated Molecular Lengths and Glass Transition Temperatures of the Different Cholesteryl-(L-lactic acid)$_{\bar{n}}$-(L-lysine)$_{Gx}$ Rodcoil Dendrons and the *d* Spacings Obtained from SAXS Experiments That Were Performed under Different Conditions of Humidity

				hydrated samples					
rodcoil dendron	mol length (Å)[a]	T_g[b] (°C)	dry samples *d* (Å)[c]	% H_2O	*d* (Å)[c]	(*hkl*)	% H_2O	*d* (Å)[c]	(*hkl*)
18	99	42	138	20	180	001	-	-	-
				20	90	002	-	-	-
19	99	44	115	20	167	001	50	232	001
				20	85	002	50	115	002
20	103	64	147	10	184	001	50	188	
				10	93	002	50	118	

[a] Average estimated length of the molecules assuming a 10_3 helical conformation of the oligo(L-lactic acid) segment (cf. ref 21). [b] Glass transition temperature of the dry material as determined by differential scanning calorimetry. [c] *d*-spacing calculated from small-angle X-ray diffraction scans.

size of the L-lysine-dendron from rodcoil dendron **18** (Figure 2b) to rodcoil dendron **20** (Figure 2d) and also prove that all rodcoil dendrons are well-defined oligomers with narrow polydispersity.

Polarized optical microscopy (POM) and small-angle X-ray scattering (SAXS) experiments were performed to investigate the supramolecular organization of the rodcoil dendrons. In the dry state, the materials are semicrystalline solids. The glass-transition temperatures (T_g) as determined by differential scanning calorimetry (DSC) for the different rodcoil dendrons are listed in Table 1. The T_g increases from 42 °C for **18**, which is substituted with the smallest L-lysine dendron, to 64 °C for cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ (**20**). Representative birefringent textures of **20**, both for the neat material and upon hydration, are shown in Figure 3. Small-angle X-ray diffraction scans of rodcoil dendrons **18**, **19**, and **20** are shown in Figure 4. Experiments were performed both on the dry materials and on hydrated samples. The *d* spacings obtained from the diffraction scans together with the estimated average length of the molecules are listed in Table 1.[21] For the dry materials, only one broad diffraction peak was observed, which makes it impossible to unambiguously describe the organization of the molecules. Among others, the width of the diffraction peaks reflects the distribution of lengths of the oligo(L-lactic acid)$_{\bar{n}}$ spacer. Exposure of the materials to water vapor strongly enhances the molecular order as is indicated by the appearance of higher-order reflections in the SAXS scans. Except for rodcoil dendron **20** at a water content of ∼50 wt %, all hydrated samples show two diffraction peaks that can be indexed as (001) and (002) and suggest a lamellar organization of the molecules. The periodicity of these layered assemblies depends on the level of hydration. For rodcoil dendron **19** at a water content of 50 wt %, a *d* spacing of 232 Å can be determined, which is slightly larger than twice the estimated average length of these molecules. This observation indicates the organization of **19** in a non-interdigitated bilayer structure, as is illustrated in Figure 5. Hydration of the L-lysine dendrons probably accounts for the difference between the observed *d* spacing and the periodicity indicated in Figure 5. For rodcoil dendron **19** at a water content of 20 wt % as well as for the other rodcoil dendrons that show both (001) and (002) reflections, a similar type of supramolecular organization can be envisioned if one assumes a certain degree of interdigitation of the cholesterol-moieties and/or the L-lysine dendrons.

The SAXS pattern of rodcoil dendron **20** at a water content of 50 wt % is different from that of the other hydrated samples. For this material also a higher order reflection is observed. However, although this signal is close to both the (220) reflection of a face-centered cubic organization as well as the (110) of an hexagonal assembly, it matches neither of these two supramolecu-

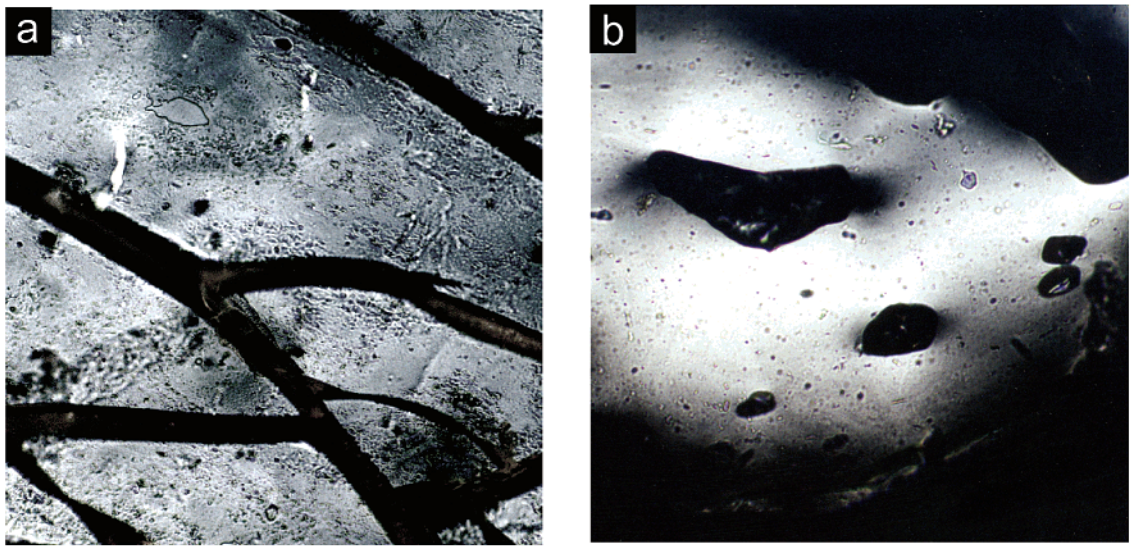


Figure 3. Polarized optical micrographs of cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ (**20**): (a) birefringent texture of the neat material in the dry state; (b) texture of the lyotropic phase of **20** obtained after hydration.

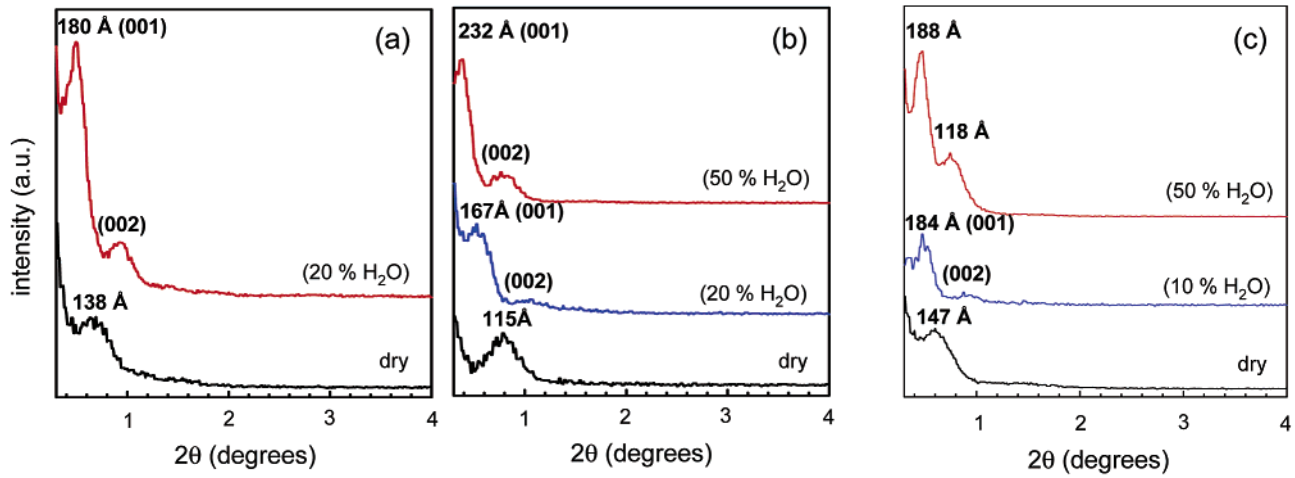


Figure 4. Small-angle X-ray diffraction scans of (a) cholesteryl-(L-lactic acid)$_{\overline{23}}$-(L-lysine)$_{G1}$ (**18**), (b) cholesteryl-(L-lactic acid)$_{\overline{21}}$-(L-lysine)$_{G2}$ (**19**), and (c) cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ (**20**). The different degrees of hydration are indicated in the scans.

lar arrangements perfectly. We feel that at these very high degrees of hydration the supramolecular organization of **20** could be similar to the behavior of this material in dilute aqueous solution (vide infra) and may involve the formation of nanosized aggregates that pack in an unconventional lattice. Despite these uncertainties, the SAXS patterns shown in Figure 4 nicely demonstrate that the supramolecular organization of the cholesteryl-(L-lactic acid)$_{\bar{n}}$-(L-lysine)$_{Gx}$ rodcoil dendrons **18**−**20** is sensitive to both the extent of hydration and the size of the L-lysine dendritic headgroup. Molecules **18** and **19**, which are substituted with, respectively, a first- and second-generation L-lysine dendron, form lamellar structures, whose periodicities depend on the degree of hydration. At low degrees of hydration, rodcoil dendron **20**, which has the largest L-lysine dendritic headgroup, also forms layered assemblies; however, at high water contents, nonlamellar morphologies are obtained. At high water contents, the sterics provided by the hydrated L-lysine dendrons apparently do not allow lamellar organization. This behavior is somewhat reminiscent of that of low molecular weight amphiphiles, which can also form a variety of different types of aggregates, depending on the effective relative sizes of the polar headgroup and the hydrophobic lipid tail.[7]

As mentioned before, all oligomers swell upon exposure to water vapor, however only the cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ (**20**), which has eight ammonium chloride end groups can be readily dissolved in water. Therefore, the supramolecular organization of this compound in dilute aqueous solution was further investigated by ^{1}H NMR spectroscopy, dynamic light scattering (DLS), atomic force microscopy (AFM), and transmission electron microscopy (TEM).

^{1}H NMR spectra of **20** in DMSO-d_6 and D_2O are shown in Figure 6. In DMSO-d_6, which is a nonselective solvent, all the characteristic resonances together with the correct integrals can be observed. In contrast, when the ^{1}H NMR experiment is performed in D_2O, the signals due to the cholesteryl-(L-lactic acid)$_{\overline{22}}$ segment disappear, and only the resonances corresponding to the L-lysine dendron are observed in the ^{1}H NMR spectrum. These observations suggest the formation of micellar-type aggregates of these rodcoil dendron oligomers in aqueous solution. Diluting a sample of cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ in D_2O to a concentration of 1 mg/mL did not affect the ^{1}H NMR spectrum.

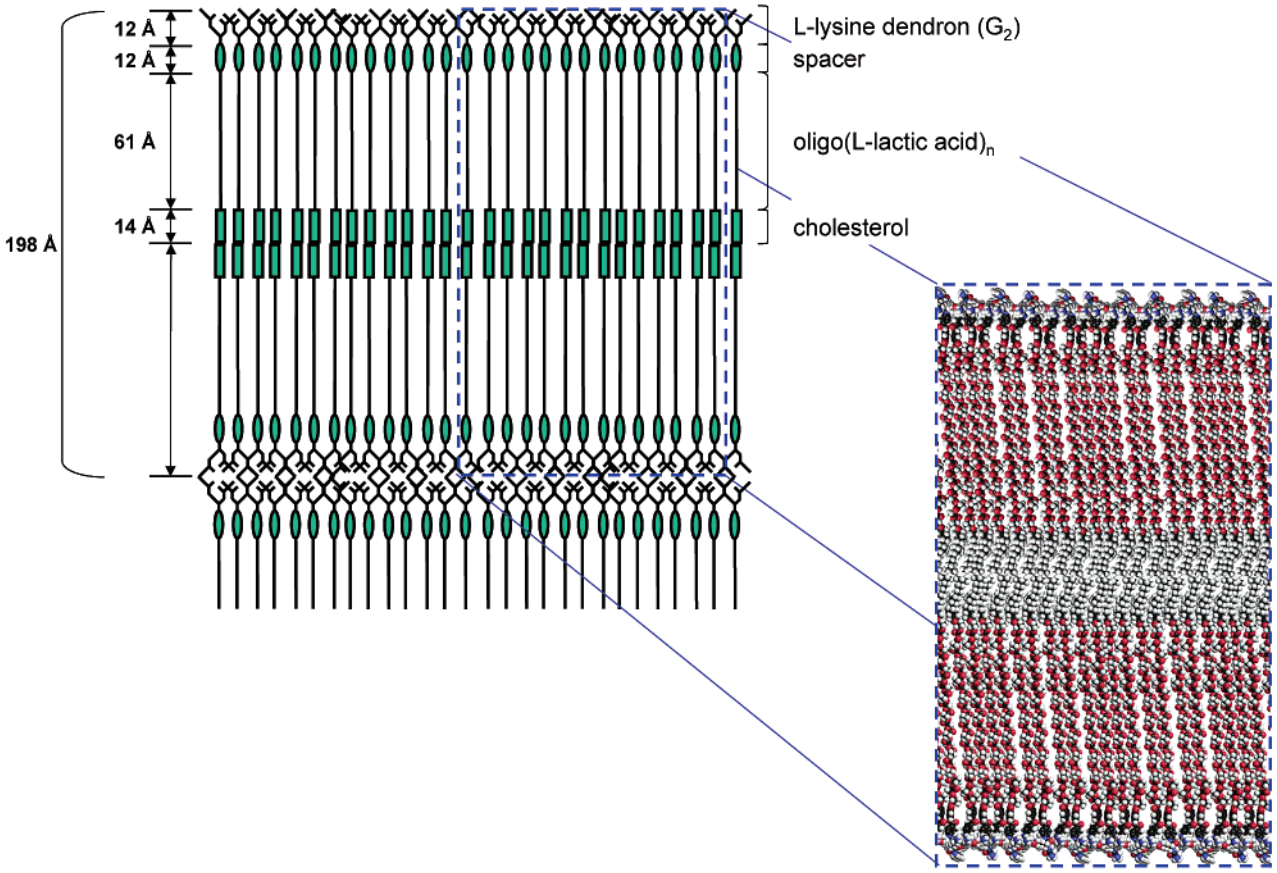


Figure 5. Schematic representation of the self-assembly of rodcoil dendron **19** at a water content of ~50 wt %. The insert shows a molecular graphics representation of part of the bilayered structure.

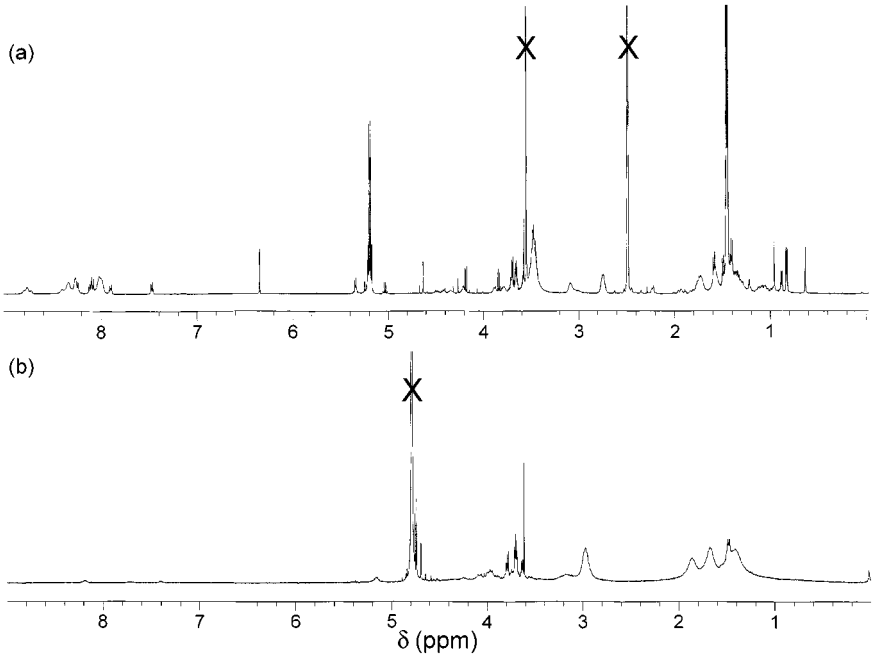


Figure 6. 500 MHz ^{1}H NMR spectra of cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ (c = 6.6 mg/mL) in DMSO-d_6 (a) and D_2O (b). Residual solvent peaks are marked with an "×".

DLS experiments with aqueous solutions of **20** at 1 × 10^{-4} M indicated an average hydrodynamic diameter of approximately 30.6 ± 0.25 nm. No signal could be observed below a concentration of 5 × 10^{-5} M, which suggests that the critical association constant of these oligomers is on the order of 5 × 10^{-5} M.

Atomic force microcopy (AFM) and transmission electron microscopy (TEM) were used to obtain more information about the size and shape of the aggregates formed by **20** in dilute aqueous solution. Figure 7 shows an AFM image of a sample obtained after casting a 1 × 10^{-4} M solution on a mica substrate. The sample was

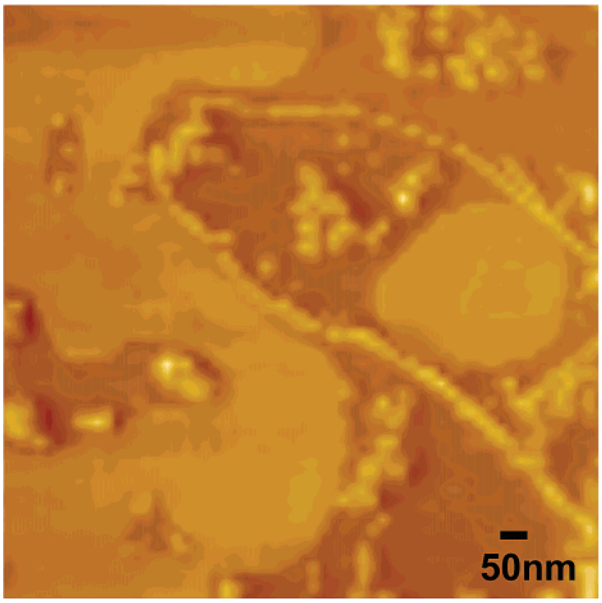


Figure 7. AFM image of cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ cast from a 1.0×10^{-4} M aqueous solution on a mica substrate. The image was acquired in the phase mode.

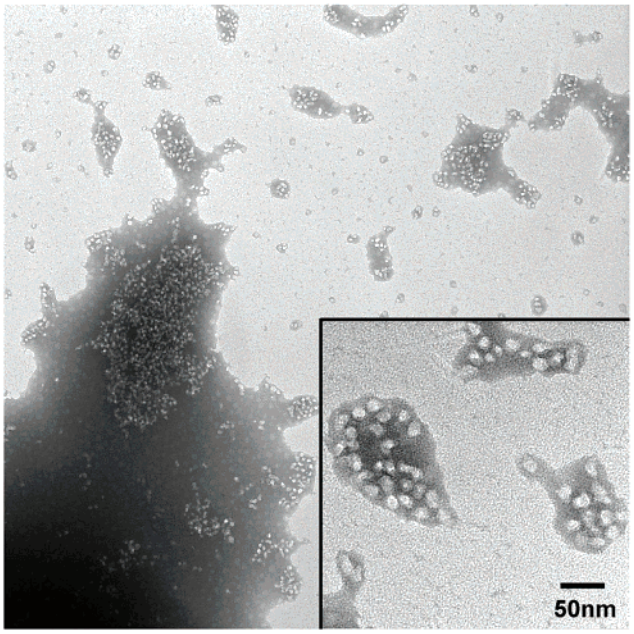


Figure 8. TEM micrograph of cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ cast from a 1.0×10^{-4} M aqueous solution on a carbon-coated copper grid. The sample was stained with phosphotungstic acid.

still partly hydrated and thus the dimensions may be close to those in solution. In addition to larger aggregates, the image, which was acquired in the phase mode, shows oval-shaped objects with widths on the order of 33 nm and heights of approximately 22 nm. These dimensions are in good agreement with the hydrodynamic diameter of the aggregates at this concentration as measured by DLS (31 nm).

A TEM image of rodcoil dendron **20** is shown in Figure 8. The sample was prepared by casting a 1×10^{-4} M solution on a carbon grid and negative staining with phosphotungstic acid. Because of the high vacuum in the TEM experiments, one expects the size and shape of the aggregates to be different from those in dilute solution. The TEM image reveals both spherical and nonspherical objects with sizes ranging from 10 to 25 nm. The insert in Figure 8 also shows larger irregular shaped structures, which are probably formed by aggregation of several smaller objects.

A model for the self-assembly of **20** in dilute aqueous solution is proposed in Figure 9. In this model, rodcoil dendron **20** forms discrete nanosized aggregates. The core of these aggregates is composed of a bilayer of cholesterol moieties, which are encapsulated in a shell of the L-lysine dendrons. The formation of aggregates such as the one depicted in Figure 9 can be rationalized by considering the bilayer type arrangements that were found for most of the rodcoil dendrons in the hydrated solid state (see Figure 5). With increasing degree of hydration, the steric hindrance of the L-lysine dendrons will increase, and it will become progressively more difficult for the molecules to self-assemble into lamellar structures as shown in Figure 5. As is evident from the SAXS patterns in Figure 4, the increase in steric bulk upon hydration of **18** and **19** is not sufficient to disrupt the layered organization of these molecules. This situation is different, however, for rodcoil dendron **20**; in this case, at sufficient degrees of hydration, the bulky L-lysine dendrons can no longer be accommodated in a layered structure but induce the formation of discrete nanosized aggregates. Assuming a 10/3 helical conformation of the L-lactic acid segment, the diameter of the aggregates would be approximately 20 nm. However, due to the sterics of the L-lysine dendron, it seems likely that the L-lactic acid chains are less ordered compared with poly(L-lactic acid) or **18** and **19** in the hydrated solid state, and therefore, they adopt a more stretched conformation. We believe that the model proposed in Figure 9 could not only apply for dilute aqueous solutions, but may also be a valid description for the solid state at very high levels of hydration. Thus, the SAXS pattern of **20** at a water content of ~50 wt % (Figure 4c) could be explained by self-assembly of the nanosized aggregates into a lattice.

Conclusions

We have described the synthesis and self-assembly of a new class of bioactive linear−dendritic block copolymers termed rodcoil dendrons. The bioactive structures based on cholesterol, oligo(L-lactic acid)$_{\bar{n}}$, and L-lysine dendrons were designed for self-assembly in water and biodegradability. Hydrated samples of all rodcoil dendrons were found to order into lamellar structures with periodicities that depended on water content. At high levels of hydration (50 wt % water) oligomers with generation 3 L-lysine dendrons form discrete nanosized aggregates. These self-assembling biomaterials offer a platform to create short-lived bioactive substrates through the dendron blocks aided by cholesterol, which has thermodynamic affinity for cell membranes and is universally necessary for eukaryotic cell survival.

Experimental Section

General Data. Unless stated otherwise, all reagents and solvents were of commercial grade and were used as received. All reactions were performed under a nitrogen atmosphere. Methylene chloride (CH_2Cl_2) and toluene were freshly distilled from P_2O_5 and sodium/benzophenone, respectively, prior to use. *N*,*N*′-Dimethylformamide (DMF) was stored over molecular sieves (4 Å). Triethylamine (TEA) was stored over KOH. Cholesterol and L-lactide were recrystallized from ethanol and

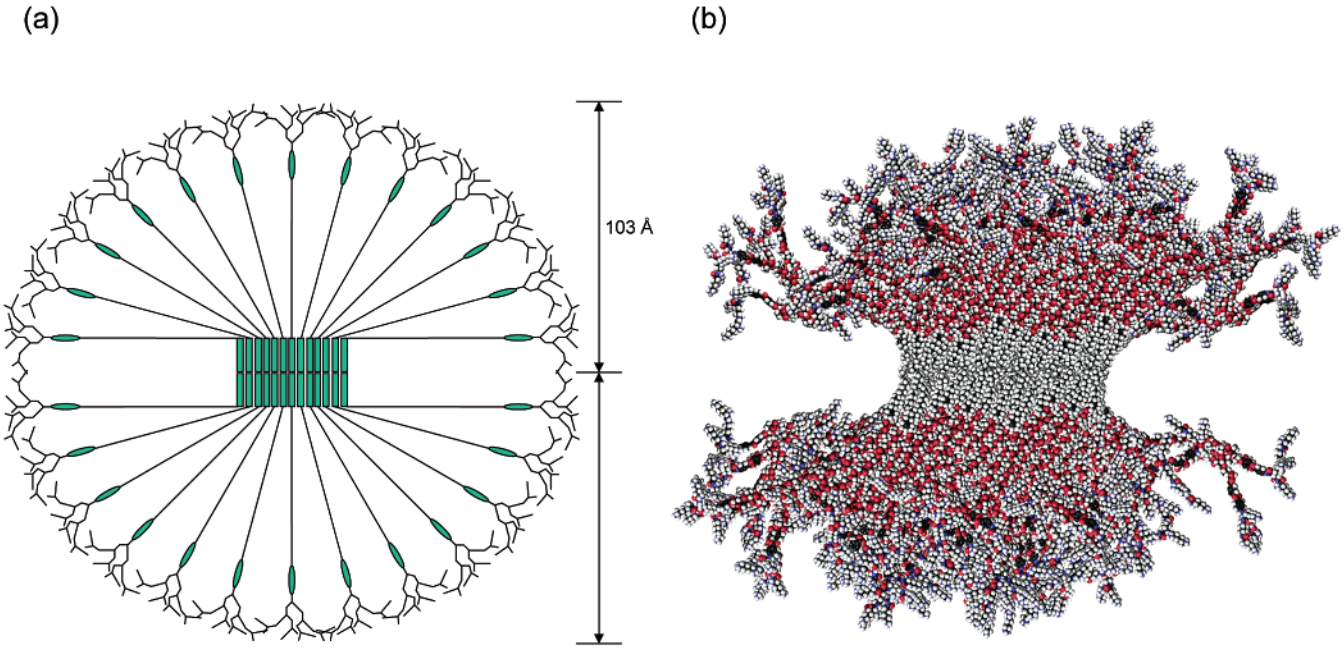


Figure 9. Schematic (a) and molecular graphics representation (b) of the proposed nanostructures formed by rodcoil dendron **20** in dilute aqueous solution.

ethyl acetate, respectively, and vacuum-dried at room temperature to constant weight. 4-(Dimethylamino)pyridinium 4-toluenesulfonate (DPTS) was prepared according to a literature procedure.[18] Reactions were monitored by thin-layer chromatography, using 0.250 mm precoated silicagel 60 F254 glass-plates (Merck). Column-chromatography was performed with Merck silica gel 60 (0.040−0.063 mm, 230−400 mesh, 60 Å).

^{1}H and ^{13}C NMR spectra were recorded on Varian U400 or U500 spectrometers at room temperature. Chemical shifts are expressed in parts per million (δ) using residual protons in the indicated solvents as internal standard. Mass-spectrometry was performed at the Mass-Spectrometry Laboratory of the School of Chemical Sciences at the University of Illinois at Urbana−Champaign. Low-resolution fast atom bombardment mass-spectra (LR−FAB) were recorded on a Micromass ZAB−SE mass-spectrometer. High-resolution fast atom bombardment mass-spectrometry (HR−FAB) was performed on a Micromass 70-SE-4F instrument. MALDI−TOF mass-spectra were acquired on a PerSeptive Biosystems Voyager-DE STR spectrometer. Elemental analysis was performed in the Microanalysis Laboratory of the School of Chemical Sciences of the University of Illinois at Urbana−Champaign. Polarized optical microscopy utilized a Leitz Laborlux 12POL optical microscope equipped with Linkham THM600 hot stage. Samples were kept under nitrogen atmosphere at elevated temperatures. Differential scanning calorimetry (DSC) experiments were performed using a TA 2920 modulated DSC instrument with a ramp speed of 10 °C/min. Dynamic light-scattering experiments were carried out with Brookhaven Instruments equipped with a HeNe laser, a goniometer with refractive index matching, temperature-controlled heat bath, and a photomultiplier tube. Unless otherwise stated, solutions for the light-scattering experiments were prepared by dissolving in Millipore water, sonicating, and then filtering with 0.22 μm Millipore filter. All solutions were checked for the absence of dust, and had fluctuations in the scattering intensity of less than 3%. Small-angle X-ray scattering (SAXS) experiments were performed using a Bruker small-angle X-ray scattering machine with an Anton Paar high-resolution small-angle camera with Hi-Star Area detector, a M18XHF22−SRA rotating anode generator, a camera distance of 630 nm, and Bruker software. Powder diffraction rings were integrated over 360° to yield the diffraction pattern, and the system was calibrated using a silver behenate standard. The samples were placed in sealed 0.7 mm diameter capillary tubes. Transmission electron microscopy utilized a Hitachi 8100 with an accelerating voltage of 200 kV. Images were acquired at a magnification of 50 000 or 100 000 and a slight defocus to enhance contrast. Samples were prepared by dissolving the material in Millipore water at a concentration of 10^{-4} M. Then, 20 μL of this suspension was pipetted directly onto a holey carbon coated 300 mesh copper grid. The suspension was allowed to sit undisturbed for 5 min after which the excess solution was wicked off to the side with filter paper. Immediately thereafter, 20 μL of a 2 wt % solution of phosphotungstic acid (adjusted to pH 7 with KOH) was pipetted onto the grid. This solution was wicked off with filter paper after 2 min. The residual film of liquid was allowed to air-dry. Atomic force microscopy (AFM) images were acquired using a Digital Instruments Multimode AFM and Nanoscope III controller. The AFM was operated in tapping mode. Typical forces were a few nanonewtons with scan rates of 0.5−1 Hz. Samples were prepared by placing a drop of a suspension of 10^{-4} M solution of **20** on freshly cleaved mica surfaces. The models proposed for the self-assembly of the rodcoil dendron molecules were visualized using Chemdraw3D and the MM2 algorithm for minimization.

Synthesis. 4-(*N*-*tert*-butoxycarbonyl)aminobenzoic Acid (1). 4-Aminobenzoicacid (10.0 g, 72.9 mmol) was added to a solution of NaOH (3.13 g, 78.3 mmol) in a mixture of dioxane (60 mL) and water (60 mL). This mixture was stirred until all of the 4-aminobenzoic acid had dissolved, and was then cooled to 0 °C in an ice bath. Then, di-*tert*-butyl dicarbonate (30 mL, 131 mmol) was added, and the reaction mixture stirred at 0 °C. After 3 h, the ice bath was removed and the reaction mixture stirred overnight at room temperature. After that, the reaction mixture was extracted once with ethyl acetate. The ethyl acetate extract was discarded and the aqueous phase was cooled to 0 °C, diluted with ethyl acetate, and neutralized with an aqueous $KHSO_4$ solution. The organic phase was separated, and the aqueous phase was extracted two more times with ethyl acetate. The ethyl acetate extracts were combined, washed with water, and dried over $MgSO_4$. The crude product obtained after filtration of the $MgSO_4$ and evaporation of the solvents was recrystallized from ethyl acetate. Yield: 10.38 g (60%). ^{1}H NMR (DMSO-d_6): δ = 7.85 (d, Ar*H*, 2H), 7.55 (d, Ar*H*, 2H), 1.45 (s, −C(C*H*$_3$)$_3$, 9H). ^{13}C NMR (DMSO-d_6): δ = 167.21, 152.65, 143.93, 130.49, 124.09, 117.34, 79.68, 28.09. MS (LR−FAB): m/z = 237.1 (M^+). MS (HR−FAB): m/z = 273.100100 (calcd 237.100108) for $C_{12}H_{15}$-

NO_4. Anal. Calcd for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.67; H, 6.36; N, 5.79.

Benzyl-4-(*N*-*tert*-butoxycarbonyl)aminobenzoate (2). DIPC (4.0 mL, 25.55 mmol) was added to a solution of **1** (2.02 g, 8.51 mmol), DPTS (5.9 g, 20.0 mmol), and benzyl alcohol (1.90 mL, 18.36 mmol) in DMF (120 mL). The reaction mixture was stirred overnight at room temperature. Then, the reaction mixture was concentrated in vacuo to approximately 50% of the initial volume, and subsequently poured into an equal volume of water. The aqueous phase was extracted with CH_2Cl_2 (3×), and the combined CH_2Cl_2 extracts were washed with water (2×) and brine (1×). The organic phase was separated, dried over $MgSO_4$, filtered, and evaporated. The solid residue was triturated with MeOH. Solids were filtered and vacuum-dried. Yield: 2.08 g (75%). ^{1}H NMR ($CDCl_3$): δ = 8.0 (d, Ar*H*, 2H), 7.4 (m, Ar*H* and Ar′*H*, 7H), 6.7 (s, N*H*, 1H), 5.35 (s, Ar′CH_2−, 2H), 1.50 (s, −C(CH_3)$_3$, 9H). ^{13}C NMR ($CDCl_3$): δ = 166.07, 152.14, 142.81, 136.18, 131.03, 128.57, 128.17, 128.14, 124.27, 117.31, 81.21, 66.47, 28.23. MS (LR−FAB): *m*/*z* = 328.1 (MH^+). MS (HR−FAB): *m*/*z* = 327.147100 (calcd 237.147058) for $C_{19}H_{21}NO_4$. Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.72; H, 6.42; N, 4.29.

Benzyl-4-aminobenzoate Trifluoroacetic Acid Salt (3). A solution of **2** (1.95 g, 5.96 mmol) in CH_2Cl_2 (60 mL) was cooled to 0 °C in an ice bath. TFA (30 mL) was added to the solution, and the reaction mixture was stirred for 1 h at 0 °C and for another 1.5 h at room temperature. Then, the reaction mixture was evaporated to dryness, and the residue triturated with *n*-hexane. Solids were filtered and dried under vacuum. Yield: 1.94 g (96%). ^{1}H NMR (DMSO-d_6): δ = 7.75 (d, Ar*H*, 2H), 7.35 (m, Ar′*H*, 5H), 6.65 (d, Ar*H*, 2H), 5.25 (s, Ar′CH_2−, 2H). ^{13}C NMR (DMSO-d_6): δ = 165.70, 151.97, 136.86, 131.27, 128.51, 127.93, 127.85, 117.16, 113.94, 65.25. MS (LR−FAB): *m*/*z* = 228.1 (M^+ − CF_3COO^-). MS (HR−FAB): *m*/*z* = 228.102500 (calcd 228.102454) for $C_{14}H_{14}NO_2$.

BOC−(L-lysine)$_{G1}$ Benzyl Ester (4). EDC (2.34 g, 12.21 mmol) was added to an ice-cooled solution of **3** (1.0 g, 2.93 mmol), N^{α},N^{ϵ}-di-BOC-L-lysine dicyclohexylammonium salt (6.18 g, 11.71 mmol), and DMAP (1.62 g, 13.26 mmol) in CH_2Cl_2 (100 mL). The reaction mixture was stirred at 0 °C for 3 h, and then the ice bath was removed and stirring continued overnight at room temperature. After that, the reaction mixture was extracted with 5% $NaHCO_3$ (1×), H_2O (1×), and brine (1×). The organic phase was separated from the aqueous phase, dried over $MgSO_4$, filtered, and evaporated to dryness. Finally, the crude product was purified by column chromatography (SiO_2, hexane/ethyl acetate 60/40 (v/v)). Yield: 1.33 g (80%). ^{1}H NMR (DMSO-d_6): δ = 10.3 (s, ArN*H*, 1H), 7.95 (d, Ar*H*, 2H), 7.75 (d, Ar*H*, 2H), 7.40 (m, Ar′*H*, 5H), 7.05 (d, N*H*, 1H), 6.75 (t, N*H*, 1H), 5.30 (s, Ar′CH_2−, 2H), 4.0 (m, C*H*, 1H), 2.85 (m, −CH_2CH_2NH−, 4H), 1.60 (m, CHCH_2CH_2−, 4H), 1.30 (s, 18H, −C(CH_3)$_3$). ^{13}C NMR (DMSO-d_6): δ = 172.18, 165.19, 155.59, 143.61, 136.30, 130.42, 128.53, 128.08, 127.97, 123.82, 118.60, 78.07, 77.32, 65.90, 55.26, 31.26, 29.23, 28.24, 28.18, 27.95, 27.54, 27.46, 22.97. MS (LR−FAB): *m*/*z* = 556.3 (MH^+). MS (HR−FAB): *m*/*z* = 556.302500 (calcd 556.302276) for $C_{30}H_{42}N_3O_7$.

General Procedure for the Removal of the BOC Protective Groups from Dendrons 4 and 7. A solution of the dendron in CH_2Cl_2 was cooled to 0 °C in an ice bath. TFA (50 vol % with respect to the CH_2Cl_2) was added, and the reaction mixture stirred at 0 °C for 1 h and at room temperature for another hour. Then, the reaction mixture was evaporated to dryness and vacuum-dried at room temperature, affording the deprotected dendrons **6** and **9** in quantitative yield.

(L-Lysine)$_{G1}$ Benzyl Ester (6). ^{1}H NMR (DMSO-d_6/THF-d_8 1/1 (v/v)) δ = 10.9 (s, ArN*H*, 1H), 8.30 (d, CHNH_3, 3H), 8.0 (d, Ar*H*, 2H), 7.75 (b, Ar*H* + CH_2NH_3, 5H), 7.35 (m, Ar′*H*, 5H), 5.30 (s, Ar′CH_2−, 2H), 4.0 (m, C*H*, 1H), 2.75 (m, −CH_2CH_2-NH_3, 4H), 1.45 (m, CHCH_2CH_2−, 4H).

(L-Lysine)$_{G2}$ Benzyl Ester (9). ^{1}H NMR (DMSO-d_6) δ = 10.55 (s, ArN*H*, 1H), 8.75 (d, N*H*, 1H), 8.45 (t, N*H*, 1H), 8.15 (dd, −CHNH_3, 6H), 7.95 (d, Ar*H*, 2H), 7.75 (b, −NH_3, 6H), 7.70 (d, Ar*H*, 2H), 7.40 (m, Ar′*H*, 5H), 5.30 (s, Ar′CH_2−, 2H), 4.40 (m, C*H*, 1H), 3.85 (m, C*H*NH$_3$, 1H), 3.65 (m, C*H*NH$_3$, 1H), 3.05 (m, CH_2NHCO, 2H), 2.70 (m, CH_2NH$_3$, 4H), 1.70 (b, CHCH_2−, 6H), 1.30 (b, −CH_2CH_2−, 12H). MS (LR−FAB): *m*/*z* = 615.4 (M^+ − 4 × CF_3COO^-).

General Procedure for the Hydrogenation of Dendrons 4, 7, and 10. Pd−C (50 wt % with respect to the dendron) was added to a solution of the dendron in EtOH, and the reaction mixture was stirred overnight at room temperature under a hydrogen atmosphere. Then, the reaction mixture was filtered over a short plug of Celite and evaporated to dryness, affording the deprotected dendrons **5**, **8**, and **11** in quantitative yield.

BOC−(L-lysine)$_{G1}$ (5). ^{1}H NMR (DMSO-d_6): δ = 10.25 (s, ArN*H*, 1H), 7.85 (d, Ar*H*, 2H), 7.65 (d, Ar*H*, 2H), 7.05 (d, CHN*H*, 1H), 6.75 (t, CH_2N*H*, 1H), 4.05 (m, C*H*, 1H), 2.85 (m, −CH_2CH_2NH, 4H), 1.55 (m, CHCH_2CH_2−, 4H), 1.35 (s, −C(CH_3)$_3$, 18H). MS (LR−FAB): *m*/*z* = 466.2 (MH^+). MS (HR−FAB): *m*/*z* = 466.255300 (calcd 466.255326) for $C_{23}H_{36}N_3O_7$.

BOC−(L-lysine)$_{G2}$ (8). ^{1}H NMR (DMSO-d_6): δ = 10.25 (s, ArN*H*, 1H), 7.95 (d, CHN*H*(C═O), 1H), 7.85 (d, Ar*H*, 2H), 7.75 (t, CH_2N*H*(C═O), 1H), 7.65 (d, Ar*H*, 2H), 6.85 (d, CHN*H*BOC, 1H), 6.75 (m, CH_2N*H*BOC, 2H), 6.65 (d, CHN*H*BOC, 1H), 4.35 (m, C*H*NH(C═O), 1H), 3.90 (m, C*H*NHBOC, 1H), 3.75 (m, C*H*NHBOC, 1H), 3.00 (m, −CH_2NH(C═O), 2H), 2.80 (m, −CH_2NHBOC, 4H), 1.70 (m, CHCH_2−, 2H), 1.55 (b, CHCH_2−, 2H), 1.45 (m, CHCH_2−, 2H), 1.30 (b, −C(CH_3)$_3$ + −CH_2CH_2−, 48H). MS (LR−FAB): *m*/*z* = 944.5 (MNa^+). MS (HR−FAB): *m*/*z* = 944.532200 (calcd 944.532056) for $C_{45}H_{75}N_7O_{13}Na$.

BOC−(L-lysine)$_{G3}$ (11). ^{1}H NMR (DMSO-d_6): δ = 10.25 (s, ArN*H*, 1H), 8.10 (d, CHN*H*(C═O), 1H), 7.85 (b, −CH_2N*H*(C═O) + Ar*H*, 3H), 7.75 (b, −CHN*H*(C═O) + −CH_2N*H*(C═O), 4H), 7.65 (d, Ar*H*, 2H), 6.90 (d, CHN*H*BOC, 2H), 6.75 (m, −CH_2N*H*BOC, 4H), 6.70 (d, CHN*H*BOC, 2H), 4.35 (m, C*H*NH-(C═O), 1H), 4.25 (m, C*H*NH(C═O), 1H), 4.15 (m, C*H*NH(C═O), 1H), 3.80 (b, C*H*NHBOC, 4H), 3.0 (b, −CH_2NH(C═O), 6H), 2.85 (b, −CH_2NHBOC, 8H), 1.30 (b, −CH_2− + −C(CH_3)$_3$, 114H). MS (LR−FAB): *m*/*z* = 1735.2 (M^+−$C_5H_7O_2$). MS (HR−FAB): *m*/*z* = 1735.088000 (calcd 1735.087253) for $C_{84}H_{148}N_{15}O_{23}$.

BOC−(L-lysine)$_{G2}$ Benzyl Ester (7). BOP (1.36 g, 3.07 mmol) was added to a mixture of **6** (0.42 g, 0.72 mmol), N^{α},N^{ϵ}-di-BOC-L-lysine dicyclohexylammonium salt (1.62 g, 3.07 mmol) and triethylamine (1.8 mL, 13 mmol) in CH_2Cl_2 (40 mL). The reaction mixture was stirred overnight at room temperature, diluted with CH_2Cl_2, and extracted with 5% $NaHCO_3$ (1×), H_2O (1×), and brine (1×). The organic phase was separated from the aqueous phase, dried over $MgSO_4$, filtered, and evaporated to dryness. The crude product was purified by column chromatography (SiO_2, 100% ethyl acetate). Yield: 0.51 g (70%). ^{1}H NMR (DMSO-d_6): δ = 10.35 (s, ArN*H*, 1H), 7.95 (m, CHN*H* + Ar*H*, 3H), 7.70 (m, CH_2N*H*(C═O) + Ar*H*, 3H), 7.35 (m, Ar′*H*, 5H), 6.85 (d, CHN*H*BOC, 1H), 6.75 (m, CH_2N*H*BOC, 2H), 6.65 (d, CHN*H*BOC, 1H), 5.30 (s, Ar′CH_2O−, 2H), 4.35 (m, C*H*NH(C═O), 1H), 3.90 (m, C*H*NHBOC, 1H), 3.75 (m, C*H*NHBOC, 1H), 3.0 (m, CH_2NH(C═O), 2H), 2.85 (m, CH_2NHBOC, 4H), 1.70 (m, CHCH_2−, 2H), 1.55 (b, CHCH_2−, 2H), 1.45 (m, CHCH_2−, 2H), 1.30 (b, −C(CH_3)$_3$ + −CH_2CH_2−, 48H). ^{13}C NMR (DMSO-d_6): δ = 172.40, 171.93, 171.33, 165.14, 155.54, 155.42, 155.26, 143.40, 136.25, 130.39, 128.51, 128.07, 127.97, 123.93, 118.64, 78.04, 77.88, 77.31, 65.92, 54.27, 53.35, 31.79, 31.50, 29.22, 28.73, 28.27, 28.18, 22.83. MS (LR−FAB): *m*/*z* = 1012.6 (MH_2^+). MS (HR−FAB): *m*/*z* = 1012.596900 (calcd 1012.597062) for $C_{52}H_{82}N_7O_{13}$.

BOC−(L-lysine)$_{G3}$ Benzyl Ester (10). BOP (1.33 g, 3.0 mmol) was added to a mixture of **9** (0.27 g, 0.25 mmol), N^{α},N^{ϵ}-di-BOC-L-lysine dicyclohexylammonium salt (1.58 g, 3.0 mmol), and triethylamine (2.4 mL, 17 mmol) in CH_2Cl_2 (30 mL). The reaction mixture was stirred overnight at room temperature, diluted with CH_2Cl_2 and extracted with 5% $NaHCO_3$ (1×), H_2O (1×), and brine (1×). The organic phase was separated from the aqueous phase, dried over $MgSO_4$, filtered, and evaporated to dryness. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 100/10 (v/v)). Yield: 0.39 g (80%). ^{1}H NMR (DMSO-d_6): δ = 10.30 (s, ArN*H*, 1H), 8.10 (d, CHN*H*(C═O), 1H), 7.90 (d, Ar*H*, 2H), 7.85 (b, −CH_2N*H*(C═O), 1H), 7.75 (d, Ar*H*, 2H), 7.70 (b, −CHN*H*(C═O) +

−CH_2NH(C=O), 3H), 7.65 (d, −CHN*H*(C=O), 1H), 7.35 (m, Ar′*H*, 5H), 6.90 (d, CHN*H*BOC, 2H), 6.75 (m, −CH_2NHBOC, 4H), 6.65 (d, CHN*H*BOC, 2H), 5.30 (s, Ar′CH_2O−, 2H), 4.35 (m, C*H*NH(C=O), 1H), 4.25 (m, C*H*NH(C=O), 1H), 4.15 (m, C*H*NH(C=O), 1H), 3.80 (b, C*H*NHBOC, 4H), 3.0 (b, −CH_2NH(C=O), 6H), 2.85 (b, −CH_2NHBOC, 8H), 1.30 (b, −CH_2− + −C(CH_3)$_3$, 114H). MS (LR−FAB): m/z = 1825.1 (M^+ − $C_5H_7O_2$). MS (HR−FAB): m/z = 1825.134800 (calcd 1825.134203) for $C_{91}H_{154}N_{15}O_{23}$.

Cholesteryl-(L-lactic acid)$_{\bar{n}}$-4-(*tert*-butoxy)benzoate (13). As a typical example the end-functionalization of a cholesteryl-(L-lactic acid)$_{\overline{21}}$ oligomer will be described: DIPC (0.70 mL, 4.5 mmol) was added to a solution of **12** (1.0 g, ∼0.4 mmol), DPTS (0.88 g, 3.0 mmol), and 4-(*tert*-butoxy)benzoic acid (0.51 g, 2.63 mmol) in CH_2Cl_2 (60 mL). After being stirred overnight at room temperature, the reaction mixture was evaporated to dryness, redissolved in CH_2Cl_2 (20 mL), and precipitated into MeOH (400 mL). Solids were filtered and dried under vacuum at room temperature. Yield: 0.90 g (82%). ^{1}H NMR ($CDCl_3$):[22] δ = 7.95 (d, Ar*H*, 2H), 7.05 (d, Ar*H*, 2H), 5.35 (d, cholesterol C-6 H, 1H), 5.30 (q, −(O(C=O)C*H*(CH_3)$_n$O(C=O)Ar, 1H), 5.15 (q, −(O(C=O)C*H*(CH_3)$_n$−, nH), 5.10 (q, cholesteryl-O(C=O)-C*H*(CH_3)−, 1H), 4.65 (m, cholesterol C-3 H, 1H), 1.55 (d, −(O(C=O)CH(CH_3)$_n$−, 3nH), 1.40 (s, −C(CH_3)$_3$, 9H), 0.65 (s, cholesterol C-18 H, 3H). ⟨DP⟩(^{1}H NMR) = 22. MS (MALDI−TOF): M_w = 2498, M_n = 2208, M_w/M_n = 1.13. ⟨DP⟩(MALDI−TOF MS) = 23.

Cholesteryl-(L-lactic acid)$_{\bar{n}}$-4-(hydroxy)benzoate (14). As a typical example, the deprotection of a cholesteryl-(L-lactic acid)$_{\overline{23}}$-4-(*tert*-butoxy)benzoate oligomer will be given: a solution of **13** (0.89 g, ∼ 0.4 mmol) in CH_2Cl_2 (80 mL) was cooled to 0 °C in an ice bath. TFA (15 mL) was added, and the reaction mixture was stirred at 0 °C for 1 h and at room temperature for another hour. Then, the reaction mixture was evaporated to dryness and the residue was redissolved in CH_2Cl_2 (10 mL) and precipitated in MeOH (200 mL). Solids were filtered and dried under vacuum at room temperature. Yield 0.74 g (86%). ^{1}H NMR ($CDCl_3$):[22] δ = 8.00 (d, Ar*H*, 2H), 6.85 (d, Ar*H*, 2H), 5.35 (d, cholesterol C-6 H, 1H), 5.30 (q, −(O(C=O)C*H*(CH_3)$_n$O(C=O)Ar, 1H), 5.15 (q, −(O(C=O)C*H*(CH_3)$_n$−, nH), 5.10 (q, cholesteryl−O(C=O)C*H*(CH_3)−, 1H), 4.65 (m, cholesterol C-3 H, 1H), 1.55 (d, −(O(C=O)CH(CH_3)$_n$−, 3nH), 0.65 (s, cholesterol C-18 H, 3H). ⟨DP⟩(^{1}H NMR) = 25. MS (MALDI−TOF): M_w = 2287, M_n = 2286, M_w/M_n = 1.01. ⟨DP⟩-(MALDI−TOF MS) = 25.

General Procedure for the Coupling of the BOC-Protected Dendrons 5, 8, and 11. As a typical example, the coupling of the protected dendrons to the terminus of a cholesteryl-(L-lactic acid)$_{\overline{29}}$-4-(hydroxy)benzoate will be described: DIPC (2 equiv) was added to a solution of **14** (1 equiv), the dendron (1.1 equiv) and DPTS (2 equiv in CH_2Cl_2). The synthesis of **17** was performed in a 10/1 (v/v) CH_2Cl_2/DMF mixture. The reaction mixture was stirred overnight at room temperature and subsequently evaporated to dryness. The crude oligomer **15** was purified over a SiO_2 column (hexane/EtAc 1/1 (v/v)). The crude rodcoil dendron oligomers **16** and **17** were purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 100/10 (v/v)).

Cholesteryl-(L-lactic acid)$_{\overline{24}}$-BOC−(L-lysine)$_{G1}$ (15). Yield: 0.08 g (37%). ^{1}H NMR ($CDCl_3$):[22] δ = 8.80 (br, Ar″N*H*, 1H), 8.15 (d, Ar′*H*(C=O)− and Ar″*H*(C=O)O−, 4H), 7.70 (d, Ar″*H*NH−, 2H), 7.30 (d, Ar′*H*O(C=O)−, 2H), 5.35 (m, cholesterol C-6 H and −(O(C=O)C*H*(CH_3)$_n$O(C=O)Ar′, 2H), 5.15 (q, −(O(C=O)C*H*(CH_3)$_n$−, nH), 5.10 (q, cholesteryl−O(C=O)-C*H*(CH_3)−, 1H), 4.65 (m, cholesterol C-3 H, 1H), 4.20 (br, −C*H*(CH_2−)NHBOC, 1H), 3.10 (br, −CH_2CH_2NHBOC, 4H), 1.55 (d, −(O(C=O)CH(CH_3)$_n$−, 3nH), 1.40 (s, −C(CH_3)$_3$, 18H), 0.65 (s, cholesterol C-18 H, 3H). ⟨DP⟩(^{1}H NMR) = 23. MS (MALDI−TOF): M_w = 2679, M_n = 2586, M_w/M_n = 1.04. ⟨DP⟩-(MALDI−TOF MS) = 24.

Cholesteryl-(L-lactic acid)$_{\overline{22}}$-BOC−(L-lysine)$_{G2}$ (16). Yield: 0.14 g (54%). ^{1}H NMR ($CDCl_3$):[22] δ = 9.20 (br, Ar″N*H*, 1H), 8.15 (dd, Ar′*H*(C=O)O− and Ar″*H*(C=O)O−, 4H), 7.75 (d, Ar″*H*NH−, 2H), 7.30 (d, Ar′*H*O(C=O)−, 2H), 5.35 (m, cholesterol C-6 H and −(O(C=O)C*H*(CH_3)$_n$O(C=O)Ar′, 2H), 5.15 (q, −(O(C=O)C*H*(CH_3)$_{\bar{n}}$, nH), 5.10 (q, cholesteryl−O(C=O)C*H*(CH_3)−, 1H), 4.50 (m, cholesterol C-3 H, 1H), 4.45 (br, −C*H*NH(C=O)−, 1H), 4.05 (br, −C*H*NHBOC, 1H), 3.55 (br, −C*H*NHBOC, 1H), 3.10 (br, −CH_2NHBOC, 4H), 1.80 (br, CHCH_2−, 2H), 1.55 (d, −(O(C=O)CH(CH_3)$_{\bar{n}}$, 3nH), 1.40 (s, −C(CH_3)$_3$, 36H), 0.65 (s, cholesterol C-18 H, 3H). ⟨DP⟩(^{1}H NMR) = 24. MS (MALDI−TOF): M_w = 3088, M_n = 3047, M_w/M_n = 1.01. ⟨DP⟩(MALDI−TOF MS) = 24.

Cholesteryl-(L-lactic acid)$_{\overline{22}}$-BOC−(L-lysine)$_{G3}$ (17). Yield: 0.13 g (80%). ^{1}H NMR ($CDCl_3$):[22] δ = 8.10 (br, Ar′*H*(C=O)O− and Ar″*H*(C=O)O−, 4H), 7.80 (br, Ar″*H*NH−, 2H), 7.30 (d, Ar′*H*O(C=O)−, 2H), 5.35 (m, cholesterol C-6 H and −(O(C=O)C*H*(CH_3)$_n$O(C=O)Ar′, 2H), 5.15 (q, −(O(C=O)C*H*(CH_3)$_{\bar{n}}$, nH), 5.10 (q, cholesteryl−O(C=O)C*H*(CH_3)−, 1H), 4.80 (br, C*H*NH(C=O), 1H), 4.65 (m, cholesterol C-3 H, 1H), 4.40 (br, C*H*NH(C=O) and −C*H*NHBOC, 5H), 4.25 (br, C*H*NH(C=O), 1H), 3.10 (br, −CH_2NH(C=O) and −CH_2NHBOC, 14H), 1.55 (d, −(O(C=O)CH(CH_3)$_{\bar{n}}$, 3nH), 1.40 (s, −C(CH_3)$_3$, 72H), 0.65 (s, cholesterol C-18 H, 3H). ⟨DP⟩(^{1}H NMR) = 25. MS (MALDI−TOF): M_w = 3988, M_n = 3893, M_w/M_n = 1.02. ⟨DP⟩(MALDI−TOF MS) = 22.

General Procedure for the Deprotection of the Rodcoil Dendrons 15, 16, and 17. The BOC-protected rodcoil dendron (∼20 mg/mL) was stirred in a 4 M solution of HCl in dioxane. After 2 h, the reaction mixture was evaporated to dryness and thoroughly vacuum-dried to afford the rodcoil dendron oligomers **18**−**20** in quantitative yield.

Cholesteryl-(L-lactic acid)$_{\overline{23}}$-(L-lysine)$_{G1}$ (18). ^{1}H NMR (DMSO-d_6):[22] δ = 9.00 (br, Ar″N*H*, 1H), 8.35 (br, −CHNH_3Cl, 3H), 8.15 (d, Ar″*H*(C=O)O−, 2H), 8.10 (d, Ar′*H*(C=O)O−, 2H), 7.90 (d, Ar″*H*NH−, 2H), 7.80 (br, −CH_2NH_3Cl, 3H), 7.50 (d, Ar′*H*O(C=O)−, 2H), 5.35 (m, cholesterol C-6 H and −(O(C=O)C*H*(CH_3)$_n$O(C=O)Ar′, 2H), 5.20 (q, −(O(C=O)C*H*(CH_3)$_{\bar{n}}$, nH), 5.05 (q, cholesteryl−O(C=O)C*H*(CH_3)−, 1H), 4.50 (m, cholesterol C-3 H, 1H and −C*H*NH_3Cl, 2H), 4.05 (m, −CH_2-NH_3Cl, 2H), 2.70 (br, −CH_2CH_2CH_2CH_2NH_3Cl, 4H), 1.45 (d, −(O(C=O)CH(CH_3)$_{\bar{n}}$, 3nH), 0.65 (s, cholesterol C-18 H, 3H). ⟨DP⟩(^{1}H NMR) = 22. MS (MALDI−TOF): M_w = 2526, M_n = 2495, M_w/M_n = 1.01. ⟨DP⟩(MALDI−TOF MS) = 23.

Cholesteryl-(L-lactic acid)$_{\overline{21}}$-(L-lysine)$_{G2}$ (19). ^{1}H NMR (DMSO-d_6):[22] δ = 8.85 (d, −CHN*H*(C=O), 1H), 8.70 (t, −CH_2-NH(C=O), 1H), 8.25 (br, −CHNH_3Cl, 6H), 8.10 (dd, Ar′*H*(C=O)O− and Ar″*H*(C=O)O−, 4H), 7.85 (br, Ar″*H*NH− and −CH_2NH_3Cl, 8H), 7.45 (d, Ar′*H*O(C=O)−, 2H), 5.35 (m, cholesterol C-6 H and −(O(C=O)C*H*(CH_3)$_n$O(C=O)Ar′, 2H), 5.20 (q, −(O(C=O)C*H*(CH_3)$_{\bar{n}}$, nH), 5.05 (q, cholesteryl−O(C=O)C*H*(CH_3)−, 1H), 4.50 (m, cholesterol C-3 H and −C*H*NH-(C=O)−, 2H), 3.90 (br, −CH_2NH(C=O)−, 2H), 3.15 (br, −C*H*NH_3Cl, 2H), 2.75 (br, −CH_2NH_3Cl, 4H), 1.80 (br, −CH_2-CH_2−, 12H), 1.45 (d, −(O(C=O)CH(CH_3)$_{\bar{n}}$, 3nH), 0.65 (s, cholesterol C-18 H, 3H). ⟨DP⟩(^{1}H NMR) = 24. MS (MALDI−TOF): M_w = 2690, M_n = 2621, M_w/M_n = 1.03. ⟨DP⟩(MALDI−TOF MS) = 21.

Cholesteryl-(L-lactic acid)$_{\overline{22}}$-(L-lysine)$_{G3}$ (20). ^{1}H NMR (DMSO-d_6):[22] δ = 8.70 (br, −CHN*H*(C=O)−, 3H), 8.30 (br, −CH_2NH(C=O)− and −CHNH_3Cl, 15H), 8.10 (dd, Ar′*H*(C=O)O− and Ar″*H*(C=O)O−, 4H), 7.95 (br, −CH_2NH_3Cl, 12H), 7.90 (d, Ar″*H*NH−, 2H), 7.45 (d, Ar′*H*O(C=O)−, 2H), 5.35 (m, cholesterol C-6 H and −(O(C=O)C*H*(CH_3)$_n$O(C=O)Ar′, 2H), 5.20 (q, −(O(C=O)C*H*(CH_3)$_{\bar{n}}$, nH), 5.05 (q, cholesteryl−O(C=O)C*H*(CH_3)−, 1H), 4.50 (m, cholesterol C-3 H, 1H), 4.40 (br, C*H*NH(C=O), 1H), 4.35 (br, C*H*NH(C=O), 1H), 4.20 (br, C*H*NH(C=O), 1H), 3.85 (br, −C*H*NH_3Cl, 4H), 3.05 (br, −CH_2-NH(C=O), 6H), 2.75 (br, −CH_2NH_3Cl, 8H), 1.80 (br, −CH_2-CH_2−, 24H), 1.45 (d, −(O(C=O)CH(CH_3)$_{\bar{n}}$, 3nH), 0.65 (s, cholesterol C-18 H, 3H). ⟨DP⟩(^{1}H NMR) = 22. MS (MALDI−TOF): M_w = 3324, M_n = 3264, M_w/M_n = 1.02. ⟨DP⟩(MALDI−TOF MS) = 22.

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