Synthesis, Characterization, and Thermal Behavior of Steroidal Dendrons

Jarmo Ropponen,[a] Jari Tamminen,[a] Manu Lahtinen,[a] Juha Linnanto,[a] Kari Rissanen,*[a] and Erkki Kolehmainen[a]

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A series of novel dendritic steroidal polyesters of first and second generation has been synthesized in convergent fashion by the use of 2,2-bis(hydroxymethyl)propionic acid as a repeating unit. The first- and second-generation hydroxy-functionalized dendrons with a variety of surface modifications were produced through the use of four bile acids: lithocholic acid (LCA), ursodeoxycholic acid (UDCA), deoxycholic acid (DCA), and cholic acid (CA). The thermal behavior of the steroidal dendrons was characterized by differential scanning calorimetry (DSC) and by thermogravimetric analysis (TGA). Finally, quantum chemical calculation methods were used to study the geometries of the dendrons and the occurrence of intramolecular hydrogen bonds in these dendritic molecules.

Introduction

The field of dendrimer chemistry is the subject of intense recent attention, as they are chemically discrete, highly branched, polymer-like macromolecules with well defined three-dimensional structures.[1−6] These characteristics of dendritic macromolecules endow them with many unique properties, such as their viscosity[7] or thermal behavior,[8] which differ significantly from those of linear polymers. Thanks to a variety of their properties, dendrimers and dendritic molecules can be used for applications in light-harvesting systems,[9−11] catalysis,[12−16] molecular encapsulation,[17−19] and biomedicine.[20−24]

In general, there are two different synthetic strategies for the construction of dendrimers. In the divergent[25−28] method, the monomers are added layer by layer around the core molecule. In the convergent[29,30] approach, the branched parts, so-called dendrons, are prepared from AB_x monomers and in the final step these parts are joined into the core molecule to form a dendrimer of a desired generation.

There is a huge variety of potential uses of dendritic structures, and a wide range of applications with dendrimers and dendrons have been explored. In fact, it is becoming clear that dendrimer chemistry itself is branching out at least in two directions: biological and materials chemistry. However, many future applications of dendritic systems are likely to be developed in the area of biomaterials.

Bile acids are polyhydroxylated steroidal acids obtained from the digestive systems of vertebrates.[31] Their physiological role is to participate in the digestion and resorption of lipids and lipophilic vitamins. Bile acids and their derivatives are also important compounds from the pharmaceutical point of view, as has been reviewed recently by Virtanen and Kolehmainen.[32] They have been used in the treatment of bile acid deficiency, liver diseases, and in dissolution of cholesterol gallstones,[33] and also have many prospective medical applications.[34−44] The high specificity and capacity of the bile acid transport system (enterohepatic circulation) forms the basis of research efforts to elaborate drug-bile acid conjugates for tissue- or organ-specific targeting, absorption enhancers of peptide drugs, and for cholesterol level-lowering agents.[45]

Their large, rigid, and curved steroidal skeletons, their chemically different hydroxy groups, their enantiomeric purities, and their unique amphiphilicity, together with their availability and low cost, make bile acids ideal building blocks for the design of novel molecular and supramolecular assemblies for molecular recognition. Interesting supramolecular applications for bile acid-based assemblies could be, for example, as molecular switches and anion[46,47] and cation[48−52] ionophores. Some bile acid derivatives have been able to act as organogelators,[53−56] important compounds in the search for new materials in the field of nanotechnology.

The uniting of dendritic structure and steroidal moieties in the same molecule might give rise to potential molecular assemblies with many interesting nano-scale applications, including as organ-targeted drug carriers, as artificial ion channels, and as molecular switches. Chen et al. have synthesized estrone dendrimers containing six estrones attached through polyoxyethylene chains (to increase their

[a] Nanoscience Center, Department of Chemistry, University of Jyväskylä,
P. O. Box 35, 40014, University of Jyväskylä, Finland
Fax: (internat.) + 358-14-2602501
E-mail: Kari.Rissanen@jyu.fi
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polarity) to a benzene core by the convergent method.[57] Maitra et al. reported the first bile acid-based chiral dendrons,[58,59] through the use of acetoxy-functionalized cholic acid (3α,7α,12α-trihydroxy-5β-cholan-24-oic acid, CA) and deoxycholic acid (3α,12α-dihydroxy-5β-cholan-24-oic acid, DCA) as starting materials in the preparation of a heptamer, a nonamer, and a decamer, also by the convergent strategy.

We have recently reported the design, synthesis, and characterization of novel steroidal dendrons based on 2,2-bis(hydroxymethyl)propionic acid (bis-MPA) and lithocholic acid (3α-acetoxy-5β-cholan-24-oic acid, LCA).[60] As an extension of our previous work in this field we now report a series of first- and second-generation bile acid-derived dendritic compounds from that study with bis-MPA as the repeating unit.

Results and Discussion

Preparation of Dendrons

2,2-Bis(hydroxymethyl)propionic acid (bis-MPA) and its derivatives **1**−**4** (Figure 1) were employed as a building blocks for the preparation of first- and second-generation dendrons.[61] A convergent route to second-generation dendrons is shown in Schemes 1 and 2.

Firstly, the benzyl ester of bis-MPA (**1**) was prepared by nucleophilic substitution of the bis-MPA potassium salt with benzyl bromide. Acetonide-[G#2]-$CO_2CH_2C_6H_5$ (**2**)

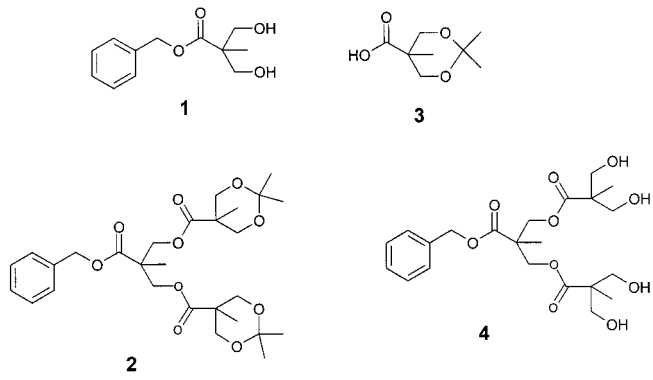
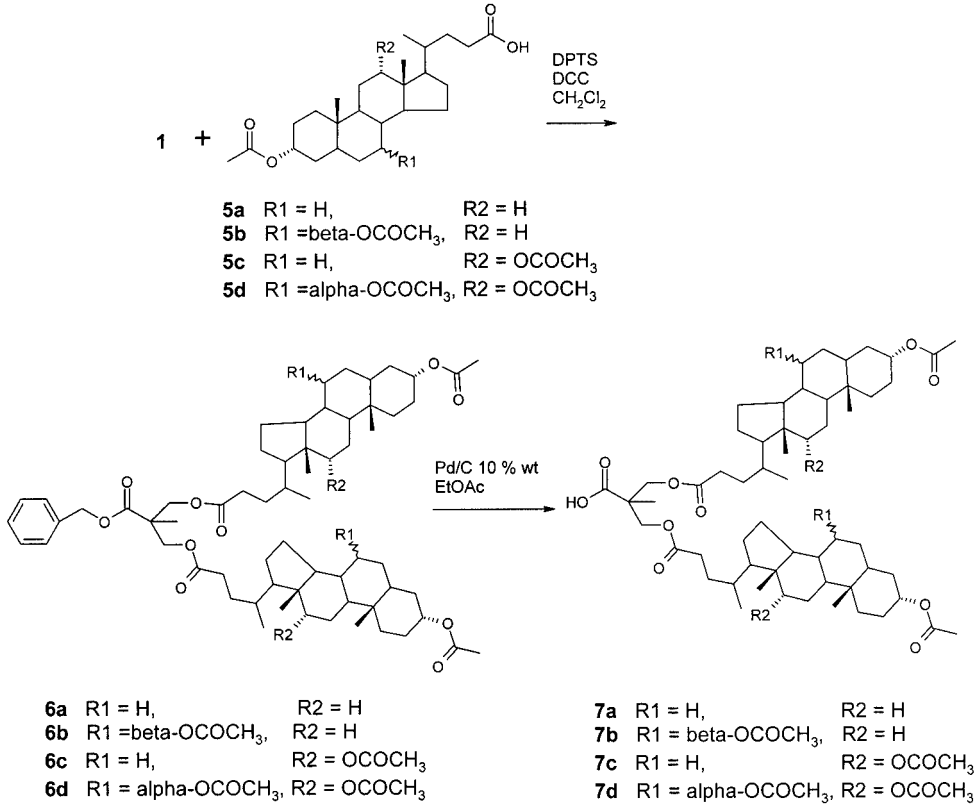


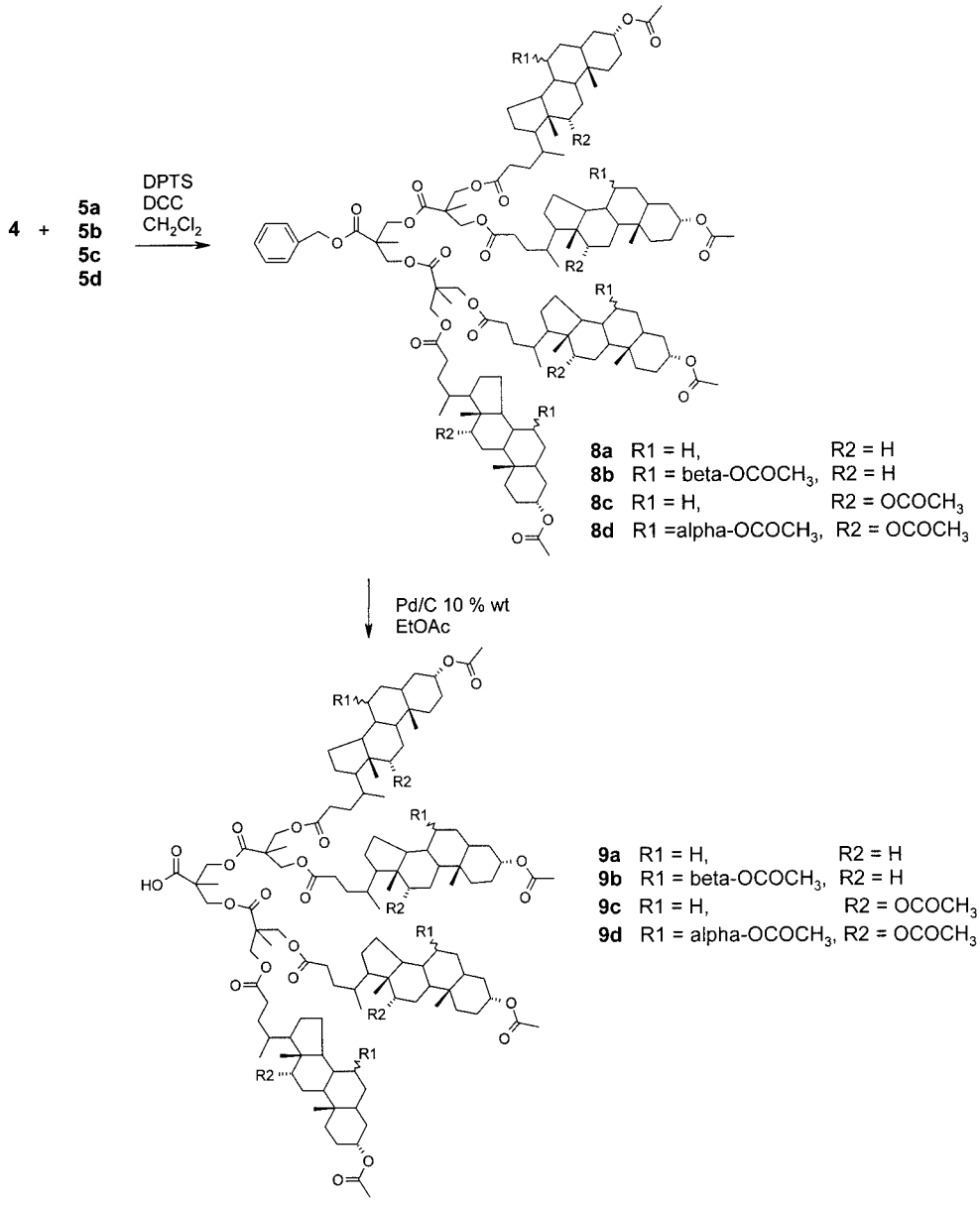
Figure 1. Bis-MPA-based dendrons **1**−**4**

was synthesized in 87% yield from **1** and **3** by *N*,*N*-dicyclohexylcarbodiimide (DCC) coupling with 4-(dimethylamino)-pyridinium *p*-toluenesulfonate (DPTS)[62] as a catalyst in dichloromethane. DOWEX, H^+ in methanol was used to cleave the acetonide, affording **4** in 97% yield.

The first-generation dendrons with steroidal surfaces were synthesized from **1** and **5a**−**d** by the same methodology. Acetyl-protected steroidal dendrons **5a**−**d** were prepared in 57%, 86%, 84%, and 71% yields, respectively, by procedures developed by Gao et al.[63] Dendron **6a** with steroidal dendrons was purified by column chromatography (SiO_2) with elution with hexane/ethyl acetate (6:4) to afford **6a**-[G#1]-$CO_2CH_2C_6H_5$ in 95% yield. Analogous coupling of the dendron **1** gave **6b**−**d** from **5b**−**d** in 82%, 71%, and



Scheme 1. Synthesis of the first-generation dendrons



Scheme 2. Synthesis of the second-generation dendrons

70% yields, respectively. The benzyl group was removed by catalytic hydrogenolysis [10% (w/w); 10% Pd/C; 6.8 atm of H_2; in ethyl acetate], affording dendrons **7a**−**d**-[G#1]-COOH in 95%, 97%, 93%, and 83% yields, respectively.

The second-generation benzyl-protected dendrons were similarly synthesized and purified by column chromatography, except that the reaction time was longer, **8a**−**d**-[G#2]-$CO_2CH_2C_6H_5$ being afforded in 83%, 86%, 70%, and 84% yields, respectively. Removal of the benzyl ester groups gave dendrons **9a**−**d**-[G#2]-COOH in 89%, 83%, 82%, and 93% yields, respectively. All the esterification and deprotection reactions were monitored by NMR spectroscopy and TLC until judged to be complete. The compounds were characterized by ESI-TOF-MS and various NMR methods such as ^1H, composite pulse proton decoupled ^{13}C, ^{13}C DEPT-135, PFG ^1H, ^{13}C HMQC[64,65] and PFG ^1H, ^{13}C HMBC[66] experiments.

Computational Methods

Quantum chemical calculation methods, semiempirical PM3 and ab initio Hartree−Fock 6-311G**, were used to study the geometries of dendrons **6**−**9** and the occurrence of intramolecular hydrogen bonds in these dendritic molecules. Calculations suggested that the dendrons **8a**−**d** to **9a**−**d** have intramolecular hydrogen bonds between the carboxy oxygen atoms of the bile acids (at position 24) and the phenyl or acid groups of the dendritic moieties. There was also another possible hydrogen bond type inside the dendritic moiety, between the carboxy groups of [G#2] and the phenyl or acid groups, but that was not as energetically fa-

vorable as the first one. Calculation methods did not produce similar intramolecular hydrogen bond structures for the shortest macromolecules – dendrons **6a–d** to **7a–d** – because these are geometrically too short. A ^{13}C NMR study also suggested similar findings for dendrons **7a–d** and **9a–d**, in which the carboxylic *C*=O signals were shifted ca. 5 ppm upfield from $\delta \approx 177$ to 172 ppm, respectively. The calculated difference was about 4.5 ppm. As a result of these intramolecular hydrogen bonds, the steroidal parts of dendrons **8a–d** and **9a–d** (or larger dendrons) might act like umbrellas above the phenyl or acid groups of the dendrons (Figure 2). In solution, on the other hand, solvent molecules might change the conformation to a more open form.

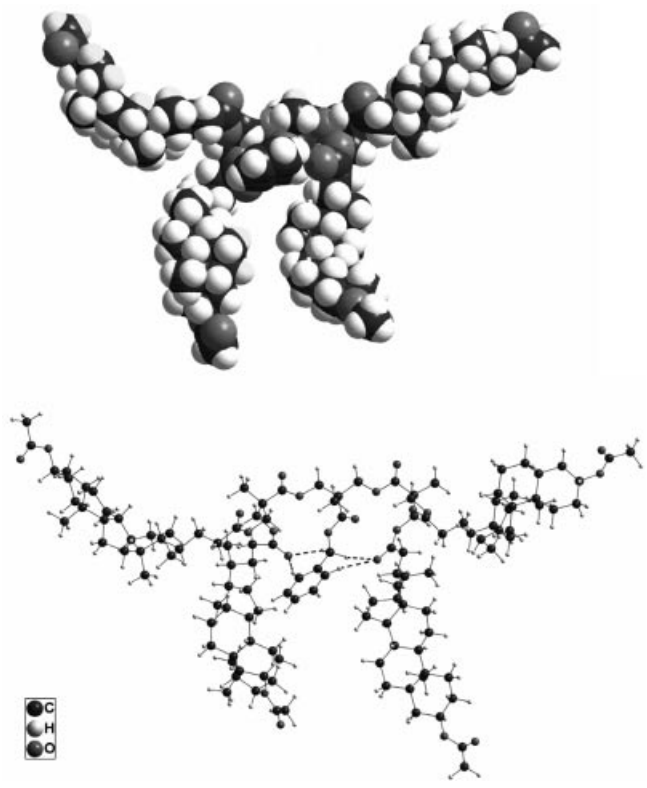


Figure 2. Ab initio HF/6-311G** optimized structure (top) of **8a**; the hydrogen bonds suggested by the calculations are shown in the lower picture (dashed lines)

Thermal Characterization

The thermal properties of the dendritic steroidal polyesters were characterized by differential scanning calorimetry (DSC) and by thermogravimetric analysis (TGA). It is well known that the glass transition temperature (T_g) is dependent on thermal history, the heating and cooling rates, and the difference between these rates, and that T_g increases with increasing rates. Macromolecular systems such as dendrimers commonly exhibit complicated DSC traces on first heating scans, with simpler and more reproducible scans being obtained on subsequent scans. The samples were therefore subjected to three consecutive heating-cooling cycles: the first cycle to erase the thermal history (caused by solidification and storage conditions) and potential solvent residue effects, the second and third cycles to observe the final glass transition temperatures. Solvent effects were observed only in **9b**, as its T_g was significantly lower on first heating than on subsequent cycles, in which the T_g shifted to the reported value. Finally, Cernošek et al.[67] have pointed out that broader supercooling temperature regions and prolonged time intervals for structural relaxation can decrease the glass transition ranges significantly with slow heating and cooling rates, and have therefore suggested the use of rates of closer to 20 °C/min to reduce the effects of the kinetic processes. However, to help comparison of the results presented with the previously reported studies on dendritic materials, the commonly used rate of 10 °C/min was selected for these experiments. The results of these experiments are tabulated in Table 1, while the DSC and TGA runs for compounds **6a–9a** and **6d–9d** are presented in Figures 3 and 5, respectively. In the case of the compounds **6b–9b** and **6c–9c**, the DSC and TGA runs are included as Supporting Information due to their graphical similarities to the former compounds (for Supporting Information see also the footnote on the first page of this article).

Table 1. T_g values of the dendritic steroidal polyesters determined by DSC

Compd.	T_g[a] [°C]	Decomp. range[b] [°C]	Compd.	T_g[a] [°C]	Decomp. range [°C]
6a	43.2	314–530	**8a**	65.4	333–520
6b	61.4	291–540	**8b**	69.5	335–540
6c	38.7	335–530	**8c**	72.8	328–530
6d	75.1	323–490	**8d**	91.5	331–510
7a	69.4	303–490	**9a**	81.1	303–490
7b	67.8	307–495	**9b**	60.7	305–500
7c	68.0	300–490	**9c**	88.7	308–490
7d	101.1	312–480	**9d**	101.2	311–505

[a] T_g values are each presented as the average of three runs, with deviation of ±0.8 °C. [b] The starting temperature of the decomposition is taken as an extrapolated onset.

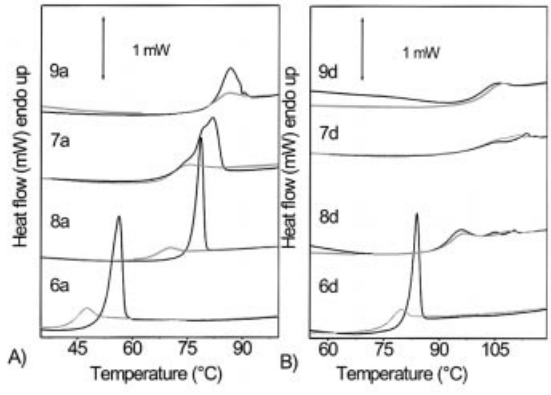


Figure 3. DSC scans of: A) LCA-substituted steroidal polyesters of **6a–9a** from the first (black) and subsequent second heating runs (gray), and B) CA-substituted polyesters of **6d–9d**; the curves have been shifted vertically for clarity

All sixteen dendrons were completely amorphous (glassy) materials showing only glass transitions on both heating and cooling runs. The non-crystallinity of the compounds was also confirmed by X-ray powder diffraction measurements with selected compounds.[68] The powder patterns showed only low diffraction humps characteristic of amorphous material in a 2θ-range of 15−30°.

The T_g values can be categorized into four groups depending on the bile acid substituent (**5a**−**d**). Furthermore, T_g within each group is further affected by increasing molecular weight and the core-type − thus by the higher dendron generation and by whether the core is either benzyl-protected or acid-type. Overall, the T_g values varied from 38.7 to 101.2 °C, being lowest for **6c** and highest for **7d** and **9d** (Table 1 and Figure 4A). The measured heat capacities (ΔC_p) varied between 0.18−0.28 J/(°Cg), decreasing slightly for higher dendron generation, although, as the temperature range of glass transition broadened at the same time, the evaluation of correct values were more difficult and no explicit tendency can be proposed. All dendrons of the CA type clearly showed higher T_g values than other dendron types. This may originate from the fact that, of the substituted bile acids, the CA has the most acetoxy groups, which might increase the probability of formation of intermolecular and/or intramolecular hydrogen bonds, as was suggested by quantum chemical calculations on dendrons **8a**−**d** and **9a**−**d**. The T_g values of CA-type dendrons increased in the order **6d** < **8d** < **7d** < **9d**, such that the benzyl-protected dendrons of both first- and second-generation had lower T_g values than dendrons with acid cores, respectively (Figure 4, A). Similar generation- and core type-dependent increasing of T_g were observed with LCA- and DCA-type dendrons, although the T_g values were lower throughout the two series, increasing from ca. 38 to 89 °C. Furthermore, if T_g values between LCA- and DCA-type dendrons are compared, it can be seen that the values were almost equal within the same generation and with same core-type (e.g., with **6a/6c** and **7a/7c**). The dendrons with UDCA components (**6b**−**9b**) deviated slightly from the other dendron types, as these dendrons seemed to be more or less unaffected by increasing generation and/or change of core type, as the T_g values varied between 60−70 °C and showed only weak parabolic tendency. If we consider the LCA, UDCA, and DCA dendrons from the structural point of view, it may be that the influence of the structural difference between DCA (one acetoxy group on R^2 site) and LCA (R^1 = R^2 = H) is not playing such a significant role because the additional acetoxy group in DCA is located on the more "crowded" side of the steroid framework, on the same side as the three methyl groups. In the case of the UDCA the acetoxy group is bonded opposite to the R^1 site, hence introducing a new branch on the opposite side of the framework and because of that, the bulkiness of the steroidal dendron increases and the free mobility of the dendron decreases relative to the LCA and DCA dendrons **6a** and **6c**. The smaller variation of the T_g in UDCA-type dendrons indicates that increasing of the dendron generation or removal of the benzyl protection do not increase the overall rigidity of the molecule to the same extent as in the other steroidal dendrons. The CA is the most bulky of the bile acid dendrons and, together with increased hydrogen bonding capability, the highest T_g values were observed for these dendrons. The influence of the hydrogen bonding capability, molecular weight, and nature of the chain ends on glass transition temperatures of dendritic macromolecules has also been verified by the thorough work of Wooley et al.[8] Furthermore, due to the bulkiness of the bile acid dendrons, the first- and second-generation dendrons − especially of the CA type − already exhibited higher T_g values than seen in, for example, dendritic polyesters with hydroxy end groups[61,69] (which commonly exhibit high T_g values) and in various dendritic macromolecules (polyethers and polyesters with different end groups) studied by Wooley et al.[8]

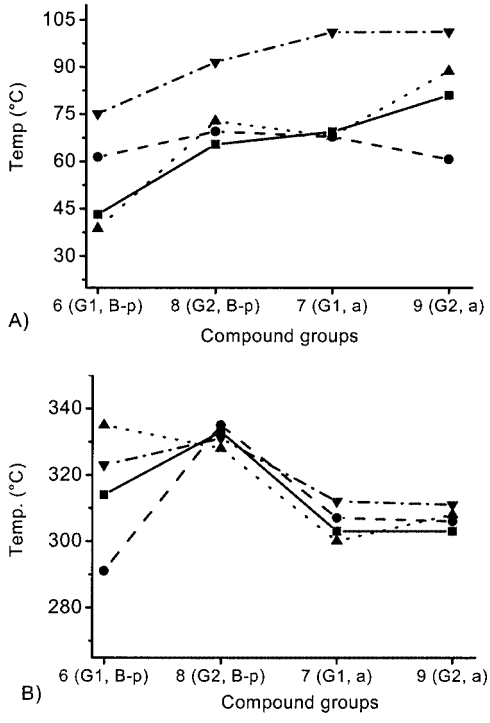


Figure 4. Comparison of (A) T_g values of the dendrons with different bile acid substitutes [(squares) compounds **6a**−**9a** with LCA, (circles) **6b**−**9b** with UDCA, (triangles up) **6c**−**9c** with DCA, (triangles down) **6d**−**9d** with CA dendron] and (B) the respective decomposition temperature onsets of the dendrons (same symbols as in A); abbreviations on *x*-axis are as follows: G1 and G2 = first- and second-generation; B-p and a = benzyl-protected and acid core, respectively

Finally, enthalpy relaxation peaks were observed on first heating runs for all dendrons except **6c**, **7d**, **8d**, and **9b**−**d** (Supporting Information), being most distinct in the cases of **6a**, **6d**, **8a**, and **8c**. This suggests that these dendrons, either during solidification or under the storage conditions, experienced structural relaxation in which the local and partial molecular ordering released the structural strain, gradually shifting the material closer to its thermal equilibrium. A few tentative DSC experiments were carried out in order to examine the relaxation conditions, and more detailed studies will be presented in further studies. Measurement conditions analogous to those noted in the Exp. Sect.

were used, except that the cooling rate was changed to 1 °C/min and one additional annealing step at constant temperature roughly 20 °C below the T_g (for 60 min) was introduced into the second heating cycle. The measurements with slow cooling suggested that the time-scale of the relaxation phenomenon was far too slow to be exhibited within the relatively short measurement time, since after slow cooling followed by an annealing step, the DSC scans showed glass transition traces similar to those observed on the second heating run with higher rates of heating and cooling (Figure 3).

The thermal stabilities of the dendrons were characterized by TGA. Studies showed that the thermal stabilities of all sixteen dendrons were quite high, as the decomposition generally started around at 300 °C and ended at close to 500 °C (Figure 5). The onset temperatures (T_e) of the decomposition are presented in Table 1 and graphically in Figure 4B. The acid core dendrons **7a−d** and **9a−d** generally showed slightly lower T_e values than the corresponding benzyl-protected dendrons, the average difference being ca. 30 °C. The weight loss paths were typical for organic compounds, as the decomposition showed two subsequent stages in which the random breakdown of the molecular bonds occurs at first, followed by the slower carbonization stage, which then ends with the fast burning of the remaining carbon-based residues at higher temperature. A few additional measurements were carried out under nitrogen by an analogous procedure (results for **8a** and **9a** presented in Figure 6). The T_g curves showed greater weight loss in the first stage than in the case of samples that were decomposed under air. It is suggested that partial oxidation processes of the steroid framework and/or polymerization of the dendrons may occur when samples are heated under air, which may counterbalance the weight loss speed before final decomposition of the dendrons.

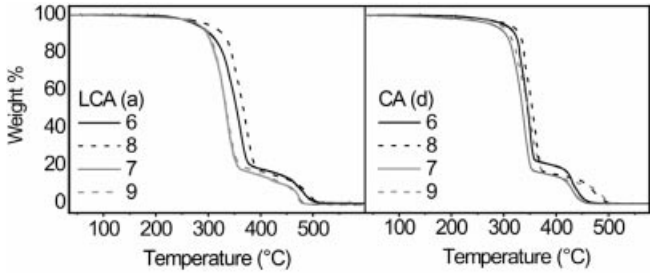


Figure 5. TGA curves of steroidal polyesters **6a−9a** and **6d−9d** measured under synthetic air atmosphere; numbers beside the curves indicate the compounds as shown on Table 1

Conclusion

The reported series of dendritic steroidal polyesters was synthesized in high yields by convergent methods, in which four different acetoxy-protected bile acids were coupled to the first- and second-generation hydroxy-terminated dendrons. The DSC runs showed clearly that all these sixteen steroidal dendrons were completely amorphous materials

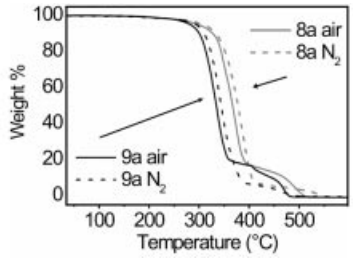


Figure 6. Comparison of TGA curves of steroidal polyesters **8a** and **9a** measured both under air and under nitrogen; the slightly higher thermal stability of the benzyl-protected dendron **8a** can be seen in the figure

showing only glass transitions. The highest T_g values were determined for the CA-type dendrons, in which the T_g values increased from 75.1 to 101.2 °C. Despite the structural differences of LCA-, DCA-, and CA-type dendrons, the T_g values behaved analogously from generation to generation of the same core type, and were dependent on the dendron generation and the core type, so that the benzyl-protected dendrons of both first and second generation showed T_g values lower than in dendrons with the corresponding acid core, suggesting that the increasing hydrogen bonding capability increased the rigidity of the dendrons. The UDCA-type dendrons were fairly independent of alteration of the generation or the core type, as their T_g values varied only in parabolic fashion between 60−70 °C. In the case of the second-generation dendrons, calculation methods suggest intramolecular hydrogen bonding between carboxy oxygens of the bile acid dendrons. However, the first-generation dendrons proved to be geometrically too short to form intramolecular hydrogen bonds. The thermal stability of the dendrons was quite high, showing a weight loss path with two subsequent stages, in which decomposition of all compounds started around at 300 °C and ended at close to 500 °C. The amorphous natures of the reported dendrons may improve the potential use of the materials in, for example, drug transport, as the solubility properties of a compound are generally improved by lowering the crystallinity. Furthermore, these amorphous dendritic steroidal esters may act as potential organic gelators.

Experimental Section

General Remarks: All chemicals were purchased from the major chemical suppliers as highest purity grade and used without any further purification. Compounds **1−4** were synthesized by a procedure reported by Hult et al.[61] DPTS was synthesized as described by Moore and Stupp.[62] All acetyl-protected bile acids were prepared by the procedure of Gao et al.[63] Column chromatography was performed with Merck silica gel 60 F_{254}, particle size 0.040−0.063 mm, with hexane/ethyl acetate mixtures. All ^1H and composite pulse proton decoupled ^{13}C NMR, as well as PFG $^1H,^{13}C$ HMQC and HMBC experiments, were performed in 0.02−0.05 M $CDCl_3$ solutions with a Bruker Avance DRX 500 NMR spectrometer working at 500.13 MHz for ^1H, and 125.77 MHz for ^{13}C experiments, respectively. Detailed lists of acquisition and processing parameters are available on request from

E. K. The ^1H and ^{13}C NMR chemical shifts were referenced to the residual signal of partly deuterated solvent: $\delta(C^{1}HCl_3) = 7.26$ ppm from the internal TMS and to the signal of solvent $\delta(^{13}CDCl_3) = 77.00$ ppm from the internal TMS, respectively. ESI-TOF MS measurements were obtained with an LCT time of flight (TOF) mass spectrometer (Micromass LCT). For the accurate mass measurements the calibration of the instrument was carried out with NaI. The reference ions were substance p for compounds **6a**−**d** and **7a**−**d** and renin for compounds **8a**−**d** and **9a**−**d**. Quantum chemical calculation methods, semiempirical PM3 and ab initio Hartree−Fock 6-311G**, were used to study the geometries of dendrons **6a**−**d** to **9a**−**d** and occurrence of intramolecular hydrogen bonds in these dendritic molecules. The absolute shieldings for the molecules were obtained by the gauge-independent atomic orbital (GIAO) method at the Hartree−Fock level of theory with use of the 6-311G** basis set and Hartree−Fock optimized geometries. Calculations were run on an AlphaServer ES-40 workstation with Gaussian98 software.[70] The DSC measurements were carried out with a Perkin−Elmer Pyris Diamond DSC instrument with intracooler with the use of 50 μL encapsulated aluminum pans with capillary holes. The temperature calibration was carried out by using onset temperatures of *n*-decane (T_m = −29.6 °C), indium (T_m = 156.6 °C), and zinc (T_m = 419.5 °C). The heat-flow was calibrated with use of the heat of fusion of indium (28.45 J/g). The DSC runs were carried out with three subsequent heating-cooling cycles under nitrogen (flow rate 50 mL/min) with heating and cooling rates of 10 °C/min on temperature range of −40 to 120 °C, except in the cases of **7d** and **9d**, which were heated to 130 °C. Sample weights of 4−5 mg were used in the measurements, and the glass transition temperatures were obtained from the third heating run as half-step temperature on ΔC_p extrapolated. The thermal decomposition paths were obtained by use of a Perkin−Elmer TGA7 thermogravimetric analyzer. Measurements were carried out in platinum pans under synthetic air atmosphere (flow rate of 50 mL/min) with a heating rate of 10 °C/min over a temperature range of 25−700 °C. In addition, a few measurements with selected compounds were made under nitrogen. The temperature calibration of the TGA equipment was carried out by use of the Curie-point calibration technique (Alumel, Ni, Perkalloy, Fe). The weight balance was calibrated by measuring the standard weight of 50 g at room temperature. The sample weights used in the measurements were about 4−5 mg.

LCA-[G#1]-$CO_2CH_2C_6H_5$ (6a) and General Esterification Procedure: 3α-Acetoxy-5β-cholan-24-oic acid (**5a**, 2.05 g, 4.91 mmol), benzyl 2,2-bis(hydroxymethyl)propionate (**1**, 0.50 g, 2.23 mmol), and DPTS (0.66 g, 2.23 mmol) were diluted in CH_2Cl_2 (40 mL) at room temp. under nitrogen. DCC (1.20 g, 5.80 mmol) was added to the solution. After the system had been stirred for four days at room temp., the formed DCC-urea was filtered off and washed with small amount of CH_2Cl_2. The crude product was purified by column chromatography (silica gel, elution with hexane/ethyl acetate, 6:4) to give the product as a white solid. Yield: 2.19 g (96%). R_f = 0.75. ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ = 7.34−7.31 (m, 5 H, Ar H), 5.15 (s, 2 H, Bz CH_2), 4.71 (m, 2 H, 3-CH^{β}), 4.23 (m, 4 H, [G#1]-CH_2), 2.29−2.24, 2.18−2.11 (m, 4 H, 23-CH_2), 1.97−1.02 (m, 52 H), 2.01 (s, 6 H, 26-CH_3), 1.25 (s, 3 H, [G#1]-CH_3), 0.92 (s, 6 H, 19-CH_3), 0.88 (d, J = 6.52 Hz, 6 H, 21-CH_3), 0.63 (s, 6 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.6 (2 C, 24-CO), 172.6 (1 C, [G#1]-CO), 170.5 (2 C, 25-CO), 135.6 [1 C, Ar(1) C_q], 128.5 [2 C, Ar(2,6) C_{ar}], 128.3 [1 C, Ar(4) C_{ar}], 128.0 [2 C, Ar(3,5) C_{ar}], 74.3 (2 C, 3-CH), 66.7 (1 C, Bz CH_2), 65.3 (2 C, [G#1]-CH_2), 56.5 (2 C, 14-C), 56.0 (2 C, 17-C), 46.4 (1 C, [G#1]-C), 42.7 (2 C, 13-C), 41.9 (2 C, 5-CH), 40.4 (2 C, 9-CH), 40.1 (2 C, 12-CH_2), 35.8 (2 C, 8-CH), 35.3 (2 C, 20-CH), 35.0 (2 C, 1-CH_2), 34.6 (2 C, 10-C), 32.2 (2 C, 4-CH_2), 31.0, 30.8 (4 C, 22-CH_2, 23-CH_2), 28.1 (2 C, 16-CH_2), 27.0 (2 C, 6-CH_2), 26.6 (2 C, 7-CH_2), 26.3 (2 C, 2-CH_2), 24.2 (2 C, 15-CH_2), 23.3 (2 C, 19-CH_3), 21.4 (2 C, 26-CH_3), 20.8 (2 C, 11-CH_2), 18.2 (2 C, 21-CH_3), 17.8 (1 C, [G#1]-CH_3), 12.0 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{64}H_{96}O_{10}$ (1025.47), $[M + Na]^+$ m/z = 1047.6901; found m/z = 1047.6920 $[M + Na]^+$. $C_{64}H_{96}O_{10}$ (1025.47): calcd. C 74.31, H 9.45; found C 74.27, H 9.43.

UDCA-[G#1]-$CO_2CH_2C_6H_5$ (6b): 3α,7β-Diacetoxy-5β-cholan-24-oic acid (**5b**, 2.76 g, 5.78 mmol), benzyl 2,2-bis(hydroxymethyl)propionate (**1**, 0.59 g, 2.63 mmol), and DPTS (0.77 g, 2.63 mmol) were diluted in CH_2Cl_2 (40 mL) at room temp. under nitrogen. DCC (1.41 g, 6.83 mmol) was added to the solution. After the system had been stirred for four days at room temp. the formed DCC-urea was filtered off and washed with a small amount of CH_2Cl_2. The crude product was purified by column chromatography (silica gel, elution with hexane/ethyl acetate, 6:4) to give the product as a white solid. Yield: 2.45 g (82%). R_f = 0.40. ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ = 7.36−7.31 (m, 5 H, Ar H), 5.16 (s, 2 H, Bz CH_2), 4.87 (q, J = 3.19 Hz, 2 H, 7-CH^{β}), 4.59 (m, 2 H, 3-CH^{β}), 4.23 (m, 4 H, [G#1]-CH_2), 2.36−2.24, 2.18−2.11 (m, 4 H, 23-CH_2), 2.05 (s, 6 H, 28-CH_3), 2.00−1.04 (m, 48 H), 2.02 (s, 6 H, 26-CH_3), 1.22 (s, 3 H, [G#1]-CH_3), 0.93 (s, 6 H, 19-CH_3), 0.89 (d, J = 6.53 Hz, 6 H, 21-CH_3), 0.64 (s, 6 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.6 (2 C, 24-CO), 172.6 (1 C, [G#1]-CO), 170.6 (2 C, 25-CO), 170.4 (2 C, 27-CO), 135.6 [1 C, Ar(1) C_q], 128.6 [2 C, Ar(2,6) C_{ar}], 128.3 [1 C, Ar(4) C_{ar}], 128.0 [2 C, Ar(3,5) C_{ar}], 74.2 (2 C, 3-CH), 71.2 (2 C, 7-CH), 66.8 (1 C, Bz CH_2), 65.4 (2 C, [G#1]-CH_2), 55.7 (2 C, 17-CH), 50.4 (2 C, 14-CH), 46.4 (1 C, [G#1]-C), 42.7 (2 C, 13-C), 41.0 (2 C, 5-CH), 39.5 (2 C, 12-CH_2), 37.9 (2 C, 8-CH), 35.2 (2 C, 20-CH), 34.9 (2 C, 1-CH), 34.8 (2 C, 10-C), 34.7 (2 C, 4-CH_2), 34.1 (2 C, 9-CH), 31.3 (2 C, 6-CH_2), 30.9 (2 C, 23-CH_2), 30.8 (2 C, 22-CH_2) 28.0 (2 C, 16-CH_2), 26.8 (2 C, 2-CH_2), 23.6 (2 C, 15-CH_2), 22.7 (2 C, 19-CH_3), 21.6 (2 C, 28-CH_3), 21.5 (2 C, 26-CH_3), 20.6 (2 C, 11-CH_2), 18.2 (2 C, 21-CH_3),17.8 (1 C, [G#1]-CH_3), 11.7 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{68}H_{100}O_{14}$ (1141.55), $[M + Na]^+$ m/z = 1163.7011; found m/z = 1163.7023 $[M + Na]^+$. $C_{68}H_{100}O_{14}$ (1141.55): calcd. C 69.36, H 8.90; found C 69.67, H 8.76.

DCA-[G#1]-$CO_2CH_2C_6H_5$ (6c): 3α,12α-Diacetoxy-5β-cholan-24-oic acid (**5c**, 2.76 g, 5.78 mmol), benzyl 2,2-bis(hydroxymethyl)propionate (**1**, 0.59 g, 2.63 mmol), and DPTS (0.77 g, 2.63 mmol) were diluted in CH_2Cl_2 (40 mL) at room temp. under nitrogen. DCC (1.41 g, 6.83 mmol) was added to the solution. After the system had been stirred for four days at room temp., the formed DCC-urea was filtered off and washed with a small amount of CH_2Cl_2. The crude product was purified by column chromatography (silica gel, elution with hexane/ethyl acetate, 6:4) to give the product as a white solid. Yield: 2.13 g (71%). R_f = 0.53. ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ = 7.29−7.22 (m, 5 H, Ar H), 5.08 (s, 2 H, Bz CH_2), 5.00 (t, J = 2.60 Hz, 2 H, 12-CH^{β}) 4.62 (m, 2 H, 3-CH^{β}), 4.15 (m, 4 H, [G#1]-CH_2), 2.22−2.15, 2.09−2.04 (m, 4 H, 23-CH_2), 2.02 (s, 6 H, 30-CH_3), 1.89−0.94 (m, 48 H), 1.95 (s, 6 H, 26-CH_3), 1.24 (s, 3 H, [G#1]-CH_3), 0.83 (s, 6 H, 19-CH_3), 0.71 (d, J = 6.52 Hz, 6 H, 21-CH_3), 0.64 (s, 6 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.2 (2 C, 24-CO), 172.3 (1 C, [G#1]-CO), 170.2 (2 C, 25-CO), 170.1 (2 C, 29-CO), 135.5 [1 C, Ar(1) C_q], 128.3 [2 C, Ar(2,6) C_{ar}], 128.1 [1 C, Ar(4) C_{ar}], 127.8 [2 C, Ar(3,5) C_{ar}] 75.6 (2 C, 12-CH), 73.9 (2 C, 3-CH), 66.5 (1 C, Bz CH_2), 65.1 (2 C, [G#1]-CH_2), 49.2 (2 C, 14-CH), 47.4 (2 C, 17-C), 46.2 (1 C, [G#1]-C), 44.8 (2 C, 13-C), 41.6 (2 C, 5-CH), 35.5 (2 C, 8-CH),

34.5 (2 C, 1-CH_2), 34.4 (2 C, 20-CH), 34.2 (2 C, 9-CH), 33.8 (2 C, 10-C), 32.1 (2 C, 4-CH_2), 30.8 (2 C, 22-CH_2), 30.5 (2 C, 23-CH_2), 28.1 (2 C, 16-CH_2), 27.0 (2 C, 6-CH_2), 26.4 (2 C, 2-CH_2), 25.7 (2 C, 7-CH_2), 25.4 (2 C, 11-CH_2), 23.2 (2 C, 15-CH_2), 22.7 (2 C, 19-CH_3), 21.2, 21.1 (2 C, 26-CH_3, 2 C, 30-CH_3), 17.6 (1 C, [G#1]-CH_3), 17.3 (2 C, 21-CH_3), 12.2 (2 C, 18-CH_3). ESI-TOF MS: Calcd. for $C_{68}H_{100}O_{14}$ (1141.55), $[M + Na]^+$ m/z = 1163.7011; found m/z = 1163.7010 $[M + Na]^+$. $C_{68}H_{100}O_{14}$ (1141.55): calcd. C 70.44, H 8.87; found C 70.64, H 8.74.

CA-[G#1]-$CO_2CH_2C_6H_5$ (6d): 3α,7α,12α-Triacetoxy-5β-cholan-24-oic acid (**5d**, 6.01 g, 11.24 mmol), benzyl 2,2-bis(hydroxymethyl)propionate (**1**, 1.20 g, 5.35 mmol), and DPTS (0.63 g, 2.14 mmol) of DPTS were diluted in CH_2Cl_2 (80 mL) at room temp. under nitrogen. DCC (2.87 g, 13.91 mmol) was added to the solution. After the system had been stirred for 20 h at room temp. the formed DCC-urea was filtered off and washed with small amount of CH_2Cl_2. The crude product was purified by column chromatography (silica gel, elution with hexane/ethyl acetate, 6:4) to give the product as a white solid. Yield 4.72 g (70%). R_f = 0.20. ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ = 7.35−7.28 (m, 5 H, Ar H), 5.14 (s, 2 H, Ar−CH_2), 5.06 (t, J = 2.74 Hz, 2 H, 12-CH^{β}), 4.89 (q, J = 2.76 Hz, 2 H, 7-CH^{β}), 4.56 (m, 2 H, 3-CH^{β}), 4.21 (s, 4 H, [G#1]-CH_2), 2.28−2.22 (m, 2 H, 23-CH_2), 2.13−1.03 (m, 46 H), 2.12 (s, 6 H, 30-CH_3), 2.07 (s, 6 H, 28-CH_3), 2.03 (s, 6 H, 26-CH_3), 1.24 (s, 3 H, [G#1]-CH_3), 0.90 (s, 6 H, 19-CH_3), 0.77 (d, J = 5.53 Hz, 6 H, 21-CH_3), 0.70 (s, 6 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.4 (2 C, 24-CO), 172.5 (1 C, [G#1]-CO), 170.4 (2 C, 25-CO), 170.4 (2 C, 29-CO), 170.2 (2 C, 27-CO), 135.6 [1 C, Ar(1) C_q], 128.5 [2 C, Ar(2) C_{ar}, Ar(6) C_{ar}], 128.3 [1 C, Ar(4) C_{ar}], 128.0 [2 C, Ar(3) C_{ar}, Ar(5) C_{ar}], 75.3 (2 C, 12-CH), 74.0 (2 C, 3-CH), 70.6 (2 C, 7-CH), 66.7 (1 C, Ar−CH_2), 65.3 (2 C, [G#1]-CH_2), 47.4 (2 C, 17-CH), 46.4 (1 C, [G#1]-C_q), 45.0 (2 C, 13-C_q), 43.3 (2 C, 14-CH), 40.9 (2 C, 5-CH), 37.7 (2 C, 8-CH), 34.7, 34.6 (4 C, 1-CH_2, 4-CH_2), 34.5 (2 C, 20-CH), 34.3 (2 C, 10-C_q), 31.2 (2 C, 6-CH_2), 30.9 (2 C, 23-CH_2), 30.6 (2 C, 22-CH_2), 28.8 (2 C, 9-CH), 27.1 (2 C, 16-CH_2), 26.9 (2 C, 2-CH_2), 25.5 (2 C, 11-CH_2), 22.8 (2 C, 15-CH_2), 22.5 (2 C, 19-CH_3), 21.6 (2 C, 28-CH_3), 21.4 (2 C, 26-CH_3), 21.4 (2 C, 30-CH_3), 17.7 (1 C, [G#1]-CH_3), 17.4 (2 C, 21-CH_3), 12.2 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{72}H_{104}O_{18}$ (1157.62), $[M + Na]^+$ m/z = 1279.7120; found m/z = 1279.7098 $[M + Na]^+$. $C_{72}H_{104}O_{18}$ (1157.62): calcd. C 67.79, H 8.36; found C 67.75, H 8.38.

LCA-[G#1]-COOH (7a) and General Procedure for Removal of the Benzyl Ester Group: Pd/C (10%, 0.15 g) was added to a solution of LCA-[G#1]-$CO_2CH_2C_6H_5$ (**6a**, 1.52 g, 2.01 mmol) in ethyl acetate (70 mL). The reaction vessel for catalytic hydrogenolysis was evacuated of air and filled with H_2. The mixture was stirred for 20 h at room temp. and the catalyst was filtered off and carefully washed with ethyl acetate. The filtrate was concentrated and dried in vacuo to give a white powder. Yield 1.32 g (95%). ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ = 4.70 (m, 2 H, 3-CH^{β}), 4.26−4.19 (m, 4 H, [G#1]-CH_2), 2.37−2.31, 2.25−2.18 (m, 4 H, 23-CH_2), 1.97−1.02 (m, 52 H), 1.96 (s, 6 H, 26-CH_3), 1.26 (s, 3 H, [G#1]-CH_3), 0.91 (s, 6 H, 19-CH_3), 0.89 (d, J = 6.52 Hz, 6 H, 21-CH_3), 0.63 (s, 6 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 177.8 (1 C, [G#1]-CO), 173.7 (2 C, 24-CO), 170.7 (2 C, 25-CO), 74.4 (2 C, 3-CH), 65.0 (2 C, [G#1]-CH_2), 56.5 (2 C, 14-CH), 56.0 (2 C, 17-C), 46.1 (1 C, [G#1]-C), 42.7 (2 C, 13-C), 41.9 (2 C, 5-CH), 40.4 (2 C, 9-CH), 40.1 (2 C, 12-CH), 35.8 (2 C, 8-CH), 35.3 (2 C, 20-CH), 35.0 (2 C, 1-CH_2), 34.5 (2 C, 10-C), 32.2 (2 C, 4-CH_2), 31.0, 30.9 (4 C, 22-CH_2, 23-CH_2), 28.1 (2 C, 16-CH_2), 27.0 (2 C, 6-CH_2), 26.6 (2 C, 7-CH_2), 26.3 (2 C, 2-CH_2), 24.2 (2 C, 15-CH_2), 23.3 (2 C, 19-CH_3), 21.4 (2 C, 26-CH_3), 20.8 (2 C, 11-CH_2), 18.2 (2 C, 21-CH_3), 17.8 (1 C, [G#1]-CH_3), 12.0 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{57}H_{90}O_{10}$ (935.35), $[M + Na]^+$ m/z = 957.6432; found m/z = 957.6491 $[M + Na]^+$. $C_{57}H_{90}O_{10}$ (935.35): calcd. C 71.81, H 9.73; found C 72.02, H 9.68.

UDCA-[G#1]-COOH (7b): Pd/C (10%, 0.19 g) was added to a solution of UDCA-[G#1]-$CO_2CH_2C_6H_5$ (**6b**, 1.93 g, 1.67 mmol) in ethyl acetate (70 mL). The reaction vessel for catalytic hydrogenolysis was evacuated of air and filled with H_2. The mixture was stirred for 20 h at room temp. and the catalyst was filtered off and carefully washed with ethyl acetate. The filtrate was concentrated and dried in vacuo to give a white powder. Yield: 1.71 g (97%). ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ = 4.86 (q, J = 2.38 Hz, 2 H, 7-CH^{β}), 4.57 (m, 2 H, 3-CHβ), 4.26−4.18 (m, 4 H, [G#1]-CH_2), 2.36−2.29, 2.26−2.16 (m, 4 H, 23-CH_2), 2.03 (s, 6 H, 28-CH_3), 2.02−1.02 (m, 48 H), 2.01 (s, 6 H, 26-CH_3), 1.25 (s, 3 H, [G#1]-CH_3), 0.91 (s, 6 H, 19-CH_3), 0.89 (d, J = 6.48 Hz, 6 H, 21-CH_3), 0.63 (s, 6 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 177.2 (1 C, [G#1]-CO), 173.6 (2 C, 24-CO), 170.7 (2 C, 25-CO), 170.5 (2 C, 27-CO), 74.2 (2 C, 3-CH), 71.2 (2 C, 7-CH), 65.0 (2 C, [G#1]-CH_2), 55.7 (2 C, 17-CH), 50.3 (2 C, 14-CH), 46.0 (1 C, [G#1]-C), 42.7 (2 C, 13-C), 40.9 (2 C, 5-CH), 39.5 (2 C, 12-CH_2), 37.8 (2 C, 8-CH), 35.2 (2 C, 20-CH), 34.9 (2 C, 1-CH), 34.8 (2 C, 10-C), 34.6 (2 C, 4-CH_2), 34.0 (2 C, 9-CH), 31.3 (2 C, 6-CH_2), 31.0 (2 C, 23-CH_2), 30.8 (2 C, 22-CH_2) 27.9 (2 C, 16-CH_2), 26.8 (2 C, 2-CH_2), 23.5 (2 C, 15-CH_2), 22.6 (2 C, 19-CH_3), 21.5 (2 C, 28-CH_3), 21.4 (2 C, 26-CH_3), 20.6 (2 C, 11-CH_2), 18.2 (2 C, 21-CH_3), 17.7 (1 C, [G#1]-CH_3), 11.7 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{61}H_{94}O_{14}$ (1051.42), $[M + Na]^+$ m/z = 1073.6541; found m/z = 1073.6499 $[M + Na]^+$. $C_{61}H_{94}O_{14}$ (1051.42): calcd. C 68.51, H 9.05; found C 68.72, H 9.01.

DCA-[G#1]-COOH (7c): Pd/C (10%, 0.17 g) was added to a solution of DCA-[G1]-$CO_2CH_2C_6H_5$ (**6c**, 1.66 g, 1.45 mmol) in ethyl acetate (70 mL). The reaction vessel for catalytic hydrogenolysis was evacuated of air and filled with H_2. The mixture was stirred for 20 h at room temp. and the catalyst was filtered off and carefully washed with ethyl acetate. The filtrate was concentrated and dried in vacuo to give a white powder. Yield: 1.42 g (93%). ^1H NMR ($CDCl_3$, 500 MHz, ppm): δ = 5.03 (t, J = 2.87 Hz, 2 H, 12-CH^{β}) 4.65 (m, 2 H, 3-CH^{β}), 4.24−4.14 (m, 4 H, [G#1]-CH_2), 2.33−2.25, 2.19−2.11 (m, 4 H, 23-CH_2), 2.06 (s, 6 H, 30-CH_3), 1.81−0.97 (m, 48 H), 1.99 (s, 6 H, 26-CH_3), 1.26 (s, 3 H, [G#1]-CH_3), 0.86 (s, 6 H, 19-CH_3), 0.75 (d, J = 6.47 Hz, 6 H, 21-CH_3), 0.68 (s, 6 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 176.9 (1 C, [G#1]-CO), 173.5 (2 C, 24-CO), 170.6 (2 C, 25-CO), 170.5 (2 C, 29-CO), 75.8 (2 C, 12-CH), 74.2 (2 C, 3-CH), 65.0 (2 C, [G#1]-CH_2), 49.3 (2 C, 14-CH), 47.6 (2 C, 17-C), 45.9 (1 C, [G#1]-C), 44.9 (2 C, 13-C), 41.7 (2 C, 5-CH), 35.6 (2 C, 8-CH), 34.6 (2 C, 1-CH_2), 34.5 (2 C, 20-CH), 34.3 (2 C, 9-CH), 33.9 (2 C, 10-C), 32.1 (2 C, 4-CH_2), 31.0 (2 C, 23-CH_2), 30.6 (2 C, 22-CH_2), 27.1 (2 C, 16-CH_2), 26.8 (2 C, 6-CH_2), 26.5 (2 C, 2-CH_2), 25.8 (2 C, 7-CH_2), 25.5 (2 C, 11-CH_2), 23.3 (2 C, 15-CH_2), 22.9 (2 C, 19-CH_3), 21.3, 21.2 (4 C, 26-CH_3, 30-CH_3), 17.7 (1 C, [G#1]-CH_3), 17.4 (2 C, 21-CH_3), 12.3 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{61}H_{94}O_{14}$ (1051.42), $[M + Na]^+$ m/z = 1073.6541; found m/z = 1073.6593 $[M + Na]^+$. $C_{61}H_{94}O_{14}$ (1051.42): calcd. C 68.51, H 9.05; found C 68.12, H 8.95.

CA-[G#1]-COOH (7d): Pd/C (10%, 0.253 g) was added to a solution of CA-[G#1]-$CO_2CH_2C_6H_5$ (**6d**, 2.53 g, 2.01 mmol) in ethyl acetate (70 mL). The reaction vessel for catalytic hydrogenolysis was evacuated of air and filled with H_2. The mixture was stirred for 16 h at room temp. and the catalyst was filtered off and carefully

washed with ethyl acetate. The filtrate was concentrated and dried in vacuo to give a white powder. Yield: 2.09 g (89%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 5.08 (q, J = 2.78 Hz, 2 H, 12-CHβ), 4.90 (q, J = 3.15 Hz, 2 H, 7-CHβ), 4.57 (m, 2 H, 3-CHβ), 4.27−4.16 (m, 4 H, [G#1]-CH_2), 2.37−2.30, 2.24−2.17 (m, 4 H, 23-CH_2), 2.13−1.03 (m, 44 H), 2.13 (s, 6 H, 30-CH_3), 2.08 (s, 6 H, 28-CH_3), 2.03 (s, 6 H, 26-CH_3), 1.26 (s, 3 H, [G#1]-CH_3), 0.91 (s, 6 H, 19-CH_3), 0.79 (d, J = 6.36 Hz, 6 H, 21-CH_3), 0.72 (s, 6 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 176.2 (1 C, [G#1]-CO), 173.5 (2 C, 24-CO), 170.6 (2 C, 29-CO), 170.6 (2 C, 25-CO), 170.4 (2 C, 27-CO), 75.4 (2 C, 12-CH), 74.1 (2 C, 3-CH), 70.7 (2 C, 7-CH), 65.1 (2 C, [G#1]-CH_2), 47.5 (2 C, 17-CH), 46.0 (1 C, [G#1]-C_q), 45.1 (2 C, 13-C_q), 43.3 (2 C, 14-CH), 40.9 (2 C, 5-CH), 37.8 (2 C, 8-CH), 34.7, 34.6 (4 C, 1-CH_2, 4-CH_2), 34.5 (2 C, 20-CH), 34.3 (2 C, 10-C_q), 31.2 (2 C, 6-CH_2), 31.1 (2 C, 23-CH_2), 30.6 (2 C, 22-CH_2), 28.9 (2 C, 9-CH), 27.0 (2 C, 16-CH_2), 26.9 (2 C, 2-CH_2), 25.6 (2 C, 11-CH_2), 22.8 (2 C, 15-CH_2), 22.5 (2 C, 19-CH_3), 21.6 (2 C, 28-CH_3), 21.4 (2 C, 26-CH_3), 21.4 (2 C, 30-CH_3), 17.7 (1 C, [G#1]-CH_3), 17.6 (2 C, 21-CH_3), 12.2 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{65}H_{98}O_{18}$ (1167.50), $[M + Na]^+$ m/z = 1189.6651; found m/z = 1189.6593 $[M + Na]^+$. $C_{65}H_{98}O_{18}$ (1167.50): calcd. C 63.91, H 8.58; found C 64.11, H 8.31.

LCA-[G#2]-$CO_2CH_2C_6H_5$ (8a): 3α-Acetoxy-5β-cholan-24-oic acid (**5a**, 2.42 g, 5.78 mmol), compound **4** (0.60 g, 1.31 mmol), and DPTS (0.77 g, 2.63 mmol) were diluted in CH_2Cl_2 (40 mL) at room temp. under nitrogen. DCC (1.41 g, 6.83 mmol) was added to the solution. After the system had been stirred for seven days at room temp. the formed DCC-urea was filtered off and washed with small amount of CH_2Cl_2. The crude product was purified by sequential column chromatography (silica gel, elution with hexane/ethyl acetate, 9:1; ethyl acetate) to give the product as a white solid. Yield: 2.26 g (83%) R_f = 0. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 7.35−7.31 (m, 5 H, Ar H), 5.15 (s, 2 H, Bz CH_2), 4.70 (m, 4 H, 3-CH^{β}), 4.30−4.09 (m, 12 H, [G#1]-CH_2 + [G#2]-CH_2), 2.37−2.27, 2.23−2.14 (m, 8 H, 23-CH_2), 1.97−1.01 (m, 104 H), 2.01 (s, 12 H, 26-CH_3), 1.25 (s, 3 H, [G#1]-CH_3), 1.15 (s, 6 H, [G#2]-CH_3), 0.91 (s, 12 H, 19-CH_3), 0.89 (d, J = 6.51 Hz, 12 H, 21-CH_3), 0.63 (s, 12 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.5 (4 C, 24-CO), 172.0 (2 C, [G#2]-CO), 171.9 (1 C, [G#1]-CO), 170.5 (4 C, 25-CO), 135.4 [1 C, Ar(1) C_q), 128.6 [2 C, Ar(2,6) C_{ar}), 128.4 [1 C, Ar(4) C_{ar}), 128.3 [2 C, Ar(3,5) C_{ar}), 74.4 (4 C, 3-CH), 67.1 (1 C, Bz CH_2), 65.7 (2 C, [G#1]-CH_2), 65.0 (4 C, [G#2]-CH_2), 56.5 (4 C, 14-C), 56.0 (4 C, 17-C), 46.7 (1 C, [G#1]-C), 46.4 (2 C, [G#2]-C), 42.7 (4 C, 13-C), 41.9 (4 C, 5-CH), 40.4 (4 C, 9-CH), 40.1 (4 C, 12-CH_2), 35.8 (4 C, 8-CH), 35.3 (4 C, 20-CH), 35.0 (4 C, 1-CH_2), 34.6 (4 C, 10-C), 32.2 (4 C, 4-CH_2), 31.0, 30.9 (8 C, 22-CH_2, 23-CH_2), 28.1 (4 C, 16-CH_2), 27.0 (4 C, 6-CH_2), 26.6 (4 C, 7-CH_2), 26.3 (4 C, 2-CH_2), 24.2 (4 C, 15-CH_2), 23.3 (4 C, 19-CH_3), 21.4 (4 C, 26-CH_3), 20.8 (4 C, 11-CH_2), 18.2 (4 C, 21-CH_3), 17.7 (2 C, [G#2]-CH_3),17.5 (1 C, [G#1]-CH_3), 12.0 (4 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{126}H_{192}O_{22}$ (2058.92), $[M + Na]^+$ m/z = 2080.3803; found m/z = 2080.3784 $[M + Na]^+$. $C_{126}H_{192}O_{22}$ (2058.92): calcd. C 72.55, H 9.42; found C 72.41, H 9.43.

UDCA-[G#2]-$CO_2CH_2C_6H_5$ (8b): 3α,7β-Diacetoxy-5β-cholan-24-oic acid (**5b**, 2.75 g, 5.76 mmol), compound **4** (0.60 g, 1.31 mmol), and DPTS (0.77 g, 2.62 mmol) were diluted in CH_2Cl_2 (50 mL) at room temp. under nitrogen. DCC (1.41 g, 6.81 mmol) was added to the solution. After the system had been stirred for seven days at room temp., the formed DCC-urea was filtered off and washed with small amount of CH_2Cl_2. The crude product was purified by column chromatography (silica gel, elution with hexane/ethyl acetate, 6:4) to give the product as a white solid. Yield: 2.59 g (86%). R_f = 0.20. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 7.35−7.31 (m, 5 H, Ar H), 5.14 (s, 2 H, Bz CH_2), 4.87 (q, J = 3.12 Hz, 4 H, 7-CH^{β}), 4.58 (m, 4 H, 3-CHβ), 4.29−4.12 (m, 12 H, [G#1]-CH_2 + [G#2]-CH_2), 2.35−2.26, 2.22−2.14 (m, 8 H, 23-CH_2), 2.05 (s, 12 H, 28-CH_3), 2.03−1.04 (m, 96 H), 2.02 (s, 12 H, 26-CH_3), 1.25 (s, 3 H, [G#1]-CH_3), 1.15 (s, 6 H, [G#2]-CH_3), 0.92 (s, 12 H, 19-CH_3), 0.89 (d, J = 6.52 Hz, 12 H, 21-CH_3), 0.63 (s, 12 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.5 (4 C, 24-CO), 172.0 (2 C, [G#2]-CO), 171.9 (1 C, [G#1]-CO), 170.6 (4 C, 25-CO), 170.3 (4 C, 27-CO), 135.4 [1 C, Ar(1) C_q), 128.7 [2 C, Ar(2,6) C_{ar}), 128.5 [1 C, Ar(4) C_{ar}), 128.3 [2 C, Ar(3,5) C_{ar}), 74.1 (4 C, 3-CH), 71.2 (2 C, 7-CH), 67.1 (1 C, Bz CH_2), 65.8 (2 C, [G#1]-CH_2), 64.9 (4 C, [G#2]-CH_2), 55.8 (4 C, 17-CH), 50.4 (4 C, 14-CH), 46.7 (1 C, [G#1]-C), 46.4 (2 C, [G#2]-C), 42.7 (4 C, 13-C), 41.0 (4 C, 5-CH), 39.5 (4 C, 12-CH_2), 37.9 (4 C, 8-CH), 35.3 (4 C, 20-CH), 34.9 (4 C, 1-CH), 34.8 (4 C, 10-C), 34.6 (4 C, 4-CH_2), 34.0 (4 C, 9-CH), 31.3 (4 C, 6-CH_2), 31.0 (4 C, 23-CH_2), 30.8 (2 C, 22-CH_2) 28.0 (4 C, 16-CH_2), 26.8 (4 C, 2-CH_2), 23.5 (4 C, 15-CH_2), 22.7 (4 C, 19-CH_3), 21.5 (4 C, 28-CH_3), 21.4 (4 C, 26-CH_3), 20.6 (4 C, 11-CH_2), 18.2 (4 C, 21-CH_3), 17.7 (2 C, [G#2]-CH_3), 17.5 (1 C, [G#1]-CH_3), 11.7 (4 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{134}H_{200}O_{30}$ (2291.07), $[M + Na]^+$ m/z = 2312.4022; found m/z = 2312.3892 $[M + Na]^+$. $C_{134}H_{200}O_{30}$ (2291.07): calcd. C 67.59, H 8.89; found C 67.76, H 8.63.

DCA-[G#2]-CO_2 $_C$$H_2C_6H_5$ (8c): 3α,12α-Diacetoxy-5β-cholan-24-oic acid (**5c**, 2.75 g, 5.76 mmol), compound **5c** (0.60 g, 1.31 mmol), and DPTS (0.77 g, 2.62 mmol) were diluted in CH_2Cl_2 (40 mL) at room temp. under nitrogen. DCC (1.41 g, 6.81 mmol) was added to the solution. After the system had been stirred for seven days at room temp., the formed DCC-urea was filtered off and washed with small amount of CH_2Cl_2. The crude product was purified by column chromatography (silica gel, elution with hexane/ethyl acetate, 6:4) to give the product as a white solid. Yield: 2.11 g (70%). R_f = 0.26. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 7.36−7.29 (m, 5 H, Ar H), 5.13 (s, 2 H, Bz CH_2), 5.06 (t, J = 2.42 Hz, 4 H, 12-CHβ), 4.68 (m, 4 H, 3-CHβ), 4.29−4.22 (m, 4 H, [G#1]-CH_2), 4.16−4.08 (m, 8 H, [G#2]-CH_2), 2.34−2.27, 2.21−2.13 (m, 8 H, 23-CH_2), 2.08 (s, 12 H, 30-CH_3), 1.84−1.00 (m, 96 H), 2.01 (s, 12 H, 26-CH_3), 1.24 (s, 3 H, [G#1]-CH_3), 1.14 (s, 6 H, [G#2]-CH_3), 0.89 (s, 12 H, 19-CH_3), 0.77 (d, J = 6.50 Hz, 12 H, 21-CH_3), 0.70 (s, 12 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.4 (4 C, 24-CO), 172.0 (2 C, [G#2]-CO), 171.9 (1 C, [G#1]-CO), 170.5 (4 C, 25-CO), 170.3 (4 C, 29-CO), 135.3 [1 C, Ar(1) C_q), 128.6 [2 C, Ar(2,6) C_{ar}], 128.5 [1 C, Ar(4) C_{ar}], 128.3 [2 C, Ar(3,5) C_{ar}), 75.8 (4 C, 12-CH), 74.1 (4 C, 3-CH), 67.1 (1 C, Bz CH_2), 65.7 (2 C, [G#1]-CH_2), 64.9 (4 C, [G#2]-CH_2), 49.4 (4 C, 14-CH), 47.7 (4 C, 17-CH), 46.7 (1 C, [G#1]-C), 46.3 (2 C, [G#2]-C), 45.0 (4 C, 13-C), 41.8 (4 C, 5-CH), 35.7 (4 C, 8-CH), 34.7 (4 C, 1-CH_2), 34.7 (4 C, 20-CH), 34.4 (4 C, 9-CH), 34.0 (4 C, 10-C), 32.2 (4 C, 4-CH_2), 31.0 (4 C, 22-CH_2), 30.7 (4 C, 23-CH_2), 27.3 (4 C, 16-CH_2), 27.9 (4 C, 6-CH_2), 26.6 (4 C, 2-CH_2), 25.8 (4 C, 7-CH_2), 25.6 (4 C, 11-CH_2), 23.4 (4 C, 15-CH_2), 23.0 (4 C, 19-CH_3), 21.4, 21.3 (8 C, 26-CH_3, 30-CH_3), 17.7 (2 C, [G#2]-CH_3), 17.5 (1 C, [G#1]-CH_3), 17.5 (4 C, 21-CH_3), 12.4 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{134}H_{200}O_{30}$ (2291.07), $[M + Na]^+$ m/z = 2312.4022; found m/z = 2312.4060 $[M + Na]^+$. $C_{134}H_{200}O_{30}$ (2291.07): calcd. C 69.14, H 8.84; found C 69.11, H 8.73.

CA-[G#2]-$CO_2CH_2C_6H_5$ (8d): 3α,7α,12α-Triacetoxy-5β-cholan-24-oic acid (**5d**, 2.33 g, 4.36 mmol), compound **4** (0.45 g, 0.99 mmol), and DPTS (0.58 g, 1.98 mmol) were diluted in CH_2Cl_2 (40 mL) at room temp. under nitrogen. DCC (1.06 g, 5.15 mmol) was added to the solution. After the system had been stirred for seven days at

room temp. the formed DCC-urea was filtered off and washed with small amount of CH_2Cl_2. The crude product was purified by column chromatography (silica gel, elution with hexane/ethyl acetate, 6:4) to give the product as a white solid. Yield: 2.10 g (84%). R_f = 0.02. ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 7.35−7.28 (m, 5 H, Ar H), 5.13 (s, 2 H, Ar−CH_2), 5.05 (t, J = 3.05 Hz, 4 H, 12-CH$^\beta$), 4.89 (q, J = 3.14 Hz, 4 H, 7-CH$^\beta$), 4.55 (m, 4 H, 3-CH$^\beta$), 4.27−4.07 (m, 12 H, [G#1]-CH_2 + [G#2]-CH_2), 2.35−2.27, 2.23−2.13 (m, 8 H, 23-CH_2), 2.00−1.05 (m, 92 H), 2.11 (s, 12 H, 30-CH_3), 2.06 (s, 12 H, 28-CH_3), 2.02 (s, 12 H, 26-CH_3), 1.24 (s, 3 H, [G#1]-CH_3), 1.13 (s, 6 H, [G#2]-CH_3), 0.89 (s, 12 H, 19-CH_3), 0.77 (d, J = 6.44 Hz, 12 H, 21-CH_3), 0.70 (s, 12 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.3 (4 C, 24-CO), 172.1 (2 C, [G#2]-CO), 171.9 (1 C, [G#1]-CO), 170.4 (4 C, 25-CO), 170.3 (4 C, 29-CO), 170.2 (4 C, 27-CO), 135.3 [1 C, Ar(1) C_q], 128.6 [2 C, Ar(2,6) C_{ar}], 128.5 [1 C, Ar(4) C_{ar}], 128.3 [2 C, Ar(3,5) C_{ar}], 75.3 (4 C, 12-CH), 74.0 (4 C, 3-CH), 70.6 (4 C, 7-CH), 67.1 (1 C, Bz CH_2), 65.2 (2 C, [G#1]-CH_2), 65.0 (4 C, [G#2]-CH_2), 47.5 (4 C, 17-CH), 46.6 (1 C, [G#1]-C), 46.3 (2 C, [G#2]-C), 45.0 (4 C, 13-C), 43.3 (4 C, 14-CH), 40.9 (4 C, 5-CH), 37.7 (4 C, 8-CH), 34.7 (8 C, 1-CH_2, 4-CH_2), 34.6 (4 C, 20-CH), 34.3 (4 C, 10-C), 31.2 (4 C, 6-CH_2), 30.9 (4 C, 23-CH_2), 30.6 (4 C, 22-CH_2), 28.8 (4 C, 9-CH), 27.1 (4 C, 16-CH_2), 26.8 (4 C, 2-CH_2), 25.5 (4 C, 11-CH_2), 22.7 (4 C, 15-CH_2), 22.5 (4 C, 19-CH_3), 21.5 (4 C, 28-CH_3), 21.4 (4 C, 26-CH_3), 21.4 (4 C, 30-CH_3), 17.6 (2 C, [G#2]-CH_3), 17.4 (4 C, 21-CH_3), 17.2 (1 C, [G#1]-CH_3), 12.2 (4 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{142}H_{208}O_{38}$ (2523.22), $[M + Na]^+$ m/z = 2544.4241; found m/z = 2544.4707 $[M + Na]^+$. $C_{142}H_{208}O_{38}$ (2523.22): calcd. C 66.64, H 8.35; found C 66.60, H 8.39.

LCA-[G#2]-COOH (9a): Pd/C (10%, 0.17 g) was added to a solution of compound **8a** (1.66 g, 0.81 mmol) in ethyl acetate (70 mL). The reaction vessel for catalytic hydrogenolysis was evacuated of air and filled with H_2. The mixture was stirred for 48 h at room temp. and the catalyst was filtered off and carefully washed with ethyl acetate. The filtrate was concentrated and dried in vacuo to give a white powder. Yield: 1.41 g (89%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 4.70 (m, 4 H, 3-CH$^\beta$), 4.34−4.14 (m, 12 H, [G#1]-CH_2 + [G#2]-CH_2), 2.36−2.28, 2.24−2.14 (m, 8 H, 23-CH_2), 1.97−0.98 (m, 104 H), 2.01 (s, 12 H, 26-CH_3), 1.27 (s, 3 H, [G#1]-CH_3), 1.22 (s, 6 H, [G#2]-CH_3), 0.91 (s, 12 H, 19-CH_3), 0.88 (d, J = 6.48 Hz, 12 H, 21-CH_3), 0.62 (s, 12 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): δ = 173.8 (2 C, [G#1]-CO), 173.7 (4 C, 24-CO), 172.0 (1 C, [G#2]-CO), 170.7 (4 C, 25-CO), 74.4 (2 C, 3-CH), 65.6 (2 C, [G#1]-CH_2), 65.0 (4 C, [G#2]-CH_2), 56.4 (2 C, 14-CH), 56.0 (2 C, 17-CH), 46.3 (2 C, [G#2]-C), 46.2 (1 C, [G#1]-C), 42.7 (4 C, 13-C), 41.8 (4 C, 5-CH), 40.3 (4 C, 9-CH), 40.1 (4 C, 12-CH_2), 35.7 (4 C, 8-CH), 35.3 (4 C, 20-CH), 35.0 (4 C, 1-CH_2), 34.5 (4 C, 10-C), 32.2 (4 C, 4-CH_2), 31.0, 30.8 (8 C, 22-CH_2, 23-CH_2), 28.1 (4 C, 16-CH_2), 27.0 (4 C, 6-CH_2), 26.6 (4 C, 7-CH_2), 26.3 (4 C, 2-CH_2), 24.1 (4 C, 15-CH_2), 23.3 (4 C, 19-CH_3), 21.4 (4 C, 26-CH_3), 20.8 (4 C, 11-CH_2), 18.2 (4 C, 21-CH_3), 17.7 (2 C, [G#2]-CH_3),17.5 (1 C, [G#1]-CH_3), 12.0 (4 C, 18-CH_3). ESI-TOF MS: Calcd. for $C_{119}H_{186}O_{22}$ (1968.80), $[M - H]^-$ m/z = 1966.3358; found m/z = 1966.3389 $[M - H]^-$. $C_{119}H_{186}O_{22}$ (1968.80): calcd. C 71.29, H 9.55; found C 71.42, H 9.56.

UDCA-[G#2]-COOH (9b): Pd/C (10%, 0.02 g) was added to a solution of compound **8b** (0.20 g, 0.086 mmol) in ethyl acetate (70 mL). The reaction vessel for catalytic hydrogenolysis was evacuated of air and filled with H_2. The mixture was stirred for 48 h at room temp. and the catalyst was filtered off and carefully washed with ethyl acetate. The filtrate was concentrated and dried in vacuo to give a clear glassy solid. Yield: 0.16 g (83%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 4.84 (q, J = 3.10 Hz, 4 H, 7-CH$^\beta$), 4.55 (m, 4 H, 3-CH$^\beta$), 4.22−4.12 (m, 12 H, [G#1]-CH_2 + [G#2]-CH_2), 2.34−2.24, 2.21−2.14 (m, 8 H, 23-CH_2), 2.02 (s, 12 H, 28-CH_3), 2.01−1.01 (m, 96 H), 1.99 (s, 12 H, 26-CH_3), 1.22 (s, 3 H, [G#1]-CH_3), 1.20 (s, 6 H, [G#2]-CH_3), 1.00 (s, 12 H, 19-CH_3), 0.89 (d, J = 6.47 Hz, 12 H, 21-CH_3), 0.61 (s, 12 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): 173.4 (4 C, 24-CO), 172.0 (2 C, [G#1]-CO), 172.0 (1 C, [G#1]-CO), 170.6 (4 C, 25-CO), 170.4 (4 C, 27-CO), 74.1 (4 C, 3-CH), 71.2 (2 C, 7-CH), 65.3 (2 C, [G#1]-CH_2), 65.0 (4 C, [G#2]-CH_2), 55.7 (4 C, 17-CH), 50.3 (4 C, 14-CH), 46.3 (1 C, [G#1]-C), 46.2 (2 C, [G#2]-C), 42.6 (4 C, 13-C), 40.9 (4 C, 5-CH), 39.4 (4 C, 12-CH_2), 37.8 (4 C, 8-CH), 35.2 (4 C, 20-CH), 34.8 (4 C, 1-CH), 34.7 (4 C, 10-C), 34.6 (4 C, 4-CH_2), 34.0 (4 C, 9-CH), 31.2 (4 C, 6-CH_2), 30.9 (4 C, 23-CH_2), 30.7 (4 C, 22-CH_2) 27.9 (4 C, 16-CH_2), 26.7 (4 C, 2-CH_2), 23.5 (4 C, 15-CH_2), 22.6 (4 C, 19-CH_3), 21.5 (4 C, 28-CH_3), 21.3 (4 C, 26-CH_3), 20.6 (4 C, 11-CH_2), 18.2 (4 C, 21-CH_3), 17.7 (2 C, [G#2]-CH_3), 17.6 (1 C, [G#1]-CH_3), 11.6 (4 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{127}H_{194}O_{30}$ (2200.94), $[M + Na]^+$ m/z = 2222.3553; found m/z = 2222.3589 $[M + Na]^+$.

DCA-[G#2]-COOH (9c): Pd/C (10%, 0.13 g) was added to a solution of compound **8c** (1.30 g, 0.567 mmol) in ethyl acetate (70 mL). The reaction vessel for catalytic hydrogenolysis was evacuated of air and filled with H_2. The mixture was stirred for 48 h at room temp. and the catalyst was filtered off and carefully washed with ethyl acetate. The filtrate was concentrated and dried in vacuo to give a white powder. Yield: 1.02 g (82%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 5.07 (s, 4 H, 12-CH$^\beta$), 4.70 (m, 4 H, 3-CH$^\beta$), 4.27−4.14 (m, 12 H, [G#1]-CH_2 + [G#2]-CH_2), 2.35−2.29, 2.22−2.15 (m, 8 H, 23-CH_2), 2.10 (s, 12 H, 30-CH_3), 1.86−1.00 (m, 96 H), 2.02 (s, 12 H, 26-CH_3), 1.26 (s, 3 H, [G#1]-CH_3), 1.22 (s, 6 H, [G#2]-CH_3), 0.90 (s, 12 H, 19-CH_3), 0.78 (d, J = 6.44 Hz, 12 H, 21-CH_3), 0.71 (s, 12 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): 173.5 (4 C, 24-CO), 172.0 (2 C, [G#1]-CO), 171.2 (1 C, [G#2]-CO), 170.6 (4 C, 25-CO), 170.6 (4 C, 29-CO), 75.9 (4 C, 12-CH), 74.2 (4 C, 3-CH), 65.8 (2 C, [G#1]-CH_2), 65.1 (4 C, [G#2]-CH_2), 49.4 (4 C, 14-CH), 47.7 (4 C, 17-CH), 46.4 (1 C, [G#1]-C), 46.3 (2 C, [G#2]-C), 45.0 (4 C, 13-C), 41.8 (4 C, 5-CH), 35.7 (4 C, 8-CH), 34.7 (4 C, 1-CH_2), 34.6 (4 C, 20-CH), 34.4 (4 C, 9-CH), 34.0 (4 C, 10-C), 32.3 (4 C, 4-CH_2), 31.0 (4 C, 23-CH_2), 30.7 (4 C, 22-CH_2), 27.2 (4 C, 16-CH_2), 26.9 (4 C, 6-CH_2), 26.6 (4 C, 2-CH_2), 25.9 (4 C, 7-CH_2), 25.7 (4 C, 11-CH_2), 23.4 (4 C, 15-CH_2), 23.0 (4 C, 19-CH_3), 21.4, 21.3 (8 C, 26-CH_3, 30-CH_3), 17.7 (2 C, [G#2]-CH_3), 17.6 (1 C, [G#1]-CH_3), 17.5 (4 C, 21-CH_3), 12.4 (2 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{127}H_{194}O_{30}$ (2200.94), $[M + Na]^+$ m/z = 2222.3553; found m/z = 2222.3677 $[M + Na]^+$. $C_{127}H_{194}O_{30}$ (2200.94): calcd. C 68.19, H 8.92; found C 68.98, H 8.82.

CA-[G#2]-COOH (9d): Pd/C (10%, 0.15 g) was added to a solution of compound **8d** (1.51 g, 0.599 mmol) in ethyl acetate (70 mL). The reaction vessel for catalytic hydrogenolysis was evacuated of air and filled with H_2. The mixture was stirred for 48 h at room temp. and the catalyst was filtered off and carefully washed with ethyl acetate. The filtrate was concentrated and dried in vacuo to give a white powder. Yield: 1.36 g (93%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ = 5.07 (s, 4 H, 12-CH$^\beta$), 4.89 (d, J = 2.19 Hz, 4 H, 7-CH$^\beta$), 4.55 (m, 4 H, 3-CH$^\beta$), 4.27−4.12 (m, 12 H, [G#1]-CH_2 + [G#2]-CH_2), 2.35−2.28, 2.25−2.15 (m, 8 H, 23-CH_2), 2.00−1.05 (m, 92 H), 2.11 (s, 12 H, 30-CH_3), 2.05 (s, 12 H, 28-CH_3), 2.01 (s, 12 H, 26-CH_3), 1.23 (s, 3 H, [G#1]-CH_3), 1.15 (s, 6 H, [G#2]-CH_3), 0.90 (s, 12 H, 19-CH_3), 0.78 (d, J = 6.42 Hz, 12 H, 21-CH_3), 0.71 (s, 12 H, 18-CH_3). ^{13}C NMR ($CDCl_3$, 126 MHz, ppm): 174.1 (1 C, [G#1]-CO),

173.5 (4 C, 24-CO), 172.2 (2 C, [G#2]-CO), 170.5 (4 C, 25-CO), 170.5 (4 C, 29-CO), 170.3 (4 C, 27-CO), 75.4 (4 C, 12-CH), 74.0 (4 C, 3-CH), 70.7 (2 C, 7-CH), 65.3 (2 C, [G#1]-CH_2), 65.1 (4 C, [G#2]-CH_2), 47.4 (4 C, 17-CH), 46.5 (1 C, [G#1]-C), 46.3 (2 C, [G#2]-C), 45.1 (4 C, 13-C), 43.3 (4 C, 14-CH), 40.9 (4 C, 5-CH), 37.7 (4 C, 8-CH), 34.7, 34.6 (8 C, 1-CH_2, 4-CH_2), 34.5 (4 C, 20-CH), 34.3 (4 C, 10-C), 31.2 (4 C, 6-CH_2), 31.0 (4 C, 23-CH_2), 30.6 (2 C, 22-CH_2), 28.8 (4 C, 9-CH), 27.1 (4 C, 16-CH_2), 26.8 (4 C, 2-CH_2), 25.5 (4 C, 11-CH_2), 22.8 (4 C, 15-CH_2), 22.5 (4 C, 19-CH_3), 21.5 (4 C, 28-CH_3), 21.4 (4 C, 26-CH_3), 21.4 (4 C, 30-CH_3), 17.7 (2 C, [G#2]-CH_3), 17.5 (4 C, 21-CH_3), 17.2 (1 C, [G#1]-CH_3), 12.2 (4 C, 18-CH_3). ESI-TOF MS: calcd. for $C_{135}H_{202}O_{38}$ (2433.99), $[M + Na]^+$ m/z = 2454.3772; found m/z = 2454.3491 $[M + Na]^+$. $C_{135}H_{202}O_{38}$ (2433.99): calcd. C 65.67, H 8.41; found C 65.78, H 8.52.

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