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Synthesis and Structure of Macrolactams of 3α-Aminodeoxycholanic Acid

Martin Feigel,*[a] Rüdiger Ladberg,[a] Manuela Winter,[a] Dieter Bläser,[b] and Roland Boese[b]

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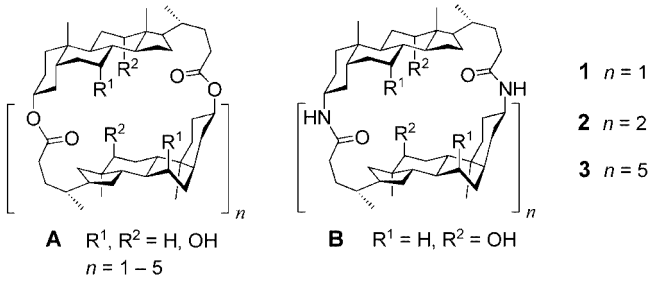
The macrolactams cyclo(3α-aminodeoxycholic amide)$_2$ (**1**) and cyclo(3α-aminodeoxycholic amide)$_3$ (**2**) were prepared in high yields (**1**: 32 %; **2**: 41 %) from the pentafluorophenyl esters of the linear precursors. The solid-state structures of both macrocycles were determined by X-ray diffraction. Compound **1** forms a cleft of C_2 symmetry which holds two methanol and two water molecules fixed by hydrogen bonds. The crystals of compound **2** contain two slightly different macrolactam rings of 7–8 Å diameter. The polar α-surface of the deoxycholanic parts and the amide NH groups are oriented into the center of the rings. The cavity formed by the ring system and the void volume between the macrocycles is filled by disordered solvent molecules.

Introduction

Cholanic acids are attractive building blocks as part of supramolecular receptors and as scaffolds for the display of molecular functions.[1–4] The rigid and curved carbon skeleton of cholanic acids has been incorporated in macrocyclic derivatives – for example, the macrolactones **A** derived from cholic (R^1 = R^2 = OH), deoxycholic (R^1 = H, R^2 = OH) or lithocholic (R^1 = R^2 = H) acid. The compounds have been used to prove the concept of dynamic combinatorial libraries[5] and to complex cations,[6] ferrocene[7] or even morphine.[8]

The solid-state structures of two macrolactones derived form deoxycholanic acid (**A**, *n* = 2, Scheme 1) and from 24-norcholanic acid (analogue of **A**, *n* = 3) have been reported recently.[9] Macrolactams containing cholanic acid derivatives have also been synthesized: e.g., lactams from a cholanic acid bearing an amino group at C17 and a carboxymethyl group at C3[10] and lactams from 3-aminocholanic acids with shortened C22–C24 steroidal side chains.[11] The present work describes the first macrolactams prepared from the parent 3α-aminocholanic acid skeleton. We report the synthesis of the rings **1**, **2**, and **3** of type **B** and detailed structure information for **1** and **2**.



Scheme 1.

Results and Discussion

Synthesis

Treatment of 3α-aminodeoxycholanic acid (**4**) with *tert*-butoxycarbonyl anhydride or thionylchloride/methanol provided the partially protected derivatives **5** or **6**, respectively (Scheme 2). Compound **6** was converted into its pentafluorophenyl ester and treated subsequently with trifluoroacetic acid to remove the Boc group. When the resulting activated "amino acid" was taken up in a two-phase system containing di- and trichloromethane and aqueous sodium hydrogen carbonate, it cyclized to the dimeric macrocycle **1** in surprisingly high yield (32%). Lactones formed by the activated carboxylate and the 12-OH group could not be detected (see, however, ref.[12]). Small amounts of the cyclotrimer **2** were also formed and could be separated from the reaction mixture by chromatography.

The cyclic trimer **2** was prepared in better yields from the linear tris(cholanamide) **8**. Standard peptide chemistry using 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide (EDC) as coupling reagent leads to compounds **7** and **8**; the latter cyclizes as activated pentafluorophenyl ester to

[a] Fakultät für Chemie, Ruhr-Universität Bochum, Universitätsstr. 150, 44780 Bochum, Germany
Fax: +49-234-321-4497
E-mail: feigel@indi-f.nsc.ruhr-uni-bochum.de
[b] Institut für Anorganische Chemie, Universität–GH Essen, Universitätsstr. 3–5, 45117 Essen, Germany
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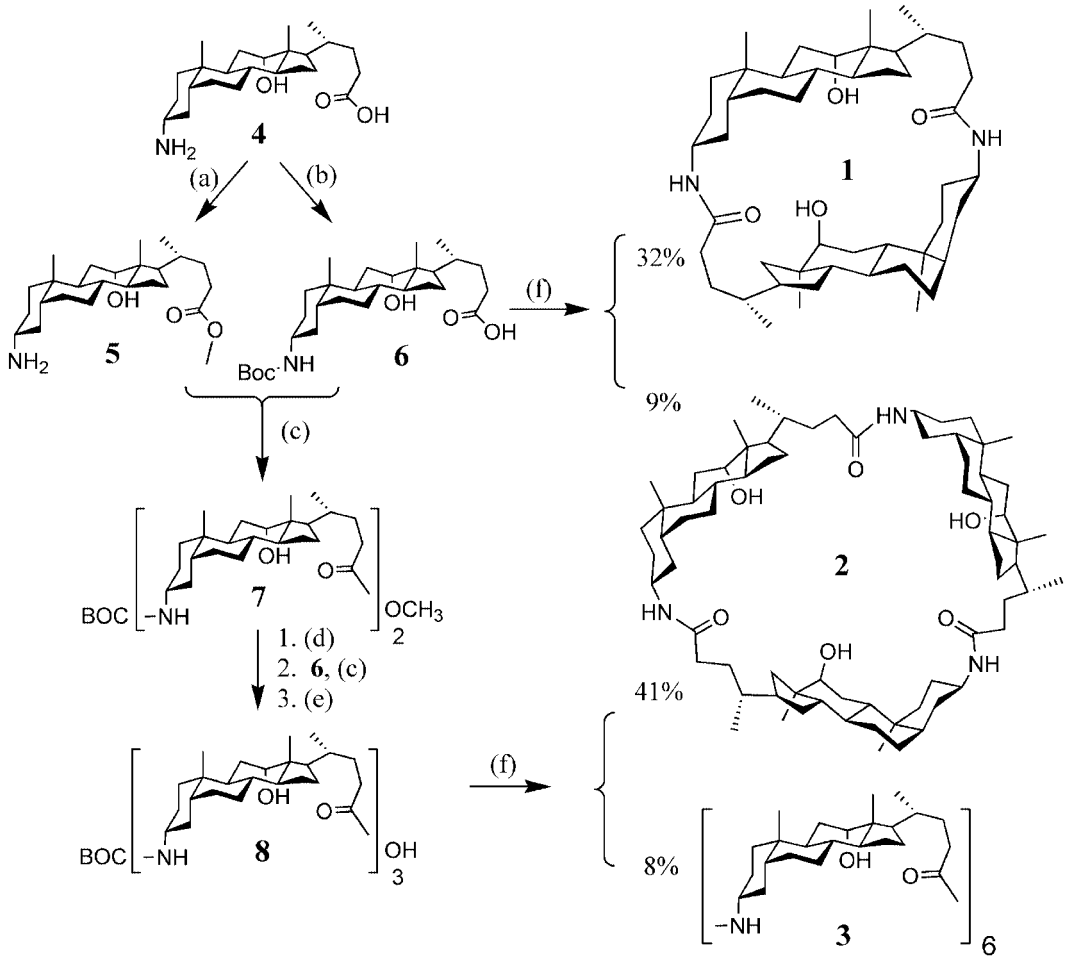

Scheme 2.

the macrocycle **2** (41% in the cyclization step). Even the cyclic hexamer **3** could be isolated from the reaction mixture after chromatography.

Structure of 1 in Solution and in the Solid State

NMR data suggest that the macrocycle **1** adopts a C_2-symmetrical form in solution. More information was obtained from a solid-state structure of crystals of **1** grown from dichloromethane/methanol. The X-ray diffraction pattern confirms a C_2-symmetrical macrocycle (Figure 1).

The two steroid parts in **1** are arranged so that the concave faces of the steroids form a small cleft. The cleft is obviously too small to encapsulate organic molecules. However, two water and two methanol molecules are fixed at the upper surface of the cleft. A net of hydrogen bonds involving the amide NH and the 12-OH groups of the steroidal part fixes the guest molecules (Figure 1).

Structure of 2 in Solution

The NMR spectrum of the trimeric macrocycle **2** in chloroform is consistent with a structure of averaged C_3 symmetry. NOE data and vicinal coupling constants point to an antiperiplanar orientation of the NH–CH(3) hydrogen atoms, also found in other 3-aminocholanic amides.[13] The chemical shift of the NH proton signal (δ = 5.2 ppm in chloroform) does not indicate strong hydrogen bonding. NOE contacts between topologically distant hydrogen atoms are not observed – all together, the NMR spectroscopic data give no indication for a preferred rigid conformation in solution.

A Monte Carlo search for structures of low energy of **2** produces some additional information. The calculation within Macromodel[14] using the Amber force field visited 5000 structures and found twenty structures within 20 kJ/mol of a global minimum by rotating the flexible dihedral angles in each of the three C20–C24 side chains of **2**. An overlay of these twenty structures is given in Figure 2 (left). A quite similar picture is obtained, when a 10 ns stochastic molecular dynamic (md) simulation at 300 K is performed (Figure 2, right) Obviously, the macrocycle **2** is not locked in a rigid single conformation but populates several different geometries of low energy. However, the overlay of the structures of low energy still exhibits a cavity, so one can expect that small organic guests could be encapsulated.

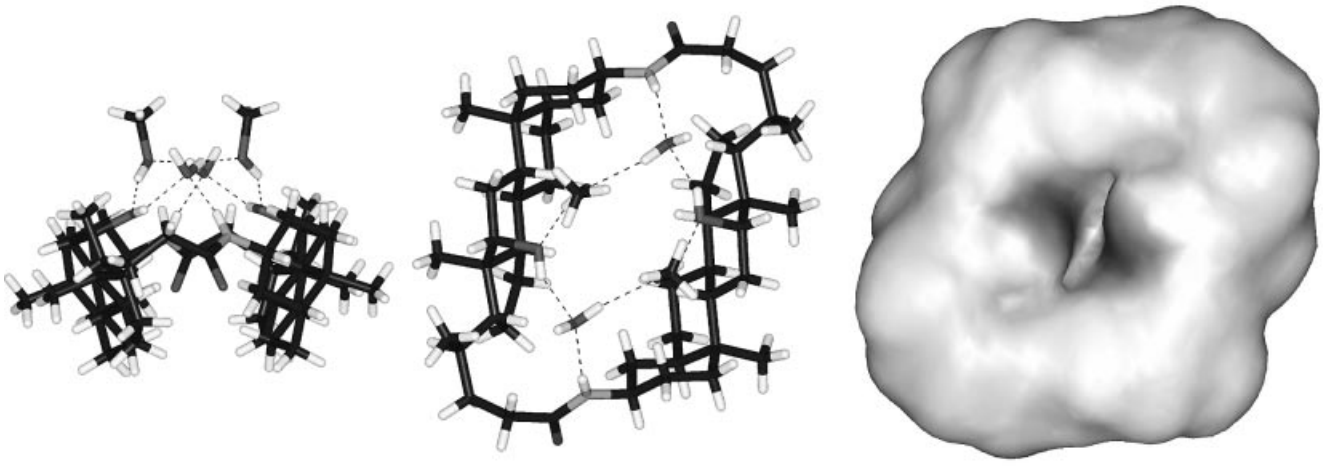

Figure 1. Solid-state structure of cyclo(3-aminodeoxycholic amide)$_2$ (**1**). The dashed lines of the stick representations indicate hydrogen bonding to attached water and methanol molecules. The molecular surface of the macrolactam (right) is obtained if the water and methanol molecules are removed. It illustrates that the cavity provided by **1** is too small to encapsulate molecular guests.

As a first test for the ability of **2** to complex organic substrates, 1 equiv. of β-dodecylglucopyranose was added to a 10 mM solution of **2** in chloroform. The host **2** is not deliberately designed to bind carbohydrates (compared to other systems[15]) but changes of the NMR chemical shifts of the proton signals of the steroidal macrocycle and of the carbohydrate were observed. Notable, the chemical shift of the signal of the three equivalent NH protons of **2** moves to lower field by 0.4 ppm. In addition, the characteristic signal pattern of the diastereotopic protons of the CH_2CON– group of the steroid part changes. A few weak intermolecular NOE contacts were observed between the carbohydrate and the steroidal host (see Supporting Information). However, the three steroid units in the complex of **2** with the carbohydrate are equivalent according to the NMR spectra; thus, the movement of the C_1-symmetrical carbohydrate guest within a cavity of averaged C_3 symmetry has to be fast on the NMR time scale.

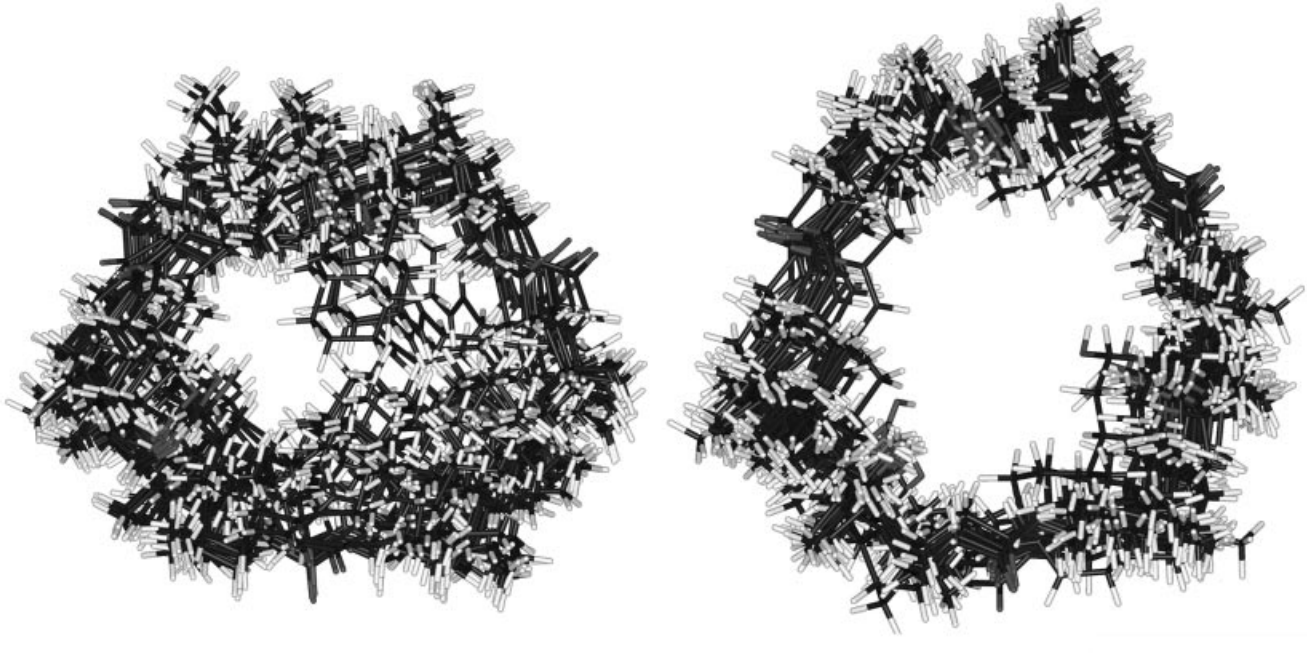

Figure 2. Left: Overlay of structures of low energy of **2** found by a Monte Carlo search within the Amber force field (Macromodel). Rotation around 12 sp^3–sp^3 bonds of the side chains C20–C24 of the macrocycle. 5000 structures were visited during the calculation, twenty structures with energies within 20 kJ/mol of the global minimum are shown. Right: Overlay of structures of **2** visited during a 10 ns molecule dynamic simulation at 300 K in chloroform [semianalytical treatment of solvation using the generalized Born equation (GB/SA)]. Twenty structures are shown, sampled at time intervals of 500 ps.

Table 1. X-ray structure determination of **1** and **2**.

	1	**2**
Empirical formula	$C_{48}H_{78}N_2O_4 \cdot 2(CH_4O) \cdot 2(H_2O)$	$2(C_{72}H_{117}N_3O_6) \cdot 3(H_2O)$
Formula mass	847.24	2289.38
Temperature	203(2) K	163(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system, space group	monoclinic, *C*2	monoclinic, *P*21
Unit-cell dimensions	a = 19.927(5) Å, b = 11.156(3) Å, c = 13.998(4) Å α = 90°, β = 129.443(7)°, γ = 90°	a = 17.525(4) Å, b = 25.939(6) Å, c = 23.895(6) Å α = 90°, β = 99.573(5)°, γ = 90°
Volume	2403.3(11) Å^3	10711(4) Å^3
Z, calculated density	2, 1.171 Mg/m^3	2, 0.710 Mg/m^3
Absorption coefficient	0.077 mm^{-1}	0.048 mm^{-1}
F(000)	932	2520
Crystal size	0.25 × 0.20 × 0.15 mm	0.37 × 0.31 × 0.26 mm
θ range for data collection	1.88–25.13°	1.55–22.50
Limiting indices	$-23 \le h \le 19$, $-13 \le k \le 13$, $-8 \le l \le 16$	$-18 \le h \le 18$, $-27 \le k \le 27$, $-25 \le l \le 25$
Reflections collected/unique	6375/4177 [R(int) = 0.0305]	85028/27954 [R(int) = 0.0663]
Completeness to θ	25.13° (99.7%)	22.50° (99.9%)
Refinement method	full-matrix least squares on F^2	full-matrix least squares on F^2
Data/restraints/parameters	4177/3/284	27954/1/1487
Goodness-of-fit on F^2	0.996	0.933
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0410, wR_2 = 0.0994	R_1 = 0.0785, wR_2 = 0.1927
R indices (all data)	R_1 = 0.0523, wR_2 = 0.1063	R_1 = 0.1076, wR_2 = 0.2099
Absolute structure parameter	0.5(11)	1.0(11)
Extinction coefficient	0.0019(6)	0.0009(2)
Largest difference peak/hole	0.179/–0.215 e·Å^{-3}	1.143/–0.616 e·Å^{-3}

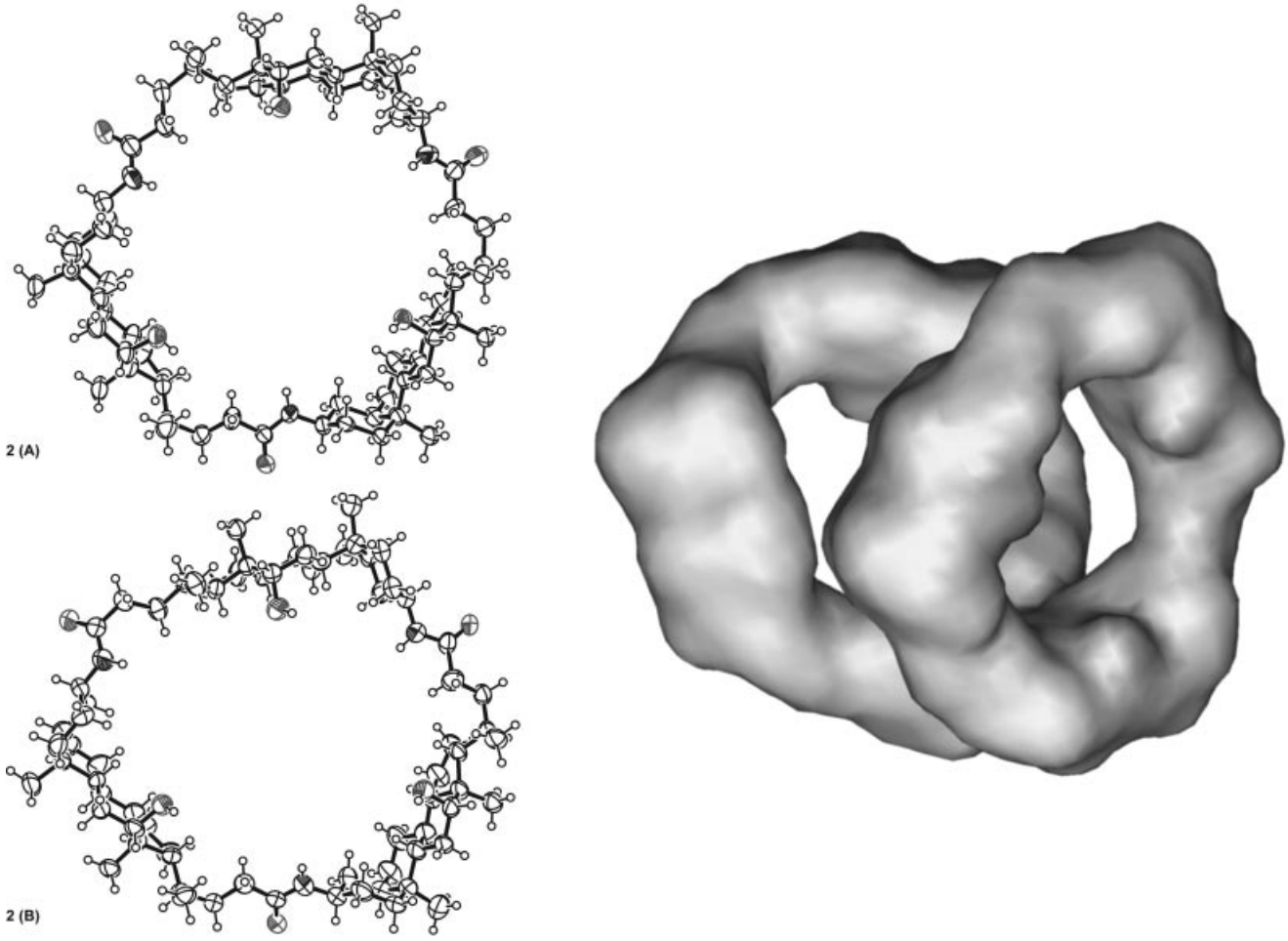

Figure 3. Conformations **2(A)** and **2(B)** found in the crystal structure of the macrocycle **2**. The ORTEP drawings (left) represent 50% of the atoms' thermal probability. The surface drawing (right) shows the relative orientation of the two macrocycles in the crystal. The structure contains large hollows filled by disordered solvent molecules (dioxane, water).

Solid-State Structure of 2

The cyclic trimer **2** crystallizes from dichloromethane/dioxane in colorless prisms. The X-ray diffraction pattern could not be resolved to a satisfactory *R* value (*R* = 19.2%) due to the substantial amount of included, partially mobile, solvent molecules (mostly dioxane and water). The application of the squeeze algorithm[16] which corrects for density identified in solvent-accessible areas, locates, however, the atoms of the macrocyclic rings with sufficient accuracy (*R* = 7.9%, see Table 1). Two slightly different conformations of **2** are found in the unit cell as shown in Figure 3.

The structures of **2(A)** and **2(B)** differ only slightly. The dihedral angle (C–C–C–N) at one of the three CH_2CH_2CONH groups in **2(B)** has a value of –59° reflecting a *syn* arrangement instead of the *anti* orientation (–168°, +172°) found at the other two CH_2–CO groups of **2(B)**. All three C–C–C–N dihedral angles of the CH_2–CO groups of **2(A)** adopt also the *anti* conformation. The cavity of **2(B)** is somewhat reduced compared to that of **2(A)** but both structures have still large cavities with diameters of 7–8 Å. The hydroxy groups at the α-surface of the cholanic acids and the NH groups of the amides are oriented inward in both structures. The CO groups and the lipophilic β-side of the cholanic acids build the outer surface. The cavities are filled with disordered dioxane molecules in the solid state – it can be expected that other molecular guests of complementary size will also fill the cavity of **2**.

Conclusions

The work presented here describes the first macrolactams prepared from the parent 3α-aminocholanic acid skeleton. The linear derivative **6** of 3α-aminodeoxycholanic acid and the linear olgioamide **8** cyclize on activation to the macrolactams **1** and **2** in high yields, suggesting the linear structures are preorganized to ease ring closure. The solid-state structures of **1** and **2** have been determined by X-ray diffraction: The concave polar surfaces of the steroid parts line the inner side of both macrocycles. The small cyclic dimer **1** does not exhibit an open cavity and binds "side on" polar solvent molecules. The large cyclic trimer **2** provides a large cavity which may be filled by solvent molecules or additional guests of complementary shape and polarity.

The cavity of **2** does obviously not collapse when the rigid steroid parts are directly connected via amide bonds. Corresponding macrolactams prepared from steroidal amino acids and natural amino acids adopt folded structures with intramolecular hydrogen bonds and do not provide such open cavities.[13]

We are looking forward to synthesize derivatives of **2** with substituted hydroxy groups pointing to the center of the cavity and being able to encapsulate and transform molecular guests.

Experimental Section

General Remarks: NMR spectra were recorded with Bruker DRX 400 and 600 MHz spectrometers. Only those NMR signals are listed below which could be unambiguously assigned (proton signals of the steroidal skeleton, appearing in the region of strong overlap between δ = 1 and 2 ppm, are not listed). FAB mass spectra were obtained with a VG AutoSpec, MALDI mass spectra were recorded with a VOYGER-DE (RP Biospectrometry). CCDC-271525 (for **1**) and -271526 (for **2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

Methyl 3α-Aminodeoxycholate Hydrochloride (5): 3α-Aminodeoxycholic acid (**4**)[17,18] (12 g, 30.6 mmol) was suspended in methanol (300 mL) and cooled to 0 °C. Thionyl chloride (4 mL) was added dropwise, the reaction mixture was heated to reflux for 3 h and stirred at 25 °C for 12 h. The solvent was removed in vacuo; excess thionyl chloride was removed by adding methanol and concentrating the mixture in vacuo three times. The remaining material was suspended in *tert*-butyl methyl ether, filtered and dried in vacuo. Yield: 11.04 g (81%), white solid. m.p. 245–250 °C (dec.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 [m (broad), 3 H, NH_3^+], 3.92 (m, 1 H, 12-H), 3.63 (s, 3 H, CO_2CH_3), 3.24 [m (broad), 1 H, 3-H], 2.39–2.31 and 2.27–2.16 (m, 2 H, 23-H), 0.94 (d, 3 H, 21-H), 0.90 (s, 3 H, 19-H), 0.64 (s, 3 H, 18-H). MS (EI, 70 eV): *m*/*z* (%) = 405 (16) [M – HCl]$^+$, 390 (21); 370 (15); 355 (8%); 331 (16%). $C_{25}H_{44}NO_3Cl \times 1{\cdot}5H_2O$ (469.1): C 64.01, H 10.10, N 2.98; found C 63.92, H 10.38, N 2.74. The compound has been already reported as the free base.[19]

3α-(*tert*-Butoxycarbonylamido)deoxycholic Acid (6): 3α-Aminodeoxycholic acid (**4**) (2.5 g, 6.4 mmol) and sodium hydrogen carbonate (0.54 g, 6.4 mmol) were dissolved in water (7 mL), di-*tert*-butyl dicarbonate (1.5 g, 7 mmol) in dioxane (14 mL) was added, the mixture was stirred at room temperature for 12 h, acidified with HCl (1 M) at 0 °C and extracted with ethyl acetate. The organic layer was washed with aqueous sodium hydrogen carbonate and water and dried with sodium sulfate. The solvent was removed in vacuo and the remaining material (2.15 g, 4.37 mmol, 68%, m.p. 103–106 °C) was used directly in the next steps. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 11.86 [s (broad), 1 H, COOH], 6.65 (d, 1 H, Boc-NH), 4.11 (d, 1 H, 12-OH), 3.78 (m, 1 H, 12-H), 3.17 [m (broad), 1 H, 3-H], 2.25–2.17 and 2.11–2.05 (2 m, 2 H, 23-H), 1.35 [s, 9 H, Boc-$(CH_3)_3$], 0.90 (s, 3 H, 19-H); 0.85 (d, 3 H, 21-H); 0.59 (s, 3 H, 18-H); $C_{29}H_{49}NO_5$ (491.7): C 70.84, H 10.04, N 2.85; found C 70.43, H 9.77, N 2.67.

General Synthetic Procedure (c): See Scheme 2. Triethylamine (1 mL), EDC (1.5 mmol) and 1-hydroxybenzotriazole (1.5 mmol) were added to a solution of the amino compound (1 mmol) and the carboxylic acid (1 mmol) in dichloromethane (30 mL). The reaction mixture was stirred at room temperature for 2 d, than diluted with ethyl acetate (100 ml), washed with aqueous solutions of potassium hydrogen sulfate (5%), sodium hydrogen carbonate (saturated) and brine. The organic phase was dried with sodium sulfate, the solvents were removed in vacuo and the residual material was either purified or used directly in the next step.

General Synthetic Procedure (d): See Scheme 2. The *N*-Boc-aminocholanic acid derivative (0.25 mmol) was dissolved in dichloromethane (15 mL), trifluoro acetic acid (7.5 mL) was added and the solvents were removed in vacuo. The remaining solid was used in the next steps without further purification.

General Synthetic Procedure (e): See Scheme 2. The methyl ester (1 mmol) was dissolved in methanol (60 mL), aqueous KOH (1 M, 5 mL) was added and the mixture stirred at room temperature for

2 d. The solvent was removed at low pressure, the residue taken up in water, tetrahydorofuran was added until the complete material had been dissolved and the mixture was acidified with HCl (1 M). The solution was extracted with either ethyl acetate or chloroform depending on the solubility of the free acid. The separated organic phase was dried with sodium sulfate, the solvent was removed in vacuo and the remaining acid characterised and used in subsequent operations.

General Synthetic Procedure (f). Cyclisation:[20] See Scheme 2. The *N*-Boc-protected aminocholanic acid (1 mmol) was dissolved in dichloromethane (10 mL), pentafluorophenol (1,5 mmol) was added, the mixture cooled to –20 °C and a solution of dicyclohexyl carbodiimide (1.25 mmol) in dichloromethane (5 mL) was added slowly. The precipitated urea was filtered off after 12 h, trifluoroacetic acid (10 mL) was added to the filtrate at 0 °C and the solvents were removed in vacuo after 1 h. Residual trifluoroacetic acid was removed by taking up the material in dichloromethane and removing the solvent in vacuo several times. The residue was taken up in dichloromethane (10 mL) and chloroform (240 mL), aqueous sodium hydrogen carbonate (50 mL, 1 M) was added and the mixture stirred at room temperature for 3 d. The organic phase was separated, washed with aqueous solutions of NaOH (0.1 M), $KHSO_4$ (5%), $NaHCO_3$ (saturated) and brine and dried with sodium sulfate. The solvents were removed in vacuo and the residual material was purified by chromatography (see below).

Methyl 3α′-(*tert*-Butoxycarbonylamido)deoxycholyl-3α-amidodeoxycholate (Boc-Dcs-Dcs-OMe) (7): Compounds **6** (0.99 g, 2.0 mmol) and **5** (0.89 g, 2.0 mmol) were used in procedure (c). The material was recrystallized from *tert*-butyl methyl ether/*n*-hexane. Yield: 1.65 g, 93%. White powder; m.p. 144–146 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.62 (d, 1 H, DCS-amide-NH); 6.64 (d, 1 H, Boc-NH); 4.17 (d, 1 H, 12-OH N-term.); 4.09 (d, 1 H, 12′-OH C-term.); 3.78 (2 m, 2 H, 12-H, 12′-H); 3.56 (s, 3 H, OCH_3); 3.48 [m (broad), 1 H, 3′-H C-term.]; 3.17 [m (broad), 1 H, 3-H N-term.]; 2.35–2.27, 2.23–2.15 (2 m, 2 H, 23′-H C-term.); 2.07–1.99, 1.93–1.87 (2 m, 2 H, 23-H N-term.); 1.35 (s, 9 H, *t*Bu CH_3); 0.90 (2 d, 6 H, 21-H, 21′-H); 0.86, 0.85 (2 s, 6 H, 19-H, 19′-H); 0.59, 0.58 (2 s, 6 H, 18-H, 18′-H). MS (FAB): *m*/*z* (%) = 901.6 (19) [M + Na]$^+$; 878.6 (3) [M]$^+$. $C_{54}H_{90}N_2O_7 \times 1H_2O$ (897.3): C 72.28, H 10.33, N 3.12; found C 72.47, H 9.94, N 3.52.

3α′′-(*tert*-Butoxycarbonylamido)deoxycholyl-3α′-amidodeoxycholyl-3α-amidodeoxycholic Acid (Boc-Dcs-Dcs-Dcs-OH) (8): The Boc group of compound **7** (1.60 g, 1.82 mmol) was removed with trifluoroacetic acid according to procedure (d) and the resulting material was coupled to the carboxylic acid **6** (0.89 g, 1.82 mmol) using procedure (c). The product was precipitated by with *n*-hexane from *tert*-butyl methyl ether. NMR spectra of that material (1.39 g) indicate, that part of the 11-OH groups of the deoxycholanic units has been converted into trifluoroacetic acid esters. The subsequent treatment with potassium hydroxide [procedure (e)] removes the trifluoroacetyl groups and cleaves the C-term. methyl ester. The material was recrystallized from dichloromethane/hexane. Yield: 1.29 g, 57%. White powder; m.p. 298–301 °C (dec.). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 11.87 [s (broad), 1 H, COOH]; 7.65 (2 d, 2 H, 2 × amide-NH); 6.68 (d, 1 H, Boc-NH); 4.18, 4.17, 4.12 (3 d, 3 H, 3 × 12-OH); 3.79 (3 m, 3 H, 3 × 12-H); 3.48 [m (broad), 2 H, 3-H center and C-term.]; 3.17 [m (broad), 1 H, 3-H N-term.]; 2.24–2.17, 2.11–2.04 (2 m, 2 H, 23-H C-term.); 2.06–1.99, 1.91–1.84 (2 m, 4 H, 23-H center and N-term.); 1.35 (s, 9 H, *t*Bu CH_3); 0.91–0.89 (3d, 9 H, 3 × 21-H); 0.86–0.85 (3 s, 9 H, 3 × 19-H); 0.59, 0.58, 0.57 (3 s, 9 H, 3 × 18-H). MS (FAB): *m*/*z* (%) = 1261.1 (9) [M + Na]$^+$, 1239.1 (3) [M + H]$^+$, 1139.1 (15). $C_{77}H_{127}N_3O_9 \times 4H_2O$ (1310.9): C 70.55, H 10.38, N 3.20; found C 70.12, H 10.21, N 3.05.

Cyclisation of 6 Producing 1 and 2: Compound **6** (0.49 g, 1 mmol) was used as starting material in the cyclisation procedure (f). The crude reaction products (0.46 g) were separated on a Silicagel 32–63 (ICN) using the solvent mixtures tetrahydrofurane/*n*-hexane/methanol (2:9:5, then 4:8:5.5). Mixed fractions containing **1** and **2** were again separated using dichloromethane/*n*-hexane/methanol (3:9:5, then 4:4:2). Yield of **1**: 0.12 g, 32%; yield of **2**: 0.034 g, 9%. Crystals of **1** were grown from dichloromethane/methanol and used for X-ray diffraction.

Cyclisation of 8 Producing 2 and 3: Compound **8** (0.50 g, 0.40 mmol) was used in the cyclisation procedure (f). The crude reaction products (0.57 g) were separated on a Silicagel 32–63 (ICN) column using first chloroform, then dichloromethane/*n*-hexane/methanol (2:12:0.5, then 5:5:1). Yield of **2**: 0.185 g, 41%; yield of **3**: 0.042 g, 9%. Crystals of **2** used in X-ray diffraction were grown from dichloromethane/dioxane.

Cyclo(3α-aminodeoxycholic amide)$_2$ (1): Colorless prisms; m.p. > 335 °C (dec.). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.71 (d, 2 H, NH); 3.83 (d, 2 H, 12-OH); 3.60 (m, 2 H, 12-H); 3.48 [m (broad), 2 H, 3-H]; 0.96 (d, 6 H, 21-H); 0.88 (s, 6 H, 19-H); 0.57, (s, 6 H, 18-H). MS (FAB): *m*/*z* (%) = 769.6 (14) [M + Na]$^+$, 747.6 (7) [M + H]$^+$, 711.6 (36). $C_{48}H_{78}N_2O_4 \times 2CH_3OH \times 2H_2O$ (847.2): C 70.88, H 10.71, N 3.31; found C 70.41, H 10.67, N 3.08.

Cyclo(3α-aminodeoxycholic amide)$_3$ (2): White powder (precipitate from chloroform); m.p. >269–271 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.21 (d, 3 H, NH); 3.97 (m, 3 H, 12-H); 3.76 [m (broad), 3 H, 3-H]; 2.19–2.13, 2.09–2.03 (2 m, 6 H, 23-H); 0.98 (d, 9 H, 21-H); 0.90 (s, 9 H, 19-H); 0.67, (s, 9 H, 18-H). MS (FAB): *m*/*z* (%) = 1142.9 (15) [M + Na]$^+$, 1120.9 (25) [M + H]$^+$, 1102.9 (3); 1084.9 (3); 1066.9 (17). $C_{72}H_{117}N_3O_6 \times 4H_2O$ (1192.8): C 72.50, H 10.56, N 3.52; found C 72.52, H 10.56, N 3.20.

Cyclo(3α-aminodeoxycholic amide)$_6$ (3): White powder (precipitate from chloroform); m.p. 247–250 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.88 (d, 6 H, NH); 3.96 (m, 6 H, 12-H); 3.80 [m (broad), 6 H, 3-H]; 2.11 (m, 12 H, 23-H); 0.98 (d, 18 H, 21-H); 0.91 (s, 18 H, 19-H); 0.67, (s, 18 H, 18-H). MS (MALDI-TOF): *m*/*z* (%) = 2268, the ion [M + Na]$^+$ is expected at 2264, errors of 4–6 mass units are common for the experimental setup used. $C_{144}H_{234}N_6O_{12} \times 10H_2O$ (2421.6): C 71.42, H 10.57, N 3.47; found C 71.35, H 10.62, N 3.11.

Supporting Information: ^{1}H NMR spectra of the macrolactam **2** and of the complex with β-1-dodecylglucopyranose (Figure S1), 2D-ROESY NMR spectrum of an equimolar solution of **2** and β-1-dodecylglucopyranose (Figure S2), low-energy structure of the complex obtained by Monte Carlo simulations (Figure S3).

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