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Dimeric Cholaphanes with Oxamide Spacers

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Summary. Two new dimeric cholaphanes with oxamide spacers were prepared. The spacers bind two identical steroidal subunits through positions 3,3′ and 24,24′ (head-to-head dimer) or positions 3,24′ and 3′,24 (head-to-tail dimer).

Keywords. Bile acids; Cholaphane; Gelator; Oxamides; Supramolecular chemistry.

Introduction

Bile acids and its derivatives are used as versatile building blocks for design and synthesis of molecular receptors, transporters or enzyme models [1–3]. In our previous paper [4] we described the synthesis of new acyclic dimers of cholic acid with oxamide and hydrazide spacers. Now we report the synthesis of two new dimeric isomeric cholaphanes **8** and **31** with oxamide spacers (Scheme 1).

Cholaphanes are bile acid-based macrocycles consisting of two to four bile acid subunits joined together by very different atom groups as spacers. The frameworks of dimeric cholaphanes are more rigid and pre-organized for strong and selective binding of ''guests'' in comparison with acyclic dimeric structures [2]. This kind of supramolecular hosts can be synthesized by various methods, preferably by macrolactonization [6, 7] or macrolactamization [8, 9]. Recently, olefin metathesis has been applied in the synthesis of cholaphanes [10].

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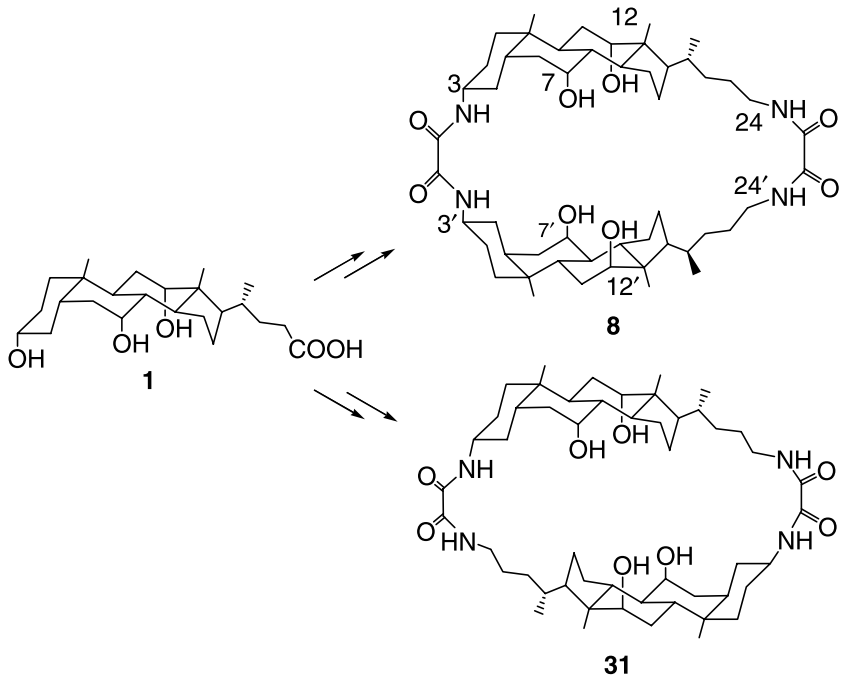
Results and Discussion

The cholaphane **8** was obtained according to Scheme 2. As a starting material in this synthesis compound **2a** was used, which was one of the intermediates in the preparation of the acyclic ''head-to-head'' dimer with oxamide spacer [4]. During the reduction of two methyl ester groups in **2a** with $LiAlH_4$ it was necessary to maintain the reaction temperature below 15°C due to partial reduction of some acetate groups. Diiodide **4** was obtained from diol **3** by treatment with a iodine/triphenylphosphine complex in benzene/pyridine solution and converted into diazide **5** by substitution with azide ion in *N*-methylpyrrolidone/acetic acid solution. The reduction of **5** with triphenylphosphine gave diamine **6** in good yield. The key step of this procedure was the reaction of **6** with oxalyl chloride. Cyclic dioxamide **7** was obtained in moderate yield when a very dilute (below 0.2%) solution of the substrate **6** was used. Under these conditions the cyclization appeared to be a favoured process compared with an intermolecular reaction. In the more concentrated solutions highly polar products (probably linear tetrameric or higher structures with terminal amine and carboxylic groups) predominated.

The second ''head-to-head'' cholaphane designed was 24,24′-bisnor analog of **8**. Its synthesis required to remove two carbon atoms from both side chains of **2a**. The synthesis plan assumed hydrolysis of methyl esters followed by a *Hunsdiecker* type reaction [11], but only the first step of this project (**2a** to

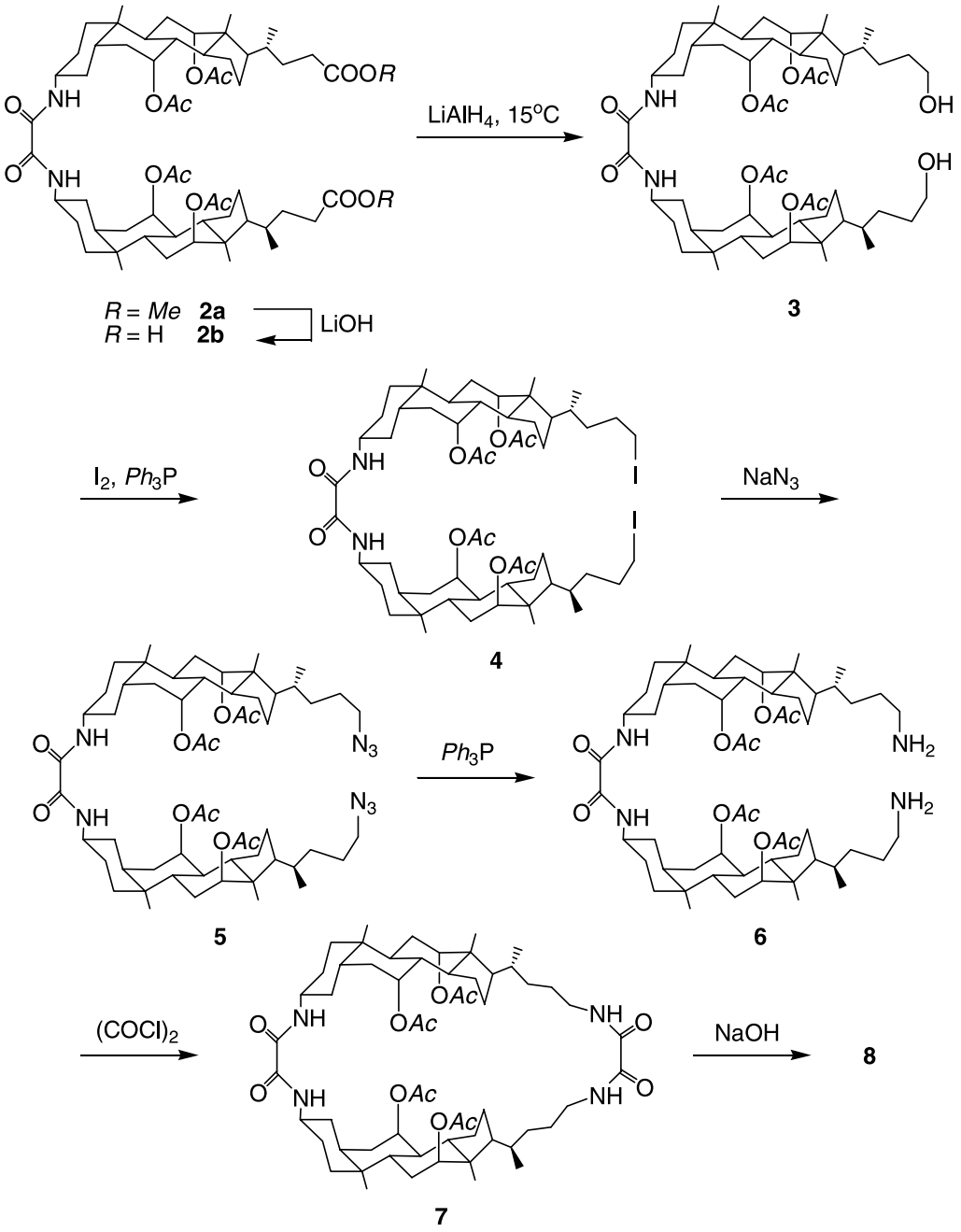


Scheme 1

2b conversion) proved successful. The diacid **2b** obtained in this reaction showed strong gelating behavior in relation to a number of organic solvents, such as chlorinated hydrocarbons (dichloromethane, chloroform, and carbon tetrachloride), benzene, ethyl acetate, methanol, and mixtures of ethyl acetate with methanol and benzene. Only in acetone it was sparingly soluble, but this is not an appropriate solvent for a radical reaction. For this reason the transformation of diacid **2b** into the corresponding diiodide could not be successfully carried out, since the reaction usually requires solubility in non-polar solvents.

The serious problem in the synthesis of cholaphane **31** was the head-to-tail coupling reaction between the two steroidal subunits. In the first approach it was planned to create a temporary ester bond between carboxylic group of the first subunit and C(3′) hydroxyl group of the second. After formation of the oxamide bond between C(3) and C(24′) carbon atoms, the auxiliary ester bond should be removed by hydride reduction. The question was if C(7), C(12), C(7′), and C(12′) acetate groups would resist to such conditions. To check the susceptibility of various ester bonds to $LiAlH_4$ reduction the model ester **11** (Scheme 3) was prepared [12] and subjected to reduction. The results of $LiAlH_4$ reduction in *THF* at 0°C are shown in Scheme 3. However, no desired selectivity favoring cleavage of a central ester group in **11** was observed. The expected product **16** was obtained in 20% yield only. Due to the failure of this approach an alternative route to dimer **31** was explored. In the first stage the C(24)-amine **22** was synthesized according to Scheme 4.

The 3α-hydroxyl group in the substrate **10** was protected as a *TBDMS* ether to prevent the C(3) position from iodination reaction (the acetate as a protecting group was useless due to susceptibility to the simultaneous partial reduction together with the methyl ester in the side chain). The 24-iodide with free 3α-hydroxyl group (**19**) was obtained by displacement of the side chain OH group with iodine using an I_2/triphenylphosphine complex. In the next step iodide **19** was substituted with azide followed by acetylation of the free OH group at C-3. The reversed order of transformations proved ineffective since iodide was easily substituted by acetate (compound **19a**), even under mild acetylation conditions. The reduction of azide **20** with triphenylphosphine in *THF* gave amine **22**.

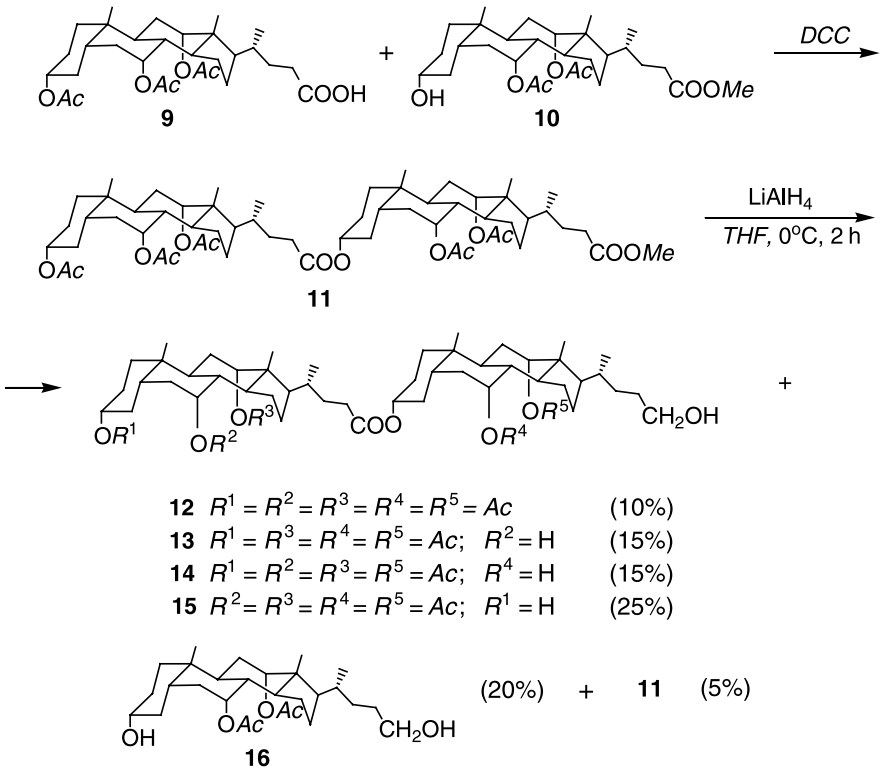


Scheme 2

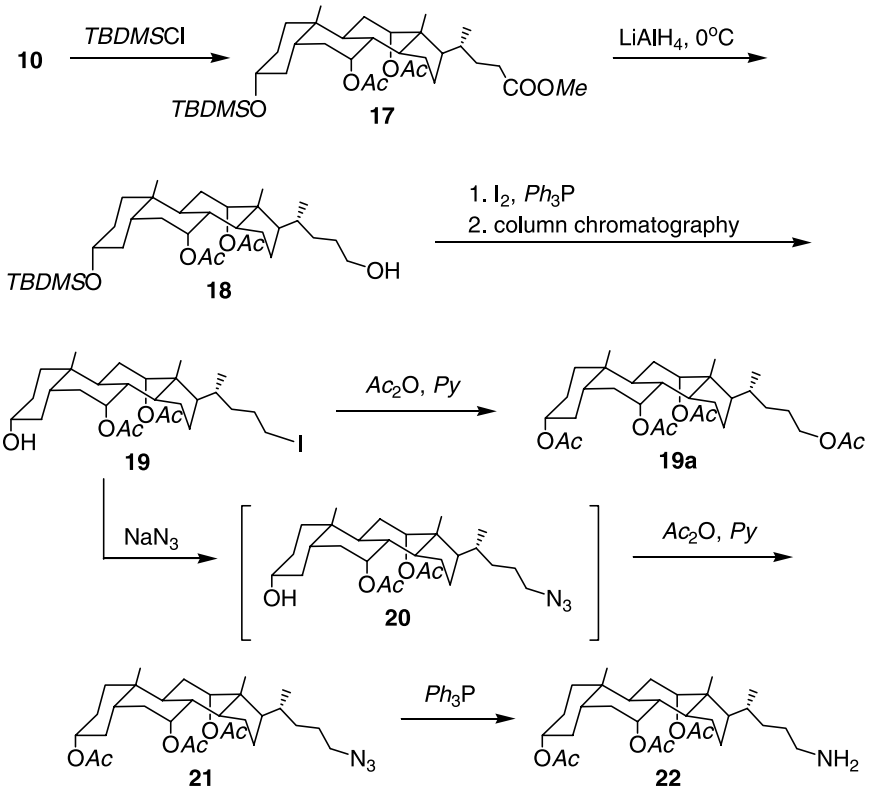
In the meantime amine **23** (Scheme 5) was prepared as described in our previous paper [4] and treated with excess oxalyl chloride. The intermediate acyl chloride **24** was immediately subjected to the reaction with **22** to form the ''head-to-tail'' acyclic dimer **25**. All transformations leading from diester **25** to the final cholaphane **31** were carried out analogously as in the case of **8** (Scheme 2).

Conclusions

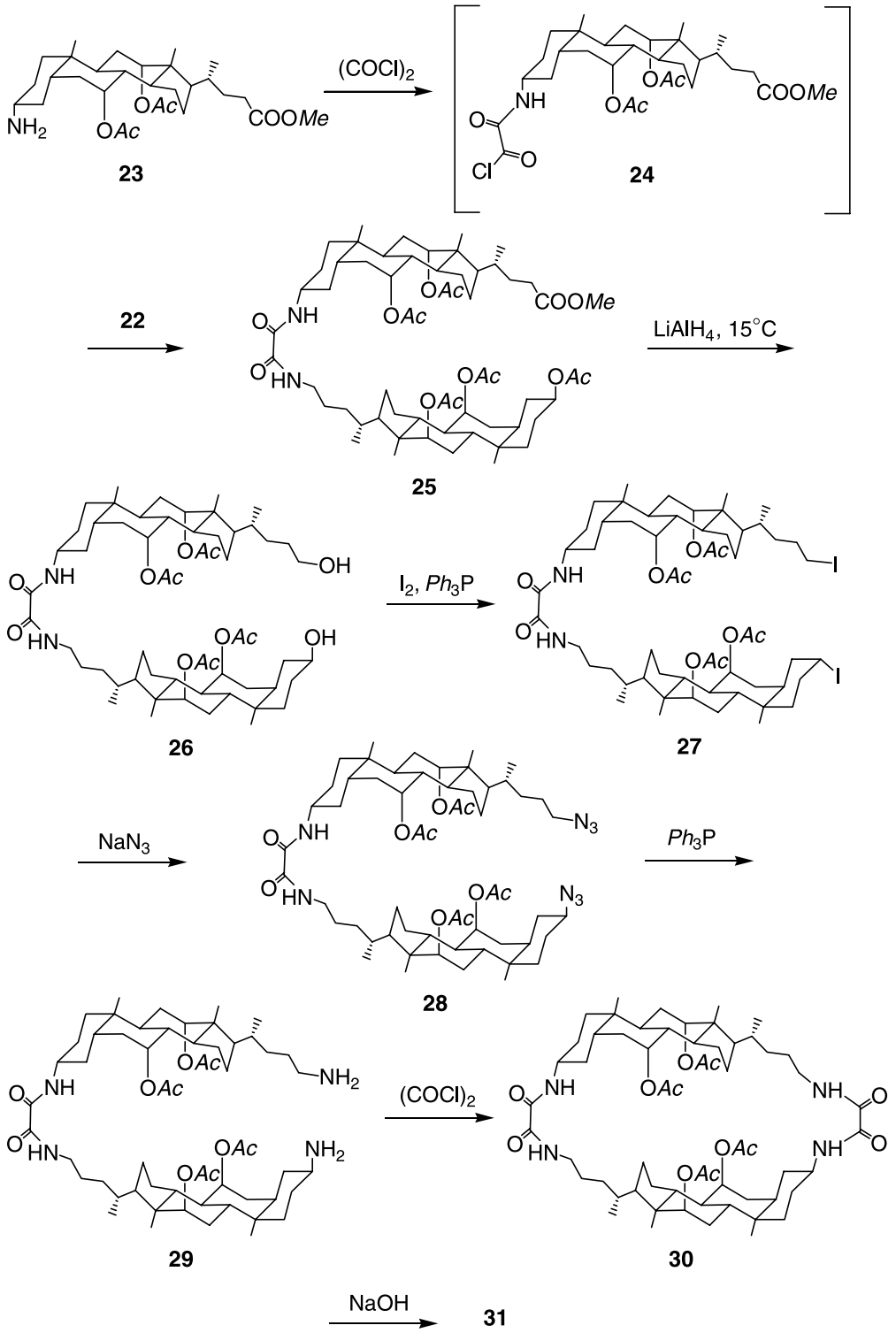
Two new dimeric cholaphanes, head-to-head isomer **8**, and head-to-tail isomer **31**, were obtained according to the procedures shown in Schemes 2, 4, and 5. Both these compounds are expected to be good supramolecular hosts for selected ions and small molecules. The physicochemical studies for guest ions and molecules complexation properties of these compounds are under way.



Scheme 3



Scheme 4



Scheme 5

Experimental

Melting points were determined on a *Kofler* apparatus of the *Boëtius* type. NMR spectra were taken with a Bruker AC 200F spectrometer with *TMS* as internal standard. Infrared spectra were recorded on a Nicolet series II Magna-IR 550 FT-IR spectrometer. Mass spectra were obtained with AMD-604 spectrometer. The reaction products were isolated by column

chromatography performed on 70–230 mesh silica gel (*J.T. Baker*). Thin-layer chromatograms were developed on aluminum TLC sheets precoated with silica gel F_{254} (*Merck*) and visualized with 50% H_2SO_4 after heating. All solvents were dried and freshly distilled prior to use. Cholic acid (**1**) was purchased from ABCR GmbH & Co. KG and it was used without further purification. 3,7,12-Triacetylcholic acid (**9**) and methyl 7,12-diacetylcholate (**10**) were prepared according to known procedures [13].

N,N′-Di(5β-cholane-7α,12α,24-triol 7,12-diacetate)-3α,3′α-oxamide (**3**, $C_{58}H_{92}N_2O_{12}$)

To a solution of 1.60 g **2a** (1.50 mmol) in 50 cm^3 anhydrous *THF* at 15°C 140 mg $LiAlH_4$ (3.68 mmol) were added portionwise with vigorous stirring under *Ar*. The progress of the reaction was controled with TLC. When all of the substrate disappeared (about 0.5 h), the excess of the reducing agent was carefully quenched with a few drops H_2O and the precipitate was filtered off. The organic layer was dried ($MgSO_4$) and the solvent was removed. The dimer **3** was purified by column chromatography (elution with 2% methanol in $CHCl_3$) to afford 0.92 g (61%) of the pure product **3**. Colorless crystals; mp 177–179°C (*n*-hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.38$ (d, $J = 8.60$ Hz, 2H, 2NH), 5.10 (m, 2H, 2 12β-H), 4.91 (m, 2H, 2 7β-H), 3.61 (m, 2H, 2 3β-H and t, 4H, 2CH_2OH), 2.18 (s, 6H, 2 12-CH_3CO), 2.07 (s, 6H, 2 7-CH_3CO), 0.94 (s, 6H, 2 19-CH_3), 0.84 (d, $J = 6.32$ Hz, 6H, 2 21-CH_3), 0.73 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.6$ (2C), 170.3 (2C), 158.9 (2C), 75.3 (2CH), 70.6 (2CH), 63.3 (CH_2), 49.9 (2CH), 47.4 (2CH), 44.9 (2C), 43.2 (2CH), 41.3 (2CH), 37.6 (2CH), 35.3 (CH_2), 35.2 (CH_2), 34.7 (2CH), 34.2 (2C), 31.5 (CH_2), 31.2 (CH_2), 29.1 (CH_2), 28.8 (2CH), 27.4 (CH_2), 27.2 (CH_2), 25.5 (CH_2), 22.7 (CH_2), 22.6 (CH_3), 21.6 (CH_3), 21.5 (CH_3), 17.8 (CH_3), 12.1 (CH_3) ppm; IR ($CHCl_3$): $\bar{\nu} = 3672$, 3513, 3390, 1724, 1670, 1255, 1024 cm^{-1}.

N,N′-Di(24-iodo-5β-cholane-7α,12α-diol 7,12-diacetate)-3α,3′α-oxamide (**4**, $C_{58}H_{90}I_2N_2O_{10}$)

To a solution of 1.38 g I_2 (5.4 mmol) in 20 cm^3 anhydrous benzene 1.38 g triphenylphosphine (5.4 mmol) and 0.88 cm^3 anhydrous pyridine (11 mmol) were added and the mixture was stirred at room temperature for 15 min. Then 0.92 g **3** (0.91 mmol) were added and the reaction mixture was heated at 40°C for 3 days. After this time benzene and pyridine were removed *in vacuo* and the residue was subjected to column chromatography. Pure diiodide **4** was eluted with hexane/ethyl acetate = 85/15 (872 mg, 78% yield). Colorless crystals; mp 170–172°C (*n*-hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.41$ (d, $J = 9.12$ Hz, 2H, 2NH), 5.10 (m, 2H, 2 12β-H), 4.91 (m, 2H, 2 7β-H), 3.58 (m, 2H, 2 3β-H), 3.14 (m, 4H, 2CH_2I), 2.19 (s, 6H, 2 12-CH_3CO), 2.07 (s, 6H, 2 7-CH_3CO), 0.94 (s, 6H, 2 19-CH_3), 0.83 (d, $J = 6.31$ Hz, 6H, 2 21-CH_3), 0.74 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.4$ (2C), 170.2 (2C), 158.9 (2C), 75.2 (2CH), 70.6 (2CH), 49.8 (2CH), 47.3 (2CH), 44.9 (2C), 43.2 (2CH), 41.3 (2CH), 37.6 (2CH), 36.5 (CH_2), 35.3 (CH_2), 35.2 (CH_2), 34.2 (2CH, 2C), 31.1 (CH_2), 30.0 (CH_2), 28.8 (2CH), 27.4 (CH_2), 27.1 (CH_2), 25.4 (CH_2), 22.7 (CH_2), 22.6 (CH_3), 21.6 (CH_3), 21.4 (CH_3), 17.9 (CH_3), 12.1 (CH_3), 7.6 (CH_2) ppm; IR ($CHCl_3$): $\bar{\nu} = 3389$, 1724, 1670, 1508, 1255, 1023 cm^{-1}.

N,N′-Di(24-azido-5β-cholane-7α,12α-diol 7,12-diacetate)-3α,3′α-oxamide (**5**, $C_{58}H_{90}N_8O_{10}$)

Diiodide **4** (870 mg, 0.78 mmol) was dissolved in 10 cm^3 *N*-methylpyrrolidone. Then 0.64 g NaN_3 (9.8 mmol) and 0.57 cm^3 acetic acid (10.0 mmol) were added into the flask. The reaction mixture was stirred at room temperature overnight and next poured into aqu. $NaHCO_3$. Crude product was extracted several times with benzene and combined organic layers were washed twice with water, dried ($MgSO_4$), and evaporated to dryness. Purification with column chromatography gave 510 mg **5** in 68% yield (elution with hexane/ethyl acetate = 80/20). Colorless crystals; mp 159–161°C (*n*-hexane/ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.38$ (d, $J = 8.60$ Hz, 2H, 2NH), 5.11 (m, 2H, 2 12β-H), 4.92 (m, 2H, 2 7β-H), 3.59 (m, 2H, 2 3β-H), 3.25 (m, 4H, 2CH_2N_3), 2.19 (s, 6H, 2 12-CH_3CO), 2.07 (s, 6H, 2 7-CH_3CO), 0.95 (s, 6H, 2 19-CH_3), 0.85 (d, $J = 6.20$ Hz, 6H, 2 21-CH_3), 0.74 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.4$ (2C), 170.2 (2C), 158.9 (2C), 75.1 (2CH), 70.5 (2CH), 51.7 (CH_2), 49.8 (2CH), 47.3 (2CH), 44.9 (2C), 43.2 (2CH), 41.2 (2CH), 37.6 (2CH), 35.3 (CH_2), 35.1 (CH_2), 34.5 (2CH), 34.1 (2C), 32.5 (CH_2), 31.1 (CH_2), 28.7 (2CH), 27.4 (CH_2), 27.1 (CH_2), 25.4 (CH_2), 25.3 (CH_2), 22.7 (CH_2), 22.6 (CH_3), 21.5 (CH_3), 21.4 (CH_3), 17.7 (CH_3), 12.1 (CH_3) ppm; IR ($CHCl_3$): $\bar{\nu} = 3390$, 2099, 1721, 1671, 1256, 1022 cm^{-1}.

N,N′-Di(24-amino-5β-cholane-7α,12α-diol 7,12-diacetate)-3α,3′α-oxamide (**6**, $C_{58}H_{94}N_4O_{10}$)

Diazide **5** (510 mg, 0.48 mmol) was dissolved in 12 cm^3 dry *THF* under *Ar*, then triphenylphosphine (503 mg, 1.92 mmol) was added and the mixture was stirred at 45°C for 15 min. After this time 0.144 cm^3 water (8 mmol) was added dropwise and the reaction mixture was stirred at room temperature with *TLC* control. When all of the substrate disappeared (about 1 day), the solvent was evaporated, the residue was dissolved in CH_2Cl_2, and the solution was dried over $MgSO_4$. Crude product was subjected to column chromatography to afford 380 mg (78%) **6** (elution with methanol/$CH_2Cl_2 = 1/1$ with a few drops aqu. NH_3). Colorless crystals; mp 174–176°C (methanol); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.36$ (d, $J = 8.60$ Hz, 2H, 2NH), 5.07 (m, 2H, 2 12β-H), 4.87 (m, 2H, 2 7β-H), 3.61 (m, 2H, 2 3β-H), 2.62 (m, 4H, 2CH_2NH_2), 2.14 (s, 6H, 2 12-CH_3CO), 2.03 (s, 6H, 2 7-CH_3CO), 0.91 (s, 6H, 2 19-CH_3), 0.79 (d, $J = 6.24$ Hz, 6H, 2 21-CH_3), 0.70 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.5$ (2C), 170.2 (2C), 158.7 (2C), 75.2 (2CH), 70.6 (2CH) 49.8 (2CH), 47.3 (2CH), 44.8 (2C), 43.1 (2CH), 42.3 (CH_2), 41.2 (2CH), 37.5 (2CH), 35.2 (CH_2), 35.1 (CH_2), 34.7 (2CH), 34.1 (2C), 32.7 (CH_2), 31.1 (CH_2), 29.7 (CH_2), 28.7 (2CH), 27.3 (CH_2), 27.1 (CH_2), 25.4 (CH_2), 22.6 (CH_2), 22.5 (CH_3), 21.5 (CH_3), 21.3 (CH_3), 17.7 (CH_3), 12.0 (CH_3) ppm; IR ($CHCl_3$): $\bar{\nu} = 3388$, 1723, 1670, 1508, 1255 cm^{-1}.

N,N′:N″,N‴-Di(5β-cholane-7α,12α-diol 7,12-diacetate)-3α,3′α:24,24′-dioxamide (**7**, $C_{60}H_{92}N_4O_{12}$)

To a solution of 343 mg **6** (0.34 mmol) in 200 cm^3 toluene (dried over CaH_2) 0.109 cm^3 dry pyridine (1.37 mmol) were added and the mixture was heated to 75°C. Then 0.043 cm^3 oxalyl chloride (0.50 mmol) were added dropwise with vigorous stirring and the heating was continued for 1 h. After this time a few drops of methanol were added and the solvent was removed *in vacuo*. Purification with column chromatography gave 100 mg **7** in 26% yield (elution with methanol/chloroform = 4/96). Colorless crystals; mp over 300°C with decomposition (*n*-hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.61$ (dd, $J_1 = 3.47$ Hz, $J_2 = 8.95$ Hz 2H, CH_2NH), 7.49 (d, $J = 8.15$ Hz, 2H, 2C(3)-NH), 5.01 (m, 2H, 2 12β-H), 4.86 (m, 2H, 2 7β-H), 3.61 (m, 2H, 2 3β-H), 3.30 (m, 2H, CH_2NH), 2.95 (m, 2H, CH_2NH), 2.16 (s, 6H, 2 12-CH_3CO), 2.00 (s, 6H, 2 7-CH_3CO), 0.86 (s, 6H, 2 19-CH_3), 0.82 (d, $J = 6.40$ Hz, 6H, 2 21-CH_3), 0.72 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.5$ (2C), 170.1 (2C), 159.8 (2C), 159.3 (2C), 75.7 (2CH), 70.7 (2CH) 50.6 (2CH), 45.2 (2CH), 44.9 (2C), 44.3 (2CH), 41.2 (2CH), 40.6 ($2CH_2$), 37.5 (2CH), 35.5 ($2CH_2$), 33.9 (2CH), 33.6 (2C), 33.3 ($2CH_2$), 32.4 ($2CH_2$), 30.9 ($2CH_2$), 29.3 (2CH), 27.2 ($2CH_2$), 25.6 ($2CH_2$), 25.5 ($2CH_2$), 23.8 ($2CH_2$), 22.5 ($2CH_2$), 22.3 ($2CH_3$), 21.6 ($2CH_3$), 21.5 ($2CH_3$), 17.7 ($2CH_3$), 12.1 ($2CH_3$) ppm; IR ($CHCl_3$): $\bar{\nu} = 3396$, 1724, 1674, 1514, 1256, 1022 cm^{-1}; MS (70 eV): $m/z = 1083.8$ ($M^+ + Na$).

N,N′:N″,N‴-Di(5β-cholane-7α,12α-diol)-3α,3′α:24,24′-dioxamide (**8**, $C_{52}H_{84}N_4O_8$)

To a solution of 40 mg **7** (0.038 mmol) in 8 cm^3 *THF* 2 cm^3 methanol and 2 cm^3 1 *M* NaOH were added and the reaction mixture was stirred at room temperature for 4 days. Then the content of the flask was poured into 50 cm^3 acidified H_2O and the product was extracted twice with $CHCl_3$. Pure end-product was isolated by means of column chromatography to afford 16 mg (48%) **8** (elution with methanol/chloroform = 1/9). Colorless crystals; mp 264–266°C (*n*-hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.58$ (m, 4H, $2CH_2NH$, 2C(3)-NH), 3.95 (m, 2H, 2 12β-H), 3.85 (m, 2H, 2 7β-H), 3.51 (m, 4H, 2 3β-H, CH_2NH), 3.00 (m, 2H, CH_2NH), 1.02 (d, $J = 6.46$ Hz, 6H, 2 21-CH_3), 0.89 (s, 6H, 2 19-CH_3), 0.70 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 159.8$ (2C), 159.4 (2C), 72.8 (2CH), 68.2 (2CH) 50.7 (2CH), 46.3 (2C), 45.0 (2CH), 42.3 (2CH), 41.5 (2CH), 40.7 ($2CH_2$), 39.4 (2CH), 35.8 ($2CH_2$), 34.6 (2CH), 34.1 (2C), 34.0 ($2CH_2$), 32.6 ($2CH_2$), 29.7 ($2CH_2$), 28.2 ($2CH_2$), 27.4 ($2CH_2$), 26.8 (2CH), 25.2 ($2CH_2$), 24.0 ($2CH_2$), 23.1 ($2CH_2$), 22.3 ($2CH_3$), 17.7 ($2CH_3$), 12.4 ($2CH_3$) ppm; IR ($CHCl_3$): $\bar{\nu} = 3397$, 1674, 1514, 1242 cm^{-1}; MS (70 eV): $m/z = 915.6$ ($M^+ + Na$); HRMS: calcd. mass for $C_{52}H_{84}N_4NaO_8$ 915.6187, found 915.6146.

N,N′-Di(7α,12α-diacetoxy-5β-cholan-24-oic acid)-3α,3′α-oxamide (**2b**, $C_{58}H_{88}N_2O_{14}$)

Compound **2a** (2.87 g, 2.70 mmol) was dissolved in 100 cm^3 methanol, then 0.5 cm^3 water and 0.13 g LiOH (5.4 mmol) were added. The suspension was vigorously stirred at room temperature for 2 days. After this time the mixture was treated with a few drops of diluted (1/1) HCl to *pH* 3–4, inorganic material was filtered off, the solution was dried over $MgSO_4$, and the solvent was removed. Crude product was subjected to column chromatography to afford 2.48 g (94%) pure diacid **2b** (elution with ethyl acetate). Colorless crystals; mp 191–194°C (ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.52$ (d, $J = 8.53$ Hz, 2H, 2NH), 5.07 (m, 2H, 2 12β-H), 4.88 (m, 2H, 2 7β-H), 3.59 (m, 2H, 2 3β-H), 2.15 (s, 6H, 2 12-CH_3CO), 2.04 (s, 6H, 2 7-CH_3CO), 0.92 (s, 6H, 2 19-CH_3), 0.80 (d, $J = 5.19$ Hz, 6H, 2 21-CH_3), 0.71 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 179.4$ (2C), 170.6 (2C), 170.4 (2C), 159.0 (2C), 75.2 (2CH), 70.6 (2CH) 53.4 ($2CH_2$), 50.0 (2CH), 47.3 (2CH), 45.0 (2C), 43.3 (2CH), 41.3 (CH), 37.6 (2CH), 35.2 ($2CH_2$), 34.5 (2CH), 34.2 (2C), 31.2 ($2CH_2$), 30.8 ($2CH_2$), 30.4 ($2CH_2$), 28.8 (2CH), 27.4 ($2CH_2$), 27.1 ($2CH_2$), 25.5 ($2CH_2$), 22.7 ($2CH_2$), 22.6 ($2CH_3$), 21.6 ($2CH_3$), 21.4 ($2CH_3$), 17.4 ($2CH_3$), 12.2 ($2CH_3$) ppm; IR ($CHCl_3$): $\bar{\nu} = 3389$, 2957, 1721, 1670, 1508, 1255 cm^{-1}; MS (70 eV): $m/z = 1059.6$ ($M^+ + Na$).

Methyl 3-t-butyldimethylsilyl-7,12-diacetylcholate (**17**, $C_{35}H_{60}O_7Si$)

To a solution of 5 g **10** (9.9 mmol) in 120 cm^3 anhydrous *DMF* imidazole (1.44 g, 21.2 mmol) and *t*-butyldimethylsilyl chloride (3.12 g, 20.8 mmol) were added with stirring. After 5 h the reaction mixture was poured into water and extracted several times with benzene, the organic layers were dried over $MgSO_4$, and the solvent was removed *in vacuo*. Crude product was subjected to column chromatography to afford 6.01 g (98%) pure **17** (elution with benzene/ethyl acetate = 9/1). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 5.07$ (m, 1H, 12β-H), 4.88 (m, 1H, 7β-H), 3.67 (s, 3H, OCH_3), 3.44 (m, 1H, 3β-H) 2.15 (s, 3H, 12-CH_3CO), 2.08 (s, 3H, 7-CH_3CO), 0.89 (m, 12H, 19-CH_3 and *t*-Bu), 0.81 (d, $J = 6.04$ Hz, 3H, 21-CH_3), 0.73 (s, 3H, 18-CH_3), 0.07 (s, 6H, $(CH_3)_2$-Si) ppm.

3α-t-Butyldimethylsilyloxy-5β-cholane-7α,12α,24-triol 7,12-diacetate (**18**, $C_{34}H_{60}O_6Si$)

Compound (4.5 g, 7.26 mmol) **17** was dissolved in 30 cm^3 dry *THF* at 0°C and 330 mg (8.68 mmol) $LiAlH_4$ were added portionwise with vigorous stirring. When all of the substrate disappeared (about 2 h), the excess reducing agent was decomposed by a few drops of water and inorganic material was filtered off. The organic layer was dried over $MgSO_4$, the solvent was evaporated, and pure product was isolated by means of column chromatography to afford 3.38 g (79%) **18** (elution with *n*-hexane/ethyl = acetate 2/8). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 5.07$ (m, 1H, 12β-H), 4.87 (m, 1H, 7β-H), 3.60 (t, $J = 6.14$ Hz, 2H, CH_2OH), 3.43 (m, 1H, 3β-H) 2.14 (s, 3H, 12-CH_3CO), 2.07 (s, 3H, 7-CH_3CO), 0.88 (m, 12H, 19-CH_3, *t*-Bu), 0.81 (d, $J = 6.37$ Hz, 3H, 21-CH_3), 0.72 (s, 3H, 18-CH_3), 0.06 (s, 6H, $(CH_3)_2$-Si) ppm; IR ($CHCl_3$): $\bar{\nu} = 3627$, 3480, 1720, 1255, 1076, 837 cm^{-1}.

24-Iodo-5β-cholane-3α,7α,12α-triol 7,12-diacetate (**19**, $C_{28}H_{45}IO_5$)

The reaction was carried out according to the procedure described for **4** with twice as little amount of iodinating agent.

Purification with column chromatography gave 2.80 g iodide **19** in 94% yield (elution with *n*-hexane/ethyl acetate = 3/7). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 5.09$ (m, 1H, 12β-H), 4.90 (m, 1H, 7β-H), 3.51 (m, 1H, 3β-H), 3.14 (m, 2H, CH_2I) 2.13 (s, 3H, 12-CH_3CO), 2.09 (s, 3H, 7-CH_3CO), 0.91 (m, 3H, 19-CH_3), 0.83 (d, $J = 6.29$ Hz, 3H, 21-CH_3), 0.73 (s, 3H, 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.4$ (2C), 75.2 (CH), 71.3 (CH), 70.7 (CH), 47.2 (CH), 44.8 (C), 43.1 (CH), 40.8 (CH), 38.4 (CH_2), 37.5 (C), 36.4 (CH_2), 34.7 (CH_2), 34.1 (CH), 31.1 (CH_2), 30.2 (CH_2), 29.9 (CH_2), 28.7 (CH), 27.0 (CH_2), 25.3 (CH_2), 22.6 (CH_2), 22.4 (CH), 21.4 (CH_3), 21.3 (CH_3), 20.8 (CH_3), 17.7 (CH_3), 12.0 (CH_3), 7.5 (CH_2) ppm; IR ($CHCl_3$): $\bar{\nu} = 3606$, 3435, 1721, 1255, 1025, 850 cm^{-1}.

24-Azido-5β-cholane-3α,7α,12α-triol 3,7,12-triacetate (**21**, $C_{30}H_{47}N_3O_6$)

The substitution reaction ($I \rightarrow N_3$) was carried out according to the procedure described for **5**. The crude azide **20** was then dissolved in 15 cm^3 dry pyridine and 5 cm^3 acetic anhydride were added. The reaction mixture was allowed to stay at room temperature overnight. After this time it was poured into acidified water and the organic material was extracted twice with CH_2Cl_2. Combined organic layers were extracted with aqu. $NaHCO_3$, dried over $MgSO_4$, and the solvent was removed. Purification with column chromatography gave 2.80 g azide **21** from iodide **19** in 94% yield (elution with *n*-hexane/ethyl acetate = 3/7). Colorless crystals; mp 142–145°C (*n*-heptane/ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 5.07$ (m, 1H, 12β-H), 4.89 (m, 1H, 7β-H), 4.56 (m, 1H, 3β-H), 3.23 (m, 2H, CH_2N_3), 2.13 (s, 3H, 12-CH_3CO), 2.07 (s, 3H, 7-CH_3CO), 2.03 (s, 3H, 3-CH_3CO), 0.90 (s, 3H, 19-CH_3), 0.81 (d, $J =$ 6.36 Hz, 3H, 21-CH_3), 0.72 (s, 3H, 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.5$ (2C), 170.3 (C), 75.3 (CH), 74.0 (CH), 70.6 (CH), 51.8 (CH_2), 47.4 (CH), 45.0 (C), 43.3 (CH), 40.9 (CH), 37.7 (CH), 34.6 (CH_2), 34.7 (CH), 34.5 (CH_2), 34.3 (C), 32.6 (CH_2), 31.2 (CH_2), 28.8 (CH), 27.2 (CH_2), 26.8 (CH_2), 25.5 (CH_2), 25.4 (CH_2), 22.7 (CH_2), 22.5 (CH_3), 21.6 (CH_3), 21.42 (CH_3), 21.38 (CH_3), 17.8 (CH_3), 12.2 (CH_3) ppm; IR ($CHCl_3$): $\bar{\nu} = 2099$, 1724, 1254, 1121 cm^{-1}.

24-Amino-5β-cholane-3α,7α,12α-triol 3,7,12-triacetate (**22**, $C_{30}H_{49}NO_6$)

The reaction was carried out according as described for **6** and thereby 2.1 g **22** were obtained from **21** in 95% yield. Colorless crystals; mp 83–84°C (methanol/ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 5.08$ (m, 1H, 12β-H), 4.90 (m, 1H, 7β-H), 4.56 (m, 1H, 3β-H), 2.65 (m, 2H, C*H*$_2$NH$_2$), 2.12 (s, 3H, 12-CH_3CO), 2.07 (s, 3H, 7-CH_3CO), 2.03 (s, 3H, 3-CH_3CO), 0.91 (s, 3H, 19-CH_3), 0.82 (d, $J = 6.30$ Hz, 3H, 21-CH_3), 0.72 (s, 3H, 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.4$ (2C), 170.2 (C), 75.3 (CH), 73.9 (CH), 70.6 (CH), 47.4 (CH), 44.9 (C), 43.2 (CH), 41.9 (CH_2), 40.8 (CH), 37.6 (CH), 34.7 (CH), 34.54 (CH_2), 34.47 (CH_2), 34.2 (C), 32.7 (CH_2), 31.1 (CH_2), 29.0 (CH_2), 28.7 (CH), 27.1 (CH_2), 26.7 (CH_2), 25.4 (CH_2), 22.7 (CH_2), 22.4 (CH_3), 21.5 (CH_3), 21.33 (CH_3), 21.29 (CH_3), 17.7 (CH_3), 12.1 (CH_3) ppm; IR ($CHCl_3$): $\bar{\nu} = 3395$, 1724, 1254, 1025 cm^{-1}.

N-(Methyl 7α,12α-diacetoxy-5β-cholanoate)-N′-(5′β-cholane-3′α,7′α,12′α-triol 3′,7′,12′-triacetate)-3α,24′-oxamide (**25**, $C_{61}H_{94}N_2O_{14}$)

To a solution of 1.5 cm^3 (17.5 mmol) oxalyl chloride in 60 cm^3 dry benzene a solution of amine **23** [4] (0.5 g, 1 mmol) in 40 cm^3 dry benzene was added dropwise with vigorous stirring. After 15 min the solvent with excess chlorinating agent was removed to dryness, the residue was dissolved in 40 cm^3 dry benzene, and a solution of amine **22** (0.47 g, 0.91 mmol) in 20 cm^3 dry benzene was slowly added with stirring. After reaction was complete (about 30 min), the solvent was removed and the crude product was subjected to column chromatography to afford 450 mg (46%) pure **25** (elution with *n*-hexane/ethyl acetate = 8/2). Colorless crystals; mp 134–136°C (*n*-heptane/ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$) $\delta = 7.53$ (t, $J = 6.01$ Hz, 1H, CH_2NH), 7.36 (d, $J = 8.54$ Hz, 1H, C(3)-NH), 5.08 (m, 2H, 2 12β-H), 4.91 (m, 2H, 7β-H), 4.57 (m, 1H, 3β-H(C–O)), 3.66 (m, 4H, OCH_3, 3β-H(C–N)), 3.28 (m, 2H, C*H*$_2$NH), 2.17 (s, 3H, CH_3CO), 2.13 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 0.93 (s, 3H, 19-CH_3), 0.91 (s, 3H, 19-CH_3), 0.81 (d, $J = 6.05$ Hz, 6H, 2 21-CH_3), 0.72 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 174.4$ (C), 170.5 (C), 170.4 (C), 170.3 (C), 170.2 (2C), 160.0 (C), 158.7 (C), 75.3 (CH), 75.2 (CH), 73.9 (CH), 70.6 (2CH), 51.4 (CH_3), 49.8 (CH), 47.3 (CH), 47.2 (CH), 44.94 (C), 44.89 (C), 43.2 (2CH), 41.3 (CH), 40.8 (CH), 40.1 (CH_2), 37.6 (2CH), 35.3 (CH_2), 35.2 (CH_2), 34.6 (CH), 34.5 (C), 34.4 (CH), 34.2 (C), 34.1 (CH_2), 32.7 (CH_2), 31.7 (CH_2), 31.1 (CH_2), 30.7 (CH_2), 30.6 (CH_2), 28.7 (2CH), 27.4 (CH_2), 27.1 (CH_2), 27.0 (CH_2), 26.8 ($2CH_2$), 25.6 (CH_2), 25.4 (CH_2), 22.58 ($2CH_2$), 22.55 (CH_3), 22.4 (CH_3), 21.6 (CH_3), 21.5 (CH_3), 21.4 (CH_3), 21.3 (CH_3), 17.7 (CH_3), 17.4 (CH_3), 14.0 (CH_3), 12.11 (CH_3), 12.08 ($2CH_3$) ppm; IR ($CHCl_3$): $\bar{\nu} = 3608$, 3394, 1725, 1673, 1254, 1024 cm^{-1}; MS (70 eV): $m/z = 1078$ (M^+), 1019, 663, 411, 253.

N-(5β-Cholane-7α,12α,24-triol 7,12-diacetate)-N′-(5′β-cholane-3′α,7′α,12′α-triol 7′,12′-diacetate)-3α,24′-oxamide (**26**, $C_{58}H_{92}N_2O_{12}$)

The reaction was carried out according to the procedure described for **3**; 340 mg diol **26** were obtained from **25** in 87% yield. Colorless crystals; mp 150–153°C (*n*-heptane/ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.51$ (t, $J = 6.02$ Hz, 1H, CH_2NH), 7.33 (d, $J = 8.63$ Hz, 1H, C(3)-NH), 5.07 (m, 2H, 2 12β-H), 4.89 (m, 2H, 7β-H), 3.65 (m, 4H, C*H*$_2$OH, 3β-H(C–O), 3β-H(C–N)), 3.24 (m, 2H, C*H*$_2$NH), 2.16 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO), 0.92 (s, 3H, 19-CH_3), 0.89 (s, 3H, 19-CH_3), 0.82 (m, 6H, 2 21-CH_3), 0.72 (s, 3H, 18-CH_3), 0.71 (s, 3H, 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.63$ (2C), 170.60 (C), 170.4 (C), 160.1 (C), 158.8 (C), 75.43 (CH), 75.39 (CH), 71.7 (CH), 70.8 (CH), 70.7 (CH), 63.4 (CH_3), 49.9 (CH), 47.5 (CH), 47.4 (CH), 45.0 (2 C), 43.4 (2CH), 43.3 (CH), 41.4 (CH), 41.0 (CH), 40.2 (CH_2), 38.7 (CH_2), 37.8 (CH), 37.7 (CH), 35.5 (CH_2), 35.3 (CH_2), 34.84 (CH_2), 34.78 (CH), 34.7 (CH), 34.3 (2C), 32.9 (CH_2), 31.6 (CH_2), 31.4 (CH_2), 31.3 (CH_2), 30.5 (CH_2),

29.7 (CH_2), 29.2 (CH_2), 28.9 (CH), 27.6 (CH_2), 27.3 (CH_2), 25.7 (CH_2), 25.5 ($2CH_2$), 22.9 (CH_2), 22.82 (CH_2), 22.79 (CH_3), 22.7 (CH_3), 22.6 (CH_3), 21.70 (CH_3), 21.66 (CH_3), 21.54 (CH_3), 21.49 (CH_3), 17.9 (CH_3), 17.8 (CH_3), 12.2 (CH_3) ppm; IR ($CHCl_3$): $\bar{\nu} = 3616$, 3394, 1723, 1673, 1511, 1255, 1024 cm^{-1}.

N-(24-Iodo-5β-cholane-7α,12α-diol 7,12-diacetate)-N′-(3′β-iodo-5′β-cholane-7′α,12′α-diol 7′,12′-diacetate)-3α,24′-oxamide (**27**, $C_{58}H_{90}I_2N_2O_{10}$)

Diiodide **27** (325 mg, 79% yield) was obtained from **26** according to the procedure described for **4**. Colorless crystals; mp 145–147°C (*n*-heptane/ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.49$ (t, $J = 6.04$ Hz, 1H, CH_2NH), 7.34 (d, $J = 8.65$ Hz, 1H, C(3)-NH), 5.09 (m, 2H, 2 12β-H), 4.91 (m, 3H, 2 7β-H, 3α-H), 3.62 (m, 1H, 3β-H(C–N)), 3.14 (m, 4H, CH_2NH, CH_2I), 2.18 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO), 1.01 (s, 3H, 19-CH_3), 0.93 (s, 3H, 19-CH_3), 0.81 (m, 6H, 2 21-CH_3), 0.73 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.6$ (C), 170.4 (C), 170.3 (C), 170.1 (C), 160.1 (C), 158.8 (C), 75.4 (CH), 75.3 (CH), 70.7 (2CH), 49.9 (CH), 47.4 (2CH), 45.1 (C), 45.0 (C), 43.34 (CH), 43.31 (CH), 41.4 (CH), 40.2 (CH_2), 38.9 (CH_2), 38.3 (CH), 38.2 (CH), 37.72 (CH), 37.68 (CH), 36.6 (CH_2), 35.5 (CH_2), 35.3 (CH_2), 35.2 (C), 34.7 (CH), 34.31 (CH), 34.28 (C), 32.9 (CH_2), 32.3 (CH_2), 31.3 (CH_2), 30.9 ($2CH_2$), 30.1 (CH_2), 29.9 (CH), 28.9 (CH), 27.5 (CH_2), 27.2 ($2CH_2$), 25.7 (CH_2), 25.5 (CH_2), 22.81 (CH_2), 22.77 (CH_3), 22.74 (CH_3), 22.70 (CH_3), 21.7 (CH_3), 21.5 (CH_3), 21.4 (CH_3), 21.0 (CH_3), 18.0 (CH_3), 17.8 (CH_3), 12.2 ($2CH_3$), 7.6 (CH_2) ppm; IR ($CHCl_3$): $\bar{\nu} = 3616$, 3394, 1724, 1673, 1511, 1254, 1023 cm^{-1}.

N-(24-Azido-5β-cholane-7α,12α-diol 7,12-diacetate)-N′-(3′α-azido-5′β-cholane-7′α,12′α-diol 7′,12′-diacetate)-3α,24′-oxamide (**28**, $C_{58}H_{90}N_8O_{10}$)

The reaction was carried out according to the procedure described for **5**; 261 mg diazide **28** were obtained from **27** in 93% yield. Colorless crystals; mp 152–155°C (*n*-heptane/ethyl acetate); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.50$ (t, $J = 6.05$ Hz, 1H, CH_2NH), 7.34 (d, $J = 8.63$ Hz, 1H, C(3)-NH), 5.09 (m, 2H, 2 12β-H), 4.91 (m, 2H, 2 7β-H), 3.62 (m, 1H, 3β-H(C–N)), 3.25 (m, 4H, CH_2NH, CH_2N_3), 2.19 (s, 3H, CH_3CO), 2.13 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO), 0.94 (s, 3H, 19-CH_3), 0.93 (s, 3H, 19-CH_3), 0.84 (m, 6H, 2 21-CH_3), 0.74 (s, 3H, 18-CH_3), 0.73 (s, 3H, 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.52$ (C), 170.47 (C), 170.35 (C), 170.28 (C), 160.0 (C), 158.7 (C), 75.3 (2CH), 70.62 (CH), 70.55 (CH), 60.7 (CH), 51.8 (CH_2), 49.8 (CH), 47.4 (2CH), 45.0 (C), 44.9 (C), 43.25 (CH), 43.20 (CH), 41.3 (CH), 41.2 (CH), 40.1 (CH_2), 37.6 (2CH), 35.4 (CH_2), 35.0 (CH_2), 34.6 (2CH), 34.3 (CH_2), 34.2 (2C), 32.8 (CH_2), 32.6 (CH_2), 31.2 (CH_2), 31.1 (CH_2), 28.8 (CH), 28.7 (CH), 28.5 (CH_2), 28.1 ($2CH_2$), 27.5 (CH_2), 27.2 (CH_2), 26.6 (CH_2), 25.8 (CH_2), 25.5 (CH_2), 25.4 (CH_2), 25.3 (CH_2), 22.7 (CH_2), 22.6 (CH_3), 22.5 (CH_3), 21.6 (CH_3), 21.51 (CH_3), 21.46 (CH_3), 21.3 (CH_3), 17.8 (CH_3), 17.7 (CH_3), 12.1 ($2CH_3$) ppm; IR ($CHCl_3$): $\bar{\nu} = 3616$, 3393, 2098, 1724, 1674, 1510, 1254 cm^{-1}.

N-(24-Amino-5β-cholane-7α,12α-diol 7,12-diacetate)-N′-(3′α-amino-5′β-cholane-7′α,12′α-diol 7′,12′-diacetate)-3α,24′-oxamide (**29**, $C_{58}H_{94}N_4O_{10}$)

Diamine **29** (202 mg, 81% yield) was obtained from **28** according to the procedure described for **6**. Colorless crystals; mp 230°C with decomposition (*n*-heptane/ethyl acetate/methanol); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.52$ (t, $J = 4.50$ Hz, 1H, CH_2NH), 7.34 (d, $J = 7.44$ Hz, 1H, C(3)-NH), 5.08 (m, 2H, 2 12β-H), 4.90 (m, 2H, 2 7β-H), 3.68 (m, 1H, 3β-H(C–NHCO)), 3.27 (m, 2H, CH_2NH), 2.82 (m, 3H, 3β-H(C–NH_2), CH_2NH_2), 2.18 (s, 3H, CH_3CO), 2.15 (s, 3H, CH_3CO), 2.12 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO), 0.92 (s, 6H, 2 19-CH_3), 0.82 (m, 6H, 2 21-CH_3), 0.72 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.64$ (C), 170.60 (C), 170.4 (C), 170.3 (C), 160.1 (C), 158.8 (C), 75.3 (2CH), 70.6 (2CH), 53.4 (CH_2), 51.5 (CH), 49.9 (CH), 47.3 (2CH), 45.0 (C), 44.9 (C), 43.6 (CH), 43.1 (CH), 41.3 (CH), 41.2 (CH), 40.8 (CH_2), 40.2 (CH_2), 37.8 (CH), 37.6 (CH), 35.8 (CH_2), 35.2 ($2CH_2$), 34.7 (2CH), 34.2 (2C), 32.8 (CH_2), 32.6 (CH_2), 31.2 (CH_2), 30.9 (CH_2), 30.2 (CH_2), 29.6 (CH_2), 28.9 (CH), 28.7 (CH), 27.8 (CH_2), 27.4 (CH_2), 25.8 ($3CH_2$), 25.7 (CH_2), 25.5 (CH_2), 22.8 (CH_2), 22.6 (CH_3), 22.5 (CH_3), 21.7 ($2CH_3$), 21.6 (CH_3), 21.5 (CH_3), 17.7 ($2CH_3$), 12.2 ($2CH_3$) ppm; IR ($CHCl_3$): $\bar{\nu} = 3615$, 3394, 1724, 1673, 1511, 1254, 910 cm^{-1}.

N,N′:N″,N‴-Di(5β-cholane-7α,12α-diol 7,12-diacetate)-3α,24′:3′α,24-dioxamide (**30**, $C_{60}H_{92}N_4O_{12}$)

The reaction was carried out according to the procedure described for **7**; 51 mg **30** were obtained from **29** in 24% yield. Colorless crystals; mp 305°C with decomposition (*n*-heptane/ethyl acetate/methanol); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.58$ (dd, $J_1 = 3.46$ Hz, $J_2 = 8.88$ Hz, 2H, CH_2NH), 7.46 (d, $J = 8.12$ Hz, 2H, 2 C(3)-NH), 5.04 (m, 2H, 2 12β-H), 4.92 (m, 2H, 2 7β-H), 3.46 (m, 4H, 2 3β-H, $2CH_2NH$), 2.98 (m, 2H, CH_2NH), 2.16 (s, 6H, 2 12-CH_3CO), 2.09 (s, 6H, 2 7-CH_3CO), 0.91 (s, 6H, 2 19-CH_3), 0.85 (d, $J = 6.69$ Hz, 6H, 2 21-CH_3), 0.76 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 170.5$ (2C), 170.1 (2C), 160.5 (2C), 158.9 (2C), 75.4 (2CH), 70.6 (2CH) 50.1 (2CH), 45.0 (2C), 44.6 (2CH), 43.9 (2CH), 41.3 ($2CH_2$), 41.1 (2CH), 37.3 (2CH), 34.8 ($2CH_2$), 34.42 (2CH), 34.37 ($2CH_2$), 33.8 (2C), 31.5 ($2CH_2$), 31.0 ($2CH_2$), 29.7 (2CH), 27.9 ($2CH_2$), 26.7 ($2CH_2$), 25.9 ($2CH_2$), 22.9 ($2CH_2$), 22.63 ($2CH_3$), 22.58 ($2CH_2$), 22.1 ($2CH_3$), 21.3 ($2CH_3$), 17.3 ($2CH_3$), 12.0 ($2CH_3$) ppm; IR ($CHCl_3$): $\bar{\nu} = 3400$, 1724, 1674, 1508, 1253, 1027 cm^{-1}; MS (70 eV): $m/z = 1083.8$ ($M^+ + Na$).

N,N′:N″,N‴-Di(5β-cholane-7α,12α-diol)-3α,24′:3′α,24-dioxamide (**31**, $C_{52}H_{84}N_4O_8$)

Dimer **31** (13 mg, 30% yield) was obtained from **30** according to the procedure described for **8**. Colorless crystals; mp 230–233°C (*n*-hexane/CH_2Cl_2); ^{1}H NMR (200 MHz,

$CDCl_3$): $\delta = 7.53$ (m, 4H, $2CH_2NH$, 2C(3)-NH), 3.96 (m, 2H, 2 12β-H), 3.84 (m, 2H, 2 7β-H), 3.51 (m, 4H, 2 3β-H, CH_2NH), 3.01 (m, 2H, CH_2NH), 1.02 (d, $J = 6.43$ Hz, 6H, 2 21-CH_3), 0.90 (s, 6H, 2 19-CH_3), 0.72 (s, 6H, 2 18-CH_3) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 159.8$ (2C), 159.3 (2C), 72.4 (2CH), 68.2 (2CH) 50.5 (2CH), 46.2 (2C), 45.0 (2CH), 42.2 (2CH), 41.5 (2CH), 40.6 ($2CH_2$), 39.6 (2CH), 35.8 ($2CH_2$), 34.5 (2CH), 34.1 (2C), 34.0 ($2CH_2$), 32.4 ($2CH_2$), 29.8 ($2CH_2$), 28.2 ($2CH_2$), 27.5 ($2CH_2$), 26.8 (2CH), 25.1 ($2CH_2$), 24.0 ($2CH_2$), 23.1 ($2CH_2$), 22.2 ($2CH_3$), 17.7 ($2CH_3$), 12.3 ($2CH_3$) ppm; IR ($CHCl_3$): $\bar{\nu} = 3396$, 1674, 1518, 1237 cm^{-1}; MS (70 eV): $m/z = 915.6$ ($M^+ + Na$); HRMS: calcd. mass for $C_{52}H_{84}N_4NaO_8$ 915.6187, found 915.6153.

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