Synthesis of neoglycolipids for the development of non-viral gene delivery systems

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Synthesis of lipid conjugates with galactose as a targeting ligand intended for the development of non-viral systems for the targeted delivery of nucleic acids into hepatocytes is described. 3,4-Diethoxycyclobut-3-ene-1,2-dione (diethyl squarate) was used to bind the galactose moiety to the lipid component.

Key words: neoglycolipids, galactose, targeting ligand, 3,4-diethoxycyclobut-3-ene-1,2-dione (diethyl squarate), hepatocytes.

Gene therapy is based on the corrections of genetic disorders and curing diseases caused by them by introduction of molecules of therapeutic DNA into the defective cells. For the successful treatment, it is necessary to provide efficient delivery of these DNA into the target cells and their prolonged functioning.[1] At present, cationic liposomes are extensively studied as prospective systems for the DNA delivery.[2—4] The DNA incorporated into a lipid membrane becomes unavailable for the destructive action of cell enzymes, whereas liposomes themselves are noninfectious and nonimmunogenic.[5]

Unfortunately, liposomal DNA delivery systems do not possess cell specificity. Therefore, the liposomal surface is modified with ligands specific to receptors on the surface of target cells to overcome this shortcoming.[6—10]

Thus hepatocytes expose asialoglycoprotein receptors on their surface[11,12] specific to glycoproteins, as well as to other molecules containing galactose groups.[13] Therefore, modification of liposomes or their lipid components with galactose residues can be used to solve the problem of specific transport of biologically active compounds into hepatocytes, in particular, for elimination of genetic disorders of liver cells and curing various pathologies and diseases caused by them.[14]

The present work deals with the synthesis of lipid conjugates with galactose as a targeting ligand, which are meant to be used for the development of vectors for targeted delivery of nucleic acids to hepatocytes.

Molecular constructions developed by us, in addition to the "targeting" carbohydrate residues, include a dialkylglycerol component, which is intended for the incorporation of the conjugate into liposomes and functions as an anchor that fixes the carbohydrate unit. It is known that among lipids with the long-chain hydrocarbon substituents, compounds containing tetradecyl residues provide the best delivery of DNA to cells,[15,16] therefore, 1,2-di-*O*-tetradecyl-*rac*-glycerol has been used as a hydrophobic component. To study the effect of the lipid conjugate structure on the transfection activity, the galactose residue was bound to the dialkylglycerol molecule with spacers of various length and nature. The structure of a spacer group can affect the lypophilic—hydrophilic balance of the molecule, which determines the structure-forming properties of glycolipid conjugates. In the case of extended oligomethylene spacers, the lypophilic—hydrophilic balance can be disturbed, since spacers of this type tend to arrange close to the alkyl chains of the diglyceride disturbing the stability of lipid aggregates and approximating the galactose residues to the surface of liposomes. The shortening of a spacer group decreases availability of the targeting ligand for the receptors on the surface of the target cells. On the contrary, incorporation of a long hydrophilic oligooxamethylene spacer into the molecule of a lipid conjugate will make the galactose residue remote from the liposome surface. Carbamoyl linker has been chosen to connect the lipid component to the spacer groups, which provides the optimum combination of stability and toxicity of the lipid conjugate.[17]

The strategy for obtaining galactose-containing lipids is based on the use of 3,4-diethoxycyclobut-3-ene-1,2-dione (diethyl squarate), which first has been used in the synthesis of neoglycopeptides.[18] Being a chemoselective reagent, which reacts with primary amino groups, diethyl squarate is also used in the synthesis of carbohydrate[19] and peptide[20] conjugates.

The binding of the galactose residue to a spacer group was performed by glycosylation of 6-(*tert*-butoxycarbonylamino)hexanol with 2,3,4,6-tetra-*O*-acetyl-α-D-galacto-

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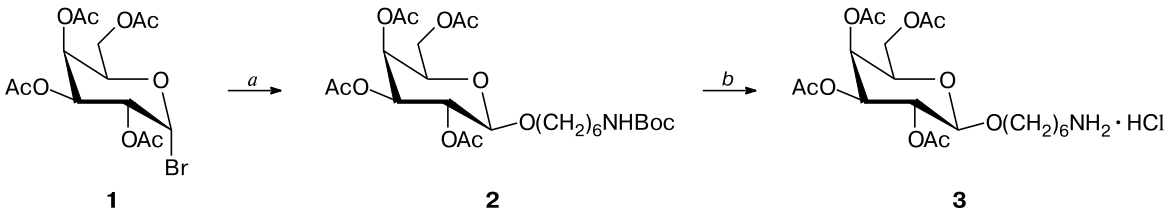
Scheme 1

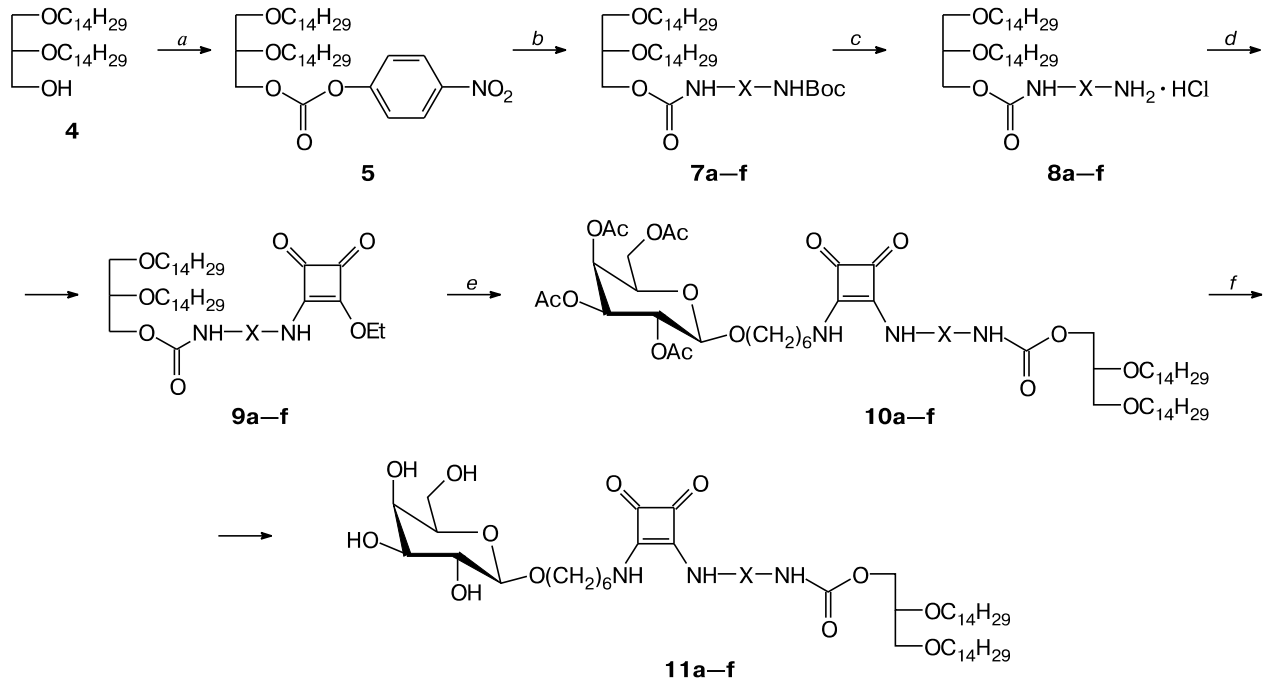


Reagents and conditions: (*a*) $BocNH(CH_2)_6OH$, $CdCO_3$, C_6H_6, 80 °C; (*b*) 4 *M* HCl, dioxane, 0 °C.

pyranosyl bromide (**1**) under conditions of the modified Koenigs—Knorr method[21] using $CdCO_3$ as a promoter (Scheme 1). Glycoside **2** was isolated by column chromatography on silica gel in 43% yield. Its ^1H NMR spectrum exhibits a signal for the anomeric proton with the chemical shift δ_H 4.37 and the spin-spin coupling constant $J_{1,2}$ = = 7.9 Hz and the ^{13}C NMR spectrum contains a signal for the anomeric carbon atom at δ_C 100.78, which indicates the β-configuration of the glycosidic bond. *tert*-Butoxycarbonyl protecting group was removed with 4 *M* hydrogen chloride in dioxane to obtain compound **3** in 97% yield.

To bind the lipid component to the spacer fragments of various length and type, we performed preliminarily the reaction of 1,2-di-*O*-tetradecyl-*rac*-glycerol (**4**) with 4-nitrophenyl chloroformate in the presence of Et_3N (Scheme 2). Carbonate **5** was obtained in 96% yield. The reaction of activated hydrophobic component **5** with mono-Boc-protected diamines **6a—f**, obtained by the previously described method,[22] led to compounds **7a—f**. Variations in the reaction time and temperature allowed us to increase the yields of compounds **7a—f** to 75—97%. Removal of the Boc-pro-

Scheme 2



Reagents and conditions: (*a*) $4\text{-}NO_2C_6H_4OCOCl$, Et_3N, 24 °C; (*b*) $NH_2XNHBoc$ (**6a—f**), Et_3N, 24—45 °C; (*c*) 4 *M* HCl, dioxane, 0 °C; (*d*) 3,4-diethoxycyclobut-3-ene-1,2-dione, Et_3N, 24 °C; (*e*) **3**, Et_3N, 24—40 °C; (*f*) MeONa/MeOH, 24 °C.

tecting groups afforded amino derivatives **8a**—**f** in 89—94% yields.

Coupling of glycerol (**8a**—**f**) and galactose (**3**) derivatives containing terminal NH_2 groups was performed by the successive substitution of the ethoxy groups in diethyl squarate. First, we performed its reaction with compounds **8a**—**f** in the presence of Et_3N. Compounds **9a**—**f** were isolated by column chromatography on silica gel in 72—99% yields. Subsequent reaction of compounds **9a**—**f** with the carbohydrate component **3** in the presence of Et_3N led to conjugates **10a**—**f** in 50—89% yields. It should be noted that an increase in the reaction time and the use of an excess of galactoside **3** (1.8 equiv.) resulted in the increase in the yields of compounds **10a**—**f**. Removal of the acetyl groups was performed by the Zemplén procedure (treatment with 0.1 *M* methanolic MeONa), to give the target galactose-containing lipids **11a**—**f** in high yields. To confirm the structures of compounds **11a**—**f** and assign the signals for the protons of the carbohydrate residue, we used two-dimensional homonuclear correlation NMR spectroscopy ($^1H,^1H$-COSY). The structures of conjugates **11a**—**f** were confirmed by the mass spectrometric data, as well.

In conclusion, using 3,4-diethoxycyclobut-3-ene-1,2-dione as the chemoselective coupling reagent we succeeded in obtaining galactose-containing lipids for the targeted delivery of nucleic acids to hepatocytes.

Experimental

Distilled solvents were used in the work (Khimmed, Reakhim), as well as 6-(*tert*-butoxycarbonylamino)hexanol, 4-nitrophenyl chloroformate (Aldrich), 3,4-diethoxycyclobut-3-ene-1,2-dione (Acros), and Et_3N (Merck). Benzene was refluxed over metallic Na and distilled directly before the reaction; CH_2Cl_2 and Et_3N were refluxed over CaH_2 and distilled. 1,2-Di-*O*-tetradecyl-*rac*-glycerol (**4**) was obtained according to the known procedure.[23] Boc-Protected diamines **6a**—**f** were obtained as described for *N*-*tert*-butoxycarbonyl-1,4-diaminobutane (**6a**).[22]

Thin-layer chromatography was performed on Kieselgel 60 F_{254} plates (Merck). Visualization of compounds on the chromatographic plates was performed by treatment with chlorine and then with a benzidine solution,[24] the Dragendorff reagent,[24] or phosphormolybdic acid—cerium(IV) sulfate with subsequent heating,[25] and under the UV light (254 nm). Column chromatography was performed on Kieselgel 60 silica gel (40—63 μm, Merck). ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 300 pulse Fourier-spectrometer in $CDCl_3$ using $SiMe_4$ as an internal standard, if not stated otherwise. Mass spectra were obtained on a Bruker Ultraflex time-of-flight mass spectrometer using laser-desorption ionizaition and 2,5-dihydroxybenzoic acid as a matrix.

[6-(*tert*-Butoxycarbonylamino)hexyl]-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (2). To a solution of 6-(*tert*-butoxycarbonylamino)hexanol (0.5 g, 2.30 mmol) in anhydrous benzene (50 mL), cadmium carbonate (0.721 g, 4.18 mmol), ground molecular sieves 4 Å, and after 15 min 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide[26] (**1**) (0.927 g, 2.25 mmol) were added. The reaction mixture was refluxed for 5 h, filtered, the solvent was evaporated *in vacuo*. The product was isolated by column chromatography; elution with the toluene—EtOAc (6 : 1) solvent system afforded compound **2** (0.525 g, 43%) as a crystallizing oil, $[\alpha]_D^{27}$ −4.95 (*c* 0.5, $CHCl_3$). MS, *m*/*z* (I_{rel} (%)): 570.307 $[M + Na]^+$ (100). Calculated for $C_{25}H_{41}NO_{12}$: 547.263 $[M]^+$. ^1H NMR, δ: 1.21—1.33 (m, 4 H, $(CH_2)_2$); 1.37 (s, 9 H, $C(Me)_3$); 1.35—1.44 (m, 2 H, $NHCH_2C\underline{H}_2$); 1.45—1.57 (m, 2 H, $OCH_2C\underline{H}_2$); 1.91, 1.98, 1.99, 2.08 (all s, 3 H each, 4 MeCO); 2.96—3.10 (m, 2 H, $NHC\underline{H}_2$); 3.40 (dt, 1 H, $OCH\underline{H}_a$, J = 6.8 Hz, J = 9.5 Hz); 3.77—3.86 (m, 2 H, H(5) Gal, $OCH\underline{H}_b$); 4.06 (dd, 1 H, J = 6.9 Hz, J = 11.1 Hz) and 4.12 (dd, 1 H, both H(6) Gal, J = 6.6 Hz, J = 11.1 Hz); 4.37 (d, 1 H, H(1) Gal, J = 7.9 Hz); 4.40—4.50 (m, 1 H, CONH); 4.94 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 10.5 Hz); 5.13 (dd, 1 H, H(2) Gal, J = 7.9 Hz, J = 10.5 Hz); 5.31 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.4 Hz). ^{13}C NMR, δ: 10.38, 13.47, 20.02, 20.10, 20.11, 20.19, 22.41, 23.17, 24.95, 25.90, 27.85, 28.35, 28.75, 29.45, 29.79, 38.16, 60.70, 66.50, 67.58, 68.36, 69.51, 70.02, 70.39, 100.78, 155.40, 168.50, 169.61, 169.71, 169.83.

(6-Aminohexyl)-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside hydrochloride (3). A solution of hydrogen chloride in dioxane (4 *M*, 5 mL) was added to a solution of compound **2** (0.315 g, 0.575 mmol) in CH_2Cl_2 (10 mL) cooled to 0 °C. After 1 h, the solvents were evaporated *in vacuo*, the product was isolated by column chromatography; elution with the $CHCl_3$—MeOH (10 : 1) → (5 : 1) solvent system afforded compound **3** (0.271 g, 97%) as a crystallizing oil, $[\alpha]_D^{27}$ −1.5 (*c* 1, $CHCl_3$). MS, *m*/*z* (I_{rel} (%)): 448.242 $[M - HCl + H]^+$ (100). Calculated for $C_{20}H_{34}NO_{10}$: 448.218 $[M - HCl + H]^+$. ^1H NMR, δ: 1.20—1.70 (m, 8 H, $(CH_2)_4$); 1.92, 1.98, 2.00, 2.09 (all s, 3 H each, 4 MeCO); 2.75—2.86 (m, 2 H, $C\underline{H}_2NH_2$); 3.41 (dd, 1 H, $OCH\underline{H}_a$, J = 7.1 Hz, J = 8.9 Hz); 3.76—3.88 (m, 2 H, H(5) Gal, $OCH\underline{H}_b$); 4.06 (dd, 1 H, J = 6.9 Hz, J = 11.2 Hz) and 4.13 (dd, 1 H, both H(6) Gal, J = 6.6 Hz, J = 11.2 Hz); 4.39 (d, 1 H, H(1) Gal, J = 7.9 Hz); 4.96 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 10.5 Hz); 5.13 (dd, 1 H, H(2) Gal, J = 7.9 Hz, J = 10.5 Hz); 5.32 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.4 Hz). ^{13}C NMR, δ: 11.35, 14.04, 20.52, 20.61, 20.63, 20.69, 20.78, 22.57, 25.16, 26.08, 27.37, 28.35, 29.03, 29.61, 30.24, 31.50, 31.84, 34.59, 36.42, 39.77, 61.16, 66.99, 67.01, 68.89, 69.75, 70.52, 70.84, 77.20, 101.18, 169.41, 170.09, 170.20, 170.33.

***rac*-1-*O*-(4-Nitrophenyloxycarbonyl)-2,3-di-*O*-tetradecylglycerol (5).** A solution of 4-nitrophenyl chloroformate (1.55 g, 7.69 mmol) in anhydrous CH_2Cl_2 (20 mL) was added dropwise to a solution of 1,2-di-*O*-tetradecyl-*rac*-glycerol (**4**) (2.42 g, 4.99 mmol) and anhydrous Et_3N (1.4 mL) in anhydrous CH_2Cl_2 (20 mL) over 30 min. The reaction mixture was stirred for 11 h at 24 °C, washed with 3% aqueous HCl (20 mL) and brine (3×20 mL) to pH 7, dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The product was isolated by column chromatography in toluene to obtain compound **5** (3.11 g, 96%) as a crystallizing oil. MS, *m*/*z* (I_{rel} (%)): 672.622 $[M + Na]^+$ (100). Calculated for $C_{38}H_{67}NO_7$: 649.492 $[M]^+$. ^1H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.9 Hz); 1.15—1.30 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.44—1.57 (m, 4 H, 2 $OCH_2C\underline{H}_2$); 3.38 (t, 2 H, $OC\underline{H}_2CH_2$, J = 6.6 Hz); 3.43 (dd, 1 H, J = 6.3 Hz, J = 10.0 Hz) and 3.49 (dd, 1 H, $OC\underline{H}_2CH$, J = 4.9 Hz, J = 10.0 Hz); 3.52 (t, 2 H, $OC\underline{H}_2CH_2$, J = 6.6 Hz); 3.61—3.69 (m, 1 H, $OCH_2C\underline{H}$); 4.25 (dd, 1 H, J = 5.9 Hz, J = 11.3 Hz) and

4.39 (dd, 1 H, $CH_2OC(O)$, J = 3.8 Hz, J = 11.3 Hz); 7.29—7.35 (m, 2 H) and 8.18—8.24 (m, 2 H, Ar).

***rac*-1-*O*-{*N*-[4-(*tert*-Butoxycarbonylamino)butyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (7a).** A solution of compound **5** (1.04 mmol) and anhydrous Et_3N (2.89 mmol) in anhydrous CH_2Cl_2 (8 mL) was added to a solution of *N*-*tert*-butoxycarbonyl-1,4-diaminobutane **6a** (1.72 mmol) in anhydrous CH_2Cl_2 (12 mL) with stirring. The mixture was heated for 30 h at 45 °C. After the starting compound **5** disappeared from the reaction mixture, it was washed with 3% aq. HCl (10 mL) and brine (4×10 mL) to pH 7, dried with Na_2SO_4, filtered, the solvent was evaporated *in vacuo*. The product was isolated by column chromatography in the toluene—EtOAc (20 : 1 → 10 : 1) solvent system to obtain compound **7a** (0.628 g, 86%) as a crystallizing oil. Found (%): C, 70.28; H, 12.05; N, 4.03. $C_{41}H_{82}N_2O_6$. Calculated (%): C, 70.44; H, 11.82; N, 4.01. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.8 Hz); 1.17—1.25 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.43 (s, 9 H, $C(Me)_3$); 1.40—1.55 (m, 8 H, 2 $OCH_2C\underline{H}_2$, 2 $NHCH_2C\underline{H}_2$); 3.00—3.17 (m, 4 H, 2 $NHC\underline{H}_2$); 3.33—3.59 (m, 7 H, 2 $OC\underline{H}_2CH_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.3 Hz, J = 11.5 Hz) and 4.13 (dd, 1 H, $CH_2OC(O)$, J = 4.2 Hz, J = 11.5 Hz); 4.49—4.55 (m, 1 H, CONH); 4.65—4.77 (m, 1 H, CONH). ^{13}C NMR, δ: 14.29, 22.83, 26.18, 26.24, 27.42, 27.52, 28.55, 29.50, 29.64, 29.79, 29.83, 30.16, 32.06, 40.30, 40.80, 64.40, 70.55, 70.74, 71.92, 77.00, 79.35, 156.13, 156.57.

Compounds **7b—f** were obtained similarly (below, the amounts of the starting reactants, reaction temperature, reaction time, eluent for chromatography, the yields, and physicochemical characteristics of compounds obtained are given).

***rac*-1-*O*-{*N*-[6-(*tert*-Butoxycarbonylamino)hexyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (7b).** *N*-*tert*-Butoxycarbonyl-1,6-diaminohexane (**6b**) (0.349 g, 1.61 mmol), compound **5** (0.610 g, 0.939 mmol), Et_3N (0.4 mL, 2.89 mmol), 45 °C, 20 h, toluene. Compound **7b** (0.553 g, 81%) was obtained as a crystallizing oil. Found (%): C, 70.81; H, 12.10; N, 3.76. $C_{43}H_{86}N_2O_6$. Calculated (%): C, 71.03; H, 11.92; N, 3.85. ^{1}H NMR, δ: 0.78 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.9 Hz); 1.14—1.28 (m, 48 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_2$); 1.30—1.56 (m, 17 H, 2 $OCH_2C\underline{H}_2$, 2 $NHCH_2C\underline{H}_2$, CMe_3); 2.93—3.10 (m, 4 H, 2 $NHC\underline{H}_2$); 3.30—3.55 (m, 7 H, 2 $OC\underline{H}_2CH_2$, OCH_2CH); 4.03 (dd, 1 H, J = 5.5 Hz, J = 11.3 Hz) and 4.15 (dd, 1 H, $CH_2OC(O)$, J = 4.2 Hz, J = 11.3 Hz); 4.48—4.60 (m, 1 H, CONH); 4.66—4.80 (m, 1 H, CONH). ^{13}C NMR, δ: 14.24, 22.80, 26.01, 26.14, 26.21, 27.43, 29.48, 29.63, 29.78, 29.82, 30.11, 32.03, 40.47, 63.55, 64.29, 70.52, 70.71, 71.21, 76.95, 77.58, 79.06, 156.12, 156.61.

***rac*-1-*O*-{*N*-[8-(*tert*-Butoxycarbonylamino)octyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (7c).** *N*-*tert*-Butoxycarbonyl-1,8-diaminooctane (**6c**) (0.359 g, 1.47 mmol), compound **5** (0.620 g, 0.954 mmol), Et_3N (0.4 mL, 2.89 mmol), 45 °C, 30 h, toluene—EtOAc (20 : 1 → 10 : 1). Compound **7c** (0.543 g, 75%) was obtained as a crystallizing oil. Found (%): C, 71.45; H, 12.25; N, 3.52. $C_{45}H_{90}N_2O_6$. Calculated (%): C, 71.57; H, 12.01; N, 3.71. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.9 Hz); 1.17—1.27 (m, 52 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_4$); 1.38 (s, 9 H, $C(Me)_3$); 1.40—1.59 (m, 8 H, 2 $OCH_2C\underline{H}_2$, 2 $NHCH_2C\underline{H}_2$); 2.98—3.13 (m, 4 H, 2 $NHC\underline{H}_2$); 3.33—3.44 (m, 4 H, $OC\underline{H}_2CH_2$, $OC\underline{H}_2CH$); 3.46—3.59 (m, 3 H, $OC\underline{H}_2CH_2$, $OCH_2C\underline{H}$); 4.02 (dd, 1 H, J = 5.4 Hz, J = 11.5 Hz) and 4.13 (dd, 1 H, $CH_2OC(O)$, J = 4.1 Hz, J = 11.5 Hz); 4.39—4.57 (m, 1 H, CONH); 4.70 (br.t, 1 H, CONH, J = 5.6 Hz). ^{13}C NMR, δ: 14.25, 22.82, 26.19, 26.24, 26.79, 26.84, 28.57, 29.31, 29.50, 29.64, 29.84, 30.08, 30.16, 32.07, 40.73, 41.18, 64.32, 70.57, 70.73, 71.92, 77.02, 79.17, 156.12, 156.54.

***rac*-1-*O*-{*N*-[12-(*tert*-Butoxycarbonylamino)dodecyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (7d).** *N*-*tert*-Butoxycarbonyl-1,12-diaminododecane (**6d**) (0.465 g, 1.55 mmol), compound **5** (0.638 g, 0.982 mmol), Et_3N (0.4 mL, 2.89 mmol), 45 °C, 6.5 h, toluene—EtOAc (20 : 1). Compound **7d** (0.663 g, 83%) was obtained as a crystallizing oil. Found (%): C, 71.92; H, 12.33; N, 3.59. $C_{49}H_{98}N_2O_6 \cdot 1/2\ H_2O$. Calculated (%): C, 71.74; H, 12.16; N, 3.41. ^{1}H NMR, δ: 0.80 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.12—1.30 (m, 60 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_8$); 1.38—1.54 (m, 17 H, 2 $OCH_2C\underline{H}_2$, 2 $NHCH_2C\underline{H}_2$, $C(Me)_3$); 2.98—3.15 (m, 4 H, 2 $NHC\underline{H}_2$); 3.32—3.43 (m, 4 H, $OC\underline{H}_2CH_2$, $OC\underline{H}_2CH$); 3.44—3.57 (m, 3 H, $OC\underline{H}_2CH_2$, $OCH_2C\underline{H}$); 4.02 (dd, 1 H, J = 5.4 Hz, J = 11.5 Hz) and 4.12 (dd, 1 H, $CH_2OC(O)$, J = 4.2 Hz, J = 11.5 Hz); 4.43—4.56 (m, 1 H, CONH); 4.70 (br.t, 1 H, CONH, J = 5.5 Hz). ^{13}C NMR, δ: 14.25, 22.82, 26.15, 26.21, 26.60, 26.89, 28.56, 29.42, 29.49, 29.62, 29.78, 29.82, 30.10, 32.04, 40.09, 41.20, 64.29, 70.48, 70.69, 71.88, 76.95, 79.21, 156.24, 156.51.

***rac*-1-*O*-{*N*-[12-(*tert*-Butoxycarbonylamino)-4,9-dioxadodecyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (7e).** *N*-*tert*-Butoxycarbonyl-4,9-dioxa-1,12-diaminododecane (**6e**) (0.552 g, 1.81 mmol), compound **5** (0.708 g, 1.09 mmol), Et_3N (0.45 mL, 3.25 mmol), 24 °C, 5 h, toluene—EtOAc (4 : 1). Compound **7e** (0.861 g, 97%) was obtained as a crystallizing oil. MS, m/z (I_{rel} (%)): 837.839 $[M + Na]^+$ (100). Calculated for $C_{47}H_{94}N_2O_8$: 814.701 $[M]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.19—1.30 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.36 (s, 9 H, $C(Me)_3$); 1.42—1.52 (m, 4 H, 2 $OCH_2C\underline{H}_2$); 1.53—1.61 (m, 4 H, 2 $OCH_2C\underline{H}_2$); 1.63—1.75 (m, 4 H, 2 $OCH_2C\underline{H}_2$); 3.10—3.26 (m, 4 H, 2 $NHC\underline{H}_2$); 3.31—3.44 (m, 12 H, 5 $OC\underline{H}_2CH_2$, $OC\underline{H}_2CH$); 3.45—3.58 (m, 3 H, $OC\underline{H}_2CH_2$, $OCH_2C\underline{H}$); 4.01 (dd, 1 H, J = 5.4 Hz, J = 11.5 Hz) and 4.12 (dd, 1 H, $CH_2OC(O)$, J = 4.4 Hz, J = 11.5 Hz); 4.80—4.92 (m, 1 H, CONH); 4.97—5.10 (m, 1 H, CONH). ^{13}C NMR, δ: 13.90, 22.47, 25.84, 25.90, 26.23, 28.22, 29.15, 29.30, 29.82, 31.71, 38.58, 38.95, 63.98, 68.77, 69.01, 70.28, 70.39, 70.52, 70.59, 71.56, 76.70, 78.89, 155.80, 156.20.

***rac*-1-*O*-{*N*-[13-(*tert*-Butoxycarbonylamino)-4,7,10-trioxatridecyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (7f).** *N*-*tert*-Butoxycarbonyl-4,7,10-trioxa-1,13-diaminotridecane (**6f**) (0.705 g, 2.20 mmol), compound **5** (0.720 g, 1.11 mmol), Et_3N (0.45 mL, 3.25 mmol), 24 °C, 3 h, toluene—EtOAc (4 : 1). Compound **7f** (0.884 g, 96%) was obtained as a crystallizing oil. MS, m/z (I_{rel} (%)): 853.858 $[M + Na]^+$ (100). Calculated for $C_{47}H_{94}N_2O_9$: 830.696 $[M]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.15—1.30 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.36 (s, 9 H, $C(Me)_3$); 1.42—1.54 (m, 4 H, 2 $OCH_2C\underline{H}_2$); 1.63—1.75 (m, 4 H, 2 $OCH_2C\underline{H}_2$); 3.10—3.26 (m, 4 H, 2 $NHC\underline{H}_2$); 3.32—3.42 (m, 4 H, $OC\underline{H}_2CH_2$, $OC\underline{H}_2CH$); 3.44—3.60 (m, 15 H, 7 $OC\underline{H}_2CH_2$, $OCH_2C\underline{H}$); 4.01 (dd, 1 H, J = 5.4 Hz, J = 11.4 Hz) and 4.11 (dd, 1 H, $CH_2OC(O)$, J = 4.3 Hz, J = 11.4 Hz); 4.87—5.00 (m, 1 H, CONH); 5.09—5.22 (m, 1 H, CONH)). ^{13}C NMR, δ: 13.90, 22.47, 25.84, 25.90, 28.24, 29.15, 29.30, 29.48, 29.83, 31.71, 38.34, 38.74, 63.95, 69.16, 69.36, 70.04, 70.31, 70.38, 71.56, 76.72, 155.84, 156.26.

***rac*-1-*O*-[*N*-(4-Aminobutyl)]carbamoyl-2,3-di-*O*-tetradecylglycerol hydrochloride (8a).** A solution of hydrogen chloride in dioxane (4 *M*, 5 mL) was added to a solution of compound **7a** (0.295 mmol) in CH_2Cl_2 (7 mL) cooled to 0 °C with stirring.

After 4 h, the solvents were evaporated, and compound **8a** (0.167 g, 89%) was isolated by chromatography in the $CHCl_3$—MeOH (12 : 1) solvent system as a crystallizing oil. Found (%): C, 67.93; H, 12.06; N, 4.48. $C_{36}H_{75}ClN_2O_4$. Calculated (%): C, 68.05; H, 11.90; N, 4.41. ^{1}H NMR, δ: 0.82 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.15—1.32 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.42—1.67 (m, 6 H, 2 $OCH_2C\underline{H}_2$, $NHCH_2C\underline{H}_2$); 1.70—1.89 (m, 2 H, $NH_2CH_2C\underline{H}_2$); 2.96 (t, 2 H, $C\underline{H}_2NH_2$, J = 7.3 Hz); 3.09—3.20 (m, 2 H, $NHC\underline{H}_2$); 3.33—3.60 (m, 7 H, 2 $OC\underline{H}_2CH_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.4 Hz, J = 11.4 Hz) and 4.11 (dd, 1 H, $CH_2OC(O)$, J = 4.3 Hz, J = 11.4 Hz); 5.35—5.48 (m, 1 H, CONH). ^{13}C NMR, δ: 13.54, 22.11, 24.37, 25.47, 25.54, 26.21, 28.80, 28.97, 29.10, 29.44, 31.36, 39.07, 39.64, 63.68, 69.83, 70.07, 71.25, 76.29, 156.07.

Compounds **8b—f** were obtained similarly (below, the amounts of compounds **7b—f**, reaction time, eluent for chromatography, the yields and physicochemical characteristics of compounds obtained are given).

***rac*-1-*O*-[*N*-(6-Aminohexyl)]carbamoyl-2,3-di-*O*-tetradecylglycerol hydrochloride (8b).** Compound **8b** (0.181 g, 90%) was obtained from compound **7b** (0.220 g, 0.303 mmol) (2 h, $CHCl_3$—MeOH (15 : 1)) as a crystallizing oil. Found (%): C, 66.83; H, 12.13; N, 4.25. $C_{38}H_{79}ClN_2O_4 \cdot H_2O$. Calculated (%): C, 66.97; H, 11.98; N, 4.11. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.13—1.38 (m, 48 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_2$); 1.40—1.55 (m, 6 H, 2 $OCH_2C\underline{H}_2$, $NHCH_2C\underline{H}_2$); 1.63—1.80 (m, 2 H, $NH_2CH_2C\underline{H}_2$); 2.85—3.00 (m, 2 H, $C\underline{H}_2NH_2$); 3.02—3.13 (m, 2 H, $NHC\underline{H}_2$); 3.30—3.70 (m, 7 H, 2 $OC\underline{H}_2CH_2$, OCH_2CH); 4.00 (dd, 1 H, J = 5.3 Hz, J = 11.5 Hz) and 4.10 (dd, 1 H, $CH_2OC(O)$, J = 4.3 Hz, J = 11.5 Hz); 5.02 (br.t, 1 H, CONH, J = 5.6 Hz). ^{13}C NMR, δ: 14.28, 22.84, 26.04, 26.18, 26.25, 27.47, 29.52, 29.67, 29.82, 29.85, 30.14, 32.07, 39.89, 40.84, 43.07, 61.76, 64.33, 70.55, 70.75, 71.25, 71.93, 72.42, 76.99, 156.64.

***rac*-1-*O*-[*N*-(8-Aminooctyl)]carbamoyl-2,3-di-*O*-tetradecylglycerol hydrochloride (8c).** Compound **8c** (0.184 g, 92%) was obtained from compound **7c** (0.219 g, 0.290 mmol) (4 h, $CHCl_3$—MeOH (15 : 1)) as a crystallizing oil. Found (%): C, 69.43; H, 12.30; N, 4.13. $C_{38}H_{79}ClN_2O_4$. Calculated (%): C, 69.47; H, 12.10; N, 4.05. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.11—1.34 (m, 52 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_4$); 1.35—1.57 (m, 6 H, 2 $OCH_2C\underline{H}_2$, $NHCH_2C\underline{H}_2$); 1.62—1.80 (m, 2 H, $NH_2CH_2C\underline{H}_2$); 2.82—3.00 (m, 2 H, $C\underline{H}_2NH_2$); 3.02—3.14 (m, 2 H, $NHC\underline{H}_2$); 3.33—3.70 (m, 7 H, 2 $OC\underline{H}_2CH_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.3 Hz, J = 11.5 Hz) and 4.12 (dd, 1 H, $CH_2OC(O)$, J = 4.1 Hz, J = 11.5 Hz); 4.72—4.84 (m, 1 H, CONH). ^{13}C NMR, δ: 13.90, 22.48, 25.84, 25.90, 26.15, 26.35, 27.33, 28.58, 28.70, 29.15, 29.30, 29.45, 29.49, 29.66, 29.81, 31.71, 39.76, 40.81, 63.99, 66.87, 70.25, 70.40, 71.58, 72.07, 76.68, 156.23.

***rac*-1-*O*-[*N*-(12-Aminododecyl)]carbamoyl-2,3-di-*O*-tetradecylglycerol hydrochloride (8d).** Compound **8d** (0.217 g, 94%) was obtained from compound **7d** (0.251 g, 0.309 mmol) (2 h, $CHCl_3$—MeOH (15 : 1)) as a crystallizing oil. MS, m/z (I_{rel} (%)): 711.814 $[M - HCl + H]^+$ (100). Calculated for $C_{44}H_{91}N_2O_4$: 711.698 $[M - HCl + H]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.10—1.33 (m, 60 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_8$); 1.35—1.57 (m, 6 H, 2 $OCH_2C\underline{H}_2$, $NHCH_2C\underline{H}_2$); 1.59—1.78 (m, 2 H, $NH_2CH_2C\underline{H}_2$); 2.81—2.98 (m, 2 H, $C\underline{H}_2NH_2$); 3.02—3.14 (m, 2 H, $NHC\underline{H}_2$); 3.29—3.63 (m, 7 H, 2 $OC\underline{H}_2CH_2$, OCH_2CH); 4.02 (dd, 1 H, J = 5.4 Hz, J = 11.5 Hz) and 4.13 (dd, 1 H, $CH_2OC(O)$, J = 4.1 Hz, J = 11.5 Hz); 4.70 (br.t, 1 H, CONH, J = 5.8 Hz). ^{13}C NMR, δ: 14.25, 22.81, 26.15, 26.21, 26.60, 26.89, 27.86, 29.09, 29.41, 29.49, 29.62, 29.78, 29.82, 30.10, 32.04, 40.08, 41.20, 64.23, 70.48, 70.69, 71.88, 76.95, 156.51.

***rac*-1-*O*-[*N*-(12-Amino-4,9-dioxadodecyl)]carbamoyl-2,3-di-*O*-tetradecylglycerol hydrochloride (8e).** Compound **8e** (0.223 g, 90%) was obtained from compound **7e** (0.269 g, 0.330 mmol) (3 h, $CHCl_3$—MeOH (15 : 1)) as a crystallizing oil. MS, m/z (I_{rel} (%)): 715.756 $[M - HCl + H]^+$ (100). Calculated for $C_{42}H_{87}N_2O_6$: 715.656 $[M - HCl + H]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.10—1.32 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.42—1.64 (m, 8 H, 4 $OCH_2C\underline{H}_2$); 1.65—1.77 (m, 2 H, $OCH_2C\underline{H}_2$); 1.86—1.98 (m, 2 H, $OCH_2C\underline{H}_2$); 3.03—3.15 (m, 2 H, $NH_2C\underline{H}_2$); 3.16—3.26 (m, 2 H, $NHC\underline{H}_2$); 3.32—3.68 (m, 15 H, 6 $OC\underline{H}_2CH_2$, OCH_2CH); 4.00 (dd, 1 H, J = 5.4 Hz, J = 11.5 Hz) and 4.10 (dd, 1 H, $CH_2OC(O)$, J = 4.3 Hz, J = 11.5 Hz); 5.45 (t, 1 H, CONH, J = 5.4 Hz). ^{13}C NMR, δ: 13.54, 22.10, 25.46, 25.53, 25.73, 25.76, 27.44, 28.78, 28.94, 29.06, 29.12, 29.44, 31.34, 38.39, 38.55, 63.59, 68.15, 68.44, 69.88, 70.04, 70.53, 71.20, 76.32, 155.90.

***rac*-1-*O*-[*N*-(13-Amino-4,7,10-trioxatridecyl)]carbamoyl-2,3-di-*O*-tetradecylglycerol hydrochloride (8f).** Compound **8f** (0.232 g, 93%) was obtained from compound **7f** (0.270 g, 0.325 mmol) (3 h, $CHCl_3$—MeOH (15 : 1)) as a crystallizing oil. R_f 0.55 (K). MS, m/z (I_{rel} (%)): 731.763 $[M - HCl + H]^+$ (100). Calculated for $C_{42}H_{87}N_2O_7$: 731.651 $[M - HCl + H]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.10—1.32 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.46—1.54 (m, 4 H, 2 $OCH_2C\underline{H}_2$); 1.68—1.78 (m, 2 H, $OCH_2C\underline{H}_2$); 1.89—2.03 (m, 2 H, $OCH_2C\underline{H}_2$); 3.03—3.15 (m, 2 H, $NH_2C\underline{H}_2$); 3.16—3.26 (m, 2 H, $NHC\underline{H}_2$); 3.32—3.68 (m, 19 H, 7 $OC\underline{H}_2CH_2$, OCH_2CH); 4.00 (dd, 1 H, J = 5.4 Hz, J = 11.5 Hz) and 4.10 (dd, 1 H, $CH_2OC(O)$, J = 4.4 Hz, J = 11.5 Hz); 5.45 (br.t, 1 H, CONH, J = 5.4 Hz). ^{13}C NMR, δ: 13.54, 22.11, 25.47, 25.53, 26.26, 28.78, 28.94, 29.07, 29.12, 29.72, 29.44, 31.34, 38.00, 39.19, 63.13, 63.64, 68.39, 69.31, 69.56, 69.86, 70.04, 71.21, 76.29, 156.19.

***rac*-1-*O*-{*N*-[4-*N*-(4-Ethoxy-1,2-dioxocyclobut-3-enyl)aminobutyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (9a).** Triethylamine (0.1 mL) and 3,4-diethoxycyclobut-3-ene-1,2-dione (0.153 mmol) were sequentially added to a solution of compound **8a** (0.076 mmol) in $CHCl_3$ (2 mL), and the mixture was stirred for 4 h at 24 °C. The solvent was evaporated *in vacuo*, the product was isolated by column chromatography; elution with $CHCl_3$ → $CHCl_3$—MeOH (70 : 1) solvent system afforded compound **9a** (44.2 mg, 80%) as a crystallizing oil. MS, m/z (I_{rel} (%)): 745.384 $[M + Na]^+$ (100). Calculated for $C_{42}H_{78}N_2O_7$: 722.581 $[M]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.15—1.30 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.35—1.66 (m, 11 H, 2 $OCH_2C\underline{H}_2$, 2 $NHCH_2C\underline{H}_2$, $OCH_2\underline{Me}$); 3.07—3.19 (m, 2 H, $NHC\underline{H}_2$); 3.31—3.68 (m, 9 H, 2 $OC\underline{H}_2CH_2$, $NHC\underline{H}_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.6 Hz, J = 11.4 Hz) and 4.12 (dd, 1 H, $CH_2OC(O)$, J = 4.0 Hz, J = 11.5 Hz); 4.64—4.75 (m, 2 H, $OC\underline{H}_2Me$); 4.80—4.93 (m, 1 H, CONH); 6.85—7.02 (m, 1 H, NH). ^{13}C NMR, δ: 13.52, 15.27, 22.10, 25.46, 25.52, 26.34, 27.08, 28.78, 28.92, 29.05, 29.11, 29.43, 31.34, 39.75, 43.76, 63.80, 69.16, 69.77, 70.02, 71.21, 76.25, 156.00, 171.86, 176.89, 182.06, 189.01.

Compounds **9b—f** were obtained similarly (below, the amounts of compounds **8b—f** and 3,4-diethoxycyclobut-3-ene-1,2-dione, the yields, and physicochemical characteristics of compounds obtained are given).

***rac*-1-*O*-{*N*-[6-*N*-(4-Ethoxy-1,2-dioxocyclobut-3-enyl)aminohexyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (9b).** Compound **9b** (84 mg, 97%) was obtained from compound **8b** (76.4 mg, 0.115 mmol) and 3,4-diethoxycyclobut-3-ene-1,2-dione (34 μL, 0.230 mmol) as a crystallizing oil. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.12—1.35 (m, 48 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_2$); 1.36—1.62 (m, 11 H, 2 $OCH_2C\underline{H}_2$, 2 $NHCH_2C\underline{H}_2$, $OCH_2\underline{Me}$); 3.02—3.12 (m, 2 H, $NHC\underline{H}_2$); 3.32—3.62 (m, 9 H, 2 $OC\underline{H}_2CH_2$, $NHC\underline{H}_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.4 Hz, J = 11.5 Hz) and 4.12 (dd, 1 H, $CH_2OC(O)$, J = 4.1 Hz, J = 11.5 Hz); 4.61—4.83 (m, 3 H, $OC\underline{H}_2Me$, CONH); 6.86—7.07 (m, 1 H, NH). ^{13}C NMR, δ: 13.52, 15.28, 22.10, 25.29, 25.46, 25.51, 28.77, 28.91, 29.26, 29.43, 29.81, 31.33, 40.18, 44.04, 63.67, 69.81, 70.00, 71.19, 76.27, 155.94, 171.86, 176.82, 182.03, 189.07.

***rac*-1-*O*-{*N*-[8-*N*-(4-Ethoxy-1,2-dioxocyclobut-3-enyl)aminooctyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (9c).** Compound **9c** (115 mg, 96%) was obtained from compound **8c** (106.0 mg, 0.153 mmol) and 3,4-diethoxycyclobut-3-ene-1,2-dione (45.4 μL, 0.306 mmol) as a crystallizing oil. ^{1}H NMR, δ: 0.80 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.10—1.29 (m, 52 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_4$); 1.33—1.62 (m, 11 H, 2 $OCH_2C\underline{H}_2$, 2 $NHCH_2C\underline{H}_2$, $OCH_2\underline{Me}$); 3.02—3.14 (m, 2 H, $NHC\underline{H}_2$); 3.29—3.61 (m, 9 H, 2 $OC\underline{H}_2CH_2$, $NHC\underline{H}_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.5 Hz, J = 11.5 Hz) and 4.12 (dd, 1 H, $CH_2OC(O)$, J = 4.2 Hz, J = 11.5 Hz); 4.60—4.85 (m, 3 H, $OC\underline{H}_2Me$, CONH). ^{13}C NMR, δ: 13.50, 15.25, 22.07, 25.44, 25.49, 25.65, 25.99, 28.34, 28.46, 28.75, 28.89, 29.05, 29.08, 29.29, 29.41, 29.89, 31.31, 40.38, 44.20, 63.59, 68.97, 69.80, 69.96, 71.14, 76.27, 155.85, 171.89, 176.73, 181.95, 189.14.

***rac*-1-*O*-{*N*-[12-*N*-(4-Ethoxy-1,2-dioxocyclobut-3-enyl)-aminododecyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (9d).** Compound **9d** (133 mg, 99%) was obtained from compound **8d** (120.4 mg, 0.161 mmol) and 3,4-diethoxycyclobut-3-ene-1,2-dione (47.6 μL, 0.322 mmol) as a crystallizing oil. MS, m/z (I_{rel} (%)): 857.520 $[M + Na]^+$ (100). Calculated for $C_{50}H_{94}N_2O_7$: 834.706 $[M]^+$. ^{1}H NMR, δ: 0.80 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.12—1.32 (m, 60 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_8$); 1.34—1.62 (m, 11 H, 2 $OCH_2C\underline{H}_2$, 2 $NHCH_2C\underline{H}_2$, $OCH_2\underline{Me}$); 3.03—3.14 (m, 2 H, $NHC\underline{H}_2$); 3.30—3.64 (m, 9 H, 2 $OC\underline{H}_2CH_2$, $NHC\underline{H}_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.5 Hz, J = 11.5 Hz) and 4.13 (dd, 1 H, $CH_2OC(O)$, J = 4.1 Hz, J = 11.5 Hz); 4.61—4.78 (m, 3 H, $OC\underline{H}_2Me$, CONH); 6.74—6.96 (m, 1 H, NH). ^{13}C NMR, δ: 13.52, 15.26, 22.09, 25.46, 25.51, 25.73, 26.14, 28.51, 28.65, 28.77, 28.91, 29.10, 29.42, 29.99, 31.33, 40.48, 44.28, 63.59, 68.98, 69.81, 69.99, 71.17, 76.28, 155.83, 171.87, 176.74, 182.03, 189.07.

***rac*-1-*O*-{*N*-[12-*N*-(4-Ethoxy-1,2-dioxocyclobut-3-enyl)-amino-4,9-dioxadodecyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (9e).** Compound **9e** (88.3 mg, 72%) was obtained from compound **8e** (109.5 mg, 0.146 mmol) and 3,4-diethoxycyclobut-3-ene-1,2-dione (43 μL, 0.290 mmol) as a crystallizing oil. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.09—1.29 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.32—1.62 (m, 11 H, 4 $OCH_2C\underline{H}_2$, $OCH_2\underline{Me}$); 1.59—1.75 (m, 2 H, $OCH_2C\underline{H}_2$); 1.75—1.86 (m, 2 H, $OCH_2C\underline{H}_2$); 3.15—3.25 (m, 2 H, $NHC\underline{H}_2$); 3.31—3.55 (m, 17 H, 6 $OC\underline{H}_2CH_2$, $NHC\underline{H}_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.5 Hz, J = 11.5 Hz) and 4.12 (dd, 1 H, $CH_2OC(O)$, J = 4.2 Hz, J = 11.5 Hz); 4.61—4.75 (m, 2 H, $OC\underline{H}_2Me$); 5.02—5.12 (m, 1 H, CONH); 6.74—6.97 (m, 1 H, NH). ^{13}C NMR, δ: 13.51, 15.25, 22.08, 25.45, 25.51, 25.80, 25.87, 28.76, 28.91, 29.09, 29.43, 31.32, 38.51, 42.60, 63.61, 68.03, 68.32, 68.87, 69.86, 69.99, 70.12, 70.39, 71.17, 76.29, 155.85, 171.94, 176.56, 182.45, 188.56.

***rac*-1-*O*-{*N*-[13-*N*-(4-Ethoxy-1,2-dioxocyclobut-3-enyl)-amino-4,7,10-trioxatridecyl]}carbamoyl-2,3-di-*O*-tetradecylglycerol (9f).** Compound **9f** (108 mg, 86%) was obtained from compound **8f** (112.7 mg, 0.147 mmol) and 3,4-diethoxycyclobut-3-ene-1,2-dione (43.4 μL, 0.294 mmol) as a crystallizing oil. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.09—1.29 (m, 44 H, 2 $(C\underline{H}_2)_{11}Me$); 1.32—1.55 (m, 7 H, 2 $OCH_2C\underline{H}_2$, $OCH_2\underline{Me}$); 1.64—1.75 (m, 2 H, $CH_2(11)$); 1.75—1.86 (m, 2 H, $CH_2(12)$); 3.14—3.28 (m, 2 H, $NHC\underline{H}_2$); 3.31—3.66 (m, 21 H, 8 $OC\underline{H}_2CH_2$, $NHC\underline{H}_2$, OCH_2CH); 4.01 (dd, 1 H, J = 5.5 Hz, J = 11.5 Hz) and 4.11 (dd, 1 H, $CH_2OC(O)$, J = 4.3 Hz, J = 11.5 Hz); 4.61—4.78 (m, 2 H, $OC\underline{H}_2Me$); 5.02—5.27 (m, 1 H, CONH); 6.95—7.10 (m, 1 H, NH). ^{13}C NMR, δ: 13.51, 15.25, 22.08, 25.45, 25.51, 28.76, 28.91, 29.05, 29.09, 29.43, 31.32, 38.51, 42.64, 63.61, 68.71, 68.79, 69.64, 69.74, 69.89, 69.97, 71.17, 76.29, 155.89, 172.06, 176.34, 182.53, 188.42.

3-[6-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-hexyl]amino-4-{4-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonylamino]butyl}aminocyclobut-3-ene-1,2-dione (10a). A mixture of compound **3** (0.077 mmol) and Et_3N (0.1 mL) in $CHCl_3$ (4 mL) was added to a solution of compound **9a** (0.042 mmol) in $CHCl_3$ (2 mL) and the mixture was kept for 36 h at 24 °C. The solvents were evaporated *in vacuo*, the product was isolated by column chromatography; elution with a $CHCl_3$—MeOH (70 : 1 → 50 : 1) solvent system afforded compound **10a** (41.8 mg, 89%) as a crystallizing oil, $[\alpha]_D^{28}$ −5.36 (*c* 0.5, $CHCl_3$). MS, m/z (I_{rel} (%)): 1147.026 $[M + Na]^+$ (100). Calculated for $C_{60}H_{105}N_3O_{16}$: 1123.749 $[M]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.11—1.35 (m, 48 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_2$); 1.40—1.68 (m, 12 H, 3 $OCH_2C\underline{H}_2$, 3 $NHCH_2C\underline{H}_2$); 1.92, 1.98, 1.99, 2.08 (all s, 3 H each, 4 MeCO); 3.08—3.20 (m, 2 H, $NHC\underline{H}_2$); 3.30—3.69 (m, 12 H, 2 $OC\underline{H}_2CH_2$, 2 $NHC\underline{H}_2$, OCH_2CH, $OCH\underline{H}_a$); 3.76—3.89 (m, 2 H, H(5) Gal, $OCH\underline{H}_b$); 3.96—4.16 (m, 4 H, H(6) Gal, $CH_2OC(O)$); 4.39 (d, 1 H, H(1) Gal, J = 7.9 Hz); 4.96 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 10.5 Hz); 5.10 (dd, 1 H, H(2) Gal, J = 7.8 Hz, J = 10.5 Hz); 5.17 (br.t, 1 H, CONH, J = 6.3 Hz); 5.33 (dd, 1 H, H(4) Gal, J = 0.9 Hz, J = 3.4 Hz); 6.89—7.02 (m, 1 H, NH); 7.04—7.17 (m, 1 H, NH). ^{13}C NMR, δ: 13.53, 20.00, 20.07, 20.10, 20.25, 22.10, 24.99, 25.47, 25.52, 25.60, 26.41, 27.07, 28.78, 28.94, 29.08, 29.46, 30.54, 31.34, 43.41, 43.96, 60.59, 63.99, 66.48, 68.48, 69.60, 69.77, 70.03, 70.09, 70.29, 71.23, 76.26, 100.79, 156.36, 167.14, 167.46, 169.11, 169.50, 169.62, 169.86, 181.93, 182.10.

Compounds **10b**—**f** were obtained similarly (below, the amounts of compounds **9b**—**f** and compound **3**, reaction temperature, reaction time, the yields, and physicochemical characteristics of compounds obtained are given).

3-[6-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-hexyl]amino-4-{6-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonylamino]hexyl}aminocyclobut-3-ene-1,2-dione (10b). Compound **10b** (56.4 mg, 74%) was obtained from compound **9b** (49.7 mg, 0.069 mmol) and compound **3** (39.9 mg, 0.082 mmol) (24 °C, 34 h) as a crystallizing oil, $[\alpha]_D^{28}$ −4.06 (*c* 1, $CHCl_3$). Found (%): C, 64.64; H, 9.59; N, 3.47. $C_{62}H_{109}N_3O_{16}$. Calculated (%): C, 64.61; H, 9.53; N, 3.65. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.10—1.37 (m, 52 H, 2 $(C\underline{H}_2)_{11}Me$, 2 $(CH_2)_2$); 1.38—1.63 (m, 12 H, 3 $OCH_2C\underline{H}_2$, 3 $NHCH_2C\underline{H}_2$); 1.91, 1.98, 1.99, 2.07 (all s, 3 H each, 4 MeCO); 3.04—3.15 (m, 2 H, $NHC\underline{H}_2$); 3.28—3.68 (m, 12 H, 2 $OC\underline{H}_2CH_2$, 2 $NHC\underline{H}_2$, OCH_2CH, $OCH\underline{H}_a$); 3.75—3.90 (m, 2 H, H(5) Gal, $OCH\underline{H}_b$); 3.95—4.19 (m, 4 H, H(6) Gal, $CH_2OC(O)$); 4.39 (d, 1 H, H(1)

Gal, J = 7.9 Hz); 4.95 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 10.5 Hz); 4.96—5.05 (m, 1 H, CONH); 5.10 (dd, 1 H, H(2) Gal, J = 7.9 Hz, J = 10.5 Hz); 5.33 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.4 Hz); 6.85—7.16 (m, 2 H, 2 NH). ^{13}C NMR, δ: 13.52, 19.99, 20.07, 20.09, 20.23, 22.08, 24.79, 24.98, 25.05, 25.46, 25.51, 25.62, 28.77, 28.92, 29.07, 29.11, 29.23, 29.44, 30.10, 30.58, 31.33, 39.93, 43.40, 43.92, 60.59, 63.99, 66.47, 68.44, 69.57, 69.72, 70.01, 70.08, 70.30, 71.22, 76.25, 100.76, 156.34, 167.29, 167.53, 169.04, 169.49, 169.63, 169.84, 181.93, 182.04.

3-[6-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-hexyl]amino-4-{8-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonyl-amino]octyl}aminocyclobut-3-ene-1,2-dione (10c). Compound **10c** (75.9 mg, 85%) was obtained from compound **9c** (58.7 mg, 0.075 mmol) and compound **3** (37.1 mg, 0.077 mmol) (24 °C, 48 h) as a crystallizing oil, $[\alpha]_D^{28}$ 1.02 (*c* 1, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 1203.016 $[M + Na]^+$ (100). Calculated for $C_{64}H_{113}N_3O_{16}$: 1179.812 $[M]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.09—1.35 (m, 56 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_2$, $(CH_2)_4$); 1.36—1.64 (m, 12 H, 3 $OCH_2C\underline{H}_2$, 3 $NHCH_2C\underline{H}_2$); 1.91, 1.98, 1.99, 2.08 (all s, 3 H each, 4 MeCO); 3.00—3.11 (m, 2 H, $NHC\underline{H}_2$); 3.32—3.64 (m, 12 H, 2 $OC\underline{H}_2CH_2$, 2 $NHC\underline{H}_2$, OCH_2CH, $OCH\underline{H}_a$); 3.80 (dt, 1 H, $OCH\underline{H}_b$, J = 6.1 Hz, J = 9.3 Hz); 3.84 (dt, 1 H, H(5) Gal, J = 1.1 Hz, J = 6.8 Hz); 3.96—4.18 (m, 4 H, H(6) Gal, $CH_2OC(O)$); 4.39 (d, 1 H, H(1) Gal, J = 7.9 Hz); 4.89—4.98 (m, 1 H, CONH); 4.96 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 10.5 Hz); 5.10 (dd, 1 H, H(2) Gal, J = 7.9 Hz, J = 10.5 Hz); 5.33 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.4 Hz); 6.82—7.10 (m, 2 H, 2 NH). ^{13}C NMR, δ: 13.53, 20.00, 20.07, 20.11, 20.25, 22.10, 25.01, 25.47, 25.51, 25.64, 25.77, 25.91, 28.48, 28.78, 28.93, 29.08, 29.12, 29.35, 29.44, 30.53, 30.57, 31.34, 40.45, 43.94, 60.60, 66.47, 68.47, 69.60, 69.74, 70.02, 70.07, 70.30, 71.22, 76.26, 100.79, 156.23, 167.28, 167.50, 169.09, 169.50, 169.63, 169.85, 181.94, 182.07.

3-[6-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-hexyl]amino-4-{12-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonyl-amino]dodecyl}aminocyclobut-3-ene-1,2-dione (10d). Compound **10d** (78.7 mg, 52%) was obtained from compound **9d** (103 mg, 0.123 mmol) and compound **3** (50.2 mg, 0.104 mmol) (24 °C, 10 h) as a crystallizing oil, $[\alpha]_D^{28}$ −7.3 (*c* 0.5, $CHCl_3$). Found (%): C, 66.06; H, 9.84; N, 3.56. $C_{68}H_{121}N_3O_{16}$. Calculated (%): C, 66.04; H, 9.86; N, 3.40. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.08—1.35 (m, 64 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_2$, $(CH_2)_8$); 1.35—1.64 (m, 12 H, 3 $OCH_2C\underline{H}_2$, 3 $NHCH_2C\underline{H}_2$); 1.91, 1.98, 1.98, 2.07 (all s, 3 H each, 4 MeCO); 3.00—3.14 (m, 2 H, $NHC\underline{H}_2$); 3.27—3.71 (m, 12 H, 2 $OC\underline{H}_2CH_2$, 2 $NHC\underline{H}_2$, OCH_2CH, $OCH\underline{H}_a$); 3.74—3.90 (m, 2 H, H(5) Gal, $OCH\underline{H}_b$); 3.95—4.18 (m, 4 H, H(6) Gal, $CH_2OC(O)$); 4.39 (d, 1 H, H(1) Gal, J = 7.9 Hz); 4.83 (br.t, 1 H, CONH, J = 5.6 Hz); 4.96 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 10.5 Hz); 5.09 (dd, 1 H, H(2) Gal, J = 7.9 Hz, J = 10.5 Hz); 5.32 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.4 Hz); 7.27—7.52 (m, 2 H, 2 NH). ^{13}C NMR, δ: 13.52, 19.98, 20.05, 20.07, 20.21, 22.09, 25.01, 25.45, 25.50, 25.67, 25.96, 26.19, 28.71, 28.76, 28.90, 29.05, 29.10, 29.42, 30.58, 30.66, 31.32, 40.51, 44.00, 44.10, 60.56, 63.73, 66.45, 68.42, 69.54, 69.79, 69.99, 70.01, 70.30, 71.18, 76.28, 100.76, 156.00, 167.19, 167.45, 168.94, 169.49, 169.61, 169.79, 181.61, 181.85.

3-[6-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-hexyl]amino-4-{12-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonyl-amino]-4,9-dioxadodecyl}aminocyclobut-3-ene-1,2-dione (10e). Compound **10e** (52.6 mg, 57%) was obtained from compound **9e** (88.3 mg, 0.103 mmol) and compound **3** (36.1 mg, 0.075 mmol) (40 °C, 37 h) as a crystallizing oil, $[\alpha]_D^{28}$ −3.7 (*c* 1, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 1263.169 $[M + Na]^+$ (100). Calculated for $C_{66}H_{117}N_3O_{18}$: 1239.833 $[M]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.09—1.37 (m, 48 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_2$); 1.39—1.63 (m, 12 H, 5 $OCH_2C\underline{H}_2$, $NHCH_2C\underline{H}_2$); 1.64—1.75 (m, 2 H, $OCH_2C\underline{H}_2$)); 1.76—1.87 (m, 2 H, $OCH_2C\underline{H}_2$); 1.91, 1.98, 1.99, 2.08 (all s, 3 H each, 4 MeCO); 3.14—3.26 (m, 2 H, $NHC\underline{H}_2$); 3.29—3.73 (m, 20 H, 6 $OC\underline{H}_2CH_2$, 2 $NHC\underline{H}_2$, OCH_2CH, $OCH\underline{H}_a$); 3.76—3.89 (m, 2 H, H(5) Gal, $OCH\underline{H}_b$); 4.00 (dd, 1 H, $CH_2OC(O)$, J = 5.5 Hz, J = 11.3 Hz); 4.04—4.16 (m, 3 H, H(6) Gal, $CH_2OC(O)$); 4.39 (d, 1 H, H(1) Gal, J = 7.9 Hz); 4.95 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 10.5 Hz); 5.11 (dd, 1 H, H(2) Gal, J = 7.9 Hz, J = 10.5 Hz); 5.05—5.18 (m, 1 H, CONH); 5.32 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.4 Hz); 6.72—6.89 (m, 2 H, 2 NH). ^{13}C NMR, δ: 13.52, 19.99, 20.06, 20.09, 20.22, 22.09, 24.97, 25.45, 25.50, 25.61, 25.78, 25.87, 28.76, 28.91, 29.06, 29.10, 29.42, 30.62, 30.68, 31.32, 38.41, 41.49, 43.85, 60.61, 63.82, 66.48, 67.49, 68.05, 68.41, 69.56, 69.73, 70.01, 70.13, 70.32, 71.23, 76.27, 100.78, 156.04, 167.28, 167.55, 169.00, 169.51, 169.64, 169.82, 182.11, 182.27.

3-[6-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyloxy)-hexyl]amino-4-{13-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonyl-amino]-4,7,10-trioxatridecyl}aminocyclobut-3-ene-1,2-dione (10f). Compound **10f** (46.8 mg, 50%) was obtained from compound **9f** (84.1 mg, 0.100 mmol) and compound **3** (35.9 mg, 0.074 mmol) (40 °C, 43 h) as a crystallizing oil, $[\alpha]_D^{28}$ −2.95 (*c* 0.5, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 1279.200 $[M + Na]^+$ (100). Calculated for $C_{66}H_{117}N_3O_{19}$: 1255.828 $[M]^+$. ^{1}H NMR, δ: 0.81 (t, 6 H, 2 $(CH_2)_{11}\underline{Me}$, J = 6.7 Hz); 1.09—1.36 (m, 48 H, 2 $(C\underline{H}_2)_{11}Me$, $(CH_2)_2$); 1.40—1.59 (m, 8 H, 3 $OCH_2C\underline{H}_2$, $NHCH_2C\underline{H}_2$); 1.64—1.75 (m, 2 H, $OCH_2C\underline{H}_2$); 1.77—1.87 (m, 2 H, $OCH_2C\underline{H}_2$); 1.91, 1.98, 1.99, 2.08 (all s, 3 H each, 4 MeCO); 3.14—3.25 (m, 2 H, $NHC\underline{H}_2$); 3.30—3.74 (m, 24 H, 8 $OC\underline{H}_2CH_2$, 2 $NHC\underline{H}_2$, OCH_2CH, $OCH\underline{H}_a$); 3.80 (dt, 1 H, $OCH\underline{H}_b$, J = 6.3 Hz, J = 9.5 Hz); 3.84 (dt, 1 H, H(5) Gal, J = 1.1 Hz, J = 6.7 Hz); 4.00 (dd, 1 H, $CH\underline{H}_aOC(O)$, J = 5.6 Hz, J = 11.3 Hz); 4.07 (dd, 1 H, J = 6.7 Hz, J = 11.1 Hz) and 4.11 (dd, 1 H, both H(6) Gal, J = 6.7 Hz, J = 11.1 Hz); 4.11 (dd, 1 H, $CH\underline{H}_bOC(O)$, J = 3.9 Hz, J = 11.3 Hz); 4.39 (d, 1 H, H(1) Gal, J = 7.9 Hz); 4.95 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 10.5 Hz); 5.11 (dd, 1 H, H(2) Gal, J = 7.9 Hz, J = 10.5 Hz); 5.12—5.19 (m, 1 H, CONH); 5.32 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.4 Hz); 6.51—6.61 (m, 1 H, NH); 6.61—6.76 (m, 1 H, NH). ^{13}C NMR, δ: 13.53, 20.00, 20.07, 20.10, 20.22, 22.09, 24.95, 25.46, 25.51, 25.58, 28.76, 28.92, 29.05, 29.06, 29.10, 29.44, 29.95, 30.75, 31.32, 31.33, 38.10, 42.00, 43.77, 60.63, 63.83, 66.49, 68.39, 68.51, 68.96, 69.40, 69.56, 69.64, 69.70, 69.76, 70.02, 70.34, 71.24, 76.25, 100.79, 156.11, 167.27, 167.63, 168.97, 169.54, 169.66, 169.84, 182.26, 182.49.

3-[6-(β-D-Galactopyranosyloxy)hexyl]amino-4-{4-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonylamino]butyl}aminocyclobut-3-ene-1,2-dione (11a). A solution of MeONa in MeOH (0.1 *M*, 0.5 mL) was added to a solution of compound **10a** (0.024 mmol) in CH_2Cl_2 (3 mL). After 40 min, the reaction mixture was neutralized with the ion-exchange resin Dowex 50×8 (H^+), filtered, the solvent was evaporated *in vacuo*. The product was isolated by column chromatography; elution with the CH_2Cl_2—MeOH (10 : 1) solvent system afforded compound **11a** (20.9 mg, 93%) as a crystallizing oil, $[\alpha]_D^{25}$ 0.3 (*c* 2, $CHCl_3$—CH_3OH, 1 : 1). MS, *m/z* (I_{rel} (%)): 978.953 $[M + Na]^+$ (100). Calculated for $C_{52}H_{97}N_3O_{12}$: 955.707 $[M]^+$. ^{1}H NMR (Py-d_5), δ: 0.81 (t, 6 H,

2 $(CH_2)_{11}$Me, J = 6.7 Hz); 1.10—1.39 (m, 48 H, 2 $(CH_2)_{11}$Me, $(CH_2)_2$); 1.40—1.79 (m, 12 H, 3 OCH_2CH_2, 3 $NHCH_2CH_2$); 3.22—3.34 (m, 2 H, $NHCH_2$); 3.36—3.46 (m, 2 H, $NHCH_2$); 3.55 (dt, 1 H, CH_aH_b, J = 6.5 Hz, J = 9.0 Hz); 3.57—3.77 (m, 8 H, 2 OCH_2CH_2, $NHCH_2$, OCH_2CH); 3.78—3.87 (m, 1 H, OCH_2CH); 3.92—4.02 (m, 2 H, H(5) Gal, OCH_aH_b); 4.07 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 9.5 Hz); 4.33 (dd, 1 H, H(2) Gal, J = 7.7 Hz, J = 9.5 Hz); 4.34—4.38 (m, 2 H, H(6) Gal); 4.41 (dd, 1 H, $CH_aH_bOC(O)$, J = 5.6 Hz, J = 11.3 Hz); 4.49 (dd, 1 H, H(4) Gal, J = 0.9 Hz, J = 3.4 Hz); 4.50 (dd, 1 H, $CH_aH_bOC(O)$, J = 4.6 Hz, J = 11.3 Hz); 4.64 (d, 1 H, H(1) Gal, J = 7.7 Hz); 7.86—8.23 (m, 3 H, 3 NH). ^{13}C NMR, δ: 14.94, 23.61, 26.69, 26.98, 27.17, 27.21, 28.05, 29.85, 30.29, 30.49, 30.51, 30.60, 30.64, 30.66, 30.83, 31.30, 32.17, 32.81, 41.56, 44.77, 44.97, 63.12, 70.26, 71.01, 71.25, 71.79, 72.44, 73.29, 75.94, 77.51, 78.41, 105.88, 158.13, 169.68, 169.77, 184.77.

Compounds **11b**—**f** were obtained similarly (below, the amounts of compounds **10b**—**f**, the yields, and physicochemical characteristics of compounds obtained are given).

3-[6-(β-D-Galactopyranosyloxy)hexyl]amino-4-{6-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonylamino]hexyl}aminocyclobut-3-ene-1,2-dione (11b). Compound **11b** (20.4 mg, 98%) was obtained from compound **10b** (24.4 mg, 0.021 mmol) as a crystallizing oil, $[\alpha]_D^{25}$ −4.12 (*c* 1, $CHCl_3$—CH_3OH, 1 : 1). MS, *m/z* (I_{rel} (%)): 1007.009 $[M + Na]^+$ (100). Calculated for $C_{54}H_{101}N_3O_{12}$: 983.738 $[M]^+$. ^{1}H NMR (Py-d_5), δ: 0.80 (t, 6 H, 2 $(CH_2)_{11}$Me, J = 6.7 Hz); 1.09—1.39 (m, 52 H, 2 $(CH_2)_{11}$Me, 2 $(CH_2)_2$); 1.39—1.62 (m, 12 H, 3 OCH_2CH_2, 3 $NHCH_2CH_2$); 3.17—3.28 (m, 2 H, $NHCH_2$); 3.35—3.44 (m, 2 H, $NHCH_2$); 3.53 (dt, 1 H, OCH_aH_b, J = 6.5 Hz, J = 9.5 Hz); 3.58—3.71 (m, 8 H, 2 OCH_2CH_2, $NHCH_2$, OCH_2CH); 3.75—3.87 (m, 1 H, OCH_2CH); 3.91—4.00 (m, 2 H, H(5) Gal, OCH_aH_b); 4.06 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 9.5 Hz); 4.31 (dd, 1 H, H(2) Gal, J = 7.6 Hz, J = 9.5 Hz); 4.32—4.37 (m, 2 H, H(6) Gal); 4.42 (dd, 1 H, $CH_aH_bOC(O)$, J = 5.6 Hz, J = 11.3 Hz); 4.48 (dd, 1 H, H(4) Gal, J = 1.0 Hz, J = 3.4 Hz); 4.51 (dd, 1 H, $CH_aH_bOC(O)$, J = 4.4 Hz, J = 11.3 Hz); 4.63 (d, 1 H, H(1) Gal, J = 7.6 Hz); 7.80—7.88 (m, 1 H, 1 CONH); 7.91—8.14 (m, 2 H, 2 NH). ^{13}C NMR, δ: 14.94, 23.30, 26.37, 26.68, 26.75, 26.86, 26.89, 27.10, 29.97, 30.17, 30.19, 30.29, 30.32, 30.35, 30.51, 30.72, 30.99, 31.90, 32.17, 32.49, 41.62, 44.66, 44.75, 62.80, 64.87, 69.94, 70.69, 70.93, 71.48, 72.12, 72.98, 75.63, 77.22, 78.12, 105.57, 157.78, 169.43, 184.49, 184.52.

3-[6-(β-D-Galactopyranosyloxy)hexyl]amino-4-{8-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonylamino]octyl}aminocyclobut-3-ene-1,2-dione (11c). Compound **11c** (51.8 mg, 85%) was obtained from compound **10c** (70.9 mg, 0.060 mmol) as a crystallizing oil, $[\alpha]_D^{26}$ −3.72 (*c* 1, $CHCl_3$—CH_3OH, 1 : 1). MS, *m/z* (I_{rel} (%)): 1034.891 $[M + Na]^+$ (100). Calculated for $C_{56}H_{105}N_3O_{12}$: 1011.770 $[M]^+$. ^{1}H NMR (Py-d_5), δ: 0.80 (t, 6 H, 2 $(CH_2)_{11}$Me, J = 6.7 Hz); 1.02—1.39 (m, 56 H, 2 $(CH_2)_{11}$Me, $(CH_2)_2$, $(CH_2)_4$); 1.41—1.65 (m, 12 H, 3 OCH_2CH_2, 3 $NHCH_2CH_2$); 3.21—3.33 (m, 2 H, $NHCH_2$); 3.34—3.44 (m, 2 H, $NHCH_2$); 3.52 (dt, 1 H, CH_aH_b, J = 6.5 Hz, J = 8.7 Hz); 3.56—3.74 (m, 8 H, 2 OCH_2CH_2, $NHCH_2$, OCH_2CH); 3.76—3.87 (m, 1 H, OCH_2CH); 3.89—4.00 (m, 2 H, H(5) Gal, OCH_aH_b); 4.05 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 9.5 Hz); 4.29 (dd, 1 H, H(2) Gal, J = 7.7 Hz, J = 9.5 Hz); 4.33 (d, 2 H, H(6) Gal, J = 6.0 Hz); 4.41 (dd, 1 H, $CH_aH_bOC(O)$, J = 5.6 Hz, J = 11.4 Hz); 4.47 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.5 Hz); 4.51 (dd, 1 H, $CH_aH_bOC(O)$, J = 4.3 Hz, J = 11.6 Hz); 4.62 (d, 1 H, H(1) Gal, J = 7.7 Hz); 7.84 (t, 1 H, CONH, J = 5.4 Hz); 7.91—8.20 (m, 2 H, 2 NH). ^{13}C NMR, δ: 14.58, 23.24, 26.32, 26.66, 26.80, 26.83, 27.00, 27.43, 29.75, 29.78, 29.92, 30.10, 30.13, 30.23, 30.26, 30.29, 30.44, 30.74, 30.93, 31.87, 32.14, 32.44, 41.72, 44.63, 44.83, 69.89, 70.64, 70.86, 71.42, 72.05, 72.89, 75.52, 77.10, 78.06, 105.49, 149.80, 150.16, 150.51, 169.32, 169.40, 184.38.

3-[6-(β-D-Galactopyranosyloxy)hexyl]amino-4-{12-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonylamino]dodecyl}aminocyclobut-3-ene-1,2-dione (11d). Compound **11d** (44.2 mg, 95%) was obtained from compound **10d** (54.1 mg, 0.044 mmol) as a crystallizing oil, $[\alpha]_D^{26}$ −2.85 (*c* 1, $CHCl_3$—CH_3OH, 1 : 1). MS, *m/z* (I_{rel} (%)): 1091.094 $[M + Na]^+$ (100). Calculated for $C_{60}H_{113}N_3O_{12}$: 1067.832 $[M]^+$. ^{1}H NMR ($CDCl_3$—CD_3OD (6 : 1)), δ: 0.80 (t, 6 H, 2 $(CH_2)_{11}$Me, J = 6.7 Hz); 1.08—1.36 (m, 64 H, 2 $(CH_2)_{11}$Me, $(CH_2)_2$, $(CH_2)_8$); 1.37—1.62 (m, 12 H, 3 OCH_2CH_2, 3 $NHCH_2CH_2$); 2.99—3.09 (m, 2 H, $NHCH_2$); 3.32—3.58 (m, 15 H, 2 OCH_2CH_2, 2 $NHCH_2$, OCH_2CH, CH_aH_b, H(2) Gal, H(3) Gal, H(5) Gal); 3.72 (dd, 2 H, H(6) Gal, J = 2.2 Hz, J = 5.8 Hz); 3.82 (dt, 1 H, OCH_aH_b, J = 6.4 Hz, J = 9.5 Hz); 3.84—3.90 (m, 1 H, H(4) Gal); 4.00 (dd, 1 H, J = 5.3 Hz, J = 11.5 Hz) and 4.09 (dd, 1 H, $CH_2OC(O)$, J = 5.4 Hz, J = 11.5 Hz); 4.15 (d, 1 H, H(1) Gal, J = 7.5 Hz); 5.32—5.40 (m, 1 H, CONH); 7.89—7.91 (m, 2 H, 2 NH). ^{13}C NMR, δ: 13.33, 21.97, 24.58, 25.07, 25.30, 25.36, 25.77, 26.09, 28.56, 28.61, 28.65, 28.78, 28.89, 28.94, 28.98, 29.23, 30.02, 30.46, 30.82, 31.22, 36.00, 40.26, 43.28, 43.77, 60.70, 63.31, 63.32, 68.35, 69.08, 69.63, 69.94, 70.64, 71.14, 72.80, 73.81, 76.18, 102.66, 156.16, 167.06, 167.35, 181.41, 181.57.

3-[6-(β-D-Galactopyranosyloxy)hexyl]amino-4-{12-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonylamino]-4,9-dioxadodecyl}-aminocyclobut-3-ene-1,2-dione (11e). Compound **11e** (26 mg, 83%) was obtained from compound **10e** (36.4 mg, 0.029 mmol) as a crystallizing oil, $[\alpha]_D^{27}$ −3.55 (*c* 1, $CHCl_3$—CH_3OH, 1 : 1). MS, *m/z* (I_{rel} (%)): 1095.060 $[M + Na]^+$ (100). Calculated for $C_{58}H_{109}N_3O_{14}$: 1071.791 $[M]^+$. ^{1}H NMR (Py-d_5), δ: 0.80 (t, 6 H, 2 $(CH_2)_{11}$Me, J = 6.7 Hz); 1.10—1.39 (m, 48 H, 2 $(CH_2)_{11}$Me, $(CH_2)_2$); 1.41—1.63 (m, 12 H, 6 OCH_2CH_2); 1.80—1.98 (m, 4 H, OCH_2CH_2, $NHCH_2CH_2$); 3.19—3.32 (m, 4 H, 2 $NHCH_2$); 3.33—3.71 (m, 15 H, 5 OCH_2CH_2, $NHCH_2$, OCH_2CH, CH_aH_b); 3.73—3.88 (m, 3 H, OCH_2CH_2, OCH_2CH); 3.90—4.01 (m, 2 H, H(5) Gal, OCH_aH_b); 4.06 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 9.5 Hz); 4.32 (dd, 1 H, H(2) Gal, J = 7.6 Hz, J = 9.4 Hz); 4.35 (d, 2 H, H(6) Gal, J = 6.0 Hz); 4.41 (dd, 1 H, $CH_aH_bOC(O)$, J = 5.6 Hz, J = 11.4 Hz); 4.47 (dd, 1 H, H(4) Gal, J = 1.1 Hz, J = 3.4 Hz); 4.51 (dd, 1 H, $CH_aH_bOC(O)$, J = 4.7 Hz, J = 11.4 Hz); 4.63 (d, 1 H, H(1) Gal, J = 7.7 Hz); 7.91 (t, 1 H, CONH, J = 5.0 Hz); 7.99—8.27 (m, 2 H, 2 NH). ^{13}C NMR, δ: 14.94, 23.61, 26.69, 27.03, 27.17, 27.20, 27.56, 30.29, 30.48, 30.50, 30.60, 30.63, 30.66, 30.82, 31.30, 31.43, 32.26, 32.77, 32.80, 39.50, 42.58, 44.99, 63.12, 65.19, 68.66, 69.25, 70.24, 71.00, 71.23, 71.54, 71.78, 72.43, 73.29, 75.95, 77.54, 78.41, 105.88, 158.10, 169.78, 169.82, 184.84, 184.92.

3-[6-(β-D-Galactopyranosyloxy)hexyl]amino-4-{13-[*rac*-2,3-bis(tetradecyloxy)propoxycarbonylamino]-4,7,10-trioxatridecyl}aminocyclobut-3-ene-1,2-dione (11f). Compound **11f** (23 mg, 80%) was obtained from compound **10f** (33.9 mg, 0.027 mmol) as a crystallizing oil, $[\alpha]_D^{27}$ −3.92 (*c* 1, $CHCl_3$—CH_3OH, 1 : 1). MS, *m/z* (I_{rel} (%)): 1111.103 $[M + Na]^+$ (100). Calculated for $C_{58}H_{109}N_3O_{15}$: 1087.786 $[M]^+$. ^{1}H NMR (Py-d_5), δ: 0.80 (t, 6 H, 2 $(CH_2)_{11}$Me, J = 6.7 Hz); 1.09—1.39 (m, 48 H, 2 $(CH_2)_{11}$Me, $(CH_2)_2$); 1.41—1.62 (m, 8 H,

4 $OCH_2C\underline{H}_2$); 1.78—1.96 (m, 4 H, $OCH_2C\underline{H}_2$, $NHCH_2C\underline{H}_2$); 3.34—3.70 (m, 23 H, 7 $OC\underline{H}_2CH_2$, 3 $NHC\underline{H}_2$, $OC\underline{H}_2CH$, $CH\underline{H}_a$); 3.72—3.86 (m, 3 H, $OC\underline{H}_2CH_2$, $OCH_2C\underline{H}$); 3.91—4.02 (m, 2 H, H(5) Gal, $OCH\underline{H}_b$); 4.06 (dd, 1 H, H(3) Gal, J = 3.4 Hz, J = 9.5 Hz); 4.32 (dd, 1 H, H(2) Gal, J = 7.7 Hz, J = 9.5 Hz); 4.35 (d, 2 H, H(6) Gal, J = 6.0 Hz); 4.41 (dd, 1 H, $CH\underline{H}_aOC(O)$, J = 5.6 Hz, J = 11.4 Hz); 4.45—4.56 (m, 2 H, H(4) Gal, $CH\underline{H}_bOC(O)$); 4.64 (d, 1 H, H(1) Gal, J = 7.7 Hz); 7.89 (t, 1 H, CONH, J = 5.6 Hz); 7.96—8.19 (m, 2 H, 2 NH). ^{13}C NMR, δ: 14.58, 23.24, 26.33, 26.67, 26.81, 26.84, 29.92, 30.11, 30.14, 30.23, 30.26, 30.29, 30.45, 30.93, 30.97, 31.90, 32.25, 32.44, 39.05, 42.16, 44.63, 62.76, 64.83, 68.74, 69.31, 69.88, 70.62, 70.83, 70.87, 71.05, 71.07, 71.42, 72.07, 72.92, 75.60, 77.19, 78.05, 105.53, 157.74, 169.41, 164.44, 184.48, 184.56.

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