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Palladium-Catalyzed Amination in the Synthesis of Nitrogen and Oxygen Heterocycles Containing Fragments of Cholane and Quinoline

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Abstract—By Mitsunobu reaction from 3,24-cholanediol and 2-hydroxy-8-chloroquinoline 24-(8-chloroquinolinyl-2-oxy)cholan-3-ol and 3,24-di(8-chloroquinolinyl-2-oxy)cholane were synthesized. These compounds were brought into reactions of palladium-catalyzed amination with propanediamine, oxaalkane diamines, and *N,N'*-bis(3-aminopropyl)ethylenediamine to obtain macrocycles of various structures, linear mono- and bis(steroid) derivatives of trioxaalkane diamine, and also cholane bis(oxaalkandiamine) derivative. The dependence was demonstrated of macrocyles and cyclooligomers yield on the polyamine nature. 4-Hydroxy-7-chloroquinoline afforded only 24-(7-chloroquinolinyl-4-oxy)cholan-3-ol.

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The chemistry of bile acids macrocyclic derivatives has been vigorously developed within the last two decades. The main trend consists in the building up macrocycles containing two steroid fragments bound by two linkers (cholaphanes) [1, 2] or macrocycles composed of a single steroid fragment and constructed by cyclophane type [3, 4]. The latter as a rule possess a larger conformational mobility. Lately the synthesis of hybrid macrocycles, containing, for example, steroid and peptoid [5], steroid and biarylester groups [6, 7] has been actively developed. The synthesis of such compounds is performed by the method of multiple multicomponent macrocyclization applying bifunctional building blocks. A method was also developed for introduction of steroids into porphyrin molecules [8, 9] by the use of dipyrrole steroid derivatives. Much research is oriented to the opportunities of applying steroid-containing macrocycles as analytic sensors [8] of metal ions [2] and organic molecules in water, on the water–air phase boarder, and in liquid double-layer membranes [3]. We developed a singular approach to the synthesis of macrocycles containing steroid fragments based on the palladium-catalyzed amination of cholanediol haloaryl derivatives with linear polyamines [10–12]. In this study we performed the catalytic synthesis of macrocycles proceeding from 3,24-cholanediol using quinoline substituents as aromatic linkers. The additional nitrogen atom in the quinoline ring may improve the complexing and fluorophore properties of the macrocycles and also enhance the biological activity of the synthesized molecules.

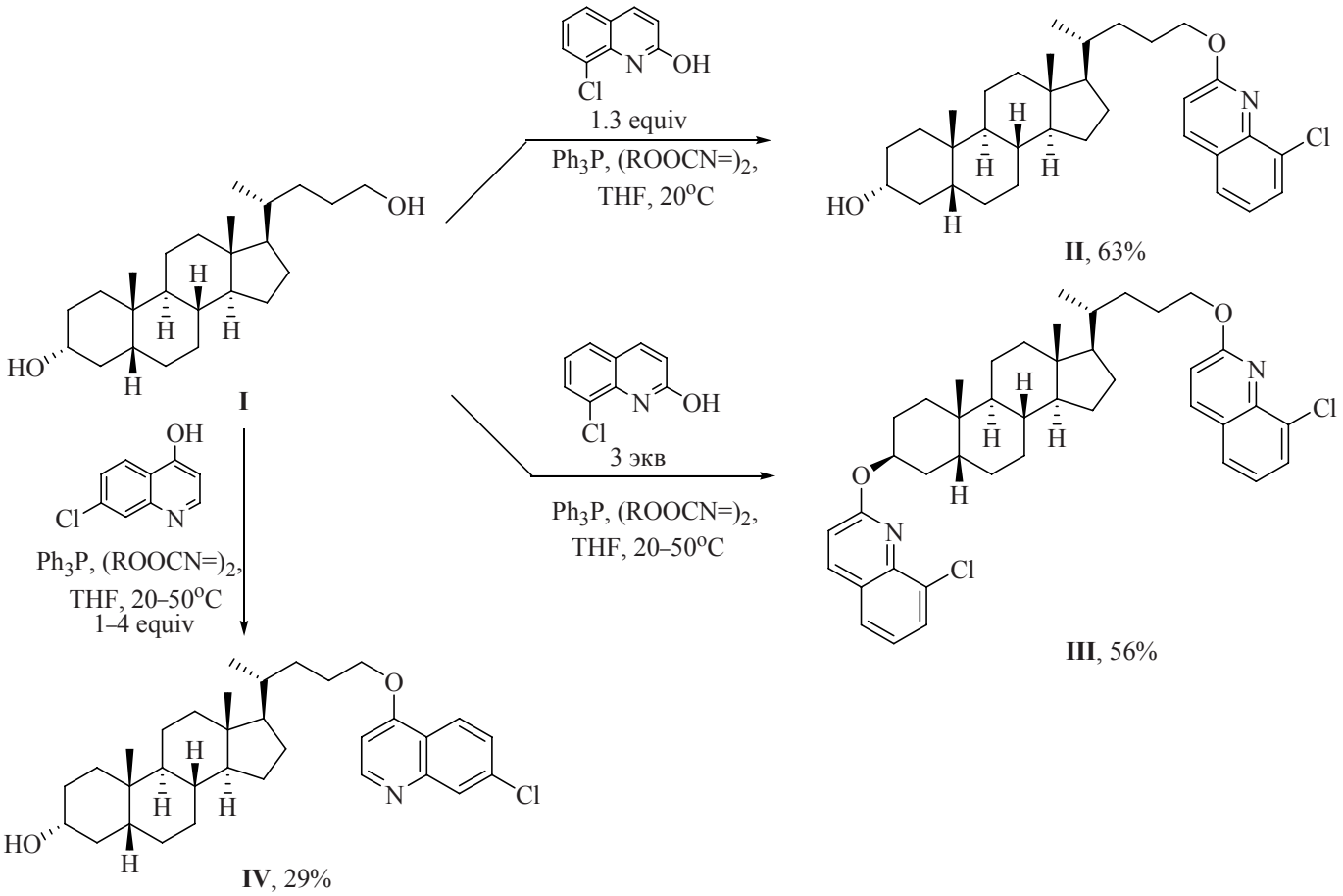
First we synthesized 24-(8-chloroquinolinyl-2-oxy)-cholan-3-ol (**II**) and 3,24-di(8-chloroquinolinyl-2-oxy)-cholane (**III**) by Mitsunobu reaction [13] from 3,24-cholanediol (**I**) obtained in its turn by the reduction of lithocholic acid with diborane in THF [10] (Scheme 1). In this study we synthesized compound **II** not from diethyl azodicarboxylate (DEAD) but from diisopropyl azodicarboxylate (DiPrAD), and we found that in reaction of equimolar amounts of reagents in THF after 24 h of stirring at room temperature the conversion of cholanediol reached 75%. After adding 0.33 equiv of 2-hydroxy-8-chloroquinoline, DiPrAD, triphenylphosphine, and the continuation of stirring for 24 h more the cholanediol conversion became 100%, and therewith in the reaction mixture notable amounts of diaryl derivative **III** were not found. Hence the hydroxy group attached at C^{24} reacted exclusively regioselectively. The yield of 24-(8-chloroquinolinyl-2-oxy)cholan-3-ol (**II**) after the chromatography on silica gel reached 63%. In the synthesis of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**)

we compared the efficiency of DEAD and DiPrAD. At the use of 2 equiv of 2-hydroxy-8-chloroquinoline, DEAD, and triphenylphosphine in reaction with cholanediol in THF after 24 h of stirring at room temperature the molar ratio of compounds **III** and **II** in the reaction mixture was 2:1. After supplementary addition of 1 equiv of 2-hydroxy-8-chloroquinoline, DEAD, and stiring for 24 h at room temperature the conversion of cholanediol into compound **III** reached 100%. At the replacement of DEAD by DiPrAD and the use of 2 equiv of reagents the molar ratio of compounds **III** and **II** reached 1:5 after 24 h at 20°C, and after addition of the third equivalent of the reagents and stirring for 5 h at 50°C we obtained the quantitative conversion into the diarylation product. The yield of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**) after chromatography was 56%.

We also attempted to bring into the Mitsunobu reaction the isomeric 4-hydroxy-7-chloroquinoline (Scheme 1). This compound proved to be practically insoluble in THF and in other organic solvents suitable for this process. Still at the use of 1 equiv of reagents after 24 h of stirring at room temperature the hydroxychloroquinoline mostly dissolved, and therewith the conversion of 3,24-cholanediol into compound **IV** was 75%. However further addition of 4-hydroxy-7-chloroquinoline, DiPrAD, and triphenylphosphine, the replacement of DiPrAD by DEAD and the heating of the reaction mixture failed to promote conversion of cholanediol into compound **IV**, and the quinoline did not dissolve more. Regretfully, the chromatographic purification of compound **IV** was hampered by the close values of R_f of compound **IV**, triphenylphosphine oxide, and diisopropyl azodicarboxylate. Even after triple chromatographic purification compound **IV** was obtained in a mixture with triphenylphosphine oxide and diisopropyl azodicarboxylate. The yield of compound **IV** calculated for the pure compound was 29%.

In the synthesis of macrocycles proceeding from 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**) in reactions with polyamines **Va–Ve** we initially applied the conditions

Scheme 1.



R = Et (DEAD), *i*-Pr (DiPrAD).

analogous to those for the synthesis of the pyridine-containing steroid polyazamacrocycles [12]: 8/9 mol% $Pd(dba)_2$/BINAP, sodium *tert*-butylate, dioxane. It turned out that sufficiently general catalytic system $Pd(dba)_2$/BINAP [14] was of low efficiency in this case, and the amination with trioxadiamine **Va** after 30 h of boiling occurred to a low extent. Therefore we applied another donor ligand, 2-dicyclohexylphosphino-2'-dimethylamino-biphenyl that was efficient in the amination of less reactive chloroarenes [15]; besides the charge of the catalyst was increased to 16 mol%. This helped to raise significantly the reaction rate, and after 39 h of boiling we obtained the desired macrocycle **VIa** that was isolated by chromatography in 24% yield (Scheme 2). Alongside the macrocycle also cyclodimer **VIIa** was obtained in the form of two regioisomers ("head to head" and "head to tail") in 9% yield, and also fractionated mixtures of cyclic and linear oligomers (50%) (see the table, run no. *1*). The reaction with dioxadiamine **Vb** gave 22% yield of desired macrocycle **VIb**; therewith cyclodimer **VIIb** was isolated in 20%, and oligomer mixture of a large molecular weight, in 43% yield (see the table, run no. *2*). Dioxadiamine **Vc** with a shorter chain afforded a lower yield both of macrocycle **VIc** and cyclodimer **VIIc** (see the table, run no. *3*), therewith the amount of oligomers regularly increased (55%). The reaction with tetramine **Vd** proceeded much worse: the yield of macrocycle **VId** decreased to 8%, besides, a significant amount formed (25%) of bis(steroid)-substituted tetramine **VIII**, a product of chlorine atom amination in one quinoline fragment and chlorine reduction in the second one. This compound can exist in the form of three isomers depending on the definite quinoline that suffered the amination ("head to head", "head to tail", and "tail to tail"). Finally, the reaction with 1,3-propanediamine **Ve** led to the formation of cyclodimer in a mixture with cyclooligomers (15%), besides, noncyclic oligomers were isolated in 56% yield.

Compounds synthesized were characterized by ^1H and ^{13}C NMR spectra, mass spectra MALDI-TOF, and UV spectra. In the NMR spectra of all macrocycles **VI** and cyclodimers **VII** the signals of the two quinoline groups are notably different. The polyamine chains in macrocycles **VI** are unsymmetrical and as a rule in the ^{13}C NMR spectra all carbon atoms are nonequivalent. A characteristic feature of the ^1H NMR spectra of macrocycles **VI** is a considerable difference in the chemical shifts of protons at the atom C^{24} of the steroid framework. Each of these protons appears as a multiplet in the region 4.3–4.6 ppm, whereas in the spectra of cyclodimers **VII** these protons give rise to a single multiplet in the region 4.3–4.4 ppm. In the spectra of macrocycles **VI** two protons at nitrogens related to two quinoline fragments differ by 0.1–0.2 ppm, and in cyclodimers **VII** they give one broadened singlet. These features are also characteristic of macrocycle containing steroid and pyridine fragments [12]. Yet the chemical shifts of protons attached to atom C^3 of steroid framework both in macrocycles **VI** and cyclodimers **VII** are identical and appear at 5.55 ppm.

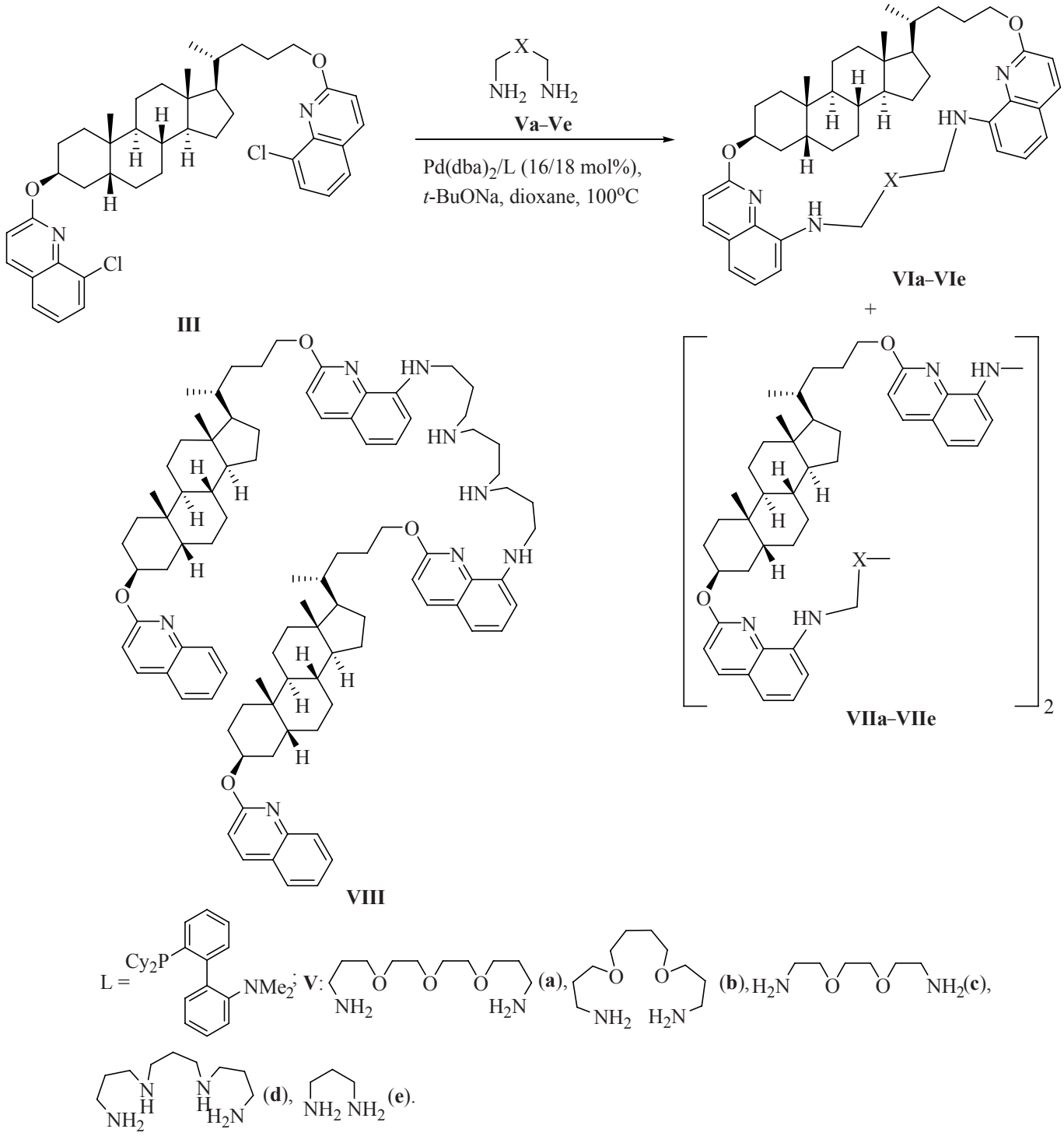
In the ^{13}C NMR spectra the most characteristic chemical shifts are those of atoms C^{14} and C^{17} of the steroid skeleton: for macrocycles **VI** the difference in their values is 1.3 ppm (**VIa**), 1.6 ppm (**VIb**, **VId**), 3.5 ppm (**VIc**), thus the difference notably grows with diminishing of the ring. This difference for cyclodimers equals about 0.5 ppm, In the spectra of cyclodimers that might exist as a mixture of two regioisomers ("head to head" and "head to tail") the signals of some atoms are either broadened or separated in two peaks of unequal intensity. In the spectra of macrocycles and cyclodimers often appears a dioxane signal, and therewith its molar fraction amounts on the average to 12–25%. This is apparently caused by the formation of sufficiently strong complexes of the macrocyclic molecules with this solvent that are not broken during chromatography on silica gel and evaporation in a vacuum. Mass spectra MALDI-TOF

Synthesis of macrocycles **VIa–VId** and cyclodimers **VIIa–VIIe**

Run no.	Polyamine	**VI**, yield, %	**VII**, yield, %	Oligomer mixture, %
1	$NH_2(CH_2)_3O(CH_2)_2O(CH_2)_2O(CH_2)_3NH_2$ (**Va**)	24	9	50
2	$NH_2(CH_2)_3O(CH_2)_4O(CH_2)_3NH_2$ (**Vb**)	22	20	43
3	$NH_2(CH_2)_2O(CH_2)_2O(CH_2)_2NH_2$ (**Vc**)	16	16	55
4	$NH_2(CH_2)_3NH(CH_2)_3NH(CH_2)_3NH_2$ (**Vd**)	8	15	33
5	$NH_2(CH_2)_3NH_2$ (**Ve**)	0	15[a]	56

[a] Contains an impurity of cycloligomers of higher molecular weight

Scheme 2.



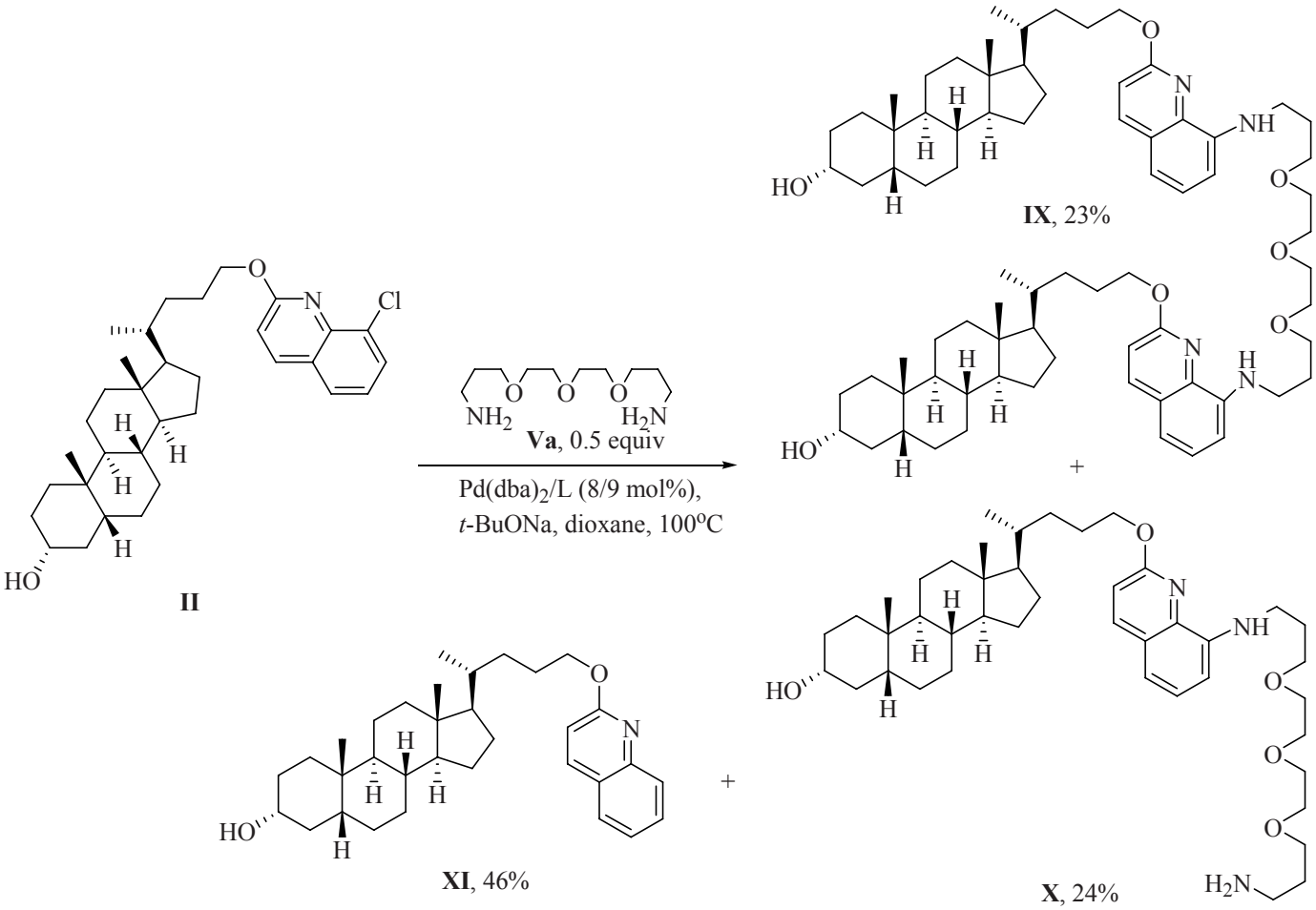
are characterized by the following feature: the intensity of peaks of molecular ions belonging to cyclodimers is significantly lower than for common macrocycles, and for cycloligomers of higher molecular weight and for linear oligomers the molecular peaks are not observed at all, therefore the analysis of their mixture becomes difficult, especially as in the NMR spectra of these compounds the signals are also broadened. On substitution of chlorine atom by nitrogen in the quinoline ring the absorption in the UV spectra considerably changes in

the region 300–350 nm: Whereas in the spectrum of 2-hy-droxy-8-chloroquinoline absorption bands are observed at 316 and 330 nm, in the spectrum of 2-hydroxy-8-aminoquinoline appear three bands of approximately equal intensity at 308–310, 324, and 350–354 nm.

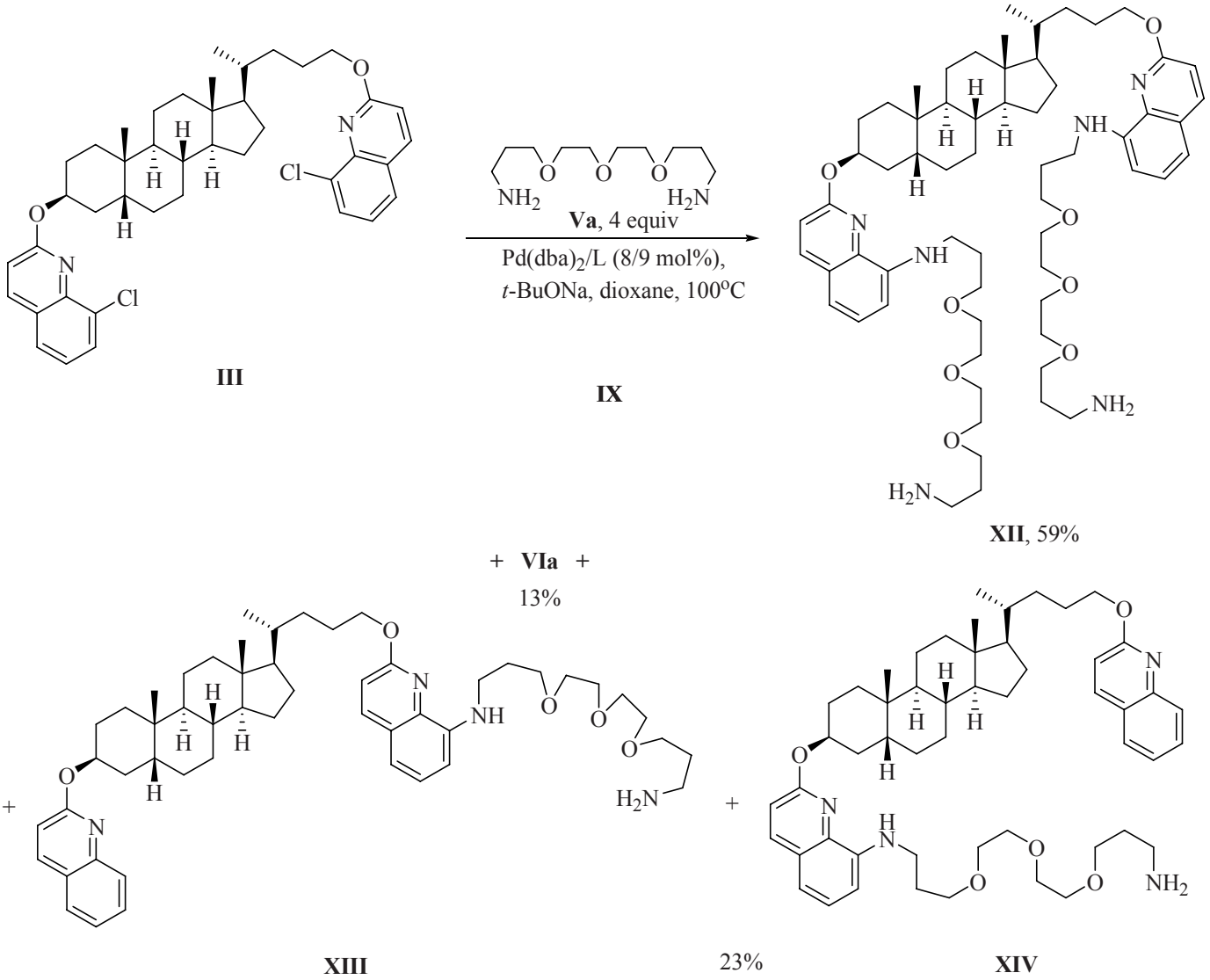
We carried out the synthesis of some linear oxadiamine derivatives of quinolinyloxycholanol by the reaction of 24-(8-chloroquinolinyl-2-oxy)cholan-3-ol (**II**) with trioxadiamine (**Va**) at various reagents ratios in the presence of the palladium catalyst (Scheme 3). By the reaction of 2 equiv of compound **II** with trioxadiamine in the presence of 8 mol% of the catalyst we obtained bis-(steroid)-substituted diamine **IX** (23%) and monosteroid derivative **X** (24%). Besides in 46% yield product **XI** formed as a result of chlorine reduction in compound **II**. At the use of smaller amount of the catalyst (6 mol%) the yield of the target product **IX** reduced to 18%. The low yields both of bis and mono derivatives of trioxa-diamaine alongside the high yield of the reduction product of initial steroid **II** may be due to the use of excess sodium *tert*-butylate necessary for the alcoholate formation at the position *3* of the steroid. Actually, in reaction of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**) with 4 equiv of trioxadiamine (**Va**) in the presence of 8 mol% of catalyst formed the corresponding bis(oxadiamine) steroid derivative **XII** in a good yield (59%), and as side products were isolated macrocycle **VIa** (13%) and a mixture of isomeric products of monoamination and reduction of chlorine **XIII** and **XIV** (23%).

This and above cited examples show that unlike the previously studied bromophenoxy- and chloropyridinyloxy-cholanes the chloroquinolinyloxycholanes in the reactions of palladium-catalyzed amination are prone to the reduction of the chlorine atom. This fact may be due to the lesser reactivity of the chlorine in these compounds with respect to amination thus increasing the yield of the products of concurrent reduction. Compound **XI** owing to the hydroxy group, and compounds **X** and **XII** thanks to the free primary amino group are ready to further modifications.

Scheme 3.



Scheme 4.



Hence we developed a synthetic procedure for preparation of steroid macrocycles including in their composition two quinoline fragments by an intramolecular palladium-catalyzed amination, the limits of the application of this reaction were shown, and also were synthesized linear oxadiamine steroid derivatives with various ratio of steroid and oxadiamine fragments.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker Avance-400 at operating frequency 400 and 100.6 MHz respectively. Mass spectra MALDI-TOF were measured on an instrument Bruker Daltonics Ultraflex using 1,8,9-anthracenetriol as matrix. UV spectra were recorded on a spectrophotometer Perkin Elmer Lambda 40. Commercially available reagents: lithocholic acid, sodium borohydride, boron trifluoride etherate, diethyl and diisopropyl azodicarboxylate, 2-hydroxy-8-chloroquinoline, 4-hydroxy-7-chloroquinoline, polyamines **Va–Ve**, 2-dicyclohexylphosphino-2'-dimethylaminobiphenyl, BINAP, sodium *tert*-butylate were used without additional purification, triphenylphosphine was recrystallized from ethanol, THF and dioxane were distilled in succession over alkali and metallic sodium, ether was distilled over alkali, dichloromethane and methanol were distilled. The column chromatography was performed on silica gel Fluka 40–60 μm. 3,24-Cholanediol was obtained by reducing lithocholoc acid with diborane in THF by method [10], $Pd(dba)_2$ was prepared by procedure [16].

24-(8-Chloroquinolinyl-2-oxy)cholan-3-ol (II). Into a flask filled with argon was charged 1.45 g (4 mmol) of 3,24-cholanediol, 720 mg (4 mmol) of 8-chloroquinolin-2-ol, 1.05 g (4 mmol) of triphenylphosphine, 100 ml of anhydrous THF was poured, 0.82 ml (808 mg, 4 mmol) of diisopropyl azodicarboxylate was added, and the mixture was stirred at room temperature for 24 h. Then 240 mg (1.33 mmol) of 8-chloroquinolin-2-ol, 350 mg (1.33 mmol) of triphenylphosphine, and 0.27 ml (270 mg, 1.33 mmol) of diisopropyl azodicarboxylate were added, and the stirring was continued at room temperature for 24 h. On completion of the reaction the mixture was evaporated in a vacuum, and the viscous residue obtained was subjected to chromatography on silica gel using dichloromethane as eluent. Yield 1.31 g (63%). Colorless crystals, mp 148–150°C. UV spectrum (CH_2Cl_2), λ_{max}, nm (log ε): 264 (3.58), 272 (3.55), 316 (3.47), 330 (3.47). ^{1}H NMR spectrum, δ, ppm: 0.64 s (3H), 0.90 s (3H), 0.95 d (3H, ^3J 6.5 Hz), 1.00–1.99 m (29H), 3.56–3.65 m (1H), 4.46–4.56 m (2H), 6.92 d (1H, ^3J 8.9 Hz), 7.25 t (1H, ^3J 7.8 Hz), 7.60 d (1H, ^3J 8.0 Hz), 7.71 d.d (1H, ^3J 7.6, ^4J 0.9 Hz), 7.95 d (1H, ^3J 8.8 Hz). ^{13}C NMR spectrum, δ, ppm: 12.0, 18.6, 20.8, 23.3, 24.2, 25.4, 26.4, 27.2, 28.2, 30.5, 32.1, 34.5, 35.3, 35.5, 35.8, 36.4, 40.1, 40.4, 42.1, 42.7, 56.1, 56.5, 66.9, 71.8, 114.1, 123.6, 126.1, 126.3, 129.5, 131.3, 138.8, 142.9, 162.6. Mass spectrum MALDI-TOF: *m/e* 523.3156 $[M]^+$. $C_{33}H_{46}ClNO_2$. Calculated *m/e* 523.3217.

3,24-Di(8-chloroquinolinyl-2-oxy)cholane (III). Into a flask filled with argon was charged 1.086 g (3 mmol) of 3,24-cholanediol, 539 mg (3 mmol) of 8-chloroquinolin-2-ol, 786 mg (3 mmol) of triphenylphosphine, 75 ml of anhydrous THF was poured, 1.4 ml of 40% solution of diethyl azodicarboxylate (3 mmol) was added, and the mixture was stirred at room temperature for 24 h. Then the same quantity of 8-chloroquinolin-2-ol, triphenylphosphine, and diethyl azodicarboxylate was added, and the stirring was continued at room temperature for 24 h. Afterwards once more the same quantity of reagents was added, and the stirring was again continued at room temperature for 24 h. At the use of diisopropyl azodicarboxylate instead of diethyl azodicarboxylate (synthesis was performed using 0.5 mmol of cholanediol) after the third addition of reagents the mixture was stirred at 50°C for 5 h. The combined reaction mixtures were partly evaporated in a vacuum to a volume of 20 ml, and 50 ml of ethyl ether was added. The separated crystalline powder of triphenylphosphine oxide was filtered off, the filtrate was evaporated in a vacuum, and the residue obtained was subjected to chromatography on silica gel using dichloromethane as eluent. Yield 1.333 g (56%). Colorless crystalline powder, mp 180–182°C. ^{1}H NMR spectrum, δ, ppm: 0.67 C (3H), 0.98 d (3H, ^3J 6.6 Hz), 1.00 s (3H), 1.01–2.14 m (28H), 4.48–4.58 m (2H), 5.72 br.s (1H), 6.92 d (1H, ^3J 7.9 Hz), 6.94 d (1H, ^3J 7.9 Hz), 7.23 t (1H, ^3J 8.0 Hz), 7.26 t (1H, ^3J 7.9 Hz), 7.59 d (1H, ^3J 8.2 Hz), 7.61 d (1H, ^3J 8.3 Hz), 7.70 d.d (1H, ^3J 7.6, ^4J 1.1 Hz), 7.72 d.d (1H, ^3J 7.6, ^4J 1.2 Hz), 7.94 d (1H, ^3J 8.5 Hz), 7.96 d (1H, ^3J 8.8 Hz). ^{13}C NMR spectrum, δ, ppm: 12.1, 18.7, 21.1, 23.9, 24.2, 24.7, 25.4, 26.3, 26.6, 28.3, 30.4, 30.9, 32.2, 35.0, 35.5, 35.7, 37.5, 40.0, 40.3, 42.8, 56.2, 56.7, 66.9, 71.9, 114.1, 114.7, 123.4, 123.6, 126.0, 126.1, 126.2, 126.3, 129.4, 129.5, 131.2, 131.3, 138.7, 138.9, 142.9, 143.0, 162.0, 162.6. Mass spectrum MALDI-TOF: *m/e* 684.3267 $[M]^+$. $C_{42}H_{50}Cl_2N_2O_2$. Calculated *m/e* 684.3249.

24-(7-Chloroquinolinyl-4-oxy)cholan-3-ol (IV). Into a flask filled with argon was charged 181 mg (0.5 mmol) of 3,24-cholanediol, 90 mg (0.5 mmol) of 7-chloroquinolin-4-ol, 131 mg (0.5 mmol) of triphenylphosphine, 12 ml of anhydrous THF was poured, 0.1 ml (101 mg, 0.5 mmol) of diisopropyl azodicarboxylate was added, and the mixture was stirred at room temperature for 24 h. Then 30 mg (0.17 mmol) of 7-chloroquinolin-4-ol, 44 mg (0.17 mmol) of triphenylphosphine, and 0.35 ml (35 mg, 0.17 mmol) of diisopropyl azodicarboxylate was added, and the stirring was again continued at room temperature for 24 h. The reaction mixture was evaporated in a vacuum, the residue was subjected to column chromatography on silica gel using the following sequence of eluents: CH_2Cl_2, CH_2Cl_2–MeOH, 100:1–3:1. With eluent CH_2Cl_2–MeOH, 3:1, the main product was isolated in a mixture with initial compounds, triphenylphosphine oxide and diisopropyl azodicarboxylate. This fraction was subjected to chromatography for the second time using the same series of eluents. Compound **IV** was isolated by the mixture CH_2Cl_2–MeOH, 50:1, together with initial cholanediol, triphenylphosphine oxide, and diisopropyl hydrazodicarboxylate in a molar ratio 1:0.3:2.5:1.5. The third attempt on chromatographic separation resulted in removal of cholanediol, but the other two components were present in the mixture with compound **IV** in a ratio 1:3.5:2.8 in the fraction eluted with CH_2Cl_2–MeOH, 50:1. Overall yield of compound **IV** 0.145 mmol (29%) in a mixture with triphenylphosphine oxide, and diisopropyl hydrazodicarboxylate. ^{1}H NMR spectrum, δ, ppm: 0.60 s (3H), 0.84 s (3H), 0.94 d (3H, ^3J 6.4 Hz), 1.00–1.98 m (29H), 3.48–3.58 m (1H), 4.05–4.13 m (2H), 6.64 d (1H,

^3J 5.2 Hz), 7.97 s (1H), 8.08 d (1H, ^3J 8.9 Hz), 8.64 d (1H, ^3J 5.1 Hz) (1 proton of quinoline fragment is overlapped by the multiplet of triphenylphosphine oxide). ^{13}C NMR spectrum, δ, ppm: 11.9, 18.5, 20.6, 23.2, 24.0, 25.3, 26.2, 27.0, 28.1, 30.3, 32.0, 34.4, 35.2, 35.3, 35.6, 36.2, 40.0, 40.2, 41.9, 42.5, 55.8, 56.3, 69.3, 71.2, 100.8, 119.7, 123.3, 126.2, 127.5, 135.5, 149.4, 152.3, 161.6.

Macrocycles VIa–VId and cyclodimers VIIa–VIIe. *General procedure.* Into a two-neck flask filled with argon was charged 0.25 mmol (171 mg) of 3,24-di-(8-chloroquinolinyl-2-oxy)cholane (**III**), 23 mg (16 mol%) of $Pd(dba)_2$, 18 mg (18 mol%) of 2-dicyclohexylphosphino-2'-dimethylaminobiphenyl, 12 ml of anhydrous dioxane, 0.25 mmol of an appropriate polyamine **Va–Vd**, 75 mg (0.78 mmol) of sodium *tert*-butylate, and the mixture was boiled at stirring for 25–30 h. Then the reaction mixture was filtered, evaporated in a vacuum, and subjected to column chromatography on silica gel using the following sequence of eluents: CH_2Cl_2; CH_2Cl_2–MeOH, 100:1–3:1; CH_2Cl_2–MeOH–aqueous NH_3, 100:20:1–10:3:1.

Macrocycle VIa was synthesized from 0.5 mmol (342 mg) of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**) and 0.5 mmol (110 mg) of trioxadiamine (**Va**). Eluent CH_2Cl_2–MeOH, 200:1. Yield 100 mg (24%). Light-yellow viscous oily substance slowly crystallizing, mp 98–100°C. UV spectrum (CH_2Cl_2), λ_{max}, nm (log ε): 310 (3.76), 324 (3.76), 354 (3.70). ^{1}H NMR spectrum, δ, ppm: 0.68 s (3H), 0.95 d (3H, ^3J 6.4 Hz), 0.99 C (3H), 1.00–2.16 m (32H), 3.35–3.45 m (4H), 3.64–3.75 m (12H), 4.33–4.41 m (1H), 4.56–4.64 m (1H), 5.55 br.s (1H), 5.70 br.s (1H), 5.79 br.s (1H), 6.63 d (1H, ^3J 7.5 Hz), 6.69 d (1H, ^3J 7.4 Hz), 6.85 d (1H, ^3J 8.9 Hz), 6.86 d (1H, ^3J 8.8 Hz), 6.97 d (1H, ^3J 8.7 Hz), 6.99 d (1H, ^3J 9.1 Hz), 7.20 t (1H, ^3J 7.9 Hz), 7.22 t (1H, ^3J 7.8 Hz), 7.89 d (1H, ^3J 8.8 Hz), 7.91 d (1H, ^3J 8.8 Hz). ^{13}C NMR spectrum, δ, ppm: 12.1, 18.6, 21.1, 23.7, 24.0, 24.3, 24.5, 26.1, 26.4, 28.2, 28.9, 29.7, 30.3, 30.9, 32.4, 34.7, 35.3, 35.4, 37.4, 40.2, 40.3, 40.4 (2C), 42.7, 55.7, 57.0, 66.6, 69.2, 69.5, 70.2 (2C), 70.8 (2C), 70.9, 105.5, 105.7, 112.9, 113.5, 113.9, 114.0, 124.5, 124.7, 129.1, 129.2, 135.2, 135.3, 138.9, 139.1, 143.2, 143.3, 159.8, 160.1. Mass spectrum MALDI-TOF: *m/e* 832.5 $[M]^+$.

Cyclodimer VIIa was obtained as side product in the synthesis of macrocycle **VIa**. Eluent CH_2Cl_2–MeOH, 100:1. Yield 37 mg (9%). Light-yellow viscous oily substance. ^{1}H NMR spectrum, δ, ppm: 0.66 s (6H), 0.96 d (6H, ^3J 6.5 Hz), 0.98 s (6H), 11.00–2.05 m (56H), 2.01 br.s (8H), 3.35–3.45 m (8H), 3.56–3.70 m (24H), 4.33–4.40 m (4H), 5.53 br.s (2H), 5.75 br.s (4H), 6.62–6.70 m (4H), 6.84 d (2H, ^3J 8.5 Hz). 6.85 d (2H, ^3J 8.7 Hz), 6.93–6.99 m (4H), 7.18 t (2H, ^3J 7.7 Hz), 7.20 t (2H, ^3J 7.7 Hz), 7.84–7.90 m (4H). ^{13}C NMR spectrum, δ, ppm: 12.1 (2C), 18.7 (2C), 21.1 (2C), 23.9 (2C), 24.2 (2C), 24.7 (2C), 25.5 (2C), 26.3 (2C), 26.6 (2C), 28.3 (2C), 29.5 + 29.6 (4C), 30.4 + 30.5 (2C), 30.8 (2C), 32.3 (2C), 35.0 (2C), 35.6 + 35.7 (4C), 37.4 (2C), 40.0 (2C), 40.3 (2C), 40.5 + 40.6 (4C), 42.8 (2C), 56.2 (2C), 56.6 + 56.7 (2C), 66.6 (2C), 69.2 (4C), 70.3 (4C), 70.7 (4C), 70.9 (2C), 105.6 (2C), 105.7 (2C), 112.8 (2C), 113.6 (2C), 114.0 (4C), 124.5 (2C), 124.7 (2C), 129.2 (2C), 129.3 (2C), 135.2 (2C), 135.3 (2C), 139.0 (2C), 139.1 (2C), 143.3 (2C), 143.4 (2C), 159.9 (2C), 160.5 (2C). Mass spectrum MALDI-TOF: *m/e* 1665.0 $[M]^+$.

Macrocycle VIb was synthesized from 0.25 mmol (171 mg) of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**) and 0.25 mmol (51 mg) of dioxadiamine **Vb**. Eluent CH_2Cl_2–MeOH, 100:1. Yield 44 mg (22%). Light-yellow viscous oily substance. UV spectrum (CH_2Cl_2), λ_{max}, nm (log ε): 310 (3.70), 324 (3.68), 352 (3.62). ^{1}H NMR spectrum, δ, ppm: 0.67 s (3H), 0.96 d (3H, ^3J 6.3 Hz), 0.98 s (3H), 0.99–2.12 m (36H), 3.34–3.65 m (12H), 4.35–4.45 m (1H), 4.53–4.63 m (1H), 5.54 br.s (1H), 5.68 br.s (1H), 5.85 br.s (1H), 6.64 d (1H, ^3J 7.7 Hz). 6.69 d (1H, ^3J 7.6 Hz), 6.85 d (2H, ^3J 8.9 Hz), 6.97 d (1H, ^3J 8.0 Hz), 6.99 d (1H, ^3J 8.1 Hz), 7.20 t (1H, ^3J 7.7 Hz), 7.21 t (1H, ^3J 7.6 Hz), 7.89 d (1H, ^3J 9.1 Hz), 7.91 d (1H, ^3J 9.1 Hz). ^{13}C NMR spectrum, δ, ppm: 12.1, 18.7, 21.1, 23.7, 24.1 (2C), 24.5, 26.1, 26.4, 26.5, 26.9, 28.2, 28.8, 29.8, 30.3, 31.0, 32.4, 34.7, 35.1, 35.4, 37.4, 40.2, 40.4, 40.5, 40.8, 42.7, 55.5, 57.1, 66.7, 68.9, 70.9, 71.0, 71.1, 71.2, 105.5, 105.7, 113.0, 113.5, 113.9, 114.0, 124.5, 124.7, 129.2, 129.3, 135.2, 135.3, 138.9, 139.2, 143.2, 143.3, 159.9, 160.2. Mass spectrum MALDI-TOF: *m/e* 816.5512 $[M]^+$. $C_{52}H_{72}N_4O_4$. Calculated *m/e* 816.5554.

Cyclodimer VIIb was obtained as side product in the synthesis of macrocycle **VIb**. Eluent CH_2Cl_2–MeOH, 100:1. Yield 40 mg (20%). Light-yellow viscous oily substance. ^{1}H NMR spectrum, δ, ppm: 0.67 sC (6H), 0.99 br.s (12H), 1.00–2.10 m (72H), 3.35–3.65 m (24H), 4.37–4.43 m (4H), 5.54 br.s (2H), 5.77 br.s (4H), 6.64 d (2H, ^3J 7.2 Hz), 6.69 d (2H, ^3J 7.1 Hz), 6.85 d (4H, ^3J 8.7 Hz), 6.97 d (2H, ^3J 7.3 Hz), 6.99 d (2H, ^3J 8.4 Hz), 7.20 t (2H, ^3J 7.7 Hz), 7.21 t (2H, ^3J 7.7 Hz), 7.89 d (2H, ^3J 8.4 Hz), 7.91 d (2H, ^3J 9.0 Hz). ^{13}C NMR spectrum, δ, ppm: 12.1 (2C), 18.7 (2C), 21.1 (2C), 23.9 (2C), 24.2 (2C), 24.7 (2C), 25.5 + 25.6 (2C), 26.2 (2C), 26.6 (2C),

26.9 (4C), 28.3 (2C), 29.7 (4C), 30.5 (2C), 30.8 (2C), 32.3 (2C), 35.0 (2C), 35.6 + 35.7 (4C), 37.4 (2C), 40.0 (2C), 40.2 (4C), 40.7 (2C), 42.7 (2C), 56.1 + 56.2 (2C), 56.6 + 56.7 (2C), 66.3 (2C), 68.7 (4C), 70.8 (4C), 70.9 (2C), 105.7 (4C), 112.8 (2C), 113.6 (2C), 114.0 (4C), 124.5 (2C), 124.7 (2C), 129.2 (2C), 129.4 (2C), 135.2 (2C), 135.3 (2C), 138.9 (2C), 139.1 (2C), 143.3 (2C), 143.4 (2C), 159.9 (2C), 160.5 (2C). Mass spectrum MALDI-TOF: *m/e* 1633.3 $[M]^+$.

Macrocycle VIc was synthesized from 0.25 mmol (171 mg) of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**) and 0.25 mmol (37 mg) of dioxadiamine **Vc**. Eluent CH_2Cl_2–MeOH, 200:1. Yield 30 mg (16%). Light-yellow viscous oily substance. UV spectrum (CH_2Cl_2), λ_{max}, nm (log ε): 308 (3.62), 324 (3.57), 352 (3.60). ^{1}H NMR spectrum, δ, ppm: 0.65 s (3H), 0.97 d (3H, ^3J 6.2 Hz), 0.98 s (3H), 0.99–2.08 m (28H), 3.43–3.53 m (4H), 3.70–3.84 m (6H), 3.90 t (2H, ^3J 5.9 Hz), 4.36–4.42 m (1H), 4.45–4.53 m (1H), 5.55 br.s (1H), 5.94 br.s (1H), 6.17 br.s (1H), 6.64–6.72 m (2H), 6.85 d (1H, ^3J 8.7 Hz), 6.87 d (1H, ^3J 8.8 Hz), 7.00 d (1H, ^3J 7.7 Hz), 7.02 d (1H, ^3J 7.7 Hz), 7.21 t (1H, ^3J 7.5 Hz), 7.25 t (1H, ^3J 7.8 Hz), 7.89 d (1H, ^3J 8.8 Hz), 7.91 d (1H, ^3J 8.9 Hz). ^{13}C NMR spectrum, δ, ppm: 12.0, 18.8, 21.1, 22.3, 23.7, 24.1, 25.0, 26.1, 28.0, 29.7, 30.3, 31.0, 34.1, 34.7, 35.3, 35.6, 37.3, 40.2, 40.3, 42.7, 43.1, 43.8, 53.8, 57.3, 66.3, 69.7, 69.8, 70.5, 71.0, 71.5, 105.9, 106.1, 113.1, 113.5, 114.4 (2C), 124.4, 124.6, 128.6 (2C), 135.2, 135.5, 139.0, 139.1, 143.2 (2C), 159.9, 160.3. Mass spectrum MALDI-TOF: *m/e* 760.4939 $[M]^+$. $C_{48}H_{64}N_4O_4$. Calculated *m/e* 760.4928.

Cyclodimer VIIc was obtained as side product in the synthesis of macrocycle **VIc**. Eluent CH_2Cl_2–MeOH, 100:1. Yield 30 mg (16%). Light-yellow viscous oily substance. ^{1}H NMR spectrum, δ, ppm: 0.65 s (6H), 0.98 br.s (12H), 0.99–2.10 m (56H), 3.44–3.54 m (8H), 3.70–3.85 m (16H), 4.35–4.42 m (4H), 5.55 br.s (2H), 6.02 br.s (4H), 6.54–6.73 m (4H), 6.82–6.87 m (4H), 6.92 d (4H, ^3J 7.7 Hz), 7.17–7.25 m (4H), 7.87–7.91 m (4H). ^{13}C NMR spectrum, δ, ppm: 12.0 (2C), 18.6 (2C), 21.1 (2C), 23.8 (2C), 24.2 (2C), 24.7 (2C), 25.5 + 25.6 (2C), 26.3 (2C), 26.5 + 26.6 (2C), 28.3 (2C), 30.4 + 30.5 (2C), 30.8 (2C), 32.3 (2C), 34.9 (2C), 35.6 (4C), 37.3 (2C), 39.9 + 40.0 (2C), 40.3 (2C), 42.6 (2C), 43.1 (4C), 56.1 (2C), 56.5 + 56.7 (2C), 66.3 (2C), 70.3 (4C), 70.4 + 70.5 (4C), 70.9 + 71.0 (2C), 105.8 (2C), 105.9 (2C), 112.9 (2C), 113.6 (2C), 114.4 (2C), 114.5 (2C), 124.5 (2C), 124.7 (2C), 135.4 (2C), 135.5 (2C), 138.8 (2C), 138.9 (2C), 143.1 (2C), 143.2 (2C), 159.9 (2C), 160.5 (2C) (4 quaternary carbon atoms are not unambiguously asigned). Mass spectrum MALDI-TOF: *m/e* 1521.0 $[M]^+$.

Macrocycle VId was synthesized from 0.25 mmol (171 mg) of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**) and 0.25 mmol (47 mg) tetramine **Vd**. Eluent CH_2Cl_2–aqueous MeOH–NH_3, 100:20:1. Yield 15 mg (8%). Light-yellow viscous oily substance. UV spectrum (CH_2Cl_2), λ_{max}, nm (log ε): 310 (3.76), 324 (3.73), 352 (3.66). ^{1}H NMR spectrum, δ, ppm: 0.66 s (3H), 0.95 d (3H, ^3J 6.6 Hz), 0.98 s (3H), 1.00–2.12 m (34H), 2.74 t (4H, ^3J 7.0 Hz), 2.86 t (2H, ^3J 7.2 Hz), 2.87 t (2H, ^3J 7.1 Hz), 3.28–3.40 m (4H), 4.42–4.50 m (1H), 4.53–4.62 m (1H), 5.53 br.s (1H), 5.61 br.s (1H), 5.67 br.s (1H), 6.63 d (1H, ^3J 7.7 Hz), 6.69 d (1H, ^3J 7.2 Hz), 6.84 d (1H, ^3J 8.8 Hz), 6.85 d (1H, ^3J 8.7 Hz), 6.97 d (1H, ^3J 8.4 Hz), 6.99 d (1H, ^3J 8.9 Hz), 7.20 t (1H, ^3J 7.9 Hz), 7.21 t (1H, ^3J 8.0 Hz), 7.88 d (1H, ^3J 8.4 Hz), 7.90 d (1H, ^3J 8.4 Hz) (2 protons NH of dialkylamino groups are not unambiguously assigned). ^{13}C NMR spectrum, δ, ppm: 12.1, 18.8, 21.1, 23.7, 24.1 (2C), 24.4, 26.2, 26.4, 28.1, 29.7, 30.5, 30.6, 30.8, 32.1, 32.2, 34.8, 35.0, 35.5, 37.4, 40.2, 40.5, 41.7 (2C), 42.7, 47.9, 48.3, 48.5, 48.6, 55.5, 57.1, 66.8, 70.9, 105.7, 105.9, 113.0, 113.4, 114.0, 114.1, 124.5, 124.7, 129.2, 129.3, 135.2, 135.3, 138.9, 139.2, 143.3, 143.4, 159.9, 160.1. Mass spectrum MALDI-TOF: *m/e* 800.5632 $[M]^+$. $C_{48}H_{64}N_4O_4$. Calculated *m/e* 800.5717.

Cyclodimer VIId was obtained as side product in the synthesis of macrocycle **VId**. Eluent CH_2Cl_2–MeOH–aqueous NH_3, 100:20:1. Yield 29 mg (15%). Light-yellow viscous oily substance. ^{1}H NMR spectrum, δ, ppm: 0.66 s (6H), 0.98 br.s (12H), 1.00–2.10 m (68H), 2.74 t (8H, ^3J 7.0 Hz), 2.84–2.89 m (8H), 3.28–3.40 m (8H), 4.34–4.42 m (4H), 5.53 br.s (2H), 5.68 br.s (4H), 6.63 d (2H, ^3J 7.7 Hz), 6.69 d (2H, ^3J 7.2 Hz), 6.84 d (2H, ^3J 8.8 Hz), 6.85 d (2H, ^3J 8.7 Hz), 6.97 d (2H, ^3J 8.4 Hz), 6.99 d (2H, ^3J 8.9 Hz), 7.20 t (2H, ^3J 7.9 Hz), 7.21 t (2H, ^3J 8.0 Hz), 7.88 d (2H, ^3J 8.4 Hz), 7.90 d (2H, ^3J 8.4 Hz) (4 protons NH of dialkylamino groups are not unambiguously assigned). ^{13}C NMR spectrum, δ, ppm: 12.1 (2C), 18.7 (2C), 21.1 (2C), 23.9 (2C), 24.2 (2C), 24.7 (2C), 25.5 (2C), 26.3 (2C), 26.6 (2C), 28.3 (2C), 29.5 (4C), 30.4 (2C), 30.9 (4C), 32.3 (2C), 34.9 (2C), 35.6 (2C), 35.7 (2C), 37.4 (2C), 40.0 (2C), 40.3 (2C), 41.7 (4C), 42.7 (2C), 47.7 (4C), 48.8 (4C), 56.1 + 56.3 (2C), 56.6 + 56.7 (2C), 66.3 + 66.4 (2C), 70.9 + 71.0 (2C), 105.6 (2C), 105.8 (2C), 112.9 (2C), 113.6 (2C), 114.1 (4C), 124.5 (2C), 124.7 (2C), 129.2 (2C), 129.3 (2C), 135.2 (2C), 135.3 (2C), 138.9 (2C), 139.0 (2C), 143.3 (2C), 143.4 (2C), 159.9 (2C), 160.2 (2C). Mass spectrum MALDI-TOF: *m/e* 1601.0 $[M]^+$.

Compound VIII was obtained as side product in the synthesis of macrocycle **VId**. Eluent CH_2Cl_2–MeOH, 3:1.

Yield 29 mg (15%). Light-yellow viscous oily substance. ^{1}H NMR spectrum, δ, ppm: 0.60–0.65 m (6H), 0.93–0.95 m (6H), 0.98 br.s (6H), 0.99–2.10 m (62H), 2.85–3.10 m (8H), 3.77–3.46 m (4H), 4.35–4.44 m (4H), 5.60 br.s (2H), 6.60–6.68 m (2H), 6.80–6.88 m (4H), 6.92–7.00 m (2H), 7.12–7.19 m (2H), 7.30–7.37 m (2H), 7.55–7.61 m (2H), 7.65–7.70 m (2H), 7.76–7.95 m (6H) (4 protons NH are not unambiguously assigned). ^{13}C NMR spectrum, δ, ppm: 12.1 (2C), 18.7 (2C), 21.1 (2C), 23.9 (2C), 24.2 (2C), 24.7 + 24.9 (2C), 25.5 + 25.6 (2C), 26.2 (2C), 26.6 (2C), 28.3 (2C), 29.6 (2C), 30.6 (2C), 30.8 (2C), 32.1 (1C), 32.4 (2C), 34.9 (2C), 35.5 + 35.6 (2C), 35.7 (2C), 37.4 (2C), 39.9 (2C), 40.2 (2C), 40.7 + 40.8 (2C), 42.7 (2C), 46.6 + 46.7 (4C), 56.1 + 56.3 (2C), 56.6 (2C), 66.4 + 66.6 (2C), 70.9 + 71.0 (2C), 105.9 (2C), 113.0 (2C), 113.3 + 113.9 (2C), 114.5 (2C), 123.6 + 123.8 (2C), 124.5 + 124.7 (2C), 127.1 (2C), 127.2 + 127.3 (2C), 129.2 + 129.3 (2C), 135.3 + 135.4 (2C), 138.4 + 138.5 (2C), 139.0 (2C), 142.8 + 142.9 (2C), 160.0 + 160.7 (2C), 161.7 + 162.3 (2C) (6 quaternary carbon atoms are not unambiguously assigned). Mass spectrum MALDI-TOF: *m/e* 1416.9 $[M]^+$.

Cyclodimer VIIe was synthesized from 0.25 mmol (171 mg) of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**) and 0.25 mmol (18 mg) of diamine **Ve**. Eluent CH_2Cl_2–MeOH, 200:1. Yield 26 mg (15%). Light-yellow viscous oily substance contains as impurity cyclooligomers of larger molecular weight. UV spectrum (CH_2Cl_2), λ_{max}, nm (log ε): 308 (4.08), 350 (3.94). ^{1}H NMR spectrum, δ, ppm: 0.63 s (6H), 0.95 br.s (12H), 0.96–2.10 m (56H), 2.21 br.s (4H), 3.52 br.s (8H), 4.32 br.s (4H), 5.38 + 5.44 C (2H), 5.84 br.s (4H), 6.70 d (2H, ^3J 7.6 Hz), 6.72 d (2H, ^3J 7.3 Hz), 6.82–6.90 m (4H), 6.95–7.04 m (4H), 7.20 t (2H, ^3J 7.6 Hz), 7.21 t (2H, ^3J 7.6 Hz), 7.85–7.94 m (4H). ^{13}C NMR spectrum, δ, ppm: 12.1 (2C), 18.7 (2C), 21.1 (2C), 23.8 (2C), 24.2 (2C), 24.6 (2C), 25.5 (2C), 26.2 (2C), 26.6 (2C), 28.3 (2C), 29.7 (2C), 30.4 (2C), 30.8 (2C), 32.3 (2C), 34.9 (2C), 35.6 (2C), 35.7 (2C), 37.4 (2C), 39.9 (2C), 40.3 (2C), 41.6 (2C), 42.7 (2C), 43.2 (2C), 56.3 (2C), 56.6 (2C), 67.1 (2C), 71.1 (2C), 105.8 + 105.9 + 106.0 (4C), 113.0 (2C), 113.7 (2C), 114.3 (2C), 114.4 (2C), 124.5 (2C), 124.7 (2C), 130.4 (2C), 130.5 (2C), 135.3 (2C), 135.4 (2C), 139.0 (2C), 139.1 (2C), 143.0 + 143.3 + 143.4 (4C), 160.0 (2C), 160.6 (2C).

Bis(steroid)-substituted trioxadiamine IX. Into a two-neck flask filled with argon was charged 0.5 mmol (261 mg) of 24-(8-chloroquinolinyl-2-oxy)cholan-3-ol (**II**), 12 mg (8 mol%) of $Pd(dba)_2$, 9 mg (9 mol%) of 2-dicyclohexylphosphino-2'-dimethylaminobiphenyl, 2.5 ml of anhydrous dioxane, 0.25 mmol (55 mg) of trioxadiamine (**Va**), 120 mg (1.25 mmol) of sodium *tert*-butylate, and the mixture was boiled at stirring for 15 h. Then the reaction mixture was filtered, evaporated in a vacuum, and subjected to column chromatography on silica gel using the following sequence of eluents: CH_2Cl_2, CH_2Cl_2–MeOH, 500:1–3:1. Yield of compound **IX** 68 mg (23%). Light-yellow viscous oily substance. Eluent CH_2Cl_2–MeOH, 50:1, 10:1. UV spectrum (CH_2Cl_2), λ_{max}, nm (log ε): 310 (3.89), 324 (3.86), 350 (3.77). ^{1}H NMR spectrum, δ, ppm: 0.64 s (6H), 0.91 s (6H), 0.96 d (6H, ^3J 6.7 Hz), 0.98–1.99 m (58H), 2.00 quintet (4H, ^3J 6.2 Hz), 3.40 t (4H, ^3J 6.8 Hz), 3.49–3.68 m (14H), 4.32–4.42 m (4H), 5.75 br.s (2H), 6.67 d (2H, ^3J 7.2 Hz), 6.84 d (2H, ^3J 8.7 Hz), 6.96 d (2H, ^3J 7.9 Hz), 7.20 t (2H, ^3J 7.9 Hz), 7.88 d (2H, ^3J 8.7 Hz). ^{13}C NMR spectrum, δ, ppm: 12.1 (2C), 18.7 (2C), 20.8 (2C), 23.4 (2C), 24.2 (2C), 25.5 (2C), 26.4 (2C), 27.3 (2C), 28.3 (2C), 29.6 (2C), 30.6 (2C), 32.3 (2C), 34.6 (2C), 35.4 (2C), 35.6 (2C), 35.8 (2C), 36.5 (2C), 40.2 (2C), 40.4 (2C), 40.7 (2C), 42.1 (2C), 42.7 (2C), 56.1 (2C), 56.5 (2C), 66.3 (2C), 69.2 (2C), 70.3 (2C), 70.7 (2C), 71.8 (2C), 105.8 (2C), 112.8 (2C), 114.0 (2C), 124.7 (2C), 129.3 (2C), 135.2 (2C), 139.0 (2C), 143.4 (2C), 160.5 (2C). Mass spectrum MALDI-TOF: *m/e* 1194.8795 $[M]^+$. $C_{76}H_{114}N_4O_7$. Calculated *m/e* 1194.8788.

Compound X was isolated as a side reaction product. Yield 42 mg (24%). Eluent CH_2Cl_2–MeOH, 10:1–3:1. ^{1}H NMR spectrum, δ, ppm: 0.64 s (3H), 0.89 s (3H), 0.95 d (3H, ^3J 6.8 Hz), 0.97–2.00 m (31H), 2.01 quintet (2H, ^3J 6.5 Hz), 3.03 br.s (2H), 3.40 t (2H, ^3J 6.7 Hz), 3.52–3.65 m (11H), 3.67 t (2H, ^3J 6.2 Hz), 4.38 t (2H, ^3J 6.6 Hz), 5.65 br.s (1H), 6.70 d (1H, ^3J 7.6 Hz), 6.84 d (1H, ^3J 8.7 Hz), 6.97 d (1H, ^3J 8.1 Hz), 7.20 t (1H, ^3J 7.8 Hz), 7.88 d (1H, ^3J 8.9 Hz) (2 protons NH are not unambiguously assigned). ^{13}C NMR spectrum, δ, ppm: 12.0, 18.7, 20.8, 23.4, 24.2, 25.5 (2C), 26.4, 27.2, 28.3, 29.6, 30.5, 32.3, 34.5, 35.3, 35.6, 35.8, 36.4, 39.4, 40.2, 40.4, 41.0, 42.1, 42.7, 56.1, 56.5, 66.4, 69.4, 69.8, 70.0 (2C), 70.2, 70.4, 71.8, 106.2, 112.9, 114.3, 124.7, 135.3, 139.1, 143.4, 160.6 (1 quaternary carbon atom was not unambiguously assigned). Mass spectrum MALDI-TOF: *m/e* 707.5237 $[M]^+$. $C_{43}H_{69}N_3O_5$. Calculated *m/e* 707.5217.

Compound XI was isolated as a side reaction product. Yield 56 mg (46%). Eluent CH_2Cl_2, CH_2Cl_2–MeOH, 500:1. ^{1}H NMR spectrum, δ, ppm: 0.65 s (3H), 0.91 s (3H), 0.96 d (3H, ^3J 6.6 Hz), 1.00–2.05 m (29H), 3.56–3.65 m (1H), 4.40–4.48 m (2H), 6.88 d (1H, ^3J 8.7 Hz),

7.35 t (1H, ^3J 7.5 Hz), 7.59 t (1H, ^3J 7.7 Hz), 7.69 d (1H, ^3J 8.0 Hz), 7.82 d (1H, ^3J 8.5 Hz), 7.95 d (1H, ^3J 8.7 Hz). ^{13}C NMR spectrum, δ, ppm: 12.0, 18.6, 20.8, 23.3, 24.2, 25.6, 26.4, 27.2, 28.2, 30.5, 32.1, 34.5, 35.3, 35.5, 35.8, 36.4, 40.2, 40.4, 42.1, 42.7, 56.2, 56.5, 67.0, 71.8, 113.3, 123.8, 125.0, 127.2, 127.3, 129.3, 138.5, 146.6, 162.3. Mass spectrum MALDI-TOF: *m/e* 489.3 $[M]^+$.

Bis(oxadiamino)-substituted cholane XII. Into a two-neck flask filled with argon was charged 0.25 mmol (171 mg) of 3,24-di(8-chloroquinolinyl-2-oxy)cholane (**III**), 12 mg (8 mol%) of $Pd(dba)_2$, 9 mg (9 mol%) of 2-dicyclohexylphosphino-2'-dimethylaminobiphenyl, 5 ml of anhydrous dioxane, 1 mmol (220 mg) of trioxadiamine (**Va**), 75 mg (0.75 mmol) of sodium *tert*-butylate, and the mixture was boiled at stirring for 16 h. Then the reaction mixture was filtered, evaporated in a vacuum, and subjected to column chromatography on silica gel using the following sequence of eluents: CH_2Cl_2, CH_2Cl_2–MeOH, 50:1–3:1; CH_2Cl_2–MeOH–aqueous NH_3, 100:20:1–10:4:1. Yield of compound **XII** 155 mg (59%). Light-yellow viscous oily substance. Eluent CH_2Cl_2–MeOH, 5:1–3:1; CH_2Cl_2–MeOH–aqueous NH_3, 100:20:1–100:20:2. ^{1}H NMR spectrum, δ, ppm: 0.68 s (3H), 0.98 d (3H, ^3J 6.8 Hz), 0.99 s (3H), 1.00–2.01 m (32H), 2.03 quintet (4H, ^3J 6.0 Hz), 3.14 t (4H, ^3J 6.0 Hz), 3.37 t (2H, ^3J 6.7 Hz), 3.40 t (2H, ^3J 6.8 Hz), 3.54–3.69 m (24H), 4.32–4.45 m (2H), 5.54 br.s (1H), 5.70 br.s (2H), 6.65 d (1H, ^3J 7.2 Hz), 6.67 d (1H, ^3J 7.6 Hz), 6.85 d (1H, ^3J 8.9 Hz), 6.86 d (1H, ^3J 8.8 Hz), 6.95 d (1H, ^3J 7.2 Hz), 6.97 d (1H, ^3J 7.2 Hz), 7.18 t (1H, ^3J 7.8 Hz), 7.20 t (1H, ^3J 7.8 Hz), 7.87 d (1H, ^3J 8.7 Hz), 7.89 d (1H, ^3J 8.8 Hz) (4 protons NH are not unambiguously assigned). ^{13}C NMR spectrum, δ, ppm: 12.1, 18.7, 21.2, 23.8, 24.2, 24.8, 25.5, 26.2, 26.6 (3C), 28.5, 29.5 (2C), 30.3, 30.9, 32.4, 34.9, 35.7, 35.9, 37.4, 39.3, 39.4, 40.1, 40.4, 40.7, 40.8, 42.8, 56.2, 56.8, 66.6, 69.3 (2C), 69.7, 69.8, 69.9 (2C), 70.1 (2C), 70.2 (2C), 70.5 (2C), 71.0, 105.8, 106.0, 112.9, 113.6, 114.2 (2C), 124.5, 124.7, 128.4 (2C), 135.3 (2C), 139.0, 139.1, 143.4, 143.4, 160.0, 160.6. Mass spectrum MALDI-TOF: *m/e* 1052.7 $[M]^+$.

Macrocycle VIa was isolated as a side reaction product. Eluent CH_2Cl_2–MeOH, 50:1. Yield 27 mg (13%).

Isomeric mono(oxadiamino)-substituted cholanes XIII and XIV were isolated as side reaction products in a mixture. Eluent CH_2Cl_2–MeOH, 20:1. Yield 48 mg (23%). ^{1}H NMR spectrum of a mixture of compounds **XIII** and **XIV**, δ, ppm: 0.66 s (6H), 0.94–0.99 m (12H), 1.00–2.08 m (64H), 3.06 br.s (4H), 3.35–3.43 m (4H), 3.52–3.69 m (24H), 4.34–4.41 m (4H), 5.52 + 5.60 br.s (2H), 5.73 br.s (2H), 6.63–6.72 m (2H), 6.81–6.89 m (4H), 6.95 d (1H, ^3J 7.2 Hz), 6.97 d (1H, ^3J 6.5 Hz), 7.18 t (1H, ^3J 7.7 Hz), 7.20 t (1H, ^3J 8.1 Hz), 7.31 t (1H, ^3J 8.1 Hz), 7.33 t (1H, ^3J 8.3 Hz), 7.56 t (1H, ^3J 8.1 Hz), 7.58 t (1H, ^3J 8.0 Hz), 7.66 d (1H, ^3J 7.9 Hz), 7.68 d (1H, ^3J 7.7 Hz), 7.77 d (1H, ^3J 8.4 Hz), 7.81 d (1H, ^3J 8.4 Hz), 7.84–7.89 m (2H), 7.92 d (1H, ^3J 8.5 Hz), 7.94 d (1H, ^3J 8.5 Hz) (4 protons NH are not unambiguously assigned). ^{13}C NMR spectrum of a mixture of compounds **XIII** and **XIV**, δ, ppm: 12.1 (2C), 18.7 (2C), 21.1 (2C), 23.8 (2C), 24.2 (2C), 24.7 (2C), 25.5 + 25.6 (2C), 26.2 (2C), 26.6 (4C), 28.3 (2C), 29.6 (2C), 30.5 (2C), 30.8 (2C), 32.3 (2C), 34.9 (2C), 35.5 (2C), 35.7 (2C), 37.3 (2C), 39.3 (2C), 40.0 (2C), 40.3 (2C), 40.6 + 40.9 (2C), 42.7 (2C), 56.1 (2C), 56.6 (2C), 66.3 + 66.4 (2C), 69.3 (2C), 69.7 (2C), 69.8 (2C), 70.0 (2C), 70.2 (2C), 70.4 (2C), 70.8 + 70.9 (2C), 105.7 (1C), 106.1 (1C), 112.8 (1C), 112.9 (1C), 113.6 (1C), 113.9 (1C), 114.2 (2C), 123.5 (1C), 123.8 (1C), 124.5 (1C), 124.7 (1C), 127.1 (2C), 127.2 (1C), 127.3 (1C), 129.2 (1C), 129.3 (1C), 135.2 (1C), 135.3 (1C), 138.3 (1C), 138.5 (1C), 138.9 (1C), 139.0 (1C), 143.3 (1C), 143.4 (1C), 146.7 (2C), 159.9 (1C), 160.6 (1C), 161.7 (1C), 162.3 (1C) (4 quaternary carbon atoms are not unambiguously assigned). Mass spectrum MALDI-TOF: *m/e* 834.6 $[M]^+$.

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