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Protonated Amine Transport and Chiral Recognition by 1,2,4-Triazole Podands and Macrocycles

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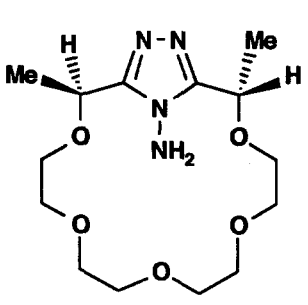
Abstract: Transport of ammonium salts across a bulk liquid membrane with chiral macrocycles and podands containing a 1,2,4-triazole subunit takes place with moderate enantioselectivity. Good transport rates were found for both podands and macrocycles, but chiral recognition was less effective with podands.

Resolution of racemic primary ammonium salts by chiral crown ethers has been achieved with moderate success by different techniques, including complexation[1], solvent extraction[2] and transport[3] experiments. However, chiral non-macrocyclic receptors (podands) have been employed for chiral recognition only in a few cases.[4] Although podands are generally considered weaker ligands than their macrocyclic analogues, some systems have been reported which showed surprisingly similar transport efficiencies of both their podand and macrocyclic forms.[5] It is also well known that a number of natural acyclic polyether antibiotics are excellent selective carriers for metal cations across biomembranes.[6]

We have recently reported on the enantioselective recognition (NMR study) of 1-(1-naphthyl)ethylammonium (HNEA$^+$) and 1-phenylethylammonium (HPEA$^+$) salts by chiral triazole-18-crown-6 ligands **1-3**.[7] Bradshaw *et al* have also studied the complexation properties of other chiral triazole-containing macrocycles for ammonium cations,[8] but no transport experiments have been reported yet for this kind of chiral ligands.



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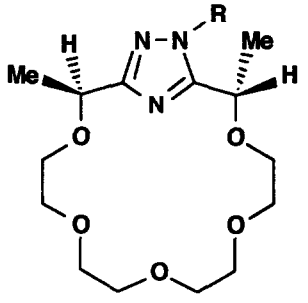
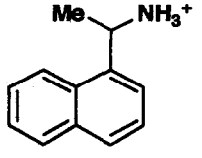
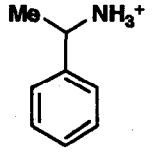


2 R = H

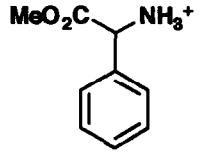
3 R = $C_{12}H_{25}$



HNEA$^+$



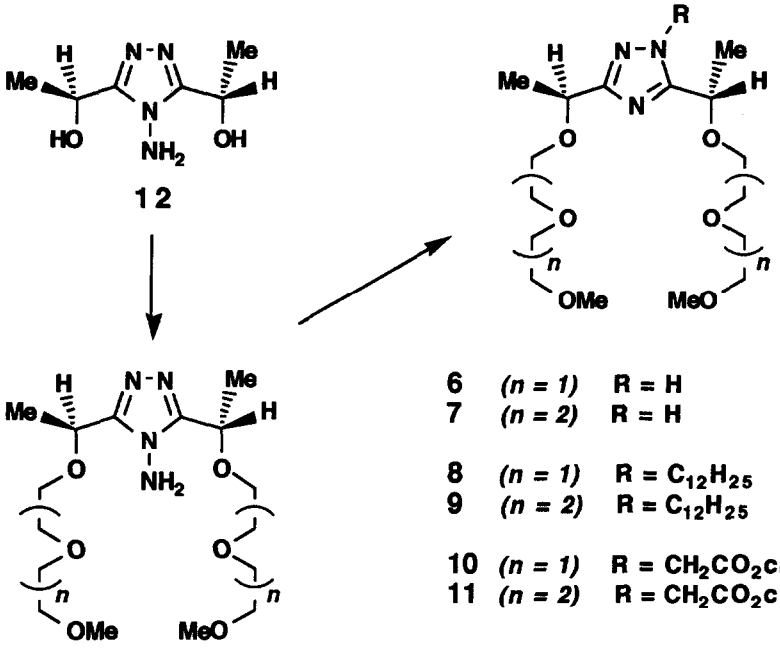
HPEA$^+$



HMPG$^+$

In the present paper, we describe the synthesis of eight new chiral podands containing 1,2,4-triazole subunits (**4-11**) and their use as carriers for chiral ammonium cations. An interesting feature of these receptors is the proximity of the chiral centers to the binding heteroatoms, and the presence of a C_2- symmetry axis in 4-amino- and 1(2)*H*-1,2,4-triazole podands, which enforces the chiral micro-environment around the bound substrates. On the other hand, *N*-alkylation provides a simple way to attach diverse side arms (functional groups, lipophilic tails) to the receptors. The transport results will be compared with those for the macrocyclic analogues **2** and **3**, whose complexation properties were studied earlier.[7,9]

Chiral podands **4-11** (n=1,2; R=H, $C_{12}H_{25}$, CH_2CO_2cholesteryl) were prepared in a few steps and good yields from *S*-lactic acid. The reaction of triazole **12**[9] with the corresponding tosylate of di- and triethyleneglycol[10] yielded amino-podands **4** and **5** (60-70 %). The *N*-amino group was removed by oxidative deamination[9,11,12] with nitrous acid to afford *N*-unsubstituted triazoles **6** and **7** (85-90 %). Alkylation with dodecyl bromide or cholesteryl chloroacetate[7] afforded the lipophilic podands **8-11**.



Transport experiments were performed using a $CHCl_3$-CCl_4 bulk liquid membrane. Results for $HNEA^+$, $HPEA^+$, and methyl phenylglycinate ($HMPG^+$) chlorides are summarized in Table 1.

$HNEA^+$ salts were found to be better transported than either $HPEA^+$ or $HMPG^+$ salts, the lipophilic macrocycles **2** and **3** showing the highest transport rates. However, rates were also high for the non-macrocyclic structures, especially for **7**, **9** and **11**, which have the longest side arms. On the contrary, podands **4** and **5** with an amino substituent at the triazole ring were found to be less efficient, probably due to the increased intramolecular hydrogen bonding, which causes a decrease in the

complexation ability of the receptors. Among macrocycles **2** and **3**, the lower transport efficiency of the former could be explained by its lower binding constants.[7]

Table 1. Transport rates (V) by receptors **2-11** (x 10^{-7} mol/h)[a]

	RS-HNEA$^+$(b)	*R*-HNEA$^+$(b)	*S*-HNEA$^+$(b)	*RS*-HPEA$^+$(c)	*RS*-HMPG$^+$(d)
2	190	--	--	--	25
3	277	--	--	--	190
4	63	--	--	3	8
5	79	92	80	14	11
6	83	--	--	16	23
7	109	130	112	22	25
8	63	--	--	16	14
9	100	112	102	20	22
10	71	--	--	(e)	11
11	89	104	90	(e)	22

(a) See experimental section for details. A 10 % error was estimated for all values.
(b) Measured at 280 nm. V_D = 13 x 10^{-7} mol.h^{-1}
(c) Measured at 257 nm. V_D = 1.0 x 10^{-7} mol.h^{-1}
(d) Measured at 260 nm. V_D = 2.0 x 10^{-7} mol.h^{-1}
(e) Complex kinetics. No linearity was found, and very long induction time was observed.

Data of Table 1 show somewhat higher rates for *R*-HNEA$^+$, within experimental error. However, most of the chiral discrimination originates during the induction time, as is shown in Figure 1 for receptor **7**.

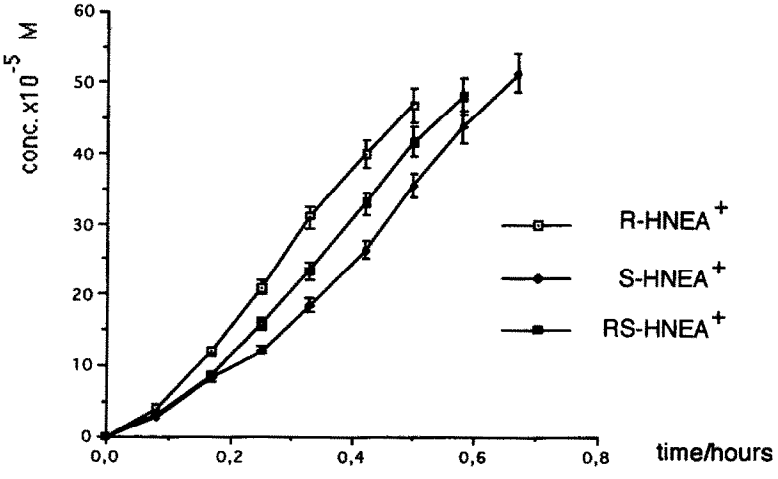


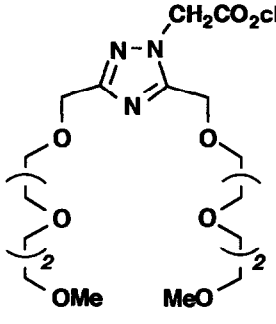
Figure 1. Plot of transport data for receptor **7** and *R*-, *S*-, and *RS*-HNEA$^+$.

Table 2. Ammonium salts enantioselective transport by receptors **2-11**.

Carrier	Guest	Time/h	Major enantiomer	Enantiomeric excess (a)
2	*RS*-HNEA$^+$	5	*R*	25
	RS-HMPG$^+$	26	*S*	24
3	*RS*-HNEA$^+$	3	*R*	9
	RS-HMPG$^+$	3.3	*S*	23
4	*RS*-HNEA$^+$	5.5	*R*	5
	RS-HMPG$^+$	50	*S*	6
5	*RS*-HNEA$^+$	5.5	*R*	8
	RS-HMPG$^+$	31	*S*	6
6	*RS*-HNEA$^+$	5.5	*R*	15
	RS-HMPG$^+$	26	*S*	11
7	*RS*-HNEA$^+$	5.5	*R*	14
	RS-HMPG$^+$	23.5	*S*	13
8	*RS*-HNEA$^+$	5.5	*R*	12
	RS-HMPG$^+$	31	*S*	10
9	*RS*-HNEA$^+$	5.5	*R*	12
	RS-HMPG$^+$	23	*S*	11
10	*RS*-HNEA$^+$	5.5	*R*	10
	RS-HMPG$^+$	32	*S*	18
11	*RS*-HNEA$^+$	5.5	*R*	14
	RS-HMPG$^+$	23	*S*	17

(a) Measured by NMR integration of Me and/or MeO signals for HNEA$^+$ and Me signals for HMPG$^+$.

Chiral recognition was determined either by independent rate measurements for each enantiomer (data for HNEA$^+$ reported in Table 1), or from racemic salts, measuring the optical purity of the ammonium salt at the receiving phase,[3] after completion of *c.a.* 10-15 % transport (Table 2). Measurements were made by ^{1}H-NMR integration of the resolved signals on the corresponding diastereomeric Mosher derivatives.[13] The small amount of HPEA$^+$ salts isolated precluded their measurement by this method. For cholesteryl containing receptors **10** and **11**, chiral recognition could be inferred from the chirality of the appended side arm. However, a control transport experiment with podand **13**, which lacks chiral centers other than cholesteryl around the triazole ring, showed no selectivity for the HNEA$^+$ enantiomers.



13

All podands and macrocycles exhibited moderate chiral recognition for the same configuration (*R*-notation for HNEA$^+$ but *S*- for HMPG$^+$). As expected, the best results were found for the more preorganized receptors,

macrocycles **2** and **3**, which showed e.e. around 25 %, with the exception of the transport of HNEA+ by **3** (only 9 %), while podands **4-11**, which have increased conformational flexibility at the chiral barriers, were found to be less selective.

Since transport efficiencies and selectivities are influenced by binding constants, lipophilicity, and many other factors, it is difficult to develop simple complexation models to account for the major transported enantiomer. Assuming that the bulkier substituent of the substrate (naphthyl or phenyl group) is pulled away from the chiral centers of the receptor, the conformation showed in Figure 2a for the complex of macrocycle **2** with *R*-HNEA+, should be preferred. On the other hand, the alternative conformation illustrated in Figure 2b could explain the chemical shifts observed by ^{1}H-NMR (stacking).[7]

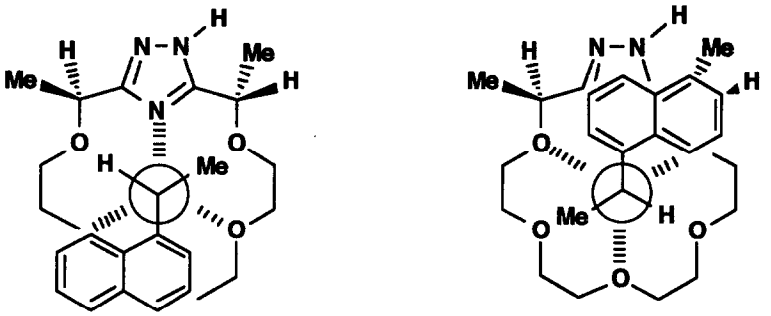


Figure 2. Proposed model for the complexation of *R*-HNEA$^+$ by **2**

It can be concluded from the present study that macrocycle formation (i.e. preorganization) has more influence on chiral discrimination than on transport efficiency. We anticipate that development of new podand systems having their chirality centers in a more rigid framework would result in efficient and selective carriers for chiral organic substrates. Experiments in this direction are currently underway and will be reported on due course.

EXPERIMENTAL PART

Transport Experiments

Transport experiments were carried out in a conventional cell consisting of an outer cylindrical glass vessel (51 mm inner diameter) and a central glass tube (24 mm inner diameter). A 0.003 M $CHCl_3$: CCl_4 (3:1) solution (50.0 ml) of the host separated the inner (12.5 ml of 0.1 M HCl) from the outer (10.0 ml of 0.08 M HCl, 0.1 M $LiPF_6$ and 0.06 M guest.HCl salt) aqueous phases. The liquid membrane was stirred at 200 r.p.m. at 20ºC and transport was followed by monitoring the absorbance (at the maximum wavelength) of the inner aqueous phase. Absorbances were reported as concentrations with the help of appropriate calibrations. Experimental transport rates (V_E) were obtained from the slope of the linear parts of the concentration/time plots after an early induction period for each carrier. Three independent curves were registered for each transport experiment. The estimated error was 10 %. Values reported in Table 1 refer to the mean of the slopes of these three curves. Control experiments in the absence of carrier allowed the measurement of diffusion rates V_D

of the hydrochoride salts through the liquid membrane. The differences V_E - V_D accounted for the corrected transport rates reported.

Experiments involving racemic substrates were stopped after 10-15% of the salt was transported to the receiving phase. A suspension of the ammonium salt isolated in chloroform (1 ml) and (*S*)-α-methoxy-α-trifluoromethylphenylacetyl chloride (ClMTPA, 1.5 molar excess) and triethylamine (2.5 molar excess) were added. The mixture was stirred at room temperature for 1 hour, diethyl ether was added and triethylamine hydrochloride was filtered off. The resulting solution was washed with water, dried over anhydrous sodium sulfate and evaporated. The diastereomeric excess was determined by ^{1}H-NMR integration.

*Podands **4** and **5**.* Over a well stirred suspension of sodium hydride (60 %, 34 mmol) in dry DMF (30 ml) was added under argon a solution of *(S,S)*- 4-amino-3,5-bis-(1-hydroxyethyl)-1,2,4-triazole (**12**) (11.6 mmol) in dry DMF (40 ml). The mixture was stirred for 30 min at room temperature and a solution of the appropriate ethyleneglycol monomethyl ether tosylate (23.6 mmol) in dry DMF (40 ml) was added slowly. The mixture was further stirred at room temperature for 24 h, and the reaction was treated with 10 % aq. ammonium chloride (10 ml). The solvent was removed and the residue was treated with CH_2Cl_2 (150 ml), filtered and evaporated. The residue was purified by column chromatography on alumina, eluting with ethyl acetate:methanol, 15:1.

(S,S)-4-Amino-3,5-bis-(1-methyl-2,5,8-trioxa-1-nonyl)-1,2,4-triazole **(4).** Yield 79 %; colourless oil.; $[\alpha]_D$ = - 22° (*c* = 0.5, chloroform); ^{1}H-NMR ($CDCl_3$): 5.62 (s, 2H, NH_2), 4.91 (c, *J* = 6.7 Hz, 2H, C<u>H</u>-CH_3), 3.7-3.5 (m, 16H, OCH_2), 3.37 (s, 6H, CH_3O), 1.68 (d, 6H, *J* = 6.7 Hz, CHC<u>H</u>$_3$); ^{13}C-NMR ($CDCl_3$): 153.9 (triazole), 71.3 (C-7), 69.7 (C-4, C-6), 69.3 (<u>C</u>HCH$_3$). 67.2 (C-3), 58.4 (CH_3O), 17.4 (<u>C</u>H$_3$CH); MS, *m/z* : 377 (M^+ + 1) Anal. Calcd. for $C_{16}H_{32}N_4O_6$: C 51.05, H 8.57 N 14.88. Found: C 50.87, H 8.31, N 14.77.

(S,S)-4-Amino-3,5-bis-(1-methyl-2,5,8,11-tetraoxa-1-dodecyl)-1,2,4-triazole **(5).** Yield 76 %, colourless oil; $[\alpha]_D$ = - 25° (*c* = 0.5, chloroform); ^{1}H-NMR ($CDCl_3$): 5.72 (s, 2H, NH_2), 4.95 (c, 2H, *J* = 6.7 Hz, C<u>H</u>CH$_3$), 3.7-3.5 (m, 24H, OCH_2), 3.36 (s, 6H, OCH_3), 1.68 (d, 6H, *J* = 6.7 Hz, CHC<u>H</u>$_3$); ^{13}C-NMR ($CDCl_3$): 154.2 (triazole), 71.7 (C-10), 70.3, 70.1 (C-4, C-6, C-7, C-9), 69.7 (<u>C</u>HCH$_3$), 67.4 (C-3), 58.8 (CH_3O), 17.8 (CH<u>C</u>H$_3$); MS, *m/z* : 465 (M^+ + 1). Anal. Calcd. for $C_{20}H_{40}N_4O_8$: C 51.44 H 8.57 N 11.75. Found: C 51.44, H 8.57, N 11.75

*Podands **6** and **7**:* To a solution of **4** or **5** (3.5 mmol) in 6 N HCl (7 ml) was slowly added at 0°C under stirring a solution of sodium nitrite (4.9 mmol) in water (5 ml). The mixture was stirred for 2 h at 0°C and then it was neutralized with solid sodium carbonate. The water was removed *in vacuo* and the product was extracted with 150 ml of CH_2Cl_2. The salts were removed by filtration and the solution was evaporated. The residue was purified by column chromatography on alumina, eluting with ethyl acetate:methanol, 15:1.

(S,S)-3,5-Bis-(1-methyl-2,5,8-trioxa-1-nonyl)-1,2,4-triazole **(6).** Yield 89 %; yellowish oil; $[\alpha]_D$ = -28° (*c* = 0.5, chloroform); ^{1}H-NMR ($CDCl_3$): 4.71 (q, 2H, *J* = 6.6 Hz, C<u>H</u>CH$_3$), 3.7-3.6 (m, 16H, OCH_2), 3.43 (s, 6H, OCH_3), 1.57 (d, 6H, *J* = 6.6 Hz, CHC<u>H</u>$_3$); ^{13}C-NMR ($CDCl_3$): 161.9 (triazole), 72.0 (C-7), 71.8 (C-4, C-6), 70.3 (<u>C</u>HCH$_3$), 68.6 (C-3), 58.9 (OCH_3), 20.7 (<u>C</u>H$_3$CH); MS *m/z* : 361 (M^+). Anal. Calcd. for $C_{16}H_{31}N_3O_6$: C, 53.17; H 8.65; N, 11.63. Found: C, 53.00; H, 8.31; N, 11.48.

(S,S)-3,5-bis-(1-methyl-2,5,8,11-tetraoxa-1-dodecyl)-1,2,4-triazole **(7).** Yield 87 %; oil; $[\alpha]_D$ = -30° (*c* = 0.5, chloroform); ^{1}H-NMR ($CDCl_3$): 4.71 (q, 2H, *J* = 6.6 Hz, C<u>H</u>CH$_3$), 3.7-3.5 (m, 24H, OCH_2), 3.37 (s, 6H, OCH_3), 1.57 (d, 6H, *J* = 6.6 Hz, CHC<u>H</u>$_3$); ^{13}C-NMR ($CDCl_3$): 161-162 (broad, triazole), 71.4 (C-

10), 69.9 ($\underline{C}HCH_3$, C-4, C-6, C-7, C-9), 67.9 (C-3), 58.4 (CH_3O), 20.2 ($CH\underline{C}H_3$); MS *m/z* : 450 ($M + 1^+$). Anal. Calcd. for $C_{20}H_{39}N_3O_8$: C, 53.44; H, 8.74; N, 9.35. Found: C, 53.47; H, 9.02; N, 9.67.

*N-Dodecyl derivatives **8** and **9**:* Finely powdered potassium carbonate (22 mmol), tetrabutyl ammonium hydrogensulfate (0.2 mmol), and dodecyl bromide (1.63 mmol) were added to a solution of the corresponding triazole **6** or **7** (1.2 mmol) in acetonitrile (60 ml). The mixture was stirred for 3 h at 60°C. The inorganic salts were filtered off and washed with acetonitrile. The filtrates were evaporated, the residue was dissolved in hexane and the solution washed with water, dried under anhydrous magnesium sulfate and evaporated to give a colourless oil. Purification was achieved by silica gel chromatography (dichloromethane-methanol, 10:1)

(S,S)-1-Dodecyl-3,5-bis-(1-methyl-2,5,8-trioxa-1-nonyl)-1,2,4-triazole **(8)**. Yield 80 %; oil; $[\alpha]_D$ =-41° (*c* = 0.5, chloroform); ^{1}H-NMR ($CDCl_3$): 4.84 (q, 1H, *J* = 6.7 Hz, $C\underline{H}CH_3$ on C_5), 4.60 (q, 1H, *J* = 6.7 Hz, $C\underline{H}CH_3$ on C_3), 4.2 (m, 2H, NCH_2), 3.7-3.5 (m, 16H, OCH_2), 3.37 (s, 6H, OCH_3), 1.9 (m, 2H, $NCH_2C\underline{H}_2$), 1.58 (d, 3H, *J* = 6.7 Hz, $C\underline{H}_3CH$ on C_5), 1.54 (d, 3H, *J* = 6.7 Hz, $C\underline{H}_3CH$ on C_3), 1.4-1.2 (m, 18H, CH_2), 0.89 (t, 3H, $C\underline{H}_3CH_2$); ^{13}C-NMR ($CDCl_3$): 162.8 (C-3), 155.2 (C-5), 71.7 (C-7, CH on C_3), 70.5, 70.2, 67.9 (CH on C_5, C-3, C-4, C-6), 58.8 (OCH_3), 48.7 (NCH_2), 31.7, 29.9, 29.4, 29.1, 26.5 ($NCH_2\underline{C}H_2$, CH_2), 22.5 ($CH_3\underline{C}H_2$), 20.3 (CH_3 on C_3), 19.4 (CH_3 on C_5), 13.9 ($\underline{C}H_3CH_2$); MS *m/z* : 530 (M^+). Anal. Calcd. for $C_{28}H_{55}N_3O_6$: C, 63.48; H, 10.47; N, 7.93. Found: C, 63.29; H, 10.47; N, 7.87.

(S,S)-1-Dodecyl-3,5-bis-(1-methyl-2,5,8,11-tetraoxa-1-dodecyl)-1,2,4-triazole **(9)**. Yield 82 %; oil; $[\alpha]_D$ = -41° (*c* = 0.5, chloroform); ^{1}H-NMR ($CDCl_3$) 4.85 (q, 1H, *J* = 6.7 Hz, $C\underline{H}CH_3$ on C_5), 4.60 (q, 1H, *J* = 6.7 Hz, $C\underline{H}CH_3$ on C_3), 4.2 (m, 2H, NCH_2), 3.7-3.5 (m, 24H, OCH_2), 3.36 (s, 6H, OCH_3), 1.9 (m, 2H, $NCH_2C\underline{H}_2$), 1.59 (d, 3H, *J* = 6.7 Hz, $C\underline{H}_3CH$ on C_5), 1.54 (d, 3H, *J* = 6.7 Hz, $C\underline{H}_3CH$ on C_3), 1.4-1.2 (m, 18H, CH_2), 0.88 (t, 3H, $C\underline{H}_3CH_2$); ^{13}C-NMR ($CDCl_3$) 162.4 (C-3), 154.8 (C-5), 71.3 (C-10, CH on C_3), 69.9, 67.4 (CH on C_5, C-3, C-4, C-6, C-7, C-9), 58.3 (OCH_3), 48.2 (NCH_2), 31.2, 29.4, 29.0, 28.9, 28.7, 28.6, 26.1 ($NCH_2\underline{C}H_2$, CH_2), 22.0 ($CH_3\underline{C}H_2$), 19.8 (CH_3 on C_3), 18.8 (CH_3 on C_5), 13.5 ($\underline{C}H_3CH_2$); MS *m/z* : 618 ($M + 1^+$). Anal. Calcd. for $C_{32}H_{63}N_3O_8$: C, 62.20; H, 10.28; N, 6.80. Found: C, 61.98; H, 9.97; N, 7.10.

*Cholesteryl derivatives **10** and **11***. A mixture of the corresponding triazole **6** or **7** (2.23 mmol), potassium carbonate (2.78 mmol), potassium iodide (1.39 mmol) and cholesteryl chloroacetate (2.23 mmol) in dry acetone (100 ml) was stirred at 50°C for 24 h. The solvent was removed under reduced pressure, the residue was extracted with CH_2Cl_2 and the solvent was evaporated. The residue was purified by column chromatography using alumina with ethyl acetate as eluent.

Cholesteryl (S,S)-3,5-bis-(1-methyl-2,5,8-trioxa-1-nonyl)-1,2,4-triazol-1-yl-acetate **(10)**. Yield, 80 %; oil; $[\alpha]_D$ = -39° (*c* = 0.5, chloroform); ^{1}H-NMR ($CDCl_3$): 5.4 (m, 1H, CH=C), 5.15 (AB system, 2H, NCH_2CO), 4.87 (q, 1H, *J* = 6.7 Hz, $C\underline{H}CH_3$ on C_5), 4.7 (m, 1H, H-3'), 4.65 (q, 1H, *J* = 6.7 Hz, $C\underline{H}CH_3$ on C_3), 3.7-3.5 (m, 16H, OCH_2), 3.4 (s, 6H, OCH_3), 1.57 (d, 3H, *J* = 6.7 Hz, $C\underline{H}_3CH$ on C_5), 1.54 (d, 3H, *J* = 6.7 Hz, $C\underline{H}_3CH$ on C_3), 1.00 (s, 3H, CH_3-19'), 0.90 (d, 3H, CH_3-21'), 0.85 (d, 6H, CH_3-26', CH_3-27'), 2.4-0.8 (m, 28H, CH, CH_2 cholest.), 0.67 (s, 3H, CH_3-18'); ^{13}C-NMR ($CDCl_3$): 166.6 (C=O), 163.3 (C-3), 156.6 (C-5), 138.8 ($\underline{C}$=CH), 122.9 (C=$\underline{C}$H), 75.5 ($\underline{C}$HOCO), 71.6 (C-7), 71.5 ($\underline{C}$H on C_3), 71.3 ($\underline{C}$H on C_5), 70.2, 68.1, 67.9 (C-3, C-4, C-6), 58.8 (OCH_3), 56.4, 55.8 (C-14', C-17'), 50.3 (CH_2N), 49.7, 42.0, 39.4, 39.2, 37.7, 36.6, 36.3, 35.9, 35.5, 31.6, 28.0, 27.7, 27.4, 24.0, 23.5 (CH_2, CH, C cholest.), 22.6, 22.3 (C-26', C-27'), 20.8 (C-11'), 20.3 ($\underline{C}H_3$ on C_3), 19.3 ($\underline{C}H_3$ on C_5), 19.0 (C-19'), 18.5 (C-21'), 11.6 (C-18'); MS *m/z* : 787 (M^+). Anal. Calcd. for $C_{45}H_{77}N_3O_8$: C, 68.58; H, 9.85; N, 5.33; Found: C, 68.36; H, 9.69; N, 5.19

Cholesteryl (S,S)-3,5-bis-(1-methyl-2,5,8-11-tetraoxa-1-dodecyl)-1,2,4-triazol-1-yl-acetate **(11)**. Yield 82 %; oil; $[\alpha]_D$ = -39° (*c* = 0.5, chloroform); ^{1}H-NMR ($CDCl_3$) 5.4 (m, 1H, CH=C), 5.15 (AB system, 2H, NCH_2CO), 4.86 (q, 1H, *J* = 6.7 Hz, $CHCH_3$ on C_5), 4.7 (m, 1H, H-3'), 4.61 (q, 1H, *J* = 6.7 Hz, $CHCH_3$ on C_3), 3.7-3.5 (m, 24H, OCH_2), 3.39 (s, 6H, OCH_3), 1.56 (d, 3H, *J* = 6.7 Hz, CH_3CH on C_5), 1.54 (d, 3H, *J* = 6.7 Hz, CH_3CH on C_3), 1.00 (s, 3H, CH_3-19'), 0.91 (d, 3H, CH_3-21'), 0.86 (d, 6H, CH_3-26', CH_3-27'), 2.4-0.8 (m, 28H, CH, CH_2 cholest.), 0.67 (s, 3H, CH_3-18'); ^{13}C-NMR ($CDCl_3$) 166.8 (C=O), 163.5 (C-3), 156.7 (C-5), 139.0 (C=CH), 123.0 (C=CH), 75.7 (CHOCO), 71.8 (C-10), 71.7 (CH on C_3), 71.5 (CH on C_5), 70.4, 70.2, 68.3, 68.1 (C-3, C-4, C-6, C-7, C-9), 58.9 (OCH_3), 56.5, 56.0 (C-14, C-17), 50.4 (CH_2N), 49.8, 42.2, 39.6, 39.4, 37.9, 36.7, 36.4, 36.0, 35.7, 31.7, 28.1, 27.9, 27.6, 24.1, 23.7 (CH_2, CH, C cholest.), 22.8, 22.5 (C-26', C-27'), 20.9 (C-11'), 20.4 (CH_3 on C_3), 19.5 (CH_3 on C_5), 19.2 (C-19'), 18.6 (C-21'), 11.7 (C-18'); MS *m/z* : 876 (M^+ + 1). Anal. Calcd. for $C_{49}H_{85}N_3O_{10}$: C, 67.17; H, 9.78; N, 4.80; Found: C, 66.98; H, 9.62; N, 4.71

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