SYNTHESIS OF HOMOCHIRAL ACYCLIC MONO- AND BIS(α-AMINO ACID)S WITH OLIGO(OXYETHYLENE) CHAINS

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Synthesis of homochiral α-amino acids **3a**–**3e** and bis(α-amino acid)s **4a**–**4e** *via* $BF_3 \cdot Et_2O$-catalyzed ring-opening of methyl (*S*)-1-[(benzyloxy)carbonyl]aziridine-2-carboxylate (**7**) with oligo(ethylene glycol)s and subsequent acid hydrolysis is reported.

Keywords: Amino acids; Oligo(ethylene glycol)s, Aziridines; Nucleophilic ring-opening reaction; Podands; Crown ethers.

Recently[1,2], we have prepared macrocyclic amino acid **1** and bis(amino acid) **2** , which are "crowned" at the glycine α-carbon with the methylene-oligo(oxyethylene)oxymethylene chain, and investigated their complexation and self-assembling properties. As an extension of this study, we wish to provide synthetic access also to the acyclic analogues **3** and **4** anticipating that the well-known metal-ion-ligating as well as hydrogen-bonding abilities of the incorporated straight-chain oligo(oxyethylene) moiety may endow also the target compounds with some unusual (podand)[3] properties.

As it is pointed out elsewhere[4,5], there is a tremendous level of interest in the *de novo* design and synthesis of novel unnatural amino acids with specific properties for the purposes of imparting enzyme-inhibitory, antimetabolite and protease resistance-inducing properties to peptides and their mimetics. As a consequence, the development of versatile methodologies for their preparation in optically pure form has emerged as a highly significant and challenging endeavor. For the homologous series of the homochiral amino acids (*S*)-**3a**–**3e** and (*S*,*S*)-**4a**–**4e**, this synthetic task has now been accomplished.

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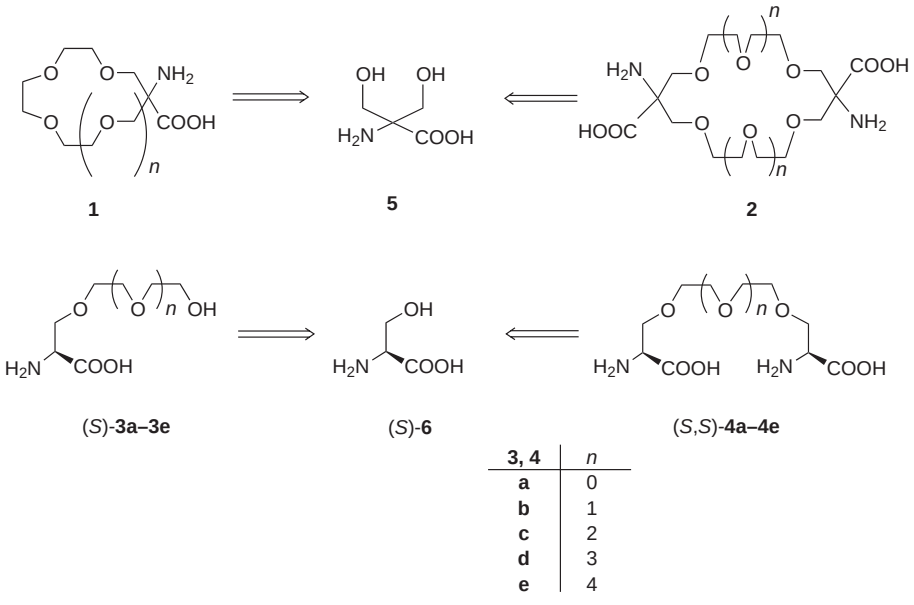
RESULTS AND DISCUSSION

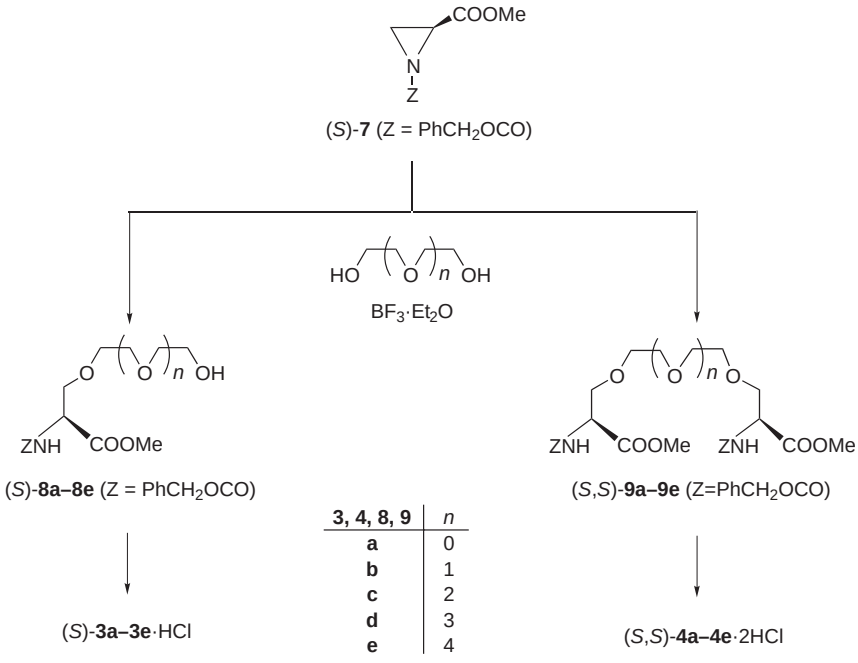
In contrast to the macrocyclic amino acids **1** and **2** pertaining retrosynthetically to 2,2-bis(hydroxymethyl)glycine **5**, the acyclic analogues **3a**–**3e** and **4a**–**4e** refer to the 2-hydroxymethylglycine (serine) homologue **6** (Scheme 1). As the most convenient synthon of **6**, we have chosen the activated derivative of (*S*)-aziridine-2-carboxylic acid **7**, which is easily accessible from the homochiral (*S*)-serine.



3, 4	*n*
a	0
b	1
c	2
d	3
e	4

SCHEME 1

Nucleophilic reactivity of aziridine **7** has been amply demonstrated[6–9]. Surprisingly enough, the reaction with free oligo(ethylene glycol)s has not been as yet reported. As we have now found, the nucleophilic ring-opening reaction of the aziridine derivative proceeds smoothly under $BF_3 \cdot Et_2O$ catalysis, yielding a mixture of the corresponding protected amino acid **8a**–**8e** and bis(amino acid) **9a**–**9e**, respectively, in proportions depending on the stoichiometry employed. A simple chromatographic separation followed by acid hydrolysis afforded the target deprotected amino acid **3a**–**3e** and bis(amino acid) **4a**–**4e** (Scheme 2). A straightforward access to novel enantiomerically uniform (*S*)-serine analogues is thus provided.



3, 4, 8, 9	*n*
a	0
b	1
c	2
d	3
e	4

SCHEME 2

EXPERIMENTAL

^{1}H NMR spectra were measured on a FT NMR spectrometer Varian Unity 200 (200 MHz, 20 °C) in $CDCl_3$ (with TMS as internal standard) and/or in D_2O (referenced to HDO signal at 4.80 ppm). Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. FAB MS spectra were recorded with a ZAB-EQ VG analytical instrument using a mixture of glycerol–thioglycerol matrix. Analytical samples were dried at 60 °C/5 kPa for 24 h. TLC chromatography was performed on Kieselgel GF254 using the Dragendorff spraying reagent. Commercial oligo(ethylene glycol)s (Aldrich, Fluka) were distilled and kept over molecular sieves 3A. Other reagents and solvents were purchased from Fluka and Aldrich and were used without further purification. Methyl (*S*)-1-[(benzyloxy)carbonyl]aziridine-2-carboxylate (**7**) was prepared by a modification of the earlier procedure[6]. Values of $[\alpha]_D$ are given in 10^{-1} deg cm^2 g^{-1}.

Methyl (*S*)-1-[(Benzyloxy)carbonyl]aziridine-2-carboxylate (**7**)

Methyl (*S*)-1-tritylaziridine-2-carboxylate[6] (6.86 g, 20 mmol) was dissolved in MeOH (20 ml) and $CHCl_3$ (20 ml). Trifluoroacetic acid (28 ml, 200 mmol) was added dropwise at 0 °C and the mixture was allowed to stand at 0 °C for 2 h. The solvents were evaporated under reduced pressure and the residue was dissolved in $CHCl_3$ (30 ml) and triethyl amine (7 ml). The resulting mixture was cooled to 0 °C and a solution of benzyl chloroformate (3.1 ml,

22 mmol) in $CHCl_3$ (20 ml) was added dropwise. The reaction mixture was allowed to stand at room temperature for 16 h and was then washed with 10% aqueous citric acid, water, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (anhydrous Na_2SO_4) and the solvent was removed by evaporation. The pure product was obtained by chromatography (ethyl acetate/petroleum ether 1:3) as oil (4.1 g, 87%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.35 (m, 5 H); 5.15 (s, 2 H); 3.71 (s, 3 H); 3.11 (dd, 1 H, *J* = 3.4 and 5.5); 2.60 (dd, 1 H, *J* = 1.2 and 3.4); 2.49 (dd, 1 H, *J* = 1.2 and 5.5). $[\alpha]_D$ –46.4 (*c* 1, MeOH); ref.[6]: $[\alpha]_D$ –47.3 (*c* 0.25).

Reactions of **7** with Oligo(ethylene glycol)s. General Procedure

Methyl (*S*)-1-[(benzyloxy)carbonyl]aziridine-2-carboxylate (**7**; 9 mmol) and an appropriate oligo(ethylene glycol) (6 mmol) was dissolved in $CHCl_3$ (4 ml) and treated with 10% solution of $BF_3{\cdot}Et_2O$ in $CHCl_3$ (2 ml). The mixture was allowed to stand at room temperature for 20 h. After dilution with $CHCl_3$ (30 ml), the mixture was shaken with 10% $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated. The products were separated by column chromatography using these eluents: EtOAc/petroleum ether from 1:1 to 3:1 (A), EtOAc/petroleum ether from 3:1 mixture to EtOAc only (B), or 5% MeOH in CH_2Cl_2 (C).

Methyl (S)-2-{[(benzyloxy)carbonyl]amino}-6-hydroxy-4-oxahexanoate (**8a**; *n* = 0). Prepared from **2** and ethylene glycol. Isolated chromatographically using eluent B; oil (0.74 g, 31%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.36 (m, 5 H); 5.81 (br d, 1 H, *J* = 8.5); 5.13 (s, 2 H); 4.53 (dt, 1 H, *J* = 8.5 and 3.4); 3.92 (dd, 1 H, *J* = 9.8 and 3.4); 3.77 (s, 3 H); 3.74–3.64 (m, 3 H); 3.59–3.51 (m, 2 H). FAB MS, *m/z*: 298 (MH^+, 41), 254 (100), 164 (29). FAB HR MS: for $[C_{14}H_{20}NO_6]^+$ calculated 298.1291, found 298.1282. $[\alpha]_D$ –11.5 (*c* 1, MeOH).

Dimethyl (S,S)-2,9-bis{[(benzyloxy)carbonyl]amino}-4,7-dioxadecanedioate (**9a**; *n* = 0). Prepared from **2** and ethylene glycol. Isolated chromatographically using eluent A; oil (1.29 g, 30%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.40–7.24 (m, 10 H); 5.80 (br d, 2 H, *J* = 8.5); 5.12 (s, 4 H); 4.48 (dt, 2 H, *J* = 8.5 and 3.4); 3.91 (dd, 2 H, *J* = 9.8 and 3.4); 3.72 (s, 6 H); 3.70–3.50 (m, 6 H). FAB MS, *m/z*: 533 (MH^+, 45), 489 (92), 399 (100). FAB HR MS: for $[C_{26}H_{33}N_2O_{10}]^+$ calculated 533.2135, found 533.2144. $[\alpha]_D$ –6.2 (*c* 1, MeOH).

Methyl (S)-2-{[(benzyloxy)carbonyl]amino}-9-hydroxy-4,7-dioxanonanoate (**8b**; *n* = 1). Prepared from **2** and diethylene glycol. Isolated chromatographically using eluent B; oil (0.70 g, 34%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.36 (m, 5 H); 6.03 (br d, 1 H, *J* = 8.6); 5.14 (s, 2 H); 4.50 (dt, 1 H, *J* = 8.6 and 3.1); 4.01 (dd, 1 H, *J* = 10.1 and 3.1); 3.77 (s, 3 H); 3.76–3.56 (m, 9 H). FAB MS, *m/z*: 342 (MH^+, 36), 298 (100), 208 (41). FAB HR MS: for $[C_{16}H_{24}NO_7]^+$ calculated 342.1553, found 342.1559. $[\alpha]_D$ –7.9 (*c* 1, MeOH).

Dimethyl (S,S)-2,12-bis{[(benzyloxy)carbonyl]amino}-4,7,10-trioxatridecanedioate (**9b**; *n* = 1). Prepared from **2** and diethylene glycol. Isolated chromatographically using eluent A; oil (1.4 g, 40%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.34 (m, 10 H); 5.88 (br d, 2 H, *J* = 8.6); 5.12 (s, 4 H); 4.47 (dt, 2 H, *J* = 8.6 and 3.4); 3.92 (dd, 2 H, *J* = 9.8 and 3.4); 3.73 (s, 6 H); 3.70–3.50 (m, 10 H). FAB MS, *m/z*: 577 (MH^+, 28), 533 (100), 443 (45). FAB HR MS: for $[C_{28}H_{37}N_2O_{11}]^+$ calculated 577.2397, found 577.2404. $[\alpha]_D$ –7.9 (*c* 1, MeOH).

Methyl (S)-2-{[(benzyloxy)carbonyl]amino}-12-hydroxy-4,7,10-trioxadodecanoate (**8c**; *n* = 2). Prepared from **2** and triethylene glycol. Isolated chromatographically using eluent C; oil (0.90 g, 39%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.36 (m, 5 H); 6.55 (br d, 1 H, *J* = 8.8); 5.13 (s, 2 H); 4.50 (dt, 1 H, *J* = 8.8 and 3.4); 3.98 (dd, 1 H, *J* = 9.5 and 3.4); 3.76 (s, 3 H); 3.75–3.54 (m, 13 H). FAB MS, *m/z*: 386 (MH^+, 36), 342 (100), 252 (62). FAB HR MS: for $[C_{18}H_{28}NO_8]^+$ calculated 386.1815, found 342.1822. $[\alpha]_D$ –5.9 (*c* 1, MeOH).

Dimethyl (S,S)-2,15-bis{[(benzyloxy)carbonyl]amino}-4,7,10,13-tetraoxahexadecanedioate (**9c**; *n* = 2). Prepared from **2** and triethylene glycol. Isolated chromatographically using eluent B; oil (1.4 g, 38%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.36 (m, 10 H); 5.91 (br d, 2 H, *J* = 8.8); 5.12 (s, 4 H); 4.47 (dt, 2 H, *J* = 8.8 and 3.4); 3.93 (dd, 2 H, *J* = 9.8 and 3.4); 3.74 (s, 6 H); 3.73 (dd, 2 H, *J* = 9.8 and 3.4); 3.75–3.50 (m, 12 H). FAB MS, *m/z*: 621 (MH^+, 35), 577 (100), 487 (66). FAB HR MS: for $[C_{30}H_{41}N_2O_{12}]^+$ calculated 621.2660, found 621.2669. $[\alpha]_D$ –7.6 (*c* 1, MeOH).

Methyl (S)-2-{[(benzyloxy)carbonyl]amino}-15-hydroxy-4,7,10,13-tetraoxapentadecanoate (**8d**; *n* = 3). Prepared from **2** and tetraethylene glycol. Isolated chromatographically using eluent C; oil (0.85 g, 33%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.36 (m, 5 H); 6.30 (br d, 1 H, *J* = 8.6); 5.13 (s, 2 H); 4.48 (dt, 1 H, *J* = 8.6 and 3.4); 3.96 (dd, 1 H, *J* = 9.8 and 3.4); 3.76 (s, 3 H); 3.76–3.52 (m, 17 H). FAB MS, *m/z*: 430 (MH^+, 33), 386 (100), 296 (24). FAB HR MS: for $[C_{20}H_{31}NO_9]^+$ calculated 430.2077, found 430.2082. $[\alpha]_D$ –6.4 (*c* 1, MeOH).

Dimethyl (S,S)-2,18-bis{[(benzyloxy)carbonyl]amino}-4,7,10,13,16-pentaoxanonadecanedioate (**9d**; *n* = 3). Prepared from **2** and tetraethylene glycol. Isolated chromatographically using eluent C; oil (1.1 g, 28%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.36 (m, 10 H); 5.90 (br d, 2 H, *J* = 8.8); 5.12 (s, 4 H); 4.47 (dt, 2 H, *J* = 8.8 and 3.4); 3.94 (dd, 2 H, *J* = 9.8 and 3.4); 3.75 (s, 6 H); 3.71 (dd, 2 H, *J* = 9.8 and 3.4); 3.78–3.63 (m, 16 H). FAB MS, *m/z*: 665 (MH^+, 30), 621 (100), 531 (54). FAB HR MS: for $[C_{32}H_{45}N_2O_{13}]^+$ calculated 665.2922, found 665.2918. $[\alpha]_D$ –6.3 (*c* 1, MeOH).

Methyl (S)-2-{[(benzyloxy)carbonyl]amino}-18-hydroxy-4,7,10,13,16-pentaoxaoctadecanoate (**8e**; *n* = 4). Prepared from **2** and pentaethylene glycol. Isolated chromatographically using eluent C; oil (1.0 g, 35%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.36 (m, 5 H); 6.07 (br d, 1 H, *J* = 8.4); 5.13 (s, 2 H); 4.48 (dt, 1 H, *J* = 8.4 and 3.6); 3.96 (dd, 1 H, *J* = 9.8 and 3.6); 3.76 (s, 3 H); 3.75–3.56 (m, 21 H). FAB MS, *m/z*: 474 (MH^+, 38), 430 (100), 252 (28). FAB HR MS: for $[C_{12}H_{28}NO_8]^+$ calculated 474.2339, found 474.2332. $[\alpha]_D$ –5.4 (*c* 1, MeOH).

Dimethyl (S,S)-2,21-bis{[(benzyloxy)carbonyl]amino}-4,7,10,13,16,19-hexaoxadocosanedioate (**9e**; *n* = 4). Prepared from **2** and pentaethylene glycol. Isolated chromatographically using eluent C; oil (1.2 g, 28%). ^{1}H NMR ($CDCl_3$, 200 MHz): 7.36 (m, 10 H); 5.91 (br d, 2H, *J* = 8.6); 5.12 (s, 4 H); 4.47 (dt, 2 H, *J* = 8.6 and 3.3); 3.95 (dd, 2 H, *J* = 9.6 and 3.3); 3.75 (s, 6 H); 3.72 (dd, 2 H, *J* = 9.6 and 3.3); 3.58 (m, 20 H). FAB MS, *m/z*: 709 (MH^+, 32), 665 (100), 575 (62). FAB HR MS: for $[C_{34}H_{49}N_2O_{14}]^+$ calculated 709.3183, found 709.3175. $[\alpha]_D$ –5.5 (*c* 1, MeOH).

Hydrolysis of Protected Amino Acids **8a**–**8e** and **9a**–**9e**. General Procedure

An appropriate amino acid (2 mmol) was refluxed in aqueous 6 M HCl under nitrogen for 16 h. After cooling, charcoal was added; the mixture was filtered and evaporated. The yields of resulting hydrochlorides of **3a**–**3e** and dihydrochlorides of **4a**–**4e** were quantitative.

(S)-2-Amino-6-hydroxy-4-oxahexanoic acid hydrochloride (**3a**; *n* = 0). Obtained from **8a** as a hygroscopic oil. ^{1}H NMR (D_2O, 200 MHz): 4.26 (dd, 1 H, *J* = 4.8 and 3.4); 4.04 (dd, 1 H, *J* = 11.0 and 4.8); 3.95 (dd, 1 H, *J* = 11.0 and 3.4); 3.70 (m, 4 H). FAB MS, *m/z*: 150 (MH^+, 100). FAB HR MS: for $[C_5H_{12}NO_4]^+$ calculated 150.0766, found 150.0757.

(S,S)-2,9-Diamino-4,7-dioxadecanedioic acid dihydrochloride (**4a**; *n* = 0). Obtained from **9a** as a hygroscopic glassy substance. ^{1}H NMR (D_2O, 200 MHz): 4.25 (dd, 2 H, *J* = 4.6 and 3.4); 4.05 (dd, 2 H, *J* = 11.0 and 4.6); 3.94 (dd, 2 H, *J* = 11.0 and 3.4); 3.74 (m, 4 H). FAB MS, *m/z*: 237 (MH^+, 100). FAB HR MS: for $[C_8H_{17}N_2O_6]^+$ calculated 237.1087, found 237.1080.

(S)-2-Amino-4,7-dioxanonanoic acid hydrochloride (**3b**; *n* = 1). Obtained from **8b** as a hygroscopic oil. ^{1}H NMR (D_2O, 200 MHz): 4.23 (dd, 1 H, *J* = 4.9 and 3.7); 4.04 (dd, 1 H, *J* = 11.0 and 4.9); 3.95 (dd, 1 H, *J* = 11.0 and 3.7); 3.78–3.62 (m, 8 H). FAB MS, *m/z*: 194 (MH^+, 100). FAB HR MS: for $[C_7H_{16}NO_5]^+$ calculated 194.1028, found 194.1033.

(S,S)-2,12-Diamino-4,7,10-trioxatridecanedioic acid dihydrochloride (**4b**; *n* = 1). Obtained from **9b** as a hygroscopic glassy substance. ^{1}H NMR (D_2O, 200 MHz): 4.26 (dd, 2 H, *J* = 4.6 and 3.4); 4.05 (dd, 2 H, *J* = 11.0 and 4.6); 3.94 (dd, 2 H, *J* = 11.0 and 3.4); 3.82–3.64 (m, 8 H). FAB MS, *m/z*: 281 (MH^+, 100). FAB HR MS: for $[C_{10}H_{21}N_2O_7]^+$ calculated 281.1349, found 281.1352.

(S)-2-Amino-12-hydroxy-4,7,10-trioxadodecanoic acid hydrochloride (**3c**; *n* = 2). Obtained from **8c** as a hygroscopic oil. ^{1}H NMR (D_2O, 200 MHz): 4.25 (dd, 1 H, *J* = 4.7 and 3.4); 4.04 (dd, 1 H, *J* = 11.0 and 4.7); 3.97 (dd, 1 H, *J* = 11.0 and 3.4); 3.78–3.62 (m, 12 H). FAB MS, *m/z*: 238 (MH^+, 100). FAB HR MS: for $[C_9H_{20}NO_6]^+$ calculated 238.1290, found 238.1299.

(S,S)-2,15-Diamino-4,7,10,13-tetraoxahexadecanedioic acid dihydrochloride (**4c**; *n* = 2). Obtained from **9c** as a hygroscopic glassy substance. ^{1}H NMR (D_2O, 200 MHz): 4.24 (dd, 2 H, *J* = 4.7 and 3.4); 4.05 (dd, 2 H, *J* = 11.0 and 4.7); 3.95 (dd, 2 H, *J* = 11.0 and 3.4); 3.78–3.68 (m, 12 H). FAB MS, *m/z*: 325 (MH^+, 100). FAB MS HR: for $[C_{12}H_{25}N_2O_8]^+$ calculated 325.1611, found 325.1614.

(S)-2-Amino-15-hydroxy-4,7,10,13-tetraoxapentadecanoic acid hydrochloride (**3d**; *n* = 3). Obtained from **8d** as a hygroscopic oil. ^{1}H NMR (D_2O, 200 MHz): 4.25 (dd, 1 H, *J* = 4.9 and 3.7); 4.05 (dd, 1 H, *J* = 11.0 and 4.9); 3.96 (dd, 1 H, *J* = 11.0 and 3.7); 3.79–3.62 (m, 16 H). FAB MS, *m/z*: 282 (MH^+, 100). FAB HR MS: for $[C_{11}H_{24}NO_7]^+$ calculated 282.1553, found 282.1557.

(S,S)-2,18-Diamino-4,7,10,13,16-pentaoxanonadecanedioic acid dihydrochloride (**4d**; *n* = 3). Obtained from **9d** as a hygroscopic glassy substance. ^{1}H NMR (D_2O, 200 MHz): 4.24 (dd, 2 H, *J* = 4.6 and 3.7); 4.05 (dd, 2 H, *J* = 11.3 and 4.6); 3.95 (dd, 2 H, *J* = 11.3 and 3.7); 3.88–3.64 (m, 16 H). FAB MS, *m/z*: 369 (MH^+, 100). FAB HR MS: for $[C_{14}H_{29}N_2O_9]^+$ calculated 369.1873, found 369.1869.

(S)-2-Amino-18-hydroxy-4,7,10,13,16-pentaoxaoctadecanoic acid hydrochloride (**3e**; *n* = 4). Obtained from **8e** as a hygroscopic oil. ^{1}H NMR (D_2O, 200 MHz): 4.25 (dd, 1 H, *J* = 4.9 and 3.7); 4.05 (dd, 1 H, *J* = 11.3 and 4.9); 3.96 (dd, 1 H, *J* = 11.3 and 3.7); 3.86–3.62 (m, 20 H). FAB MS, *m/z*: 326 (MH^+, 100). FAB HR MS: for $[C_{13}H_{28}NO_8]^+$ calculated 326.1815, found 326.1822.

(S,S)-2,21-Diamino-4,7,10,13,16,19-hexaoxadocosanedioic acid dihydrochloride (**4e**; *n* = 4). Obtained from **9e** as a hygroscopic glassy substance. ^{1}H NMR (D_2O, 200 MHz): 4.25 (dd, 2 H, *J* = 4.9 and 3.7); 4.05 (dd, 2 H, *J* = 11.0 and 4.9); 3.96 (dd, 2 H, *J* = 11.0 and 3.7); 3.87–3.63 (m, 20 H). FAB MS, *m/z*: 413 (MH^+, 100). FAB HR MS: for $[C_{16}H_{33}N_2O_{10}]^+$ calculated 413.2135, found 413.2142.

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REFERENCES

1. Bělohradský M., Císařová I., Holý P., Pastor J., Závada J.: *Tetrahedron* **2002**, *58*, 8811.

2. Bělohradský M., Buděšínský M., Císařová I., Dekoj V., Holý P., Závada J.: *Tetrahedron* **2003**, *59*, submitted.
3. Vőgtle F., Weber E.: *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 753.
4. Williams R. M.: *Aldrichim. Acta* **1992**, *25*, 11.
5. Duthaler R. O.: *Tetrahedron* **1994**, *50*, 1539.
6. Larsson U., Carlson R.: *Acta Chem. Scand.* **1994**, *48*, 511.
7. Tanner D.: *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599.
8. Nakajima K., Takai F., Tanaka T., Okawa K.: *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1577.
9. Okawa K., Nakajima K.: *Biopolymers* **1981**, *20*, 1811.