Synthesis of 1,2,3-Triazole Analogues of Lincomycin

by **Marie-Pierre Collin**[a]), **Sven N. Hobbie**[b]), **Erik C. Böttger**[b]), and **Andrea Vasella***[a])

[a]) Laboratorium für Organische Chemie, Department Chemie und Angewandte Biowissenschaften, ETH-Zürich, HCI Hönggerberg, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich

[b]) Institut für Medizinische Mikrobiologie, Universität Zürich, Gloriastrasse 30/32, CH-8006 Zürich

In search for new antibiotics we replaced the amide moiety of lincomycin **1** by a 1,2,3-triazole ring. The 1,2,3-triazoles **10a**–**10k** were obtained as single regioisomers by 'click reaction' of azide **5** with the alkyne **9k**, derived from propyl hygric acid, and the alkyl, aryl, or cycloalkyl alkynes ribosomes **9a**–**9j**. The new analogues proved inactive towards wild-type and A2058G mutant.

Introduction. – Lincomycin (**1**; *Scheme 1*), isolated from *Streptomyces lincolnensis*, is a broad-spectrum antibiotic active against most *Gram*-positive bacteria [1][2]. It is an amide derived from methyl 6-amino-6,8-dideoxy-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside (lincosaminide (MLT); **2**) and *trans*-*N*-methyl-4-propyl-L-proline (propylhygric acid (PHA); **4**) [3][4]. Lincomycin (**1**) is used therapeutically for the treatment of mixed anaerobic and aerobic infections, and as alternative in the treatment of patients allergic to penicillin [5]. It inhibits peptide bond-formation by binding to 23S rRNA of the bacterial ribosome, and thereby affects the peptide chain initiation at the 50S subunit exit tunnel [2][6].

The known analogues of lincomycin can be categorized into three groups, according to whether the glycosyl [7][8], the prolinyl [9], or the amide moiety [10][11] is modified. Two analogues possessing a modified amide group are known, *viz*., the thioamide that is four times less active than lincomycin [11], and deoxolincomycin that is two times less active than lincomycin [10]. These results evidence that the C=O group is necessary for high activity [12], and suggest synthesizing additional lincomycin analogues with a modified amide group.

1,2,3-Triazoles, readily prepared by cycloaddition [13–15], are known peptide analogues [13][16][17] resistant to hydrolytic cleavage and oxidative transformations that may affect esters, thioesters, and thioamides [12][18]. 1,2,3-Triazoles may act as H-bond acceptors only, or also as H-bond donors, depending on their substitution. In 1,4-disubstituted 1,2,3-triazoles, N(2) and N(3) act as H-bond acceptors. The strong dipole moment of triazole polarizes H–C(5) to a degree that it may function as a weak H-bond donor [13][14][16][17][19]. The crystal structures of amprenavir, an HIV-1 protease inhibitor ($K_i = 0.6$ nM), and of two biologically active 1,2,3-triazole analogues ($K_i = 1.7$ and 4 nM) in complex with the HIV-1 protease establish a near overlap of the amide moiety of amprenavir with the 1,4-disubstituted triazole ring of its analogues, demonstrating that the 1,2,3-triazole ring may act as bioisoster of the amide moiety [17][20]. The *trans* configuration of the amide group of clindamycin is evidenced by the

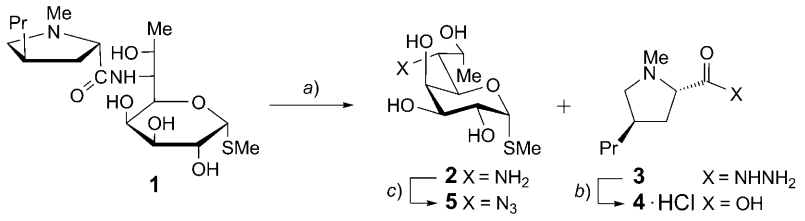
crystal structure of clindamycin (=(7*S*)-7-chloro-7-deoxylincomycin [8][21]) in complex with the 50S ribosomal subunit of the eubacterium *Deinococcus radiodurans* [22]. The distance of 3.42 Å between the C=O group and O–C(2′) of G2505[1]) indicates a weak H-bond.

To probe the interaction of the triazole analogue of clindamycin, we docked it into the above-mentioned 50S ribosomal subunit[2]). This resulted in two conformations, A and B, in favour of A (ΔE *ca.* 22 kcal/mol). In A, the amide and the triazole moieties of clindamycin and its analogue occupy the same position, with O–C(2′) of G2505 at a distance of 3.1 and 2.8 Å, respectively, from N(2) and N(3) of the triazole ring, suggesting a rather strong H-bond [23]. In conformation B, the triazole ring is rotated by 180° relative to its position in conformation A. The comparison of A and B with clindamycin shows no difference in the orientation of the proline moiety. According to conformation A, but not B, the triazolyl analogue may possess antibiotic properties.

In most of the proline-modified lincomycin derivatives that show antibacterial activity, the ring size of the proline moiety was modified, the *N*-Me group was replaced by other alkyl or by carbamoyl groups, and/or the propyl chain was replaced by other alkyl groups, maintaining or changing the configuration and/or location on the ring [9][24]. The convenience of the 'click reaction' [13–15] suggested examining the structure–activity relation of a series of triazole analogues where the proline ring is replaced by alkyl or aryl groups. We planned to synthesize and test a small library of 1,2,3-triazole analogues of lincomycin, substituting the proline ring by acyclic substitutents, cycloalkyl groups, or by an aromatic ring.

Results and Discussion. – The known hydrazinolytic cleavage of lincomycin (**1**) provided lincosaminide (**2**) and the hydrazide **3** that was hydrolyzed to PHA (**4**; *Scheme 1*) [4]. The amino group of lincosaminide (**2**) was transformed into the azide **5** by diazo transfer in the presence of $ZnCl_2$ and NEt_3 in H_2O/MeOH/CH_2Cl_2 1:3:1 to yield **5** (75% from **1**) [25].

Scheme 1



a) $H_2NNH_2 \cdot H_2O$, reflux. *b*) 6N HCl, reflux. *c*) TfN_3, $ZnCl_2$, Et_3N, CH_2Cl_2/MeOH/H_2O; 75%. Tf = Trifluoromethylsulfonyl.

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[1]) All rRNA residues in this article are numbered according to their homologous position in *Escherichia coli* 16S rRNA.

[2]) Molecular modeling was performed using the *Moloc* programme. We thank *Paul Gerber*, *Gerber Molecular Design*, for access to the programme.

Crystals of **5** were obtained by slow evaporation of a solution in MeOH, and their structure was established by X-ray analysis[3]). As expected, the pyranose ring adopts the $^4C_1$ conformation (*Fig. 1*) that is also preferred in CD_3OD solution, as evidenced by the coupling constants compiled in *Table 2* (see *Exper. Part*). The conformation of the side chain is discussed below.

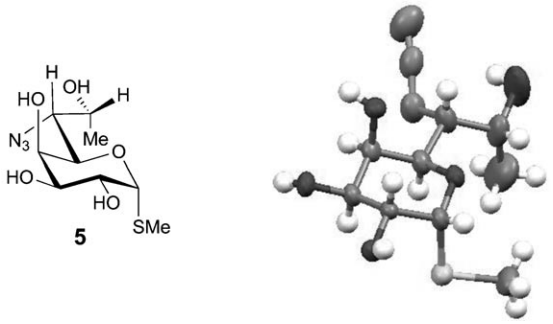

Fig. 1. *ORTEP Representation of the crystal structure of the azide* **5**

The alkyne **9k** was prepared from PHA (**4**) *via* aldehyde **8** (*Scheme 2*). Treating **4** with $SOCl_2$ in MeOH yielded 80% of the methyl ester **6** [26] that was reduced to the alcohol **7** ($LiAlH_4$ in Et_2O; >98%) and oxidized to the aldehyde **8**. The alkyne **9k** was obtained by treating crude **8** with a solution of $Ph_3P{=}CBr_2$ in CH_2Cl_2 and then with BuLi, followed by chromatography, to afford the alkyne **9k** in 30% yield from **6** [27].

The reaction of azide **5** with the acetylenes **9a**–**9k** (*Scheme 2*) in the presence of $CuSO_4 \cdot 5\ H_2O$ and ascorbic acid in a 1:1 mixture of H_2O and i-PrOH [13–15] afforded the expected 1,4-disubstituted triazoles **10a**–**10k**. It was not necessary to protect the OH groups of **5**. The triazoles were obtained as single regioisomers in moderate-to-good yields.

The chemical shifts for C(4) and C(5) of the 1,2,3-triazolyl unit of **10a**–**10k** (142.8–155.2 and 124.7–129.6 ppm) confirm the formation of 1,4-disubstituted 1,2,3-triazoles[4]). As expected, the $^4C_1$ conformation of the pyranose ring is also preferred for the triazole analogues **10a**–**10k** in CD_3OD (see *Table 2* in the *Exper. Part*).

The conformation of the side chain of crystalline **5** is characterized by the *trans*-arrangement between C(6)–N_3 and C(5)–*O*, and a *gauche* arrangement between the N_3 group and C(4) (*tg* conformation about C(5)–C(6)). C(7)–*O* is *gauche* to the N_3 group and *trans* to C(5) (*gt* conformation about C(6)–C(7)). The (5,6)*tg*/(6,7)*gt* conformation is also adopted by **5** in CD_3OD solution, as evidenced by *J*(5,6) of 10.2 and *J*(6,7) of 2.7 Hz. A similar conformation is adopted by lincomycin hydrochloride in the solid state (*Fig. 2* [29]), by lincomycin in a buffered aqueous solution (pH 7.6)

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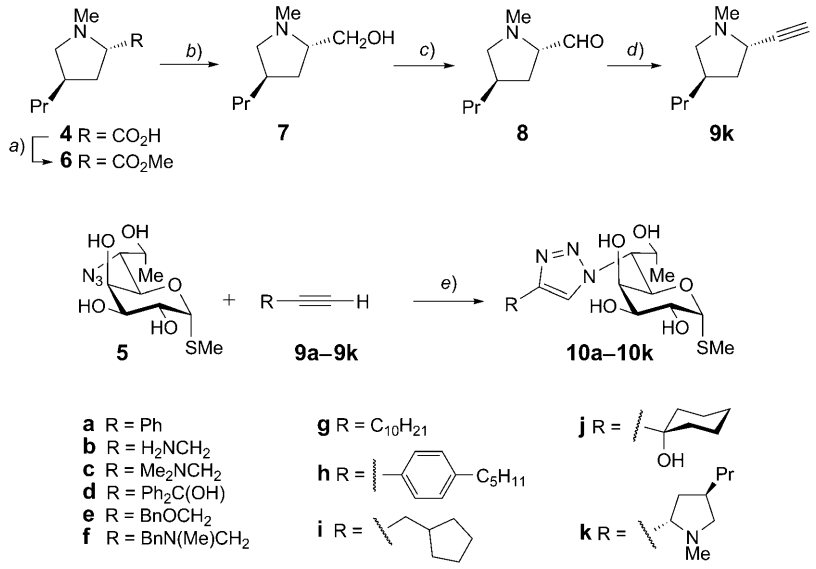
[3]) The crystallographic data have been deposited with the *Cambridge Cryistallographic Data Centre* as deposition No. CCDC-688469. Copies of the data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif (or from the *Cambridge Christallographic Data Centre*, 12 Union Road, Cambridge CB21EZ (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

[4]) Typical C(4) and C(5) chemical shifts for 1,4-disubstituted 1,2,3-triazoles are 143–148 and 117–126 ppm, differing from the C(4) and C(5) chemical shifts of 1,5-disubstituted 1,2,3-triazoles (131 and 139 ppm) [28].

Scheme 2



a) $SOCl_2$, MeOH, 0°; 80%. *b*) $LiAlH_4$, Et_2O; quant. *c*) $C_2O_2Cl_2$, DMSO, NEt_3, CH_2Cl_2, −78°; quant. *d*) 1. CBr_4, Ph_3P, CH_2Cl_2, 0°; quant.; 2. BuLi, THF, −78°; 30% from **6**. *e*) $CuSO_4$, ascorbic acid, i-PrOH, H_2O; 66% of **10a**, 47% of **10b**, 43% of **10c**, 70% of **10d**, 55% of **10e**, 94% of **10f**, 75% of **10g**, 74% of **10h**, 88% of **10i**, 90% of **10j**, 60% of **10k**.

[30][31] and in complex with the ribosome [22], and by peracetylated lincomycin in $CDCl_3$ [32]. As expected, H-bonding in aqueous solution does not play a decisive role for the conformation. However, both lincomycin and its hydrochloride in CD_3OD solution are characterized by $J(5,6)$ of 6.8 Hz and $J(6,7)$ of 6.4 Hz, evidencing a *ca.* 1:1 equilibrium of the (5,6)*tg*/(6,7)*gt* and the (5,6)*gg*/(6,7)*tg* conformers (*Fig. 2*). The population of the (5,6)*gg*/(6,7)*tg* conformation in CD_3OD solution suggests a partially persistant C(7)N–H···O–C(4) H-bond that is completely cleaved in aqueous solution. The ^{1}H-NMR spectra of the triazoles **10a**–**10k** in CD_3OD solution show a

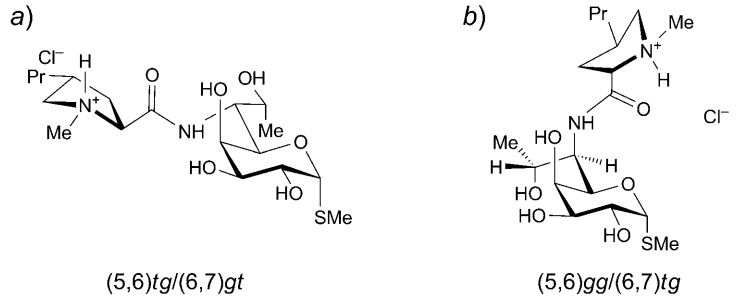


Fig. 2. *Conformations of lincomycin in the solid state* (*a*) *and in CD_3OD solution* (*a* and *b*)

large $J(5,6)$ and a small $J(6,7)$ value (see *Table 2* in the *Exper. Part*), evidencing a (5,6)*tg*/(6,7)*gt* conformation of the side chain similar to the one of the azide **5** and of the lincomycin hydrochloride in the solid state.

Biological Studies. – The antibacterial activity of the triazoles **10a**–**10k** was assessed by determining minimal inhibitory concentrations (MICs) against both lincomycin-sensitive and lincomycin-resistant *Mycobacterium smegmatis* strains in at least three independent broth microdilution experiments, as described in [33].

Growth of wild-type *M. smegmatis* cells was completely inhibited at lincomycin concentrations as little as 4–8 μg/ml, while *M. smegmatis* cells with a drug-resistance adenine to guanine mutation at 23S rRNA position 2058 [34–36] were highly resistant to lincomycin (*Table 1*). As compared to lincomycin, all 1,2,3-triazole analogues proved inactive against the wild-type and A2058G mutant *M. smegmatis* cells.

Table 1. *Ribosomal Drug Susceptibility*[a])

	Wild type	2058A → G
Lincomycin	4–8	1024
10a–**10d**, **10f**, **10h**–**10j**	>512	>512
10e	128–256	512
10g	64–128	64–128
10k	>256	>256

[a]) As minimal inhibitory concentrations (*MIC* [μg/ml])

We thank Dr. *B. Bernet* for checking the analytical data, and Dr. *P. Seiler* for determining the crystal structure.

Experimental Part

General. Solvents were distilled: Et_2O from Na/benzophenone, and MeOH, CH_2Cl_2, Et_3N from CaH_2. Reactions were carried out under N_2, unless stated otherwise. Qual. TLC: precoated silica-gel glass plates (*Merck* silica gel 60 F_{254}); detection by heating with 'mostain' (400 ml of 10% H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24}\cdot 6\,H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash Chromatography (FC): silica gel *Merck* (0.04–0.063 mm), using distilled technical solvents as eluent. M.p.: uncorrected. Optical rotation ($[\alpha]_D^{25}$): 1-dm cell, at 589 nm and 25°; concentration *c* in g/100 ml. FT-IR Spectra: neat (ATR), absorption in cm^{-1}. ^1H- and ^{13}C-NMR spectra: chemical shift δ in ppm rel. to $SiMe_4$ as external standard; coupling constants *J* in Hz. HR-MALDI-MS and HR-ESI-MS: in gentisic acid (=2,5-dihydroxybenzoic acid, DHB) or 3-hydroxypropanal matrix.

Methyl 6-Azido-6,8-dideoxy-1-thio-D-erythro-α-D-galacto-*octopyranoside* (**5**). A vigorously stirred suspension of NaN_3 (5 g, 400 mmol) in CH_2Cl_2 (75 ml) was treated dropwise with Tf_2O (13.2 ml, 80 mmol). 18-Crown-6 (53 mg, 0.2 mmol) was added, and the mixture was stirred at 25° for 24 h. It was treated carefully with H_2O until complete dissolution of NaN_3. The aq. phase was extracted with CH_2Cl_2 (2 × 60 ml). The combined org. layers were washed with $NaHCO_3$ soln. The resulting soln. of TfN_3 in CH_2Cl_2 (200 ml) was used for azidation without further purification; a 50% conversion to TfN_3 was assumed. A soln. of crude lincosaminide (**2**; 5 g, 20 mmol), obtained from commercial lincomycin according to a standard procedure [4], and $ZnCl_2$ (28 mg, 0.2 mmol) in H_2O (200 ml) was treated with Et_3N (8.4 ml, 60 mmol) and slowly with MeOH (600 ml). A CH_2Cl_2 soln. of TfN_3 (200 ml, *ca.* 40 mmol) was radiply added to the above vigorously stirred soln. The mixture was kept at 25° for 24 h, and

evaporated. Crystallisation from MeOH/CH_2Cl_2 gave **5** (4.1 g, 75% from lincomycin). Colourless crystals. R_f (AcOEt/MeOH 9:1) 0.77. M.p. 195–196°. $[\alpha]_D^{25} = +255.6$ ($c = 0.96$, MeOH). IR (ATR): 3217*w* (br.), 2977*w*, 2923*w*, 2881*w*, 2117*s*, 1451*m*, 1392*w*, 1347*w*, 1318*w*, 1295*m*, 1260*m*, 1240*m*, 1147*w*, 1123*m*, 1102*m*, 1078*m*, 1038*s*, 988*m*, 952*w*, 918*w*, 900*w*, 866*m*, 830w, 802*m*, 738*m*, 703*m*, 668*m*, 613*s*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 2.07 (*s*, MeS). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 13.80 (*q*, MeS). HR-ESI-MS: 302.0779 (100, $[M+H]^+$, $C_9H_{18}N_3O_5S^+$; calc. 302.0781). Anal. calc. for $C_9H_{17}N_3O_5S$ (279.32): C 38.70, H 6.13, N 15.04; found: C 38.55, H 6.03, N 14.83.

Table 2. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz], *and ^{13}C-NMR Chemical Shifts* [ppm] *of the Azide* **5** *and of the Triazoles* **10a**–**10k** *in CD_3OD*

	5	**10a**	**10b**	**10c**	**10d**	**10e**	**10f**	**10g**	**10h**	**10i**	**10j**	**10k**
H–C(1)	5.21	5.34	5.32	5.32	5.31	5.34	5.32	5.32	5.34	5.32	5.32	5.33
H–C(2)	4.08	4.12	4.10	4.10	4.10	4.10	4.11	4.10	4.12	4.11	4.10	4.11
H–C(3)	3.49	3.53	3.49	3.49	3.51	3.50	3.51	3.50	3.53	3.50	3.50	3.50
H–C(4)	3.96	3.36	3.24	3.24	3.34	3.27	3.28	3.26	3.36	3.27	3.26	3.21
H–C(5)	3.80	4.93	4.88–4.84	4.90–4.84	4.88	4.90	4.91–4.82	4.89–4.84	4.93	4.86	4.88–4.84	4.86
H–C(6)	3.98	5.05	4.97	4.99	4.95	5.01	4.94	4.94	5.04	4.95	4.98	4.98
H–C(7)	4.15	4.42	4.36	4.37	4.37	4.37	4.38	4.36	4.41	4.37	4.37	4.38
Me(8)	1.15	1.18	1.13	1.12	1.13	1.13	1.15	1.15	1.18	1.10	1.12	1.13
J(1,2)	5.7	5.7	5.7	6.0	6.0	5.7	5.7	5.7	6.0	5.7	6.0	5.4
J(2,3)	10.5	10.2	10.2	10.2	10.2	10.5	10.2	10.2	10.2	10.2	10.2	10.2
J(3,4)	2.7	3.3	3.6	3.3	3.3	3.3	3.0	3.2	3.3	3.3	3.3	3.3
J(4,5)	0.8	[a])	0.9	0.9	[a])	0.9	[a])	0.9	1.2	0.6	0.6	[a])
J(5,6)	10.2	10.2	10.2	10.5	10.5	10.2	10.2	10.2	10.5	10.5	10.2	10.2
J(6,7)	3.0	3.6	3.6	3.7	3.9	3.6	3.9	3.6	3.6	3.9	3.6	3.9
J(7,8)	6.3	6.3	6.6	6.3	6.6	6.6	6.6	6.3	6.6	6.6	6.3	6.3
C(1)	90.02	90.19	90.18	90.21	90.25	90.20	90.20	90.13	90.22	90.17	90.15	90.13
C(2)	68.98	68.82	68.93	68.90	68.86	68.90	68.92	68.82	68.90	68.90	68.88	68.84
C(3)	71.81	71.50	71.55	71.55	71.56	71.54	71.57	71.50	71.58	71.63	71.55	71.51
C(4)	69.87	69.05	69.03	69.07	69.15	69.07	69.13	69.04	69.14	69.18	69.10	68.97
C(5)	70.76	70.18	70.30	70.28	70.28	70.27	70.31	70.29	70.28	70.40	70.34	70.33
C(6)	66.64	65.67	65.56	65.59	65.51	65.65	65.57	65.31	65.72	65.37	65.47	65.60
C(7)	67.97	66.75	66.83	66.78	66.74	66.81	66.85	66.83	66.86	66.95	66.87	66.70
C(8)	15.60	16.90	17.09	17.07	17.03	17.07	17.12	16.96	17.09	17.16	17.09	17.00

[a]) Not assigned.

X-Ray Analysis of **5**. Crystals of **5** were obtained by slow evaporation of a soln. of **5** in MeOH (dimensions of the analyzed crystal: cube $0.21 \times 0.19 \times 0.17$ mm). $C_9H_{17}N_3O_5S \cdot MeOH$, M_r 311.36, monoclinic C_2; $a = 32.416(7)$, $b = 7.9775(16)$, $c = 5.8808(12)$, $\alpha = 90.000$, $\beta = 93.190(3)$, $\gamma = 90.00°$, $V = 1518.4(5)$ Å^3, $D_x = 1.362$ Mg/m^3, $Z = 4$. The reflections were measured on a *Bruker Nonius-KappaCCD* diffractometer (graphite monochromator, MoK_α radiation, $\lambda = 0.71070$) at 250 K. All the calculations were performed using maXus *(Bruker Nonius, Delft & MacScience, Japan)*. The structure was solved by direct methods and refined by full-matrix least-squares analysis (SHELXL-97) including an isotropic extinction correction. All non-H-atoms were refined anisotropically (H-atoms isotropic, whereby H-positions are based on stereochemical considerations). $R = 0.0735$, $Rw = 0.2006$ for 194 parameters and 2762 reflections, $\theta < 26.03°$.

Methyl (2S,4R*)-1-Methyl-4-propylpyrrolidine-2-carboxylate* (**6**). A soln. of **4**·HCl (1 g, 4.8 mmol) in MeOH (10 ml) was treated dropwise at 0° with $SOCl_2$ (1.76 ml, 24.1 mmol), warmed to 25°, stirred for

18 h, and evaporated. A soln. of the residue in AcOEt was washed with a sat. $NaHCO_3$ soln. The aq. layer was extracted four times with AcOEt. The combined org. layers were dried ($MgSO_4$) and evaporated to afford **6** (700 mg, 80%), which was used for the next step without further purification. Colourless oil. R_f (AcOEt) 0.77. $[\alpha]_D^{25} = -76.3$ ($c = 0.98$, $CHCl_3$). IR (ATR): 2953*m*, 2924*m,* 2844*w*, 2773*w*, 1734*s*, 1454*m*, 1435*m*, 1358*w*, 1275*m*, 1194*s*, 1171*s*, 1138*m*, 1114*m*, 1037*m*, 1016*m*, 910*w*, 820w, 762*w*, 733*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.64 (*s*, MeO); 3.14 (*dd*, $J = 9.0, 6.9$, H_a–C(5)); 2.91 (*dd*, $J = 9.6, 6.6$, H–C(2)); 2.29 (*s*, MeN); 2.25–2.14 (*m*, H–C(4)); 2.09–1.98 (*m*, H_a–C(3)); 1.87 (*t*, $J = 9.0$, H_b–C(5)); 1.71–1.61 (*m*, H_b–C(3)); 1.27–1.14 (*m*, $Me(CH_2)_2$); 0.83–0.78 (*m*, $Me(CH_2)_2$). ^{13}C-NMR (300 MHz, $CDCl_3$): 173.99 (*s*, C=O); 67.15 (*d*, C(2)); 63.11 (*t*, C(5)); 51.86 (*q*, MeO); 41.29 (*q*, MeN)); 36.91 (*d*, C(4)); 36.72 (*t*, C(3)); 36.39 (*t*, $MeCH_2CH_2$); 21.40 (*t*, $MeCH_2CH_2$); 14.17 (*q*, $MeCH_2CH_2$). EI-MS: 126.1278 (100, $[M - CO_2Me]^+$, $C_8H_{16}N^+$; calc. 126.1283).

(2S,4R)-1-Methyl-4-propylpyrrolidine-2-methanol (**7**). A soln. of **6** (500 mg, 2.7 mmol) in Et_2O (10 ml) was treated at 0° with $LiAlH_4$ (205 mg, 5.4 mmol), warmed to 25°, stirred for 1 h, treated with ice cubes, and stirred for 30 min. Filtration through a pad of *Celite* and evaporation of the filtrate gave crude **7** (420 mg, quant.), which was used for the next step without further purification. Colourless oil. R_f (AcOEt) 0.77. $[\alpha]_D^{25} = -11.1$ ($c = 1.01$, $CHCl_3$). IR (ATR): 3395*w* (br.), 2954*s,* 2917*s*, 2870*s*, 2844*s*, 2781*s*, 1454*s*, 1378*w*, 1210*w*, 1186*w*, 1159*m*, 1086*m*, 998*m*, 977*w*, 920*w*, 771*w*, 741*w*, 661*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.59 (*dd*, $J = 11.1$, 3.6, CH_a–C(2)); 3.37 (*dd*, $J = 11.1$, 2.7, CH_b–C(2)); 3.11 (*dd*, $J = 8.4$, 6.0, H_a–C(5)); 2.46–2.39 (*m*, H–C(2)); 2.29 (*s*, MeN); 2.11–2.00 (*m*, H–C(4)); 1.98–1.88 (*m*, H_b–C(5), H_a–C(3)); 1.53–1.42 (*m*, H_b–C(3)); 1.31–1.24 (*m*, $Me(CH_2)_2$); 0.91–0.83 (*m*, $Me(CH_2)_2$). ^{13}C-NMR (300 MHz, $CDCl_3$): 65.83 (*d*, C(2)); 64.12 (*t*, C(5)); 61.99 (*t*, CH_2OH); 40.62 (*q*, MeN); 36.99 (*d*, C(4)); 36.67 (*t*, $MeCH_2CH_2$); 34.64 (*t*, C(3)); 21.40 (*t*, $MeCH_2CH_2$); 14.15 (*q*, $MeCH_2CH_2$). HR-ESI-MS: 158.1540 (23, $[M + H]^+$, $C_9H_{20}NO^+$; calc. 158.1539), 140.1434 (52, $[M - OH]^+$, $C_9H_{18}N^+$; calc. 140.1434), 96.0807 (100, $C_6H_{10}N^+$, $[M - C_3H_7O]^+$; calc. 96.0813).

(*2S,4R*)-*1-Methyl-4-propylpyrrolidine-2-carbaldehyde* (**8**). A soln. of $C_2O_2Cl_2$ (215 µl, 2.54 mmol) in CH_2Cl_2 (10 ml) at −78° was treated dropwise with a soln. of DMSO (360 µl) in CH_2Cl_2 (2 ml), stirred for 30 min, treated dropwise with a soln. of **7** (200 mg, 1.27 mmol) in CH_2Cl_2 (1.5 ml), and stirred for 1 h. The mixture was treated with Et_3N (890 µl, 6.35 mmol), warmed to 0°, stirred for 30 min, and diluted with sat. $NaHCO_3$ soln. The aq. layer was extracted twice with Et_2O. The combined org. layers were dried ($MgSO_4$) and evaporated to afford **8** (200 mg, quant.), which was used for the next step without further purification. Colourless oil. R_f (AcOEt/MeOH 9:1) 0.77. IR (ATR): 2955*m,* 2924*m*, 2871*m*, 2846*m*, 2779*m*, 1729*s*, 1451*m*, 1379*w*, 1294*w*, 1264*w*, 1210*w*, 1160*m*, 1114*w*, 1086*w*, 1055*w*, 1024*w*, 915*w,* 807*w*, 761*w*, 741*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.47 (*d*, $J = 3.6$, CHO); 3.20 (*dd*, $J = 8.4, 6.3$, H_a–C(5)); 2.76 (*ddd*, $J = 9.9$, 6.6, 3.3, H–C(2)); 2.36 (*s*, MeN); 2.28–2.14 (*m*, H–C(4)); 2.04 (*ddd*, $J = 12.9$, 9.0, 6.3, H_a–C(3)); 1.98 (*dd*, $J = 9.6$, 9.0, H_b–C(5)); 1.62 (*ddd*, $J = 12.9$, 9.9, 7.5, H_b–C(3)); 1.35–1.22 (*m*, $Me(CH_2)_2$); 0.92–0.85 (*m*, $Me(CH_2)_2$). ^{13}C-NMR (75 MHz, $CDCl_3$): 202.46 (*d*, CHO); 72.84 (*d*, C(2)); 129.56 (*t*, C(5)); 41.40 (*q*, MeN); 37.83 (*d*, C(4)); 36.43 (*t*, $MeCH_2CH_2$); 32.20 (*t*, C(3)); 21.37 (*t*, $MeCH_2CH_2$); 14.04 (*q*, CH_2CH_2Me). EI-MS: 126.1276 (100, $[M - CHO]^+$, $C_8H_{16}N^+$; calc. 126.1283).

(*2S,4R*)-*2-Ethynyl-1-methyl-4-propylpyrrolidine* (**9k**). A stirred soln. of PPh_3 (2.67 g, 10.18 mmol) in CH_2Cl_2 (5 ml) was cooled to −5° to −10° and treated with a soln. of CBr_4 (1.69 g, 5.09 mmol) in CH_2Cl_2 (2 ml). The resulting orange-brown suspension was stirred at −10° for 15 min, and decanted at −10° to give a light brown soln. and a yellow precipitate. The soln. was added *via* a syringe to a vigorously stirred and cooled (−10° to −5°) soln. of **8** (200 mg, 1.27 mmol) in CH_2Cl_2 (5 ml). The resulting brown soln. was stirred at −5° to −10° for 40 min, and treated dropwise with Et_3N (1.27 ml) and sat. aq. $NaHCO_3$ soln. The mixture was passed through a short pad of silica gel, and the main product was collected.

A stirred soln. of the above crude product (dibromoethene) in THF (8 ml) was cooled to −78°, and treated dropwise with 1.6M BuLi in hexane (2 ml, 2.54 mmol). The yellow soln. was stirred at −76° for 1 h, warmed to 25°, diluted with Et_2O, and washed with sat. $NaHCO_3$ soln. The combined org. layers were dried and evaporated. FC (hexane/AcOEt 95:5 to 3:1) gave **9k** (60 mg, 30% from **6**). Orange oil. R_f (hexane/AcOEt 9:1) 0.77. IR (ATR): 3310*w*, 2956*s*, 2926*s*, 2872*m*, 2843*m*, 2772*m*, 2105*w*, 1643*w*, 1452*m*, 1378*w*, 1343*w*, 1259*w*, 1233*w*, 1189*w*, 1159*w*, 1138*w*, 1116*w*, 1079*w*, 1040*w*, 930*w*, 795*w*, 741*w*, 642*s*, 623*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.10 (*ddd*, $J = 8.0$, 6.0, 2.1, H–C(2)); 3.08 (*dd*, $J = 9.0$, 7.8, H_a–C(5)); 2.36 (*s*, MeN); 2.34–2.20 (*m,* H–C(4)); 2.25 (*d*, $J = 1.8$, C≡CH); 2.08 (*ddd*, $J = 12.6, 9.6, 6.3$, H_a–C(3)); 1.97

(*dd*, J = 9.3, 7.8, H_b–C(5)); 1.70 (*ddd*, J = 12.4, 7.8, 6.6, H_b–C(3)); 1.35–1.17 (*m*, Me(CH_2)$_2$); 0.89–0.83 (*m*, *Me*(CH_2)$_2$). ^{13}C-NMR (75 MHz, $CDCl_3$)[5]: 83.61 (*s*, *C*≡CH)); 71.65 (*d*, C≡*C*H); 61.64 (*d*, C(2)); 56.06 (*t*, C(5)); 40.02 (*q*, MeN); 39.17 (*d*, C(4)); 37.72 (*t*, *C*H_2CH$_2$Me); 36.20 (*t*, C(3)); 21.38 (*t*, Me*C*H_2CH$_2$); 14.22 (*q*, *Me*CH_2CH$_2$). EI-MS: 152.1364 (27, $[M+H]^+$, $C_{10}H_{18}N^+$; calc. 152.1434), 150.1265 (67, $[M-H]^+$, $C_{10}H_{16}N^+$; calc. 150.1283), 126.1271 (100, $[M-C\equiv CH]^+$, $C_8H_{16}N^+$; calc. 126.1283), 68.9949 (100, C_4H_6N, $[C_{10}H_{18}N]^+$; calc. 68.0500).

General Procedure for the Triazole Synthesis (*GP*). To a stirred soln. of **5** (50 mg, 0.17 mmol) in i-PrOH/H_2O 1:1 (1 ml) were added $CuSO_4$ (0.05 equiv.), ascorbic acid (0.2 equiv.), and the corresponding alkyne (1.5 equiv.). The mixture was heated to 60° for 1 to 12 h, cooled to 25°, and evaporated to give the crude triazole.

*Methyl 6,8-Dideoxy-6-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10a**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 4:1) gave **10a** (45 mg, 66%). White solid. R_f (AcOEt/MeOH 9:1) 0.14. M.p. 183–185°. $[\alpha]_D^{25} = +199.3$ (c = 1.05, MeOH). IR (ATR): 3364*w* (br.), 2975*w*, 2922*w*, 1657*w*, 1609*w*, 1581*w*, 1483*m*, 1435*w*, 1381*w*, 1302*w*, 1219*m*, 1077*m*, 1050*m*, 983*w*, 910*w*, 865*w*, 801*w*, 770*s*, 714*w*, 694*m*, 664w, 631*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 8.29 (*s*, H–C(5) of triazolyl); 7.85–7.80 (*m*, 2 arom. H); 7.46–7.40 (*m*, 2 arom. H); 7.36–7.30 (*m*, 1 arom. H); 2.19 (*s*, MeS). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 147.26 (*s*, C(4) of triazolyl); 131.25 (*s*); 129.56 (*d*, C(5) of triazolyl); 128.89 (*d*, 2 C); 126.25 (*d*, 2 C); 124.76 (*d*); 13.66 (*q*, MeS). HR-MALDI-MS: 382.1433 (100, $[M+H]^+$, $C_{17}H_{24}N_3O_5S^+$; calc. 382.1431).

*Methyl 6-[4-(Aminomethyl)-1*H*-1,2,3-triazol-1-yl]-6,8-dideoxy-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10b**). *GP* and FC (amino phase gel, AcOEt/MeOH 95:5 to 0:1) gave **10b** (28 mg, 47%). Colourless oil. R_f (AcOEt/MeOH 1:1) 0.33. $[\alpha]_D^{25} = +235.1$ (c = 0.83, MeOH). IR (ATR): 3348*m* (br.), 2979*w*, 2921*w*, 1651*w*, 1377*w*, 1338*w*, 1244*w*, 1076*s*, 1048*s*, 978*s*, 907*w*, 864*w*, 799*m*, 699*w*, 678*w*, 630*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.82 (*s*, H–C(5) of triazolyl); 3.89 (*s*, NH_2CH_2); 2.07 (*s*, MeS). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 147.94 (*s*, C(4) of triazolyl); 125.87 (*d*, C(5) of triazolyl); 37.21 (*t*, CH_2NH_2); 13.88 (*q*, MeS). HR-MALDI-MS: 357.1199 (25, $[M+Na]^+$, $C_{12}H_{22}N_4NaO_5S^+$; calc. 357.1203), 335.1385 (100, $[M+H]^+$, $C_{12}H_{23}N_4O_5S^+$; calc. 335.1384).

*Methyl 6,8-Dideoxy-{6-[4-(dimethylamino)methyl]-1*H*-1,2,3-triazol-1-yl}-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10c**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 3:1) gave **10c** (28 mg, 43%). Colourless oil. R_f (AcOEt/MeOH 4:1) 0.22. $[\alpha]_D^{25} = +228.1$ (c = 1.07, MeOH). IR (ATR): 3353*m* (br.), 2889*w*, 1642*w*, 1458*m*, 1336*m*, 1303*w*, 1242*m*, 1174*s*, 1094*s*, 1078*s*, 1047*s*, 1029*m*, 1009*m*, 982*s*, 908*w*, 851*w*, 801*m*, 749*s*, 700*m*, 678*m*, 664*m*, 630*w*, 591*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.87 (*s*, H–C(5) of triazolyl); 3.66, 3.60 (2*d*, J = 13.8, Me_2NCH_2); 2.27 (*s*, Me_2N); 2.18 (*s*, MeS). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 142.87 (*s*, C(4) of triazolyl); 127.79 (*d*, C(5) of triazolyl); 53.93 (*t*, Me_2NCH_2); 44.64 (*q*, Me_2N); 13.84 (*q*, MeS). HR-MALDI-MS: 385.1517 (13, $[M+Na]^+$, $C_{16}H_{32}N_4NaO_5S^+$; calc. 385.1516), 363.1700 (100, $C_{16}H_{33}N_4O_5S^+$, $[M+H]^+$; calc. 363.1697).

*Methyl 6,8-Dideoxy-6-{4-[hydroxy(diphenyl)methyl]-1*H*-1,2,3-triazol-1-yl}-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10d**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 3:1) gave **10d** (60 mg, 70%). Colourless oil. R_f (AcOEt/MeOH 4:1) 0.50. $[a]_D^{25} = +109.5$ (c = 1.58, MeOH). IR (ATR): 3374*m* (br.), 3009*w*, 2922*w*, 1634*w*, 1491*w*, 1448*w*, 1297*w*, 1216*w*, 1076*m*, 1048*m*, 1011*m*, 982*m*, 892*w*, 801*w*, 750*s*, 699*s*, 665*w*, 638*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.62 (*s*, H–C(5) of triazolyl); 7.39–7.21 (*m*, 10 arom. H); 2.15 (*s*, MeS). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally 153.95 (*s*, C(4) of triazolyl); 147.10 (*s*, 2 C); 128.38 (*d*, 4 C); 128.05 (*d*, 4 C); 127.84 (*d*, 2 C); 127.02 (*d*, C(5) of triazolyl); 77.46 (*s*, Ph_2C); 13.85 (*q*, MeS). HR-MALDI-MS: 526.1405 (28, $[M+K]^+$, $C_{24}H_{29}KN_3O_6S^+$; calc. 526.1409), 510.1660 (38, $[M+Na]^+$, $C_{24}H_{29}N_3NaO_5S^+$; calc. 510.1669), 488.1849 (31, $[M+H]^+$, $C_{24}H_{30}N_3O_6S^+$; calc. 488.1850), 470.1738 (100, $[M-OH]^+$, $C_{24}H_{28}N_3O_5S^+$; calc. 470.1744).

*Methyl 6-{4-[(Benzyloxy)methyl]-1*H*-1,2,3-triazol-1-yl}-6,8-dideoxy-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10e**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 4:1) gave **10e** (42 mg, 55%). Colourless oil. R_f (AcOEt/MeOH 9:1) 0.14. $[\alpha]_D^{25} = +218.0$ (c = 0.64, CH_3OH). IR (ATR): 3362*w*

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[5]) Displays 'bizarre' signals for the C≡CH group in the DEPT spectrum due to large ^1J(C,H) and ^2J(C,H) couplings [37].

(br.), 2889*w*, 2765*w*, 1635*w*, 1495*s*, 1452*m*, 1370*w*, 1336*w*, 1299*w*, 1230*m*, 1075*s*, 1044*s*, 1028*m*, 981*m*, 907*w*, 863*w*, 800w, 747*s*, 698*s*, 664*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.94 (*s*, H–C(5) of triazolyl); 7.38–7.24 (*m*, 5 arom. H); 4.64 (*s*, BnOCH_2); 4.58 (*s*, PhCH_2O); 2.18 (*s*, MeS). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 144.23 (*s*, C(4) of triazolyl); 138.73 (*s*); 128.99 (*d*, 2 C); 128.68 (*d*, C(5) of triazolyl); 128.42 (*d*, 2 C); 127.56 (*d*); 73.15 (*t*, Ph*C*H$_2$O); 63.67 (*t*, PhCH$_2$O*C*H$_2$); 13.87 (*q*, MeS). HR-MALDI-MS: 464.1254 (27, $[M+K]^+$, $C_{19}H_{27}KN_3O_6S^+$; calc. 464.1252), 448.1512 (36, $[M+Na]^+$, $C_{19}H_{27}N_3NaO_6S^+$; calc. 448.1513), 426.1686 (100, $[M+H]^+$, $C_{19}H_{28}N_3O_6S^+$; calc. 426.1693).

*Methyl 6-(*4-*{[(Benzyl(methyl)amino]methyl}-1*H*-1,2,3-triazol-1-yl)-6,8-dideoxy-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10f**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 3:1) gave **10f** (74 mg, 94%). Colourless oil. R_f (AcOEt/MeOH 9:1) 0.13. $[\alpha]_D^{25} = +192.2$ ($c = 1.03$, MeOH). IR (ATR): 3364*w* (br.), 2980*w*, 2922*w*, 2795*w*, 1638*w*, 1495*w*, 1453*w*, 1368*w*, 1333*w*, 1219*m*, 1074*m*, 1049*m*, 982*w*, 908*w*, 861*w*, 801*w*, 771*s*, 699*w*, 664*w*, 631*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.87 (*s*, H–C(5) of triazolyl); 7.37–7.22 (*m*, 5 arom. H); 3.73, 3.70 (2*d*, $J \approx 11.1$, BnNCH_2); 3.56 (*s*, PhCH_2N); 2.21 (*s*, MeN); 2.07 (*s*, MeS). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 143.47 (*s*, C(4) of triazolyl); 138.59 (*s*); 130.17 (*d*, 2 C); 128.95 (*d*, C(5) of triazolyl); 128.01 (*d*, 2 C); 127.74 (*d*); 61.96 (*t*, Ph*C*H$_2$N); 51.99 (*t*, PhCH$_2$N*C*H$_2$); 41.83 (*q*, MeN); 13.89 (*q*, MeS). HR-MALDI-MS: 439.2009 (100, $[M+H]^+$, $C_{20}H_{31}N_4O_5S^+$; calc. 439.2010).

*Methyl 6-(4-Decyl-1*H*-1,2,3-triazol-1-yl)-6,8-dideoxy-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10g**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 4:1) gave **10g** (60 mg, 75%). White solid. R_f (AcOEt/MeOH 9:1) 0.15. M.p. 120–122°. $[\alpha]_D^{25} = +144.3$ ($c = 1.2$, MeOH). IR (ATR): 3344*m* (br.), 2923*m*, 2854*m*, 2493*w*, 1647*w*, 1556*w*, 1530*w*, 1455*w*, 1377*w*, 1324*w*, 1239*w*, 1240*m*, 1087*m*, 1048*s*, 1028*w*, 1007*w*, 983*m*, 908*w*, 874*w*, 794*w*, 754*w*, 698*w*, 647*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.68 (*s*, H–C(5) of triazolyl); 2.68 (*t*, $J = 7.5$, Me(CH$_2$)$_8$CH_2); 2.17 (*s*, MeS); 1.67 (*quint.*, $J =$ 7.5, Me(CH$_2$)$_7$CH_2CH$_2$); 1.40–1.22 (*m*, 14 H); 0.89 (*t*, $J = 6.9$, *Me*(CH$_2$)$_8$CH$_2$). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 147.62 (*s*, C(4) of triazolyl); 125.50 (*d*, C(5) of triazolyl); 32.64, 30.32, 30.27, 30.15, 30.07, 30.05, 29.91, 25.84, 23.31 (9*t*, Me(*C*H$_2$)$_9$); 14.04 (*q*, MeS); 13.64 (*q*, *Me*(CH$_2$)$_9$). HR-MALDI-MS: 468.2507 (10, $[M+Na]^+$, $C_{21}H_{39}NaN_3O_5S^+$; calc. 468.2503), 446.2687 (100, $[M+H]^+$, $C_{21}H_{40}N_3O_5S^+$; calc. 446.2683).

*Methyl 6,8-Dideoxy-6-[4-(4-pentylphenyl)-1*H*-1,2,3-triazol-1-yl]-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10h**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 4:1) gave **10h** (60 mg, 74%). White solid. R_f (AcOEt/MeOH 9:1) 0.14. M.p. 182–185°. $[\alpha]_D^{25} = +186.7$ ($c = 1.08$, MeOH). IR (ATR): 3423*w*, 3341*w*, 3281*w*, 3172*w* (br.), 2927*w*, 2853*w*, 1501*w*, 1467*w*, 1445*w*, 1421*w*, 1378*w*, 1338*w*, 1322*w*, 1292*m*, 1263*w*, 1233*m*, 1206*w*, 1186*w*, 1140*m*, 1125*m*, 1084*s*, 1049*s*, 1037*s*, 1028*w*, 1003*w*, 984*s*, 908*w*, 881*w*, 842*m*, 795*s*, 785*s*, 756*w*, 735*w*, 707*w*, 685*w*, 646*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 8.24 (*s*, H–C(5) of triazolyl); 7.75–7.70 (br. *d*, $J = 8.1$, 2 arom. H); 7.25 (br. *d*, $J = 8.4$, 2 arom. H); 2.63 (*t*, $J = 7.2$, Me(CH$_2$)$_3$CH_2); 2.19 (*s*, MeS); 1.64 (*quint.*, $J = 7.5$, Me(CH$_2$)$_2$CH_2CH$_2$); 1.40–1.28 (*m*, Me(CH_2)$_2$CH$_2$CH$_2$); 0.90 (*t*, $J = 6.9$, *Me*(CH$_2$)$_3$CH$_2$). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 147.30 (*s*, C(4) of triazolyl); 143.93 (*s*); 129.55 (*d*, 2 C); 128.61 (*d*, C(5) of triazolyl); 126.21 (*d*, 2 C); 124.40 (*d*); 33.36, 32.33, 32.05, 23.33 (4*t*, Me(*C*H$_2$)$_4$); 14.16 (*q*, MeS); 13.87 (*q*, *Me*(CH$_2$)$_4$). HR-MALDI-MS: 452.2218 (100, $[M+H]^+$, $C_{21}H_{40}N_3O_5S^+$; calc. 452.2214).

*Methyl 6-[4-(Cyclopentylmethyl)-1*H*-1,2,3-triazol-1-yl]-6,8-dideoxy-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10i**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 4:1) gave **10i** (61 mg, 88%). White solid. R_f (AcOEt/MeOH 9:1) 0.14. M.p. 165–167°. $[\alpha]_D^{25} = +216.5$ ($c = 1.45$, MeOH). IR (ATR): 3288*w* (br.), 2977*w*, 2966*m*, 2938*m*, 2923*m*, 2866*m*, 2844*m*, 1557*w*, 1454*w*, 1372*w*, 1359*w*, 1345*w*, 1322*w*, 1239*w*, 1220*m*, 1095*m*, 1050*s*, 1032*s*, 1006*s*, 952*w*, 908*w*, 876*w*, 854*w*, 791*m*, 772*m*, 685*m*, 648*m*, 597*m*, 579*m*, 536*m*, 522*m*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.70 (*s*, H–C(5) of triazolyl); 2.69 (*d*, $J = 7.5$, CH_2C=CH); 2.18 (*heptet*, $J = 7.5$, CH$_2$C*H*CH$_2$); 2.17 (*s*, MeS); 1.82–1.50 (*m*, 6 H); 1.30–1.17 (*m*, 2 H). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 147.04 (*s*, C(4) of triazolyl); 125.79 (*d*, C(5) of triazolyl); 41.11 (*d*, C(1) of cyclopentyl); 33.13 (*t*, C(2) and C(5) of cyclopentyl); 32.00 (*t*, *C*H$_2$C=CH), 25.76 (*t*, C(3) and C(4) of cyclopentyl); 13.86 (*q*, MeS). HR-MALDI-MS: 398.1900 (100, $[M+H]^+$, $C_{17}H_{30}N_3O_5S^+$; calc. 398.1901).

*Methyl 6,8-Dideoxy-6-{4-[(1-hydroxycyclohexyl)]-1*H*-1,2,3-triazol-1-yl}-1-thio*-D-erythro-*α*-D-galacto-*octopyranoside* (**10j**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 3:1) gave **10j** (65 mg,

90%). Colourless oil. R_f (AcOEt/MeOH 4:1) 0.33. M.p. 100–102°. $[\alpha]_D^{25} = +176.5$ ($c = 1.12$, MeOH). IR (ATR): 3358*m* (br.), 2930*w*, 2854*w*, 2766*w*, 1635*w*, 1446*w*, 1337*w*, 1303*w*, 1244*m*, 1215*m*, 1076*s*, 1043*s*, 1029*w*, 979*m*, 906*w*, 850*w*, 801*w*, 750*s*, 699*w*, 664*w*, 632*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.78 (*s*, H–C(5) of triazolyl); 2.18 (*s*, MeS); 2.07–1.97 (*m*, 2 H); 1.85–1.70 (*m*, 4 H); 1.63–1.33 (*m*, 4 H); 1.12 (*d*, $J = 6.3$, Me). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 155.13 (*s*, C(4) of triazolyl); 124.76 (*d*, C(5) of triazolyl); 69.95 (*s*, C(1) of cyclohexyl); 38.56 (*t*, 2 C); 26.32 (*t*); 22.82 (*t*, 2 C); 13.83 (*q*, MeS). HR-MALDI-MS: 442.1415 (16, $[M + K]^+$, $C_{17}H_{29}KN_3O_6S^+$; calc. 442.1409), 426.1676 (20, $[M + Na]^+$, $C_{17}H_{29}N_3NaO_6S^+$; calc. 426.1669), 404.1848 (100, $[M + H]^+$, $C_{17}H_{30}N_3O_6S^+$; calc. 404.1850).

*Methyl 6,8-Dideoxy-6-{4-[(2S,4R)-1-methyl-4-propylpyrrolidin-1-yl]-1*H*-1,2,3-triazol-1-yl}*-1-thio-D-erythro-α-D-galacto-*octopyranoside* (**10k**). *GP* and FC (amino phase gel, AcOEt/MeOH 98:2 to 4:1) gave **10k** (46 mg, 60%). White solid. R_f (AcOEt/MeOH 9:1) 0.13. M.p. 90–92°. $[\alpha]_D^{25} = +169.6$ ($c = 1.04$, MeOH). IR (ATR): 3352*w* (br.), 2956*w*, 2921*w*, 2874*w*, 2848*w*, 2791*w*, 1552*w*, 1453*w*, 1379*w*, 1299*w*, 1216*w*, 1138*w*, 1094*m*, 1076*m*, 1049*s*, 980*m*, 945*w*, 908*w*, 865*w*, 801*w*, 749*s*, 700*w*, 683*w*, 665*w*, 630*w*. ^{1}H-NMR (300 MHz, CD_3OD): see *Table 2*; additionally, 7.88 (*s*, H–C(5) of triazolyl); 3.53–3.47, 3.30–3.27 (2*m*, 2 H of pyrrolidinyl); 2.41–2.31, 2.25–2.20 (2*m*, 2 H of pyrrolidinyl); 2.25 (*s*, MeN); 2.18 (*s*, MeS); 2.08–2.01 (*m*, 2 H of pyrrolidinyl); 1.95–1.85 (*m*, 2 H of pyrrolidinyl); 1.30–1.17 (*m*, $Me(CH_2)_2$); 0.94 (*t*, $J = 6.9$, $Me(CH_2)_2$). ^{13}C-NMR (75 MHz, CD_3OD): see *Table 2*; additionally, 148.19 (*s,* C(4) of triazolyl); 126.17 (*d*, C(5) of triazolyl); 68.84 (*d*, C(2) of pyrrolidinyl); 64.43 (*t*, C(5) of pyrrolidinyl); 40.52 (*q*, MeN); 39.48 (*t*, $MeCH_2CH_2$); 38.10 (*t*, C(3) of pyrrolidinyl); 36.83 (*d*, C(4) of pyrrolidinyl); 21.99 (*t*, $MeCH_2CH_2$); 14.19 (*q*, MeS); 13.70 (*q*, $MeCH_2CH_2$). HR-MALDI-MS: 431.2329 (100, $[M + H]^+$, $C_{19}H_{35}N_4O_5S^+$; calc. 431.2323).

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