Synthesis of Methyl *N*-Acetyl-4-amino-2,4,6-trideoxy-3-*C*-methyl-α-L-rhamnohexopyranoside − Towards Elucidation of the Relative Configuration of Saccharocarcin E Sugar

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Dedicated to Professor Peter Welzel on the occasion of his 65th birthday.

Keywords: Amino sugars / Antibiotics / Configuration determination

L-Olivomycal **8**, obtained from L-rhamnose (**10**) in six steps, was used as a precursor for the preparation of methyl *N*-acetyl-4-amino-2,4,6-trideoxy-3-*C*-methyl-α-L-rhamnohexopyranoside (**5b**). The amino group at C-4 of **5b** was introduced by intramolecular nucleophilic displacement of a (trichloromethyl)imidate derived from **8**, yielding the 3,4-*trans*-(trichloromethyl)oxazoline **13** with retention of configuration. Compound **13** was further converted into the *N*-acetamide **14** by basic hydrolysis and subsequent acetylation. *N*-Iodosuccinimide-promoted glycosylation and reductive dehalogenation yielded the target molecule **5b**, together with its β epimer **5c** (α/β = 85:15). Comparison of the NMR spectroscopic data of **5b** with those of saccharocarcin E sugar and several other 4-amino-2-deoxyhexoses revealed similarities between saccharocarcin E sugar and kijanimicin derivative **23**, which suggest the proposed β-L-*xylo*-hexopyranose configuration **4d** for saccharocarcin E sugar.

Introduction

Amino sugars are important building blocks of many antibiotic or cytotoxic natural products and play a major role in their biological modes of action.[1] Prominent members of this family are L-vancosamine **1** and its derivatives, which are well explored from a synthetic point of view (Scheme 1).[2] Recently, 4-amino-2-deoxyhexoses **2**−**5** have been discovered in various antibiotics: **2** and **3** − for example − in cyclic thiazolyl peptides MJ347−81F4 A and B,[3] **2a** in the thiazolyl peptide glycothiohexide α[4] and the tetrahydroisoquinoline antibiotic lemonomycin,[5] **4** in saccharocarcins A−F,[6] and **6** in macrolide L-708,299.[7] Unlike those of the 3-amino-2-deoxyhexoses represented by L-vancosamine **1**, however, the relative and absolute configurations of several 4-amino-2-deoxyhexoses, most notably **2**−**4** and **6**, have not yet been established. In order to elucidate the stereochemistry of these interesting amino sugars and to explore structure-activity relationships it would be highly desirable to develop a synthetic route to these compounds. We were particularly interested in the type-E sugar **4** of saccharocarcins A−F **7** (Scheme 2), natural products from the fermentation broth of a soil actinomycete *Saccharothrix aerocolongenes subsp. antibiotica*,[8] the structures of which were proposed in 1997 on the basis of NMR and MS data, with the stereochemical issues remaining unsolved.[6] Initially we surmised that the saccharocarcin E sugar **4** might be stereochemically related to the amino sugar **2a** found in glycothiohexide α and lemonomycin,[4,5] and so the hypothetical structure of methyl glycoside **5a** was identified as a possible synthetic target (Scheme 3). We anticipated that the acetamido group in **5a** might be introduced by nucleophilic displacement of the hydroxy group at C-4 in the known glycal **8**, which is available from enone **9** by stereospecific methylation as described by Thiem.[9] Enone **9** can be traced back to L-rhamnose **10** as the starting material. Our results relating to the synthesis and stereochemical issues of **5a** are discussed below.

Results and Discussion

L-Rhamnose (**10**) was converted into L-rhamnal (**11**) in four steps and in 53% overall yield by use of a procedure reported by Pigman and Roth (Scheme 4).[10] The attempted allylic oxidation of diol **11** to the enone **9** with MnO_2 turned out to be capricious.[11] Even in the presence of freshly prepared MnO_2 the desired enone **9** was isolated in very low yields. The oxidation was therefore performed

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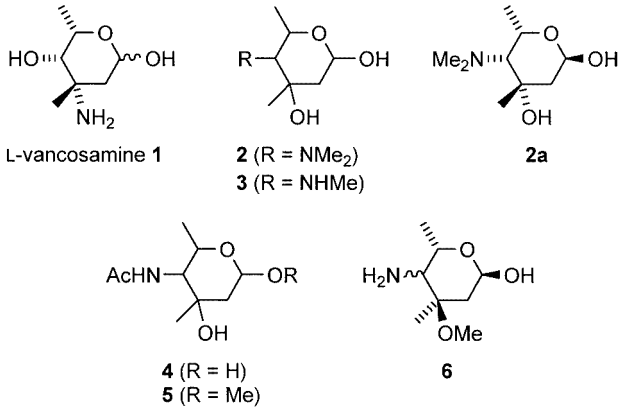
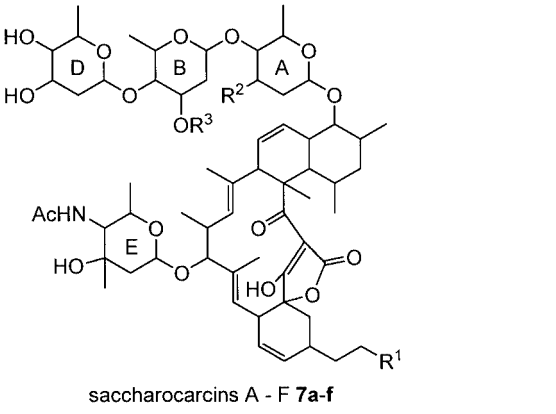
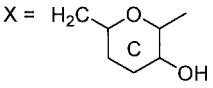


Scheme 1

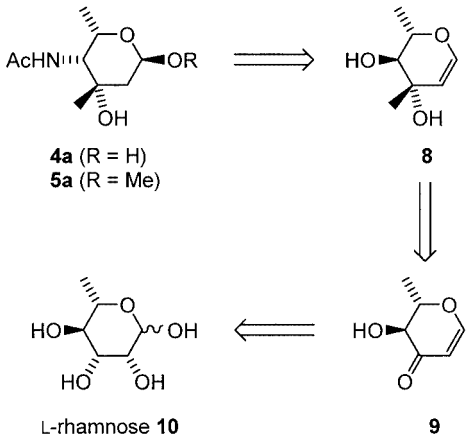


7		R^1	R^2	R^3
a	A	H	OH	X
b	B	Me	OH	X
c	C	H	H	H
d	D	H	H	X
e	E	Me	H	H
f	F	Me	H	X

X =

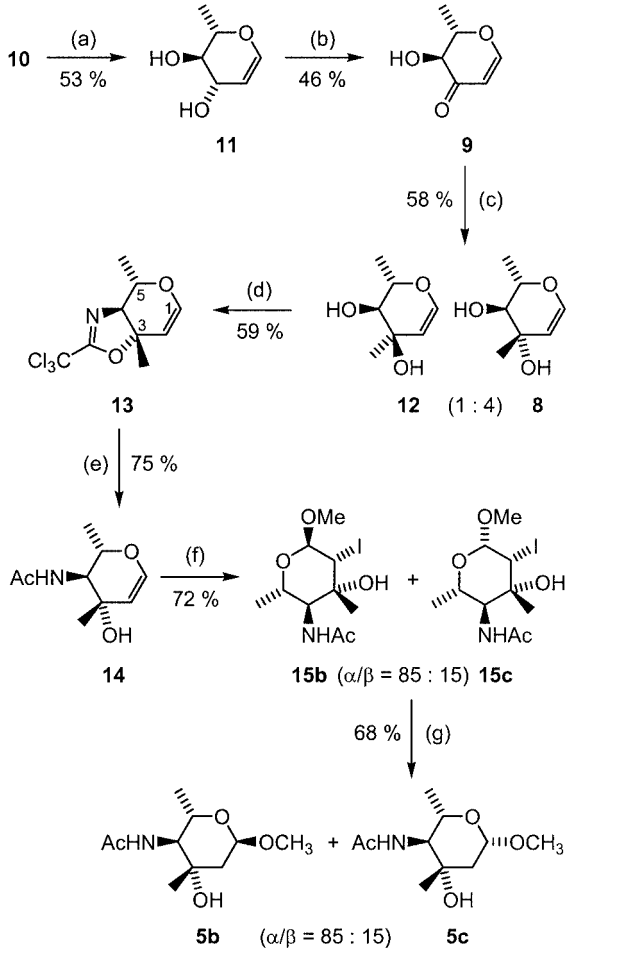


Scheme 2



Scheme 3

with pyridinium dichromate by Thiem's procedure,[9a] giving the enone **9** in 46% yield. Treatment of enone **9** with a reagent prepared in situ at −78 °C from 1.5 equiv. of $ZrCl_4$ and 6 equiv. of MeLi yielded a mixture (4:1) of diastereomers **8** and **12**, from which the major diastereomer, L-olivomycal **8**, was obtained in 58% yield after recrystallization. For the introduction of a nitrogen functionality on C-4, we decided to convert the 1,2-diol **8** into the corresponding (trichloromethyl)oxazoline **13** by a method reported by Danishefsky.[12] It was anticipated that the 1,2-bis-trichloroacetimidate produced in situ should undergo preferential intramolecular nucleophilic substitution at the secondary position on C-4. Upon deprotonation of 1,2-diol **8** with NaH and subsequent treatment with trichloroacetonitrile and $BF_3{\cdot}OEt_2$ the (trichloromethyl)oxazoline **13** was indeed formed regioselectively. To our surprise, however, the vicinal coupling constants in the ^1H NMR spectrum revealed the presence of a *trans*-configured oxazoline **13** ($J_{4,5}$ = 9.1 Hz). Basic hydrolysis of **13** and subsequent *N*-acetylation gave



Scheme 4. Preparation of α-L-rhamnohexopyranoside derivative **5b** from L-rhamnose (**10**); reagents and conditions: (a) 1) Ac_2O, NaOAc, reflux, 1 h; 2) HBr (47%), AcOH, 10 °C, 30 min; 3) Zn, AcOH, Ac_2O, NaOAc; 4) NaOMe, MeOH. (b) PDC, EtOAc, AcOH, room temp., 14 h. (c) MeLi, $ZrCl_4$, toluene, Et_2O, −78 °C, 3.5 h. (d) 1) NaH (2.4 equiv.), CH_2Cl_2, 0 °C, 30 min; 2) Cl_3CCN (5 equiv.), $BF_3{\cdot}Et_2O$ (2 equiv.), room temp., 2 h, 120 °C, 2.5 h. (f) NIS, MeOH, MeCN, room temp., 4 h. (g) Bu_3SnH, AIBN, toluene, 60 °C, 2 h

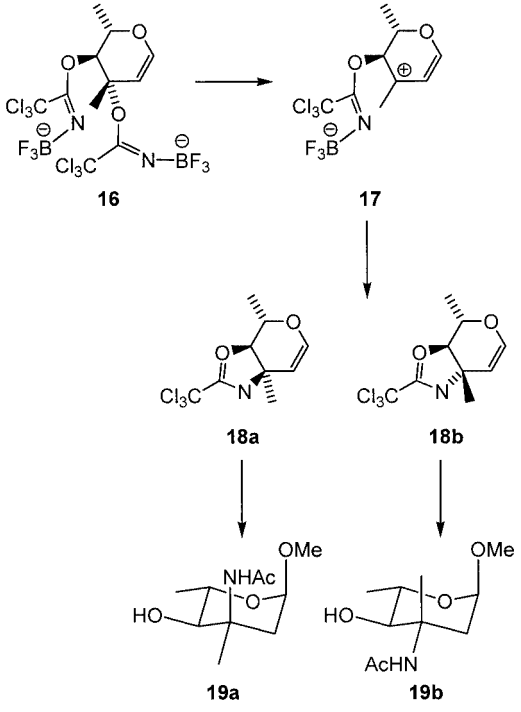
the acetamide **14** in 75% yield.[13] Treatment of acetamide **14** with *N*-iodosuccinimide in MeOH gave the 2-iodomethyl-α-glycoside **15b**, together with the β epimer **15c** (α/β = 85:15). Again, the vicinal coupling constants provided clear evidence for the presence of a 4,5-*trans* configuration. The ^{1}H NMR signal for 4-H appeared as a doublet at δ = 3.46 ppm ($J_{4,5}$ = 9.1 Hz), while 5-H appeared as a doublet of quadruplets ($J_{4,5}$ = 9.1, $J_{5,6}$ = 6.1 Hz) at δ = 4.26 ppm. The iodo substituent was reductively removed with nBu$_3$SnH and catalytic amounts of AIBN[14] to give methyl *N*-acetyl-4-amino-2,4,6-trideoxy-3-*C*-methyl-α-L-rhamnohexopyranoside (**5b**) in 68% yield, together with the corresponding β epimer **5c** (α/β = 85:15).

The configuration of **5b** was confirmed by NMR investigations. In the ^{1}H NMR spectrum of **5b** the signal for 4-H appears as a doublet (J = 9.3 Hz) at δ = 3.36 ppm and that of 5-H as a doublet of quadruplets ($J_{4,5}$ = 9.3, $J_{5,6}$ = 6.2 Hz), indicating a *trans-diequatorial* relationship between the *N*-acetyl group at C-4 and the methyl group (C-6). 1D NOE and NOESY experiments showed diagnostic NOEs for 1-H/2-H$_{ax}$, 1-H/2-H$_{eq}$, 1-H/OMe, 2-H$_{eq}$/3-Me, 3-Me/OMe, 5-H/6-H, 4-H/6-H, 4-H/3-Me, 5-H/COCH$_3$, and 6-H/OMe.

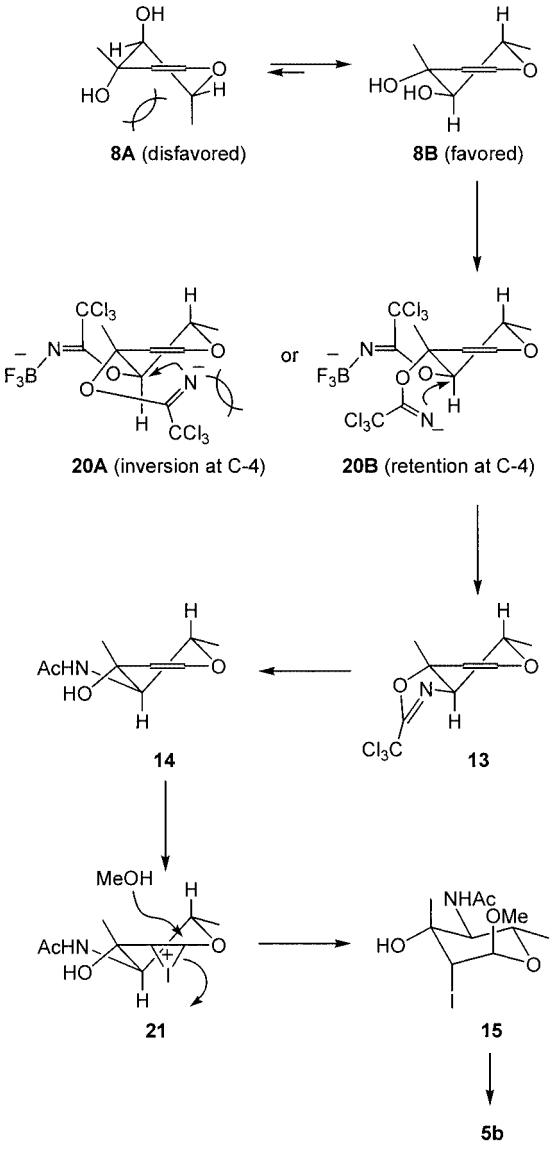
Both the regioselectivity and the stereochemical outcome of the synthetic sequence were unexpected. As far as the regioselectivity is concerned, an alternative pathway seems conceivable. With BF_3 catalysis, the imidate group at C-3 might act as the leaving group even if OR at C-3 were pseudoequatorial, yielding the allylic cation **17**, which might undergo intramolecular nucleophilic attack either with overall inversion, to afford the *cis*-(trichloromethyl)oxazoline **18a**, or with retention of the stereochemistry, to provide the *trans*-(trichloromethyl)oxazoline **18b** (Scheme 5). Whereas the *cis* diastereomer **18a** would be further transformed into methyl glycoside **19a**, the *trans* diastereomer **18b** would give the corresponding C-3 epimeric glycoside **19b**.

However, the observation of an NOE for 3-Me/OMe does not agree with structure **19a**. Furthermore, the observed NOEs for 5-H/COCH$_3$ and 4-H/3-Me can be taken as evidence against structure **19b**. The NOESY data therefore seem to support structure **5b**. It remains unclear why displacement of the C-4 imidate is strongly favored over displacement of the C-3 imidate despite the fact that the latter case should result in a stabilized tertiary allylic cation **17**.

The stereochemical outcome was even more surprising since the formation of the (trichloromethyl)oxazoline **13** must have occurred with retention of configuration.[16] For the rhamnal derivative **8**, two conformers **8A** and **8B** need to be considered (Scheme 6). Conformer **8A** is probably disfavored, due to the presence of an *axial* methyl group at C-

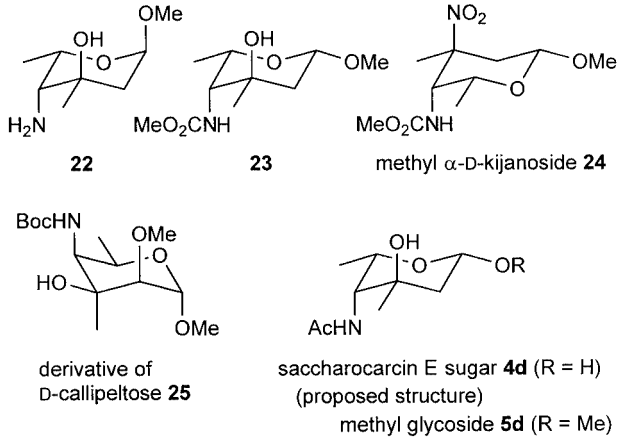


Scheme 5



Scheme 6

5. Intramolecular nucleophilic displacement of the imidate at C-4 should then preferably occur with retention (**20B**). In contrast, displacement with inversion (**20A**) should be disfavored due to steric crowding below the rhamnal ring, especially between C-6 and the lone pairs of nitrogen and the trichloromethyl group. (Trichloromethyl)oxazolines have been used in carbohydrate chemistry in two different reaction types: S_N2-type intramolecular displacement of an imidate or an acetal by an imidate[12,13] or electrophile-induced cyclization of an allylic imidate.[15] In both cases the *cis*-configured (trichloromethyl)oxazolines were formed exclusively, affording the corresponding *cis*-1,2-amino alcohols after hydrolysis. However, *trans* fusion of five-membered rings is not completely unknown.[17] Schmidt and Vankar have very recently obtained a 1,2-*trans*-fused bicyclic lactam − which could not be epimerized even under forcing conditions − from a galactosyl *C*-glycoside.[18]



Scheme 7

Comparison of the spectroscopic data for methyl glycoside **5b** with those reported for saccharocarcin E sugar[6] clearly showed that the latter has a different configuration. We wondered whether comparison of the experimental data obtained for **5b** with those for known amino sugars might be used for elucidation of the stereochemistry of the E sugar **4**. To this end, the ^{13}C NMR chemical shifts of C-1, C-3, and C-4 and the ^1H NMR chemical shifts and coupling constants of 1-H, 4-H, and 5-H of several amino sugars of known configurations (**2a**, **22**−**25**) were compared (Scheme 7).[4−6,19,20] The results summarized in Table 1 and 2 indicate that the kijanimicin derivative **23**[19] and saccharocarcin E sugar **4**[6] are most closely related in terms of chemical shifts and coupling constants. In particular, both compounds possess a $4_{axial},5_{equatorial}$-*cis* relationship and an *equatorial* methoxy group at C-1. We thus conclude that the relative configuration of the saccharocarcin E sugar can be described as a β-L-*xylo*-hexopyranose **4d** as shown in Scheme 7. In order further to corroborate the stereochemical assignment at the quaternary carbon C-3, density functional calculations were carried out for the C-3/C-4 epimers of **5b** and **5d** by the PBEPBE (G-311++G**) method.[21] The calculations showed that the ^{13}C chemical shift of C-4 for a given C-4 epimer is strongly dependent on the configuration of the quaternary center at C-3. The ^{13}C NMR signal for C-4 is shifted approximately δ = 10 ppm downfield when an *equatorial* OH group, rather than an *axial* OH group, is present at C-3. All remaining ^{13}C NMR shifts are reasonably insensitive to the configuration at the C-3 center. Although the calculated shifts refer to the gas phase and so

Table 1. Selected ^1H NMR chemical shifts and coupling constants of various amino sugars

Compound	Derived from	Solvent	δ (1-H) [ppm]	*J* [Hz]	δ (4-H) [ppm]	*J* [Hz]	δ (5-H) [ppm]	*J* [Hz]	Ref.
22	kijanimicin	$CDCl_3$	4.74	dd, 4.0, 1.0	2.35	dd, 2.0, 1.0	4.32	dq, 6.0, 2.0	[19]
23	kijanimicin	$CDCl_3$	4.68	dd, 10.0, 3.0	3.45	ddd, 10.0, 2.0, 1.0	4.27	dq, 6.0, 2.0	[19]
4	saccharocarcin	$CDCl_3$	4.56	dd, 10.0, 2.0	3.68	d, 10.0	4.22	dq, 6.0, 1.0	[6]
24	D-kijanose	$CDCl_3$	4.59	dd, 4.0, 1.0	4.40	dd, 10.0, 1.0	4.10	dq, 6.0, 1.0	[19]
2a	glycothiohexide α	[D_6]DMSO	4.96	d, 4.5	2.06	br. s	3.79	m	[4]
2a	lemonomycin	D_2O	5.08	br. d, 4.4	3.13	br. s	3.98	br. q, 7.2	[5]
5b		C_6D_6	4.29	dd, 4.9, 2.9	3.36	d, 9.3	3.07	dq, 9.3, 6.2	
25	D-callipeltose	$CDCl_3$	5.13	d, 5.9	3.38	d, 1.9	4.06	dq, 6.5, 1.9	[20]

Table 2. Selected ^{13}C NMR chemical shifts of various amino sugars

Compound	Derived from	Solvent	δ (C-1) [ppm]	δ (C-3) [ppm]	δ (C-4) [ppm]	Ref.
22	kijanimicin	$CDCl_3$	99.2	74.1	58.3	[19]
23	kijanimicin	$CDCl_3$	100.5	72.6	52.4	[19]
4	saccharocarcin	$CDCl_3$	98.4	72.7	55.5	[6]
24	D-kijanose	$CDCl_3$	96.9	86.0	52.8	[19]
2a	glycothiohexide α	[D_6]DMSO	94.9	67.3	68.2	[4]
2a	lemonomycin	D_2O	99.9	69.7	72.7	[5]
5b		C_6D_6	98.4	60.1	81.1	
25	D-callipeltose	$CDCl_3$	98.6	68.0	83.0	[20]

do not include specific interactions of the amino sugar with the solvent, the overall tendency agrees well with the experimentally measured values listed in Table 2.

Conclusion

A synthesis of the 4-*N*-acetylamino-2-deoxyhexose **5b** from L-rhamnose (**10**) has been developed, via the 3,4-*trans*-(trichloromethyl)oxazoline **13** as a key intermediate. Compound **5b** is a formal C-4 epimer of the amino sugars found in glycothiohexide α and lemonomycin. Comparison of the NMR spectroscopic data for **5b** and those for several known amino sugars resulted in assignment of the relative configuration of saccharocarcin E sugar as a β-L-*xylo*-hexopyranose **4d**.

Experimental Section

General: All reactions were carried out under nitrogen by use of standard Schlenk techniques. Solvents were dried and deoxygenated by standard procedures. Analytical TLC was performed on precoated Macherey−Nagel SIL G/UV_{254} plates (0.25 mm thickness) and the products were viewed by UV detection or by use of phosphomolybdic acid (5 wt.% in EtOH). Flash chromatography[22] was carried out with Merck silica gel 60 (230−400 mesh). NMR spectra: Bruker AM 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz), Bruker AC 200 (^{1}H: 200 MHz, ^{13}C: 50 MHz). Multiplets in ^{13}C NMR spectra were assigned with the aid of DEPT experiments. Optical rotations (1-dm cells, 1-mL capacity, room temp.): Perkin−Elmer Model 241 polarimeter. Melting points: Gallenkamp melting point apparatus, uncorrected. IR: Nicolet 320 FT-IR spectrometer. MS: Finnigan Model MAT 8430 (EI). L-Rhamnal **11** was prepared according to ref.[10]

1,5-Anhydro-2,6-dideoxy-L-erythrohex-1-enitulose (9): HOAc (12.8 mL) and pyridinium dichromate (25.0 g, 70.0 mmol) were added to a solution of L-rhamnal **11** (8.59 g, 66.6 mmol) in ethyl acetate (320 mL) and CH_2Cl_2 (110 mL), and the deep red solution was stirred for 14 h at room temp. The mixture was then filtered through a short pad of SiO_2 in a fritted funnel and washed with ethyl acetate. The combined filtrates were evaporated and the crude product was purified by recrystallization from Et_2O/*n*-pentane (2:1) to give 3.91 g (46%) of colorless needles; m.p. 87 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, *J* = 6.2 Hz, 3 H, 6-H), 3.51 (br. s, 1 H, OH), 3.91 (d, *J* = 13.1 Hz, 1 H, 4-H), 4.13 (m, 1 H, 5-H), 5.39 (d, *J* = 5.8 Hz, 1 H, 2-H), 7.32 (d, *J* = 5.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17. 9 (C-6), 72.7 (C-5), 79.9 (C-4), 103.4 (C-2), 164.7 (C-1), 194.2 (C-3) ppm. Spectroscopic data were in accordance with ref.[9b]

L-Olivomycal (8): MeLi (83.0 mL, 0.13 mol, 1.6 M solution in Et_2O) was added dropwise at −78 °C to a cooled suspension of $ZrCl_4$ (7.64 g, 33.0 mmol) in toluene (130 mL) and Et_2O (90 mL). The solution was warmed to 0 °C, stirred at 0 °C for 35 min, and then cooled again to −78 °C. A solution of **9** (2.80 g, 22.0 mmol) in Et_2O (44 mL) and toluene (66 mL) was then added dropwise over 40 min. The resulting mixture was stirred at −78 °C for 3.5 h, and was then allowed to warm to 0 °C and hydrolyzed carefully with satd. $NaHCO_3$ (250 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (4 × 50 mL), the combined organic layers were dried over $MgSO_4$, and the solvents were evaporated to give 1.84 g (58%) of a (4:1) mixture of L-olivomycal (**8**) and L-mycaral (**12**). The crude product was recrystallized from Et_2O/*n*-pentane (1:1) to give 1.47 g (46%) of colorless crystals; m.p. 101 °C. ^{1}H NMR (400 MHz, C_6D_6): δ = 1.21 (s, 3 H, 7-H), 1.32 (d, *J* = 6.2 Hz, 3 H, 6-H), 3.39 (d, *J* = 10.1 Hz, 1 H, 4-H), 3.7 (dq, *J* = 10.1, 6.2 Hz, 1 H, 5-H), 4.49 (d, *J* = 6.1 Hz, 1 H, 2-H), 6.02 (d, *J* = 6.1 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 18.1 (C-6), 24.1 (C-7), 70.8 (C-3), 73.9 (C-5), 78.2 (C-4), 108.3 (C-2), 142.8 (C-1) ppm.

L-Mycaral (12): ^{1}H NMR (400 MHz, C_6D_6): δ = 1.12 (s, 3 H, 7-H), 1.36 (d, *J* = 6.2 Hz, 3 H, 6-H), 3.45 (dq, *J* = 10.4, 6.2 Hz, 1 H, 5-H), 4.42 (d, *J* = 5.9 Hz, 1 H, 2-H), 6.06 (d, *J* = 5.9 Hz, 1 H, 1-H) ppm. Spectroscopic data were in accordance with ref.[9c]

Bicyclic Olivomycal Derivative 13: NaH (165 mg, 6.86 mmol, 60% dispersion in mineral oil) was added at 0 °C to a cooled solution of L-olivomycal (**8**) (440 mg, 3.05 mmol) in CH_2Cl_2 (50 mL). After the mixture had been stirred at 0 °C for 30 min, trichloroacetonitrile (1.50 mL, 15.0 mmol) was added dropwise and the resulting mixture was stirred for 90 min at room temp. and cooled to 0 °C. $BF_3{\cdot}Et_2O$ (0.73 mL, 6.10 mmol) was then added dropwise. After stirring at room temp. for 3 h, the mixture was hydrolyzed with satd. $NaHCO_3$ (60 mL), the layers were separated, and the organic layer was washed with H_2O (20 mL). The combined aqueous layers were extracted with ethyl acetate (3 × 50 mL), and the combined organic layers were dried over $MgSO_4$. The solvent was evaporated and the crude product was purified by flash chromatography on SiO_2 (hexanes/ethyl acetate, 80:1) to give a colorless, amorphous solid (490 mg, 59%). $[\alpha]_D^{23}$ = −47.7 (*c* = 1.5, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1664, 1641, 1005, 1047, 780 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, 3-Me), 1.36 (d, *J* = 6.4 Hz, 3 H, 6-H), 3.58 (dq, *J* = 9.1, 6.3 Hz, 1 H, 5-H), 4.26 (d, *J* = 9.1 Hz, 1 H, 4-H), 5.10 (d, *J* = 6 Hz, 1 H, 2-H), 6.44 (d, *J* = 6 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 (C-6), 26.9 (3-Me), 66.6 (C-3), 70.3, 88.5 (C-4, C-5), 77.2 (CCl_3), 106.2 (C-2), 145.5 (C-1), 160.6 (C-8) ppm. MS (EI): *m*/*z* (%) = 269 (30) [M$^+$], 254 (98), 242 (76), 177 (32), 109 (44), 97 (100), 83 (38), 41 (35). $C_9H_{10}Cl_3NO_2$ (270.54): calcd. C 39.96, H 3.73, N 5.18, Cl 39.31; found C 40.03, H 3.71, N 5.20, Cl 39.17.

4-*N*-Acetyl-4-amino-L-olivomycal (14): A suspension of (trichloromethyl)oxazoline **13** (310 mg, 1.15 mmol) and NaOH (970 mg, 24.3 mmol) in H_2O (18 mL) and MeOH (18 mL) was heated at reflux for 2 h. The solvent was removed in vacuo and the residue was extracted with ethyl acetate (4 × 20 mL). The combined organic layers were evaporated to give a colorless, solid residue, which was dissolved in pyridine (10 mL), treated with Ac_2O (3.20 mL, 34.5 mmol), and stirred at room temp. for 2 h. The mixture was then heated at 120 °C for 2.5 h and then evaporated. The residue was dissolved in ethyl acetate (30 mL) and the organic layer was washed with satd. NH_4Cl (30 mL) and satd. $NaHCO_3$ (30 mL) and dried over $MgSO_4$, and the solvents were evaporated. The crude product was purified by flash chromatography (hexanes/ethyl acetate, 20:1) to give a colorless, amorphous solid (160 mg, 75%). $[\alpha]_D^{20}$ = −37.5 (*c* = 1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3537, 3394, 3443, 1706, 1648 cm^{-1}. ^{1}H NMR (400 MHz, C_6D_6): δ = 1.01 (d, *J* = 5.9 Hz, 3 H, 6-H), 1.14 (s, 3 H, 3-Me), 1.30 (br. s, 2 H, OH, NH), 2.29 (s, 3 H, $COCH_3$), 3.14−3.21 (m, 2 H, 4-H, 5-H), 5.43 (d, *J* = 6.2 Hz, 1 H, 2-H), 5.99 (d, *J* = 6.2 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 16.9 (C-6), 24.4 ($CO\mathit{C}H_3$), 27.7 (3-Me), 57.6 (C-3), 70.6, 80.4 (C-4, C-5), 103.2 (C-2), 145.2 (C-1), 170.0 (CO) ppm.

Methyl *N*-Acetyl-4-amino-2,4,6-trideoxy-2-iodo-3-*C*-methyl-α-L-rhamnohexopyranoside (15b): MeOH (0.79 mL, 1.00 mmol) and *N*-

iodosuccinimide (109 mg, 0.49 mmol) were added to a solution of **14** (60.0 mg, 0.32 mmol) in acetonitrile (4 mL) and the resulting mixture was stirred at room temp. for 4 h. The mixture was washed with satd. $Na_2S_2O_3$ (20 mL) and satd. Na_2CO_3 (20 mL). The aqueous layer was extracted with ethyl acetate (2 × 30 mL), the combined organic layers were dried over $MgSO_4$, and the solvents were evaporated to give a pale yellow oil (80 mg, 72%) as a mixture of α/β epimers (α/β = 85:15). ^{1}H NMR (200 MHz, C_6D_6): δ = 1.02 (d, *J* = 6.1 Hz, 3 H, 6-H), 1.61 (s, 3 H, 3-Me), 2.46 (s, 3 H, $COCH_3$), 2.90 (s, 3 H, OMe), 3.46 (d, *J* = 9.1 Hz, 1 H, 4-H), 4.26 (dq, *J* = 9.4, 6.1 Hz, 1 H, 5-H), 4.84 (s, 1 H, 2-H), 5.23 (d, *J* = 1 Hz, 1 H, 1-H) ppm. ^{13}C NMR (50 MHz, C_6D_6): δ = 19.7 (C-1), 25.4 (3-Me), 26.4 ($COCH_3$), 32.2 (C-2), 55.6 (OMe), 61.8 (C-3), 66.9, 81.2 (C-4, C-5), 104.8 (C-1) ppm.

Methyl *N*-Acetyl-4-amino-2,4,6-trideoxy-3-*C*-methyl-α-L-rhamnohexopyranoside (5b): *n*Bu_3SnH (0.08 mL, 0.30 mmol) and AIBN (4 mg) were added to a solution of **15** (70 mg, 0.20 mmol) in toluene (2 mL), and the resulting mixture was heated at 60 °C for 2 h. After evaporation of the solvent, the crude product was purified by flash chromatography on SiO_2 (hexanes → hexanes/ethyl acetate, 20:1) to give a colorless oil (30 mg, 68%) as a mixture of α/β epimers **5b** and **5c** (α/β = 85:15). $[\alpha]_D^{20}$ = −1.1 (*c* = 1.5, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3632, 3548, 3401, 1709 cm^{-1}. ^{1}H NMR (400 MHz, C_6D_6): δ = 1.06 (d, *J* = 6.1 Hz, 3 H, 6-H), 1.28 (s, 3 H, 3-Me), 2.08 (dd, *J* = 15.0, 4.9 Hz, 1 H, 2-H), 2.32−2.37 (m, 4 H, 2-H, $COCH_3$), 3.03 (s, 3 H, OMe), 3.07 (dq, *J* = 9.3, 6.2 Hz, 1 H, 5-H), 3.36 (d, *J* = 9.3 Hz, 1 H, 4-H), 4.29 (dd, *J* = 4.9, 2.9 Hz, 1 H, 1-H) ppm; signals of the β anomer **5c**: 1.16 (s, 3 H, 3-Me), 2.00 (dd, *J* = 14.7, 6.8 Hz, 1 H, 2-H), 2.34 (s, 3 H, $COCH_3$), 3.00 (s, 3 H, OMe), 3.55 (dq, *J* = 9.0, 6.2 Hz, 1 H, 5-H), 4.19 (d, *J* = 5.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 18.6 (C-1), 25.0, 25.4 (3-Me, $COCH_3$), 36.7 (C-2), 55.0 (OMe), 60.1 (C-3), 68.3, 81.1 (C-4, C-5), 98.4 (C-1), 170.6 (CO) ppm; signals of the β anomer **5c**: 18.7 (C-1), 25.1 ($COCH_3$), 25.2 (3-Me), 34.5 (C-2), 54.8 (OMe), 60.1 (C-3), 64.8, 81.7 (C-4, C-5), 97.5 (C-1) ppm. $C_{10}H_{19}NO_4$ (217.26): calcd. C 55.28, H 8.81, N 6.45; found C 55.22, H 8.80, N 6.53.

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