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Syntheses of Specifically Labelled 2,3,6-Trideoxyhexoses

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Abstract: Two synthetic approaches producing L-(-) and D-(+)-rhodinose (6 and 13 respectively), L-(-)-(19)- and D-(+)- amicetose and L- and D-enopyranose 15 specifically deuterated at C-2 and C-3 are described. The strategy which starts from threonine also offers the opportunity for the synthesis of the [1-^{13}C]-labelled compounds.

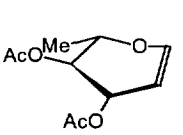
The 2,3,6-trideoxyhexoses rhodinose and amicetose are found as glycosidic components in a wide range of antibiotics including the landomycins[1] and kerriamycins[2], in which the sugar is always linked to an aglycone. Recently L-rhodinose was found in pure carbohydrate metabolites called narbosines[3]. As part of our ongoing studies on the biogenesis of 2,3,6-trideoxyhexoses, it became necessary to develop methods for the synthesis of specifically labelled deoxygenated sugars. Apart from a series of papers by *Liu* concerning the preparation of the stereospecifically deuterated 3-deoxy hexoses L-ascarylose, D-abequose and D-paratose[4], a very limited number of examples of labelled deoxygenated carbohydrates have appeared in the literature[5].

It is commonly excepted that deoxygenated hexoses are biosynthetically derived from D-glucose[6]. In the biosynthesis of L-hexoses, an enzymatically promoted epimerization at C-5 is involved. Up to now, it is unclear at which stage this conversion takes place. Therefore, we needed both enantiomers of rhodinose and amicetose, for which various synthetic approaches have been described[7], as well as their 2,3 unsaturated derivatives, all of which should be specifically deuterated at C-2 and C-3. Additionally, we were interested in the corresponding [1-^{13}C]-compounds, which are exceptionally useful for studying the distribution of these deoxyhexoses in oligoglycosylated secondary metabolites.

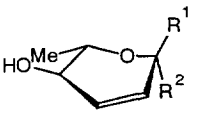
In the first phase of this project we envisaged 4,6-di-O-acetyl-L-rhamnal **1**[8] as starting material for the preparation of (2*S*, 3*R*) [2,3- $^{2}H_2$]-L-rhodinose. As depicted in scheme 1, *Ferrier* rearrangement of **1**[9] in the presence of benzyl alcohol and $BF_3{\cdot}OEt_2$ followed by saponification (MeOH, NEt_3, H_2O 3:1:1) afforded alcohols **2a** and **2b** in 88 % yield. In addition, we isolated 2,6-dideoxyhexoses **2c** and **2d** in a 3:1 ratio. Their formation can be understood as an attack of benzyl alcohol onto C-3 of the oxonium intermediate which is postulated for the *Ferrier* rearrangement[9]. In a second stereoselective step, acid catalyzed addition of benzyl alcohol onto the enol ether followed by deprotection leads to **2c** and **2d**. For determining the stereoselectivity in the labelling step, anomerically pure material was necessary. Thus, we separated the 5:1 mixture of α,β-anomers **2a,b** at this point and continued the synthesis with each anomer. Inversion of configuration at C-4 was accomplished under standard *Mitsunobu*-type reaction conditions[10]. While the *α*-anomer was smoothly

converted into benzoate **3a**[11](95 %) the β-anomer yielded an unseparable mixture of benzoates **3b** and **4**[12] (~ 5:1; 94 %). Formation of **4** can be rationalized as a stereocontrolled S_N2'-attack of benzoic acid onto the intermediate alkoxy phosphonium salt.

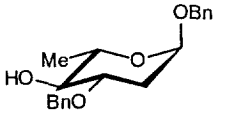
Scheme 1



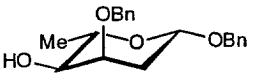
1



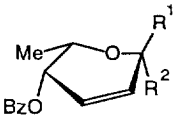
2a: R^1= OBn; R^2= H
2b: R^1= H; R^2= OBn



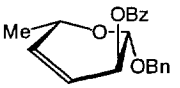
2c



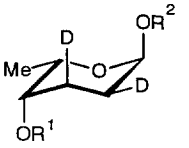
2d



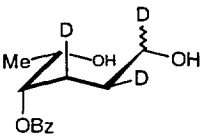
3a: R^1= OBn; R^2= H
3b: R^1= H; R^2= OBn



4



5a: R^1= Bz; R^2= Bn
5b: R^1= H; R^2= Bn
6: R^1= R^2= H
7a: R^1= Bz; R^2= H

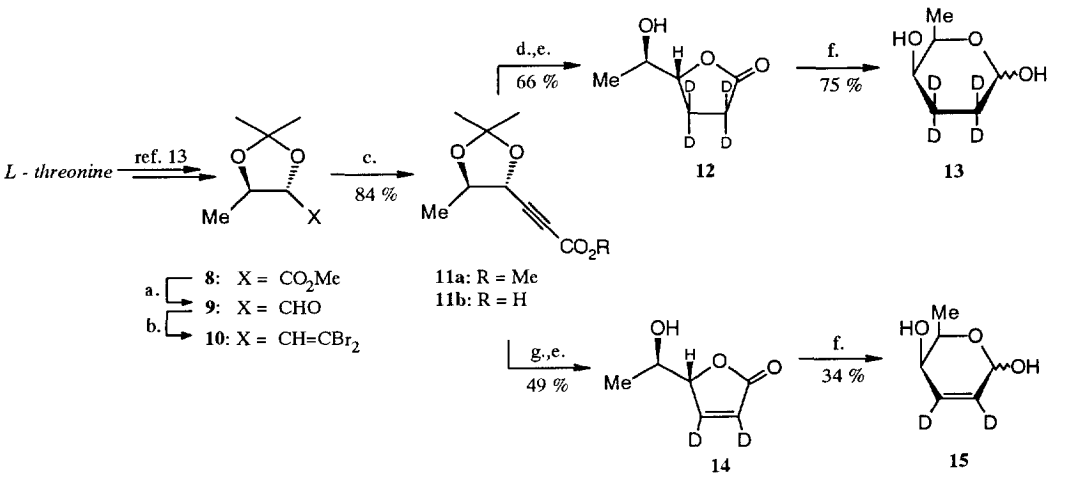


7b

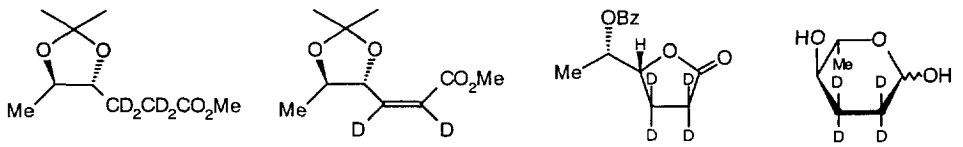
Subsequent catalytic deuteration (Pd/C, D_2, ether) of **3a** followed by saponification (HOMe, $NaOMe_{cat.}$) furnished **5b** as a single isomer in 76 % overall yield. Finally, deprotection of the anomeric benzyl group under acidic conditions gave the desired (2*S*, 3*R*) bis-deuterated L-rhodinose **6** as a mixture of anomeric furanoses and pyranoses[7]. This stepwise procedure turned out to be more efficient than direct hydrogenolysis of the benzyl group along with the olefinic double bond in **5a**. Under these conditions, formation of **7a** ($[\alpha]^{21}_D$ -15.8° (c 1.70, $CHCl_3$)) and diol **7b** ($[\alpha]^{19}_D$ +18.7° (c 1.81, $CHCl_3$)) was observed. In contrast, catalytic hydrogenation of **2a** with $^2H_2$, which eventually leads to 2,3-deuterated L-amicetose was nonselective yielding a mixture of reduction products.

Therefore, a more flexible strategy was pursued which enabled us to synthesize all four possible 2,3,6-trideoxy hexoses labelled at C-2 and C-3 as well as their 2,3- unsaturated derivatives. The strategy relies on the preparation of key intermediate **11** from optically pure *threo*-2,3-dihydroxybutanoic ester **8**[13] as outlined in scheme 2. Dibal-H promoted reduction gave **9** which was converted into 1,1-dibromo olefin **10** (61 % from **8**) and further into **11a** under well documented conditions[14]. At this point a ^{13}C-label may be introduced by employing $^{13}CO_2$ as electrophile, furnishing **11b** (79 % for $^{12}CO_2$). Partial *syn*- or exhaustive catalytic deuteration gave **16** and **17**, respectively, which after acid promoted cyclization gave γ-lactones **12** and **14** exclusively. Reduction of **12** accomplished the synthesis of 2,2',3,3'-tetradeuterated D-rhodinose (**13**). In an analogous fashion **15** was obtained from **14**. Lactol **15** which predominantly is present in the furanose form turned out to be very labile as it easily adds water or alcohols affording the corresponding 2.6-dideoxyhexoses.

Scheme 2



a. 1.2 equ. dibal-H, CH_2Cl_2, -78 °C, 1h ; b. PPh_3, Zn, CBr_4, CH_2Cl_2, rt, 24h, then addition of aldehyde, rt, 2h; c. 2.2 equ. n-BuLi, -78°C, 1h and rt, 1.5h, then $ClCO_2CH_3$, THF, -78 °C to rt, 0.5h: **11a**, or CO_2, rt, 2h: **11b**; d. Pd/C, $^2H_2$, MeOH, rt, 1.5h; e. 2N HCl, THF (1:2), rt, 12h; f. 2.5 equiv. dibal-H, CH_2Cl_2, -78°C, 0.5h; g. Pd/$BaSO_4$, quinoline, $^2H_2$, ether, rt, 3d.



The scope of this strategy was further expanded by inverting C-5 in **12** in the presence of diethyl azodicarboxylate (DEAD), triphenylphoshine (TPP) and benzoic acid[10] affording **18** (76 %), which after one-pot reductive deprotection at C-5 and partial reduction at C-1 gave access to L-amicetose (**19**) in 68 % yield. Due to the α-acidity of saturated lactones, partial exchange (~25%) of deuterium at C-2 was observed in the ^1H and ^{13}C NMR spectra of **12** and **18**. When D-threonine was employed as starting material, *ent*-**13** (L), *ent*-**15** (L) and *ent*-**19** (D) were obtained.

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Experimental

General information. All temperatures quoted are uncorrected. Optical rotations were measured in a Perkin-Elmer 141 polarimeter. Infrared spectra (IR) were obtained using a Perkin Elmer 399 spectrophotometer and wavelengths (ν) are reported in cm^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AC 250P or AMX 400 spectrometer, respectively. ^{13}C NMR multiplicities were determined by the DEPT-135 method. Tetramethylsilane (TMS) was used as internal standard. All solvents used were reagent grade and were further dried. Reactions were monitored by TLC on silica gel 60 PF^{254} (E. Merck, Darmstadt) and detected by UV-absorption and either by charring with 5% H_2SO_4 in ethanol or with a mixture of H_2SO_4, AcOH and 4-methoxy benzaldehyde in methanol. Preparative column chromatography (cc) and flash chromatography (fc) was performed on silica gel 60 (E. Merck, Darmstadt). Di-O-acetyl-L-rhamnal **1** was prepared according to the literature[8]. **8** was synthesized as previously described[13,7d].

***Ferrier* rearrangement of 1**

The pyranosides **2a** and **2b** were prepared in 88 % yield as anomers (α:β 5:1) according to *Ferrier's*[9b] procedure followed by removal of the 4-O-acetyl group in a mixture of MeOH, NEt_3 and H_2O (3:1:1) at rt. Furthermore, careful cc on silica gel (PE/ EE 2:1) yielded **2c** and **2d** (3:1; 10 %).

1st fraction: **Benzyl 2,3,6-Trideoxy-α-L-*erythro*-hex-2-enopyranoside (2a)**: crystals, m.p. 48-49 °C; $[\alpha]^{18}_D$ -44.5° (c 1.12, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.35 (m, 5H), 5.94 (broad d, 1H, *J*= 10.4 Hz), 5.78 (dt, 1H, *J*= 10.4, 2.4 Hz), 5.04 (m, 1H), 4.78, 4.59 (2d, 2H, *J*= 12.0 Hz), 3.86 (broad t, 1H, *J*= 8.6 Hz), 3.76 (dq, 1H, *J*= 8.8, 6.2 Hz), 1.42 (d, 1H, *J*= 8.4 Hz), 1.30 (d, 3H, *J*= 6.2 Hz); ^{13}C NMR ($CDCl_3$): δ 138.0, 133.5- 126.8, 93.6, 70.1, 69.8, 68.2, 17.9.

2nd fraction: **Benzyl 2,3,6-Trideoxy-β-L-*erythro*-hex-2-enopyranoside (2b)**:colorless oil; $[\alpha]^{19}_D$ -9.7° (c 1.02, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 5H), 5.96 (ddd, 1H, *J*= 10.2, 2.6, 1.6 Hz), 5.81 (dt, 1H, *J*= 10.2, 1.6 Hz), 5.18 (dt, 1H, *J*= 1.8, 1.6 Hz), 4.86, 4.61 (2d, 2H, *J*= 12.0 Hz), 3.91 (broad d, 1H, *J*= 6.4 Hz), 3.67 (dq, 1H, *J*= 6.4 Hz), 1.92 (b, 1H), 1.39 (d, 3H, *J*= 6.4 Hz); ^{13}C NMR ($CDCl_3$): δ 137.7, 132.0, 128.8- 128.0, 127.7, 95.5, 74.5, 69.6, 68.4, 18.4.

3rd fraction: **Benzyl 4-O-Benzyl-6-deoxy-α-L-*arabino*-pyranoside (2c)**: colorless oil; $[\alpha]^{20}_D$ -60.1° (c 1.37, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 10H), 4.98 (d, 1H, *J*= 3.6 Hz), 4.68, 4.66, 4.48, 4.45 (4d, 4H, *J*= 12.0 Hz), 3.81 (ddd, 1H, *J*= 11.6, 9.4, 5.2 Hz), 3.75 (dq, 1H, *J*= 9.4, 6.2 Hz), 3.26 (dt, 1H, *J*= 9.2, 2.0 Hz), 2.45 (d, 1H, *J*= 2.0 Hz), 2.33 (ddd, 1H, J= 12.8, 5.2, 1.4 Hz), 1.66 (ddd, 1H, *J*= 12.8, 11.6, 4.0 Hz), 1.30 (d, 3H, *J*= 6.2 Hz); ^{13}C NMR ($CDCl_3$): δ 138.3, 137.7, 128.5- 127.7, 96.6, 77.1, 76.2, 71.1, 68.7, 67.7, 34.8, 17.9.

4th fraction: **Benzyl 4-O-Benzyl-6-deoxy-β-L-*ribo*-pyranoside (2d)**: colorless oil; $[\alpha]^{21}_D$ +30.3° (c 1.13, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30 (m, 10H), 4.91, 4.68, 4.56, 4.44 (4d, 4H, *J*= 11.6 Hz), 4.85 (dd, 1H, *J*= 9.6, 2.0 Hz), 3.92 (broad q, 1H, *J*= 3.2 Hz), 3.69 (dq, 1H, *J*= 9.6, 6.2 Hz), 3.27 (ddd, 1H, *J*= 10.8, 9.6, 3.6 Hz), 2.30 (ddd, 1H, *J*= 14.0, 3.6, 2.0 Hz), 2.24 (d, 1H, J= 10.8 Hz), 1.71 (ddd, 1H, *J*= 14.0, 9.6, 2.6 Hz), 1.34 (d, 3H, *J*= 6.2 Hz); ^{13}C NMR ($CDCl_3$): δ 138.5, 128.6- 127.7, 96.9, 75.5, 72.5, 71.4, 71.0, 70.4, 34.3, 18.2.

***Mitsunobu*-Inversion at C-4 of 2**

Benzyl 4-O-Benzoyl-2,3,6-trideoxy-α-L-*threo*-hex-2-enopyranoside (3a): To a solution of **2a** (0.23 g, 1.04 mmol) in toluene (2.2 ml) at 0 °C were added triphenyl phosphine (0.967 g, 3.62 mmol) and benzoic acid (0.448 g, 3.62 mmol). DEAD (0.56 ml, 3.62 mmol) was dissolved in toluene (1.8 ml) and added dropwise to the reaction mixture. The resulting solution was allowed to warm to rt. After 30 min the precipitate was filtered and washed with toluene. The combined extracts were evaporated under reduced pressure and purified by cc (PE/ EE 3:1) to afford **3a** (0.32 g, 0.99 mmol, 95 %); colorless oil; $[\alpha]^{18}_D$ +222.7° (c 1.35, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.08- 7.38 (m, 10H), 6.21 (ddd, 1H, *J*= 10.4, 5.6, 0.8 Hz), 6.08 (dd, 1H, *J*= 10.4, 3.2 Hz), 5.19 (dd, 1H, *J*= 3.2, 0.8 Hz), 5.16 (dd, 1H, *J*= 5.6, 2.6 Hz), 4.81, 4.65 (2d, 2H, *J*= 12.0 Hz), 4.38 (dq, 1H, *J*= 6.6, 2.6 Hz), 1.27 (d, 3H, *J*= 6.6 Hz); ^{13}C NMR ($CDCl_3$): δ 166.2, 137.9, 133.1- 126.1, 129.9, 93.6, 70.0, 65.6, 65.1, 16.1.

Under identical conditions **2b** (80 mg, 0.36 mmol) afforded an inseparable mixture of **(3b)** and **(4)** (110 mg, 0.34 mmol, 94 %) in a 5:1 ratio: **Benzyl 4-O-Benzoyl-2,3,6-trideoxy-β-L-*threo*-hex-2-enopyranoside (3b)**: ^1H NMR ($CDCl_3$): δ 8.10- 7.30 (m, 10H), 6.16 (ddd, 1H, *J*= 10.0, 4.8, 1.2 Hz), 6.04 (d, 1H, *J*= 10.0 Hz), 5.28 (dt, 1H, *J*= 4.8, 3.0, 1.4 Hz), 5.24 (d, 1H, *J*= 1.2 Hz), 4.92, 4.78 (2d, 2H, *J*= 12.0 Hz), 4.03 (dq, 1H, *J*= 6.6, 3.0 Hz), 1.37 (d, 3H, *J*= 6.6 Hz); ^{13}C NMR ($CDCl_3$): δ 166.3, 137.7, 133.2- 127.1, 96.3, 69.4, 69.0, 66.6, 16.6. **Benzyl 2-O-Benzoyl-3,4,6-trideoxy-β-L-*erythro*-hex-3-enopyranoside (4)**: ^1H NMR ($CDCl_3$): δ 8.0-7.30 (m, 10H), 5.85 (dddd, 1H, *J*= 10.4, 3.0, 1.6, 1.0 Hz), 5.77 (broad dt, 1H, *J*= 10.4, 2.5 Hz), 5.52 (ddd, 1H, *J*= 6.0, 3.6, 2.0 Hz), 4.84 (d, 1H, *J*= 6.0 Hz), 4.93, 4.71 (2d, 2H, *J*= 11.8 Hz), 4.42 (broad q, 1H, *J*= 6.2 Hz), 1.37 (d, 3H, *J*= 6.2 Hz).

(2*S*, 3*R*) [2,3- $^2H_2$] Benzyl 4-O-Benzoyl-2,3,6-trideoxy-α-L-*threo*-pyranoside (5a): A suspension of **3a** (0.2 g, 0.59 mmol) and Pd/C (9.7 mg) in ether (18 ml) was stirred at rt under an atmosphere of D_2 (~ 99.8 %) for 4.5 h. Filtration and evaporation *in vacuo* afforded **5a** (190 mg, 0.55 mmol, 94 %); colorless oil; $[\alpha]^{19}_D$ -68.3° (c 1.62, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.18- 7.30 (m, 10H), 5.07 (broad d, 1H, *J*= 2.0 Hz), 5.02 (d, 1H, *J*= 3.0 Hz), 4.74, 4.57, (2d, 2H, *J*= 11.6 Hz), 4.16 (broad q, 1H, *J*= 6.4 Hz), 2.02 (broad t, 1H, *J*= 4.0 Hz), 2.02 (broad t, 1H, *J*= 3.6 Hz), 1.18 (d, 3H, *J*= 6.4 Hz); ^{13}C NMR ($CDCl_3$): δ 166.2, 138.1, 133.0- 127.7, 96.3, 70.0, 69.0, 65.4, 24.2 (t), 23.0 (t), 17.3.

(2*S*, 3*R*) [2,3- $^2H_2$] Benzyl 2,3,6-Trideoxy-α-L-*threo*-pyranoside (5b): To a solution of **5a** (0.19 g, 0.55 mmol) in methanol (10 ml) was added sodium (10 mg; 0.43 mmol). After stirring for 3 d at rt the reaction mixture was concentrated *in vacuo*. Fc (PE/ EE 3:1) afforded **5b** (100 mg, 0.45 mmol, 81 %); colorless oil; $[\alpha]^{20}_D$ -116.3° (c 1.24, $CHCl_3$); for undeuterated **5b**: $[\alpha]^{20}_D$ -120.9° (c 1.04, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.32 (m, 5H), 4.90 (d, 1H, *J*= 3.2 Hz), 4.69, 4.51, (2d, 2H, *J*= 12.0 Hz), 4.01 (broad q, 1H, *J*= 6.6 Hz), 3.58 (broad d, 1H, *J*= 2.8 Hz), 2.01- 1.92 (m, 2H), 1.73 (broad t, 1H, *J*= 3.2 Hz), 1.19 (d, 3H, *J*= 6.6 Hz); ^{13}C NMR ($CDCl_3$): δ 138.1, 130.5- 127.6, 96.4, 69.8, 67.3, 66.3, 25.4 (t), 22.9 (t), 17.1.

(2*S*, 3*R*) [2,3- $^2H_2$] L-Rhodinose (6): A solution of **5b** (0.45 g, 2.03 mmol) in aqu. 0.5 N HCl (5 ml) at rt was stirred for 1h, neutralized with aqu. $NaHCO_3$ and evaporated *in vacuo*. Purification by fc (PE/ EE 2.5:1 to EE) afforded **6** as a mixture of furanoses and pyranoses (0.24 g, 1.82 mmol, 90 %). colorless oil; $[\alpha]^{18}_D$ -4.0° (c 0.57, $CHCl_3$); for undeuterated **6**: $[\alpha]^{18}_D$ -6.1° (c 1.01, $CHCl_3$). Spectroscopic data are in agreement with those published in the literature[7].

Alkyne 11a from ester 8

To a cold (-78 °C) solution of **8** (20 g, 114.8 mmol) in ether (120 ml), dibal-H in n-hexane (140 ml, 1.0 M, 140 mmol) was added dropwise. The mixture was stirred for 25 min at this temp. and H_2O (60 ml) was added. After stirring for 15 min at rt, the mixture was filtered through a pad of Celite, concentrated under reduced pressure and, finally, traces of water were co-distilled with toluene. Thus, 16.6 g of practically pure aldehyde **9** were obtained which were dissolved in CH_2Cl_2 (130 ml) and directly added to a suspension, which had been prepared as follows. To a cold (0 °C) suspension of CBr_4 (114.8 g, 346.2 mmol) and Zn (22.68 g, 346.8 mmol) in CH_2Cl_2 (480 ml), triphenylphosphine (90.8 g, 346.6 mmol) in CH_2Cl_2 (240 ml) was added dropwise. After 24 h at rt, the crude aldehyde **9** was slowly added over a period of 1 h. After addition was complete, the mixture was stirred for 2 h at 0°C, poured into PE (800 ml), filtered, and the filtrate was concentrated under reduced pressure. The residue was diluted with PE (800 ml), triphenylphospine oxide was removed by filtration and washed with PE. This procedure was repeated until no 1,1 dibromo olefin was detected by tlc (PE/ EE 7:1). The filtrates and washings were concentrated *in vacuo* to give 27 g. Distillation ($bp_{0.01}$ 55 °C) afforded **10** (21 g, 70 mmol, 61 %) as a yellowish oil; $[\alpha]^{20}_D$ -2.6° (c 1, $CHCl_3$); IR ν 1625; ^1H NMR ($CDCl_3$): δ 6.42 (d, 1H, *J*= 8.4 Hz), 4.21 (t, 1H, *J*= 8.4 Hz), 3.86 (dq, 1H, *J*= 8.4, 6.0 Hz), 1.41, 1.36 (2s, 6H), 1.31 (d, 3H, *J*= 6.0 Hz); ^{13}C NMR ($CDCl_3$): δ 135.4, 109.3, 93.7, 82.1, 75.9, 27.3, 26.7, 17.0.

To a cold (-78 °C) of **10** (10 g, 33.4 mmol) in THF (150 ml), n-BuLi (45.9 ml, 1.6 M, 73.5 mmol) in hexane was added dropwise. The mixture was stirred at -78°C for 1h and at rt for 1.5h. After addition of methyl chloroformate (2.8 ml, 36.7 mmol) at -65 °C, stirring was continued for 10 min at -65 °C and at rt for 20 min. The reaction mixture was poured onto crushed ice and extracted with ether (3x). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to give 6.6 g. Distillation (bp_4 65 °C) afforded **11a** (5.56 g, 28 mmol, 84 %); colorless oil; $[\alpha]^{20}_D$ -1.9° (c 1.04, $CHCl_3$); IR ν 2240, 1740. ^1H NMR ($CDCl_3$): δ 4.22 (m, 2H), 3.79 (s, 3H), 1.45, 1.43 (2s, 6H), 1.38 (d, 3H, *J*= 5.6 Hz); ^{13}C NMR ($CDCl_3$): δ 153.3, 110.6, 83.5, 77.1, 76.6, 71.1, 52.8, 27.1, 25.9, 17.3. Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.71; H, 6.99.

γ-Lactone 12 from alkyne 11a

A suspension of **11a** (2.0 g, 10.1 mmol) and Pd/C (16 mg) in methanol (60 ml) was stirred at rt under an atmosphere of D_2 (~ 99.8 %) for 1.5 h. Addition of a drop of NEt_3, filtration, evaporation *in vacuo* followed by kugelrohr distillation afforded **16** (1.9 g, 9.19 mmol, 91 %) oil; $[\alpha]^{20}_D$ +13.8° (c 1, $CHCl_3$); for undeuterated **16**: $[\alpha]^{19}_D$ 14.8° (c 1.13, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.70 (m, 4H), 3.50 (d, 1H, *J*= 8.2 Hz), 1.38, 1.34 (2s, 6H), 1.26 (d, 3H, *J*= 6.0 Hz). ^{13}C NMR ($CDCl_3$): δ 173.7, 108.0, 81.3, 76.5, 51.6, 30.2 (m), 27.3, 27.2, 26.7 (m), 17.4. Anal. Calcd. for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97. Found: C, 59.35; H, 9.03. A solution of **16** (1.9 g, 9.19 mmol) in THF and aqu. 2 N HCl (24 ml, 2:1) was stirred for 12 h at rt, neutralized

with icecold aqu. $NaHCO_3$, extracted with EE, dried ($MgSO_4$) and evaporated *in vacuo*. Purification by fc (PE/ EE 1:2) afforded **12** (0.89 g, 6.62 mmol, 72 %); colorless oil; $[\alpha]^{20}_D$ -61.1° (c 1.34, $CHCl_3$); for undeuterated **12**: $[\alpha]^{20}_D$ -61.5° (c 1.09, $CHCl_3$); lit.[15] **L-12**: $[\alpha]^{25}_D$ +51.6° (c 2.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 4.36 (broad d, 1H, *J*= 5.6 Hz), 3.80 (broad pent, 1H, *J*= 6.0 Hz), 2.63 (broad, 1H), 1.26 (d, 1H, *J*= 6.2 Hz). 177.3, 84.1, 69.7, 28.3 (m), 23.6 (m), 18.4. Anal. Calcd. for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.49; H, 7.65.

[2,2′,3,3′- $^2H_4$] D-Rhodinose (13):

To a cold (-78 °C) solution of **12** (0.89 g, 6.62 mmol) in ether (10 ml), dibal-H in n-hexane (16.5 ml, 1.0 M, 16.5 mmol) was added. The mixture was stirred for 25 min at this temp. and H_2O (3.5 ml) was added. After stirring for 15 min at rt, the mixture was filtered through a pad of Celite, concentrated under reduced pressure and finally traces of water were co-distilled with toluene. Purification by fc (PE/ EE 2.5:1 to EE) afforded **6** as a mixture of furanoses and pyranoses (0.68 g, 4.97 mmol, 75 %). Spectroscopic data are in agreement with those published in the literature[7].

γ-Lactone 14 from alkyne 11a

A suspension of **11a** (2.15 g, 10.8 mmol), $Pd/BaSO_4$ (32 mg) and quinoline (29 µl) in ether (20 ml) was stirred at rt under an atmosphere of D_2 (~ 99.8 %) for 3d. Filtration, evaporation *in vacuo* followed by cc (PE/ EE 1:1) afforded **17** (1.64 g, 8.1 mmol, 75 %); colorless oil; $[\alpha]_D^{17}$ -57.1° (c 1.17, $CHCl_3$); IR ν 1745, 1660. ^1H NMR ($CDCl_3$): δ 5.22 (d, 1H, *J*= 8.0 Hz), 3.84 (dq, 1H, *J*= 8.0, 6.0 Hz), 3.73 (s, 3H), 1.45, 1.43 (2s, 6H), 1.34 (d, 3H, *J*= 6.0 Hz). ^{13}C NMR ($CDCl_3$): δ 165.9, 145.2 (t), 122.2 (t), 109.2, 51.5, 27.4, 27.1, 17.1. Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.99; H, 8.05. Found: C, 60.12; H, 7.97. Acid-promoted cyclization of **17** (0.51 g, 2.5 mmol) was achieved as described for the preparation of **13**. After cc (PE/EE 1:1 to 1:3), **14** (0.21 g, 1.6 mmol, 65 %) was obtained as a colorless oil; $[\alpha]_D^{20}$= -41.2° (c 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 4.97 (d, 1H, *J*= 5.2 Hz), 3.97 (broad pent., 1H, *J*= 6.4 Hz), 3.14 (broad, 1H), 1.32 (d, 1H, *J*= 6.4 Hz); ^{13}C NMR ($CDCl_3$): δ 173.3, 153.5 (t), 122.4 (t), 87.2, 68.0, 18.8. Anal. Calcd. for $C_6H_8O_3$: C, 56.25; H, 6.29. Found: C, 56.04; H, 6.33.

[2,3- $^2H_2$] 2,3,6-Trideoxy-α,β-D-*threo*-hex-2-enopyranose (15):

Dibal-H-promoted reduction of **14** (0.11 g, 0.47 mmol) was achieved as described for the preparation of **13**. Purification by fc (PE/ EE 2.5:1 to EE) afforded **14** (0.021 g, 0.16 mmol, 34 %); colorless oil. Spectroscopic data are in agreement with those published in the literature[7].

***Mitsunobu*-Inversion of 12**

To a solution of **12** (0.5 g, 1.04 mmol) in toluene (10 ml) at 0 °C were added triphenyl phosphine (1.54 g, 3.62 mmol) and benzoic acid (0.71 g, 3.62 mmol). DEAD (0.9 ml, 3.62 mmol) was dissolved in toluene (4 ml) and added dropwise to the reaction mixture. The resulting solution was allowed to warm up to rt. After 14 h the precipitate was filtered and washed with toluene. The combined extracts were evaporated under reduced pressure and purified by cc (PE/ EE 2.5:1) to afford **18** (0.68 g, 0.99 mmol, 76 %); crystals, m.p. 103- 105 °C; $[\alpha]^{18}_D$ +20.2 (c 1.87, $CHCl_3$); for undeuterated **18**: $[\alpha]^{20}_D$ +18° (c 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.0 -7.4

(m, 5H), 5.33 (dq, 1H, *J*= 6.6, 4.6 Hz), 4.64 (broad d, 1H, *J*= 4.6 Hz), 1.42 (d, 1H, *J*= 6.6 Hz); ^{13}C NMR ($CDCl_3$): δ 173.3, 153.5 (t), 122.4 (t), 87.2, 68.0, 18.8. Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.49; H, 6.18.

[2,2',3,3'- $^2H_4$]-L-Amicetose (19): Dibal-H-promoted reduction of **18** (0.4 g, 1.68 mmol) was achieved as described for the preparation of **13**.Purification by fc (PE/ EE 1:1 to EE) afforded **19** (0.15 g, 1.1 mmol, 68 %); colorless oil; $[\alpha]^{21}_D$ -39.8° (c 1.34, acetone). Spectroscopic data are in agreement with those published in the literature[7].

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