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3,3′-Dideoxytrehaloses via dimerisation of 2-hydroxyglycal esters☆

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Abstract

The susceptibility of 2-hydroxyglycal esters i.e., 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol and its D-*lyxo* analog towards dimerization to 2,3-unsaturated α,α-trehaloses is described, smoothly occurring in moist dichloromethane or acetone solution in the presence of iodine or boron trifluoride. The reaction involves Ferrier ionization and addition of water at C-1 of the delocalized glycosyl oxocarbenium ion, followed by addition of the hex-2-enopyranose thus formed, with its 1-OH, onto the educt still present. Hydrogenation of the dimers thus formed, i.e., 2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranosyl 2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranoside and its D-*threo*/D-*threo* analog proceeds with high stereoselectivity to give the peracetylated 3,3′-dideoxy-α,α-trehaloses with D-*ribo*/D-*ribo* and D-*lyxo*/D-*lyxo* configuration.

Keywords: 3,3′-Dideoxy-α,α-trehaloses; 2-Hydroxyglycal esters; Allylic rearrangement; Dihydropyrans

1. Introduction

Aside from glycals, which have extensively been exploited as precursors for a variety of naturally occurring products [2], the 2-acyloxyglycals of type **1** and **2**, although just as accessible [3], have found considerably less attention. In fact, their unique enolester-masked carbonyl group at C-2 adds a structural function that considerably extends the variability of their ensuing reactions [4], and, hence, their utility as enantiopure building blocks. Thus, the C-2 carbonyl group in the D-glucose-derived 2-acetoxy- and 2-benzoyloxy-glucal esters **1** and **2** can be liberated by *N*-bromosuccinimide-induced methanolysis to afford ulosyl bromides of type **3** [5] that proved to be particularly efficient 'indirect' β-D-mannosyl donors [5,6]. Similar potential as 'indirect' β-D-mannosaminyl donors [7] applies to the oximinoglycosulosyl bromides **5**, smoothly derived from **1** and **2** by a high-yielding 3-step procedure involving hydroxylaminolysis (→**4** [8]), benzoylation, and photobromination [9,10]. Other important hydroxyglycal ester transformations involve Lewis acid-induced allylic rearrangements to 3-deoxy-hex-2-enopyranoses by intra- or intermolecular addition at the anomeric center of an acetoxy group (**1**→**6** [11]), of alkoxy residues (**1**→**7** [12]), or of an acylperoxy group, which by fragmentation of the primary adduct leads to pyranoid enollactones (→**8** [13]) (Scheme 1).

☆ Enantiopure building blocks from sugars, Part 25. For Part 24, see Ref. [1].

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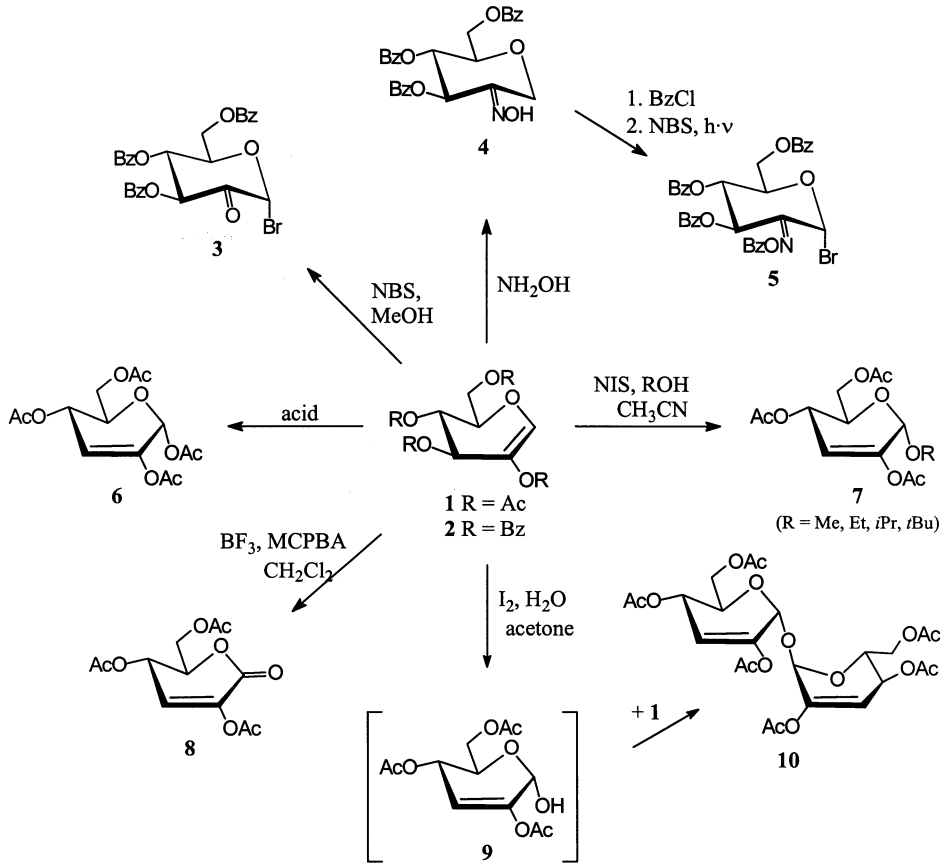


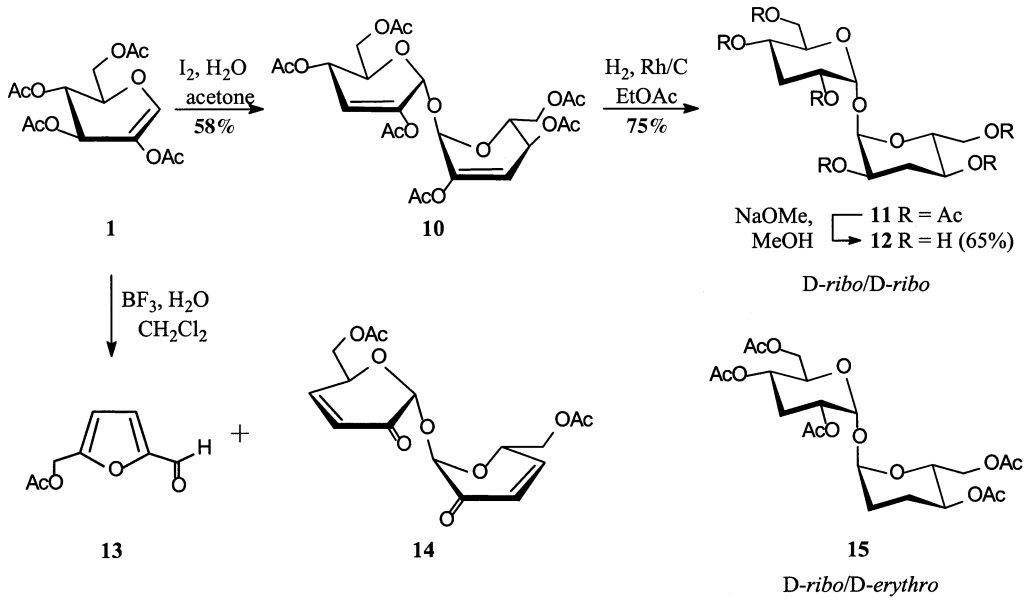
Scheme 1.

Described herein is a useful addition to this multifaceted array of versatile building blocks, namely the Lewis acid-promoted allylic rearrangement of 2-acetoxyglucal triacetate **1** and its galactose-derived 4-epimeric analog **16** and subsequent dimerization to 2,3:2′,3′-unsaturated trehalose-type dimers (**10** and **18**). This reaction, which has its analogy in the Lewis acid-induced dimerization of tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (tri-*O*-acetyl-D-glucal) [14], opened up the way to 3,3′-dideoxy-α,α,-trehalose analogs that are of interest as trehalase inhibitors.

2. Results and discussion

2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (**1**) in boiling acetic acid [11a] or cold acetic anhydride in the presence of zinc chloride [11b], or in benzene with catalytic amounts of boron trifluoride etherate [11c], undergoes Ferrier rearrangement to an anomeric mixture of 3-deoxyhex-2-enopyranoses in which the α anomer **6** is the preponderant product. When the solvents used are not absolutely dry, or by the deliberate addition of small amounts of water, the Ferrier rearrangement is followed by further reactions, the respective products then depending on the conditions used. Exposure of **1** in dichloromethane solution to borotrifluoride diethyl etherate in the presence of water rapidly forms a mixture of three main components, characterized as acetoxymethylfurfural (**13**), the α,α dimer **10**, and the bis-enone **14**. Their formation can be readily rationalized by **14** arising from **10** via hydrolytic cleavage of the enolester and subsequent elimination of the 4-acetoxy group, whereas **13** is an ensuing product of the intermediate hexenopyranose **9** (Scheme 2).

Evaluation of various other catalyst/solvent combinations, e.g., zinc chloride/dichloromethane, *N*-iodosuccinimide or iodine/acetonitrile, eventually led to iodine/acetone in the presence of water as the most suitable conditions for the conversion **1**→**10**:



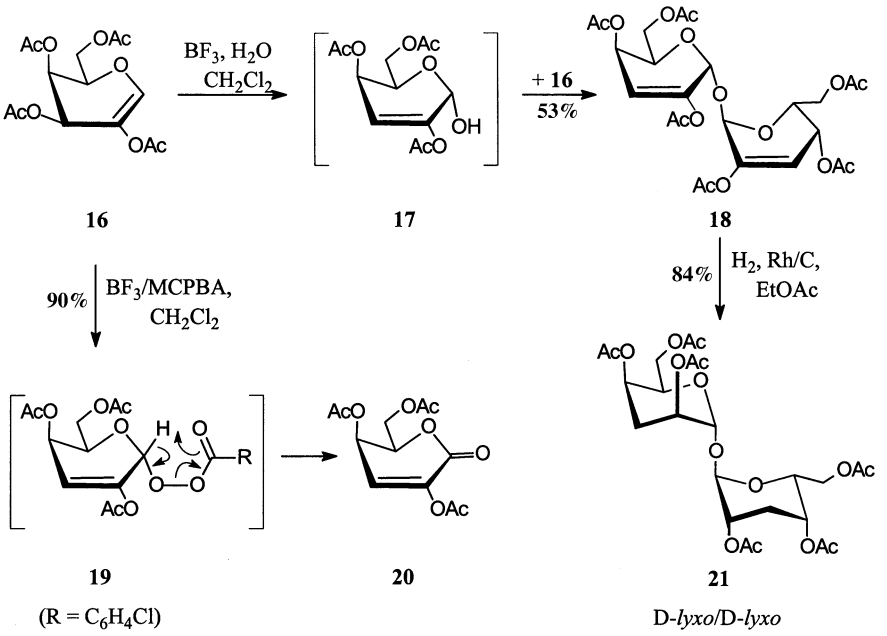
Scheme 2.

the reaction is rapid (30 min, 0 °C) and allows the isolation of **10** in 58% yield. Saturation of the two enolester double bonds was readily effected only when hydrogenation was performed over 5% rhodium on carbon in ethyl acetate, providing the 3,3′-dideoxy-trehalose in the form of its peracetate **11** (75% isol. yield), or in its free form **12** following standard O-deacetylation. Over Pd, Pd/C and Pt/C catalysts, the hydrogenation of **10** proceeded sluggishly and stereochemically non-uniformly, whereas the use of rhodium on carbon catalyst and educt in a 1:1 ratio led to some reductive deacetoxylation as evidenced by the isolation of 8% of the 2,3:3′-trideoxy derivative **15**.

This simple 3-step sequence for the conversion of **1** into a 3,3′-dideoxy-α,α-trehalose, i.e., **1** → **10** → **11** → **12**, appears to be generally applicable, since the respective D-*lyxo*-hex-1-enitol derivative **16** was also readily converted into the D-*threo*/D-*threo*-trehalose analog **18**. Interestingly, the 2-acetoxy-D-galactal **16** was considerably less reactive than its D-glucal counterpart—a reactivity difference that has previously been observed [15] in the acid-induced Ferrier rearrangement to the hex-2-enopyranose tetraacetate (4-epimer of **6**). Thus, exposure of **16** to iodine in aqueous acetone had no effect; under somewhat more forcing conditions, i.e., boron trifluoride in dichloromethane containing water, however, the conversion was readily achieved to yield (53%) the nicely crystalline D-*threo*/D-*threo* dimer **18**; it was hydrogenated with remarkable stereoselectivity (84% isol. yield) to the equally crystalline D-*lyxo*/D-*lyxo*-3-3′-dideoxy trehalose hexaacetate **20** (Scheme 3).

It is interesting to note that the coupling of the α-D-hexenopyranose intermediate **17** with unreacted **16**, i.e., **16** + **17** → **18**, cannot be intercepted by other reagents, e.g., by *m*-chloroperbenzoic acid to form the enollactone **20**. Only when the BF_3-mediated peroxidation of **16** was effected under strictly anhydrous conditions requiring the removal of water from the commercially available MCPBA, a high yield (90%) of the enollactone could be obtained—obviously via fragmentation of the 1-peroxyacyl-hexenopyranose intermediate **19** [13].

Although configurational assignments could readily be inferred from ^1H and ^{13}C NMR data, the high crystallinity of the D-galactal-derived dimer **18** invited structural verification by X-ray crystallography. As depicted in Fig. 1, the molecular geometry of **18** clearly unveils the two *O*-linked dihydropyrane rings to be in a $^{O}H_5$ halfchair conformation, in which the ring oxygen is slightly more above the plane formed by carbons 1–4 than C-5 is below (0.36 vs. 0.32 Å). The bond lengths and bond



Scheme 3.

angles are within the expected ranges [16], the dihedral angles in the two pyranoid rings differ only slightly from each other (cf. Table 1, forms A and B, respectively), and, moreover are in very close agreement to those found for the α-D-*threo*-hex-2-enopyranose analogs **22** [17] and **23** [18]. The C-4–C-5–O-5–C-1 dihedral angles are uniformly in the 64° range, evidence for an essentially identical $^{O}H_{5}$ conformation of **18**, **22** and **23**.

3. Experimental

General methods.—^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded at 25 °C with a Bruker AC 300 spectrometer. Chemical shifts (δ) are given in ppm relative to the signal for internal Me_4Si ($CDCl_3$). Column chromatography was performed on Kieselgel 60 (E. Merck, 230 mesh) and fractions were monitored by TLC on Kieselgel 60 F_{254} (E. Merck) by detection with UV light and then charring with H_2SO_4. Optical rotations were measured for solutions in $CHCl_3$ at 20 °C with a Perkin–Elmer 241 polarimeter, using a 10 cm/1 mL cell.

2,4,6-Tri-O-*acetyl-3-deoxy*-α-D-erythro-*hex-2-enopyranosyl 2,4,6-tri*-O-*acetyl-3-deoxy*-α-D-erythro-*hex-2-enopyranoside* (**10**).—A solution of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (**1**, 3.96 g, 12 mmol) [3e] in dry acetone (8 mL) was cooled (0 °C), iodine (3.05 g, 12 mmol) and water (0.12 mL, 8 mmol) was added, and the mixture

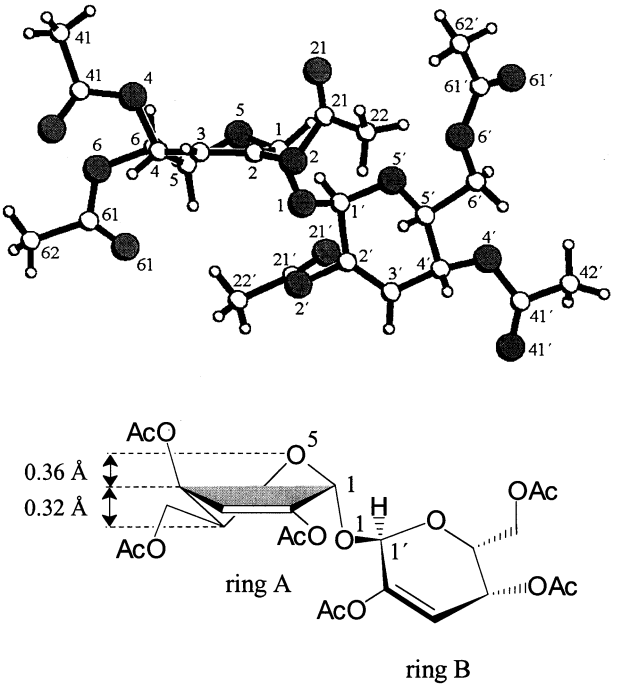
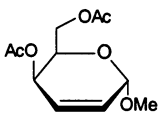
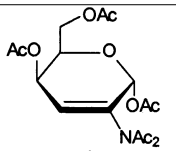


Fig. 1. Perspective drawing of the molecular structure of 2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*threo*-hex-2-enopyranosyl 2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*threo*-hex-2-enopyranoside (**17**), revealing a $^{O}H_{5}$ halfchair conformation for each of the pyranoid rings.

Table 1
Selected torsion angles (°) for **18**, and the monomeric analogs methyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (**22**) [17] and 1,4,6-tri-*O*-acetyl-2-(*N*,*N*-diacetylamido)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranose (**23**) [18]

Dihedral angels	**18**			
	A	B	**22** [a]	**23** [b]
Pyranoid ring				
O-5–C-1–C-2–C-3	+12.2	+14.4	+13.2	+14.4
C-1–C-2–C-3–C-4	+3.6	+1.9	+1.2	+6.4
C-2–C-3–C-4–C-5	+12.8	+12.1	+14.8	+7.1
C-3–C-4–C-5–O-5	−44.4	−42.3	−46.6	−40.5
C-4–C-5–O-5–C-1	+64.4	+62.6	+64.9	+64.1
C-5–O-5–C-1–C-2	−46.1	−46.5	−46.8	−49.3
Glycosidic linkage				
O-5–C-1–O-1–C-1′	+74.5	+76.5	+67.0	+76.8
Substituent angles				
C-2–C-3–C-4–O-4	−107.8	−108.6	−102.4	−113.0
O-4–C-4–C-5–C-6	−41.3	−38.7	−53.2	−39.5
O-4–C-4–C-5–O-5	+76.0	+79.6	+68.7	+80.8
Cremer–Pople puckering parameters [20]				
Q	0.466	0.444	0.466	0.475
Θ	52.4	51.0	51.3	55.1
Φ	328.1	331.9	326.0	336.0
Conformation	$^{O}H_5$	$^{O}H_5$	$^{O}H_5$	$^{O}H_5(\rightarrow {}^{O}E)$

[a] Dihedral angles not given in Ref. [17] and the Cremer–Pople parameters were calculated by S. Immel from the original coordinates (REFC THHXPY).
[b] Cremer–Pople parameters were calculated by S. Immel from the original coordinates (REFC AAXTHP).

was stirred at 0 °C for 30 min. The reaction was quenched with satd. $Na_2S_2O_3$/satd. $NaHCO_3$ solution (3:1, 40 mL), extracted with CH_2Cl_2, followed by consecutive washing of the organic phase with water (30 mL), satd. $NaHCO_3$ (2 × 20 mL) and water (30 mL), drying ($MgSO_4$), and evaporation to dryness. Purification of the syrupy residue by elution from a silica gel column (3 × 30 cm) with 4:1 toluene–EtOAc afforded, after removal of the solvents in vacuo, 1.95 g (58%) of **10** as a colorless syrup; R_f 0.45 in 1:1 toluene–EtOAc; $[\alpha]_D^{20} + 64.6°$ (c 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 5.83 (d, 1 H, H-3), 5.47 (ddd, 1 H, H-4), 5.42 (bs, 1 H, H-1), 4.26 (dd, 1 H, H-6b), 4.13 (m, 2 H, H-5, H-6a), 2.18, 2.10, 2.09 (three 3 H-s, AcCH_3), $J_{1,4} \sim 0.7$, $J_{3,4}$ 2.0, $J_{4,5}$ 9.5, $J_{5,6a} \sim 2.6$, $J_{5,6b}$ 12.0 Hz. ^{13}C NMR ($CDCl_3$): δ 170.6 (3 AcCO), 169.9, 167.8, 145.6 (C-2), 115.8 (C-3), 89.4 (C-1), 67.5 (C-5), 65.3 (C-4), 62.5 (C-6), 20.8, 20.8, 20.6 (3 CH_3); FD MS: m/z 581 [$M^+ + Na$]. Anal. Calcd for $C_{24}H_{30}O_{15}$ (558.5): C, 51.60; H, 5.41. Found: C, 51.41; H, 5.32.

When performing the reaction of **1** in CH_2Cl_2 (990 mg in 20 mL) with $BF_3{\cdot}Et_2O$ (0.6 mL) in the presence of water (0.1 mL) by stirring at ambient temperature for 1 h, an approximate 2:1:1 mixture of dienone **14**, α,α dimer **10**, and furfural **13** (R_f 0.6, 0.45 and 0.4, resp., in 1:1 toluene–EtOAc), which, on workup as described above, could be separated on a silica gel column by elution with 4:1 toluene–EtOAc. The product eluted first was secured as a colorless oil (55 mg, 11 %) and proved to be 5-acetoxymethyl-2-furanaldehyde (**13**) by identity of its ^{1}H NMR data with that of an authentic sample (from Sigma–Aldrich Chemie). The fraction closely following was rich in **10** (TLC, ^{1}H NMR). The dienone **14**, eluted last, gave upon evaporation of the appropriate fraction, 125 mg (23 %) of a colorless syrup; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.98 (dd, 1 H, H-4), 6.18 (dd, 1 H,

H-3), 5.28 (s, 1 H, H-1), 4.83 (ddd, 1 H, H-5), 4.39 and 4.28 (two 1 H-dd, two H-6), 2.10 (s, 3 H, AcC*H*$_3$), $J_{3,4}$ 10.7, $J_{3,5}$ 2.4, $J_{4,5}$ 1.7, $J_{5,6a}$ 4.5, $J_{5,6b}$ 5.1, $J_{6,6}$ 11.8 Hz; FD MS : $m/z + 377$ [M + Na$^+$].

*Hexa-*O*-acetyl-3,3′-dideoxy-α,α-trehalose (2,4,6-Tri-*O*-acetyl-3-deoxy-α-*D*-ribo-hexopyranosyl 2,4,6-tri-*O*-acetyl-3-deoxy-α-*D*-ribo-hexopyranoside)* (**11**).—A solution of *erythro*-disaccharide **10** (340 mg, 0.6 mmol) in EtOAc (10 mL) was hydrogenated over 100 mg of 5 % rhodium on charcoal at ambient temperature for 20 h. The solution was then filtered over Celite and the residue was washed with EtOAc (80 mL), followed by removal of the solvent in vacuo. The resulting syrup was subjected to purification on a silica gel column (2 × 30 cm) with 9:1 CH_2Cl_2–EtOAc. The eluates carrying **11** (R_f 0.38 in 1:1 toluene–EtOAc) were collected and evaporated to dryness, 260 mg (75 %) of a colorless syrup of $[\alpha]_D^{20} + 132$ (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.22 (d, 1 H, H-1), 4.96 (ddd, 1 H, H-2), 4.83 (ddd, 1 H, H-4), 4.20 and 4.08 (two 1 H-dd, two H-6), 3.98 (ddd, 1 H, H-5), 2.36 (ddd, 1 H, H-3e), 2.08 (6 H, 3 AcCH$_3$) and 2.07 (3 H), 2.05 (m, 1 H, H-3a); $J_{1,2}$ 3.4, $J_{2,3a}$ 12.3, $J_{2,3e}$ 4.6, $J_{3a,4}$ 10.8, $J_{3e,4}$ 4.8, $J_{4,5}$ 10.5, $J_{5,6a}$ 2.1, $J_{5,6b}$ 5.9, $J_{6,6}$ 12.1 Hz; ^{13}C NMR ($CDCl_3$): δ 170.8 (3 C=O), 169.6, 169.6, 90.9 (C-1), 68.6 (C-5), 67.4 (C-2), 65.9 (C-4), 62.3 (C-6), 28.9 (C-3), 20.9 (3 CH_3), 20.7, 20.7; FD MS: *m/z* 563 [MH$^+$], 562 [M$^+$], 273 [tri-*O*-acetyl-3-deoxyglycosyl$^+$]. Anal. Calcd for $C_{24}H_{34}O_{15}$ (562.5): C, 51.24; H, 6.09. Found: C, 51.09; H, 6.02.

*4,6-Di-*O*-acetyl-2,3-dideoxy-α-*D*-erythro-hexopyranosyl 2,4,6-tri-*O*-acetyl-3-deoxy-α-*D*-ribo-hexopyranoside* (**15**).—When using larger amounts of catalyst in the hydrogenation of **10** as described above, e.g., a 1:1 ratio in mg, a minor product was detectable in the reaction mixture (R_f 0.43 in 1:1 toluene–EtOAc) which could be eluted separately from a column and was obtained as a colorless syrup (28 mg, 8 %), which proved to be the 4-deoxygenation product **15**; $[\alpha]_D^{20} + 114°$ (*c* 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): (a) *erythro* part: δ 5.16 (broadened s, 1 H, H-1), 4.73 (ddd, 1 H, H-4), 4.20 and 4.06 (1 H-dd each, two H-6), 3.95 (ddd, 1 H, H-5), 2.06–1.90 (7 H-m, 2 AcC*H*$_3$, H-3b), 1.83 (3 H-m, two H-2, H-3a), $J_{1,2} \leq 0.5$, $J_{4,5}$ 10.0, $J_{5,6}$ 2.1 and 6.1, $J_{6,6}$ 11.7 Hz; (b) *ribo* part: δ 5.24 (d, 1 H, H-1), 4.96 (ddd, 1 H, H-2), 4.86 (ddd, 1 H, H-4), 4.24 and 4.10 (two 1 H-dd, two H-6), 3.89 (ddd, 1 H, H-5), 2.32 (ddd, 1 H, H-3b), 2.05 (10 H-m, H-3a, 3 AcC*H*$_3$); $J_{1,2}$ 3.5, $J_{2,3a}$ 4.7, $J_{2,3b}$ 12.4, $J_{3a,4}$ 4.9, $J_{3b,4}$ 10.8, $J_{4,5}$ 10.1, $J_{5,6a}$ 2.4, $J_{5,6b}$ 5.2, $J_{6,6}$ 11.8 Hz; FD MS: *m/z* 505 [MH$^+$], 504 [M$^+$].

*3,3′-Dideoxy-α,α-trehalose (3-deoxy-α-*D*-ribo-hexopyranosyl 3-deoxy-α-*D*-ribo-hexopyranoside)* (**12**).—To a solution of hexaacetate **11** (170 mg, 0.3 mmol) in MeOH (5 mL) was added 0.33 mL of N methanolic MeONa and the mixture was kept at ambient temperature for 1 h, then quenched with AcOH (1 mL), and evaporated to dryness. Purification of the residue by elution from a silica gel column (1.5 × 20 cm) with 2:1 $CHCl_3$–MeOH gave, after evaporation of the appropriate fraction, 83 mg (86 %) of **12** as a chromatographically uniform solid; R_f 0.34 in 2:1 $CHCl_3$–MeOH; $[\alpha]_D^{20} + 161°$ (*c* 1.3, MeOH); ^{1}H NMR (300 MHz, MeOH-d_4): δ 5.08 (d, 1 H, H-1), 3.8–3.5 (unresolved m, 5 H, H-2, H-4, H-5, and two H-6), 2.09 (m, 1 H, H-3b), 1.94 (m, 1 H, H-3a), $J_{1,2}$ 3.4 Hz; ^{13}C NMR (75.5 MHz, MeOH-d_4): δ 92.7 (C-1), 70.4 (C-5), 67.4 (C-2), 65.3 (C-4), 61.8 (C-6), 35.3 (C-3); FD MS: *m/z* 333 [M$^+$ + Na], 310 [M$^+$], 293 [M$^+$–OH]. Anal. Calcd for $C_{12}H_{22}O_9$ (310.3): C, 46.45; H, 7.15. Found: C, 46.35; H, 7.03.

*2,4,6-Tri-*O*-acetyl-3-deoxy-α-*D*-threo-hex-2-enopyranosyl 2,4,6-tri-*O*-acetyl-3-*deoxy-α-*D*-threo-hex-2-enopyranoside* (**18**).—A solution of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-*D*-*lyxo*-hex-1-enitol (**16**, 660 mg, 2 mmol) [3e,15,19] in CH_2Cl_2 (10 mL) was stirred with $BF_3 \cdot Et_2O$ (803 μL, 20 mmol) for about 5 min at room temperature. Water (360 μL, 20 mmol) was then added, followed by stirring for another 5 min and quenching the reaction by pouring into satd aq $NaHCO_3$ (20 mL). The mixture was diluted with CH_2Cl_2 (50 mL), and the organic phase was separated, dried ($MgSO_4$), evaporated to dryness, and the syrupy residue was purified by elution from a silica gel column (1.5 × 25 cm) with 9:1 CH_2Cl_2–EtOAc. Removal of the solvents gave a syrup, which crystallized from *t*-BuOMe/*n*-pentane: 290 mg (53%) of **18** as colorless prisms; mp 156.0–156.5 °C; $[\alpha]_D^{20}$ −194.8° (*c*

1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 6.06 (d, 1 H, H-3), 5.53 (s, 1 H, H-1), 5.31 (ddd, 1 H, H-4), 4.39–4.32 (m, 2 H, H-5, H-6b), 4.22 (ddd, 1 H, H-6a), 2.24 (3 s, 3 H each, 3 AcCH_3), 2.14, 2.12; $J_{3,4}$ 6.1, $J_{4,5}$ 2.2, $J_{4,6a} \sim 1.0$, $J_{5,6a}$ 3.6, $J_{6a,b}$ 9.8 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 170.4, 170.1, 167.7 (3 Ac*C*O), 148.6 (C-2), 112.4 (C-3), 88.6 (C-1), 67.0 (C-5), 64.0 (C-4), 62.2 (C-6), 20.8 (3 $AcCH_3$), 20.7, 20.6; FI MS: m/z 558 [M^+]. Anal. Calcd for $C_{24}H_{30}O_{15}$ (558.49): C 51.60; H 5.41. Found: C 51.58; H 5.35.

The crystal of **18**, subjected to X-ray analysis, had the dimensions $0.55 \times 0.375 \times 0.175$ mm, was monoclinic, space group $P2_1$ with $a = 7.859$ (4), $b = 22.401$ (7), and $c = 8.092$ (4) Å, $\alpha = \gamma = 90°$, $\beta = 108.16$ (4)°, $V = 1353.1$ Å^3, $Z = 2$, $T = 298$ K, μ(Mo Kα) = 0.11 mm^{-1}, and Dc = 1.37 g cm^{-3}. A total of 2444 reflections were collected on a Enraf–Nonius CAD4 diffractometer, equipped with a graphite-monochromated Mo Kα ($\lambda = 0.71093$ Å) radiation using 1928 independent reflections to refine the complete structure, i.e., $R(F)$ 0.0357 for 1860 reflections with $I \geq 2\sigma I$, $wR(F^2)$, and 0.0961 for all 1928 reflections ($w = 1/(\sigma^2(F_0^2) + (0.0725)^2 + 0.248P)$; $P = (F_0^2 - 2F_c^2)/3$. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms on the molecule were considered in calculated positions with the $1.2 \times U_{eq}$ value of the corresponding atom. Data reduction was done by a Stoe-REDU4 program, structural resolution and refinement by SHELXS-86 and SHELXL-93 [21]. For atomic coordinates and further details, see Section 4.

2,4,6-Tri-O-*acetyl-3-deoxy*-α-D-lyxo-*hexopyranosyl 2,4,6-tri*-O-*acetyl-3-deoxy*-α-D-lyxo-*hexopyranoside* (**21**).—In a hydrogenation vessel, rhodium on carbon (5 %, 30 mg) was added to an EtOAc solution of *threo*/*threo*-disaccharide **18** (140 mg, 0.25 mmol, in 15 mL), and the mixture was hydrogenated over H_2 for 16 h. Subsequent filtration through Kieselgur, thorough washing with EtOAc and removal of the solvent in vacuo left a syrup which crystallized from 2-propanol: 120 mg (84 %) of **20** as colorless, waddy needles; mp 201 °C; [α] +48.9° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.21 (bs, 1 H, H-1), 4.90 (bs, 1 H, H-4), 4.75 (bs, 1 H, H-2), 4.26–4.13 (m, 3 H, H-5, two 6-H), 2.38 (brm, 1 H, H-3b), 2.16 (m, 1 H, H-3a), 2.11, 2.10, 2.05 (three 3 H-s, 3 AcCH_3); $J_{1,2} < 0.5$ Hz; ^{13}C NMR ($CDCl_3$): δ 170.6, 170.3, 169.9 (3 Ac*C*O), 91.6 (C-1), 67.5 (C-5), 66.0 (C-2), 64.8 (C-4), 63.0 (C-6), 26.7 (C-3), 21.0, 21.0, 20.6 (3 $AcCH_3$); FD MS: m/z 562 [$M^+ - H$]. Anal. Calcd for $C_{24}H_{34}O_{15}$ (562.5): C, 51.24; H, 6.09. Found: C, 51.19; H, 6.15.

2,4,6-Tri-O-*acetyl-3-deoxy*-D-threo-*hex-2-enono-1,5-lactone [(5*R*,6*R*)-3,5-bis(acetoxy)-6-acetoxymethyl-5,6-dihydro-2*H*-pyran-2-one]* (**20**).—A solution of 1.0 g (3 mmol) of **16** [15] in CH_2Cl_2 (10 mL) was stirred for 20 min at ambient temperature, then cooled to −20 °C and followed by the addition of $BF_3 \cdot Et_2O$ (267 μL, 2.2 mmol) and of a solution of anhydrous, 85 % *m*-chloroperbenzoic acid[1] in CH_2Cl_2 (600 mg, 3.5 mmol, in 6 mL). After vigorous stirring for 15 min at −20 °C, the mixture was quenched by pouring into satd. $NaHCO_3$ solution (15 mL) containing 10–20 mg of $Na_2S_2O_3$ (i.e., without prior warming to ambient temperature). The organic phase is removed, and the aqueous layer is extracted with CH_2Cl_2 (2 × 15 mL), followed by concentration of the combined organic phases in vacuo to a syrup, which was purified by elution from a silica gel column (2 × 25 cm) with 2:1 toluene–EtOAc. Removal of the solvents from the eluates with R_f 0.30 (TLC in 2:1 toluene–EtOAc) gave 786 mg (90 %) of enelactone **20** as a colorless syrup; $[\alpha]_D^{20}$ −151.5° (*c* 1, $CHCl_3$); lit. [22] : $[\alpha]_D^{25}$ −150° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.64 (d, 1 H, H-3), 5.44 (dd, 1 H, H-4), 4.93 (dt, 1 H, H-5), 4.36 (d, 2 H, 7-H_2), 2.20 (three 3 H-s, 3 AcCH_3), 2.04, 2.03, $J_{4,5}$ 6.4, $J_{5,6}$ 2.6, $J_{6,7}$ 6.3 Hz; ^{13}C NMR ($CDCl_3$): δ 170.5, 169.8, 168.1

[1] The *m*-chloroperbenzoic acid used was the commercially available anhydrous 85% grade, i.e., containing 15% *m*-chlorobenzoic acid. Since the overall reaction requires the BF_3-induced generation of an allylcarboxonium ion intermediate subsequently undergoing peroxidation, conditions have to be strictly anhydrous (e.g., dry CH_2Cl_2 as the solvent) in order to prevent hydrolysis of the Lewis acid. By consequence, it is essential that lower grade MCPBA (e.g., 55% with 30–35% of water and 10–15% 3-chlorobenzoic acid) is freed from water before use. This is readily effected by dissolving 55% MCPBA in CH_2Cl_2 (5 g in 100 mL of freshly distilled solvent to exclude the presence of small amounts of HCl), separating the aqueous layer, drying of the organic phase (Na_2SO_4), and removal of the solvent in vacuo (bath temp. below 35 °C) to yield a fluffy solid that can directly be used.

(3 Ac*C*O), 157.6 (C-1), 141.7 (C-2), 124.6 (C-3), 76.2 (C-5), 63.0 (C-4), 61.3 (C-6), 20.6, 20.4, 20.3 (3 Ac*C*H$_3$); FI MS: $m/z = 287$ [MH$^+$], 286 [M$^+$]. Anal. Calcd for $C_{12}H_{14}O_8$ (286.2): C, 50.37; H, 4.91. Found: C, 50.33; H, 4.96.

4. Supplementary material

Tables of atomic coordinates, bond lengths and bond angles have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-121452. Copies of this data can be obtained, free of charge, from CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336-033 or e-mail: deposit@ccdc.cam.ac.uk).

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