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STEREOSELECTIVE SYNTHESIS OF *C*-GLYCOSYL COMPOUNDS *via* MICHAEL ADDITION OF TRIMETHYLSILYL ENOL ETHERS AND ENAMINES TO HEX-1-ENOPYRAN-3-ULOSES

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ABSTRACT

The titanium(IV)-catalyzed addition of trimethylsilyl enol ethers to 2,4,6-tri-*O*-acylhex-1-enopyran-3-uloses (**3** and **4**) gave stereoselectively 3,6-di-*O*-acyl-4-deoxy-β-D-*glycero*-hex-3-enopyranosyl-2-ulose derivatives. The formation of the *C*-glycosyl bond was accompanied by a 2→3 acyl shift, followed by the elimination of the 4-acyloxy substituent. Similarly, the reaction of 1-pyrrolidinocyclohexene with **3** and **4** also led stereoselectively to 2-(2,4,6-tri-*O*-acyl-β-D-*ribo*-hexopyranosyl)cyclohexanones. In this Michael addition, among the eight possible diastereomers, only one was formed. The high stereocontrol of both *C*-glycosyl compound syntheses is explained in terms of cyclic transition complexes **A** and **C**.

INTRODUCTION

The synthesis of *C*-glycosyl compounds is receiving increasing attention owing to the number of important natural products possessing *C*-glycosyl bonds, *e.g.*, the *C*-nucleosides[1] and *C*-glycosylflavonoids[2]. Furthermore, synthetic *C*-glycosyl compounds represent interesting chiral synthons, suitable for the synthesis of complex molecules, since they contain a large number of chiral centers and functional groups. For these reasons, new methods for the synthesis of these compounds have been recently developed. Whereas the earlier methods only allowed the introduction of one C-atom, *e.g.*, *via* cyanide[3], the new procedures open up ways to connect larger structures at C-1. Most of these *C*-glycosyl compound syntheses involve the attack of *C*-nucleophiles at the anomeric center of glycosyl halides, lactones[5], or thioglycosides[6]. Another *C*-glycosyl compound synthesis utilizes the addition of glycosyl adicals to double-bond systems[7]. A new flexible concept is based on the "Umpolung" of the chemical reactivity at the anomeric center. Carbanions of 1-deoxy-1-nitro-monosaccharides[8] and, more generally, glycosyllithium compounds[9] have been converted successfully into C-glycosyl compounds by treatment with various electrophiles.

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1 R = Ac
2 R = Me_3CCO

3 R = Ac
4 R = Me_3CCO

RESULTS AND DISCUSSION

In this report, we describe a new method for the synthesis of highly functionalized C-glycosyl compounds consisting of the reaction of 2,4,6-tri-*O*-acetyl- (**3**) and 2,4,6-tri-*O*-pivaloyl-1-deoxy-D-*erythro*-hex-1-enopyran-3-ulose (**4**) with trimethylsilyl enol ethers[10]. The acyl-protected enuloses **3** and **4**, which act as the Michael acceptors in these Mukaiyama reactions[11], were best obtained from the corresponding 1,2,4,6-tetra-*O*-acylglycopyranoses (**1** and **2**) by means of the oxidation of the free OH-3 with dimethyl sulfoxide and acetic anhydride or chlorosulfonyl isocyanate in dichloromethane[12]. In compounds **3** and **4**, the orbital-controlled reacting electrophilic terminus of the α,β-unsaturated carbonyl system is located at the anomeric carbon atom. In contrast to alcohols, which cannot be added to this center stereoselectively[1], the trimethylsilyl enol ethers of ketones **5–8**, aldehyde **9**, and ester **10** reacted highly stereoselectively, in the presence of titanium(IV) catalyst, with the acetyl-protected enulose **3** to form the *C*-glycosyl compounds **11–17**. The reactions took place in dichloromethane at $-78°$ in the presence of titanium(IV) chloride or titanium(IV) chloride–titanium(IV) isopropylate. The reactions were accompanied by an intensive red or orange color and could be monitored by t.l.c.. The nucleophilic addition of the silyl enol ether is apparently followed by a 2→3 acyl shift and subsequent elimination of the acyloxy-4 substituent. After the reaction was finished, the titanium complex was removed by sodium carbonate and, if necessary, the *C*-glycosyl compounds were purified by flash chromatography. The results are summarized in Table I.

As shown in Table I, the reaction of **3** with cyclohexenyl trimethylsilyl ether **5** gave a *C*-glycosyl compound **11** having two new chiral centers (C-1,2′). Among four possible diastereomers, only one was formed in high yield. Analogously, the trimethylsilyl enol ethers of acetophenone (**7**), acetone (**8**), isobutyraldehyde (**9**), and *tert*butyl acetate (**10**) stereospecifically gave **13–16** which, on the basis of their ^{1}H-n.m.r. spectra, have the β-D configuration.

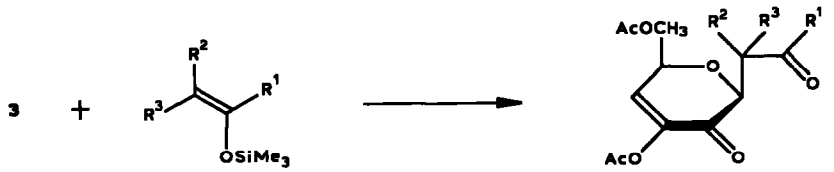
In the reaction of the cyclopentenyl trimethylsilyl ether **6**, a second diastereomer **13** was formed beside the main product **12**. This by-product presumably also has the β-D configuration at the anomeric center, but an opposite configuration relative to **12** at glycosylated C-2′. The cyclopentyl derivative **6** is relatively planar. This property may cause the lower stereocontrol during the approach to **3** as the

TABLE I

SYNTHESIS OF COMPOUNDS 11-16 FROM TRIMETHYLSILYL ENOL ETHERS AND 2,4,6-TRI-*O*-ACETYL-1-DEOXY-D-*erythro*-HEX-1-ENOPYRAN-3-ULOSE (3)[a]

Trimethylsilyl enol ether	*C-Glycosyl compound*	*Ratio of $TiCl_4$ to Ti-isopropylate*	*Reaction time (h)*	*Yield (%)*
5	11	1:0	0.5	90
6	12[b]	1:0	0.5	55[b]
7	13	2:1	4	76
8	14	2:1	20	50
9	15	2:0	17	47
10	16	1:0	17	40

[a]In dichloromethane at −78°. [b]A 5:1 mixture of diastereomers, see Results and Discussion, and Experimental sections.

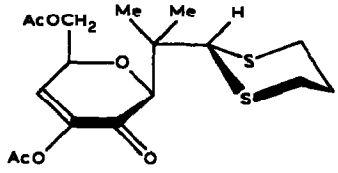


5 $R^1, R^2 = -(CH_2)_4-, R^3 = H$
6 $R^1, R^2 = -(CH_2)_3-, R^3 = H$
7 $R^1 = Ph, R^2 = R^3 = H$
8 $R^1 = Me, R^2 = R^3 = H$
9 $R^1 = H, R^2 = R^3 = Me$
10 $R^1 = OBu^t, R^2 = R^3 = H$

11 $R^1, R^2 = -(CH_2)_4-, R^3 = H$
12 $R^1, R^2 = -(CH_2)_3-, R^3 = H$
13 $R^1 = Ph, R^2 = R^3 = H$
14 $R^1 = Me, R^2 = R^3 = H$
15 $R^1 = H, R^2 = R^3 = Me$
16 $R^1 = OBu^t, R^2 = R^3 = H$

reacting partner. The *C*-glycosyl compound **15** obtained from isobutyraldehyde retained traces of unpolar impurities. Therefore, it was converted into the dithioacetal **17** with 1,3-propanedithiol.

The n.m.r. spectroscopic determination of the structure of the synthesized *C*-glycosyl compounds is rather problematic owing to the lack of the commonly evaluated H-1–H-2 coupling. The assignment of the structure of the products **11–16** was, in most cases, almost exclusively based on the comparison of their ^{1}H-n.m.r. data with those of structurally analogous glycosides[13–16] and was deduced from the magnitude of the H-4–H-5 coupling. For the structurally similar glycosides, a coupling constant $J_{4,5}$ ~3.5 Hz has been observed for the β-D series, whereas the corresponding α-D anomers have shown a constant $J_{4,5} \leqq 2$ Hz. Since, in the spectra of **11-16**, these couplings ranged from $J_{4,5}$ = 4.34 (**12**) to 3.54 Hz (**16**), all the compounds formed selectively possess the β-D configuration. By use of this analogy, only the structure of the minor product of the cyclopentenyl trimethylsilyl ether addition (isolated with **12**) remains somewhat uncertain, the coupling ($J_{4,5}$ 3.8 Hz) in



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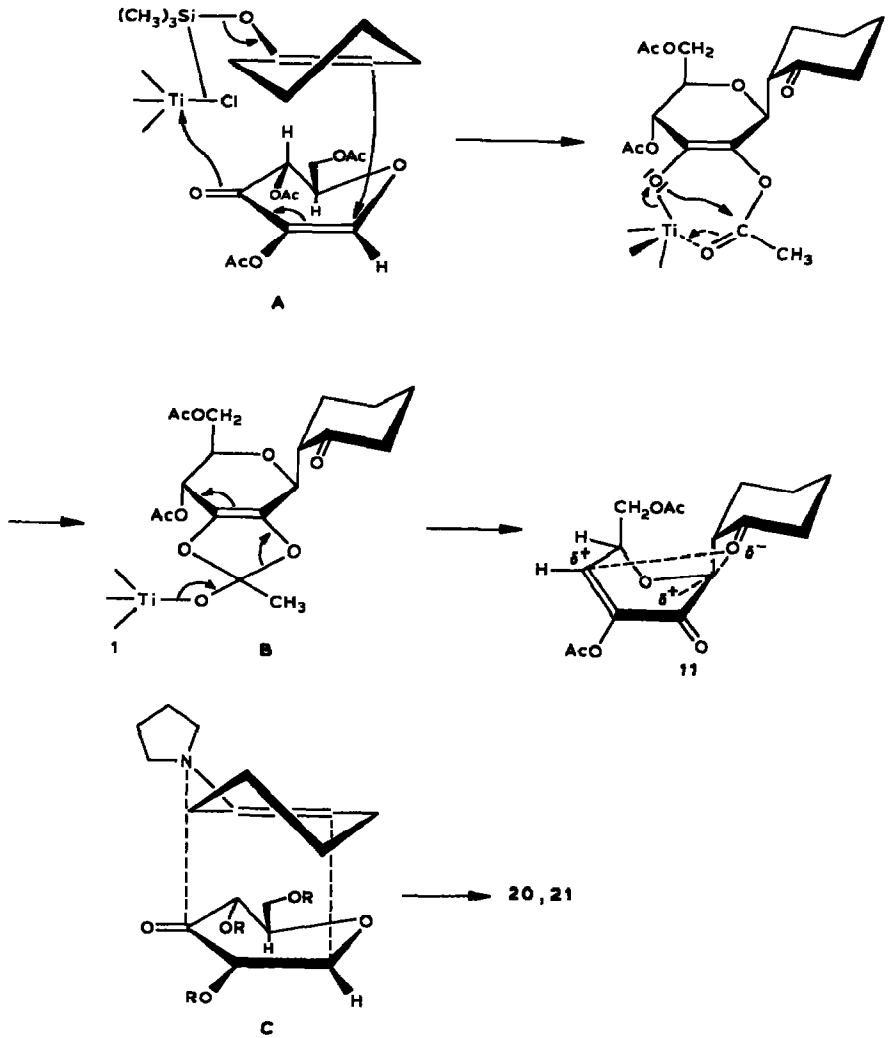
its spectrum is lower than that of **12**, but the value clearly is larger than those of α-D glycosides. Therefore, we corrected the assignment made earlier[10] and suggest that this side product belongs to the β-D series and has a configuration at C-2′ opposite to that of **12**. An additional support for the structural assignments of **11–17** can be

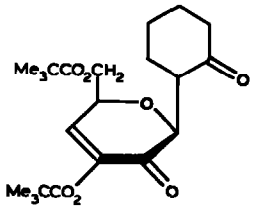


Scheme 1

drawn from the observation of Köll *et al.*[17] who found that the structurally similar *C*-α-D-glycosyl compounds having aromatic side chains at C-1 show a low coupling $J_{4,5} \leqq 2$ Hz.

The larger H-4–H-5 coupling in the β-D series of these compounds has been explained in terms of a reduced dihedral angle between the bonds of H-4 and H-5, and consequently by a dominating ^1H_O(D) conformation[13–16], in which the large-size substituents have to take the quasi-axial orientation. For the *C*-glycosyl compounds **11–17**, this normally unfavored arrangement may be stabilized by intramolecular dipole interactions between the carbonyl oxygen atom in the side chain and the electrophilic ring-atoms C-2 and C-4.

The high stereocontrol of the *C*-glycosyl compound synthesis described herein may be explained in terms of a cyclic transition complex **A** (formulated for the formation of **11**) in which the C–C bond formation is assisted by a titanium-mediated interaction between the silyl group and the carbonyl oxygen atom. The approach of the silyl enol ether **5** from the upper (*Si*) side of the enulose **3** was obviously preferred, since the reactant approaching from below causes a steric repulsion with the 4-acetoxy substituent. The formation of the C–C bond was followed by an 2→3 acetyl shift, probably giving an orthoester-type intermediate **B** which, then, underwent an elimination of the 4-acetoxy substituent to form the *C*-glycosyl compound **11** (see Scheme 1). This accompanying rearrangement is hindered where the wandering acyl group is bulky. Consistent with this proposal, the pivaloyl-protected enulose **4** reacted with the trimethylsilyl enol ether **5** to give **18** in only 34% yield.



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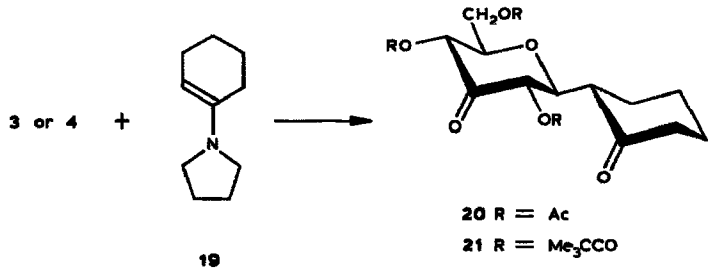
The suggestion outlined for the mechanism and the structural assignment for compounds **11–18** were both strongly supported by the results obtained in the Michael addition of 1-(1-cyclohexen-1-yl)pyrrolidine (**19**) to the enuloses **3** and **4**. In these reactions, compounds **20** and **21** having three newly created chiral centers at C-1,2, and 2′ were obtained. Here also, these reactions proceeded with high stereoselectivity. Among eight possible diastereomers, only one was formed. The structure of the 2-(2,4,6-tri-*O*-acyl-β-D-*ribo*-hexopyranosyl-3-ulose)cyclohexanones **20** and **21** was elucidated from the highfield ^{1}H-n.m.r. spectra, in which the doublets for H-4 and -2 occurred at δ 5.26 and 5.21 (**20**), and δ 5.23 and 5.18 (**21**), respectively. The



larger coupling constants $J_{4,5}$ 10.23 (**20**) and 10.55 Hz (**21**) reflected, in both cases, in the double triplets of H-5 proved the preferred $^4C_1$(D) conformation of these *C*-glycosyl compounds. Furthermore, the large coupling $J_{2,1}$ 10.88 Hz also observed in the signals of the anomeric protons at δ 4.37 (**20**) and 4.43 (**21**) is evidence for the β-D configuration of both compounds. All the assignments were confirmed by double-resonance experiments.

The high stereocontrol in the formation of **20** and **21** may be explained, once again, by the postulation of an intermediate, cyclic-transition complex **C** involving the orbital-controlled C–C bond formation and a cooperating interaction between the enamine nitrogen and the carbonyl carbon atoms (see Scheme 1). Model considerations revealed the favored enamine approach from the *Si*-site owing to the sterically hindered alternative *Re*-site reaction. Furthermore, in both C-glycosyl syntheses, the nonpolar ring members of the silyl enol ether **5** in **A**, as well as those of the enamine **19** in **C** would prefer the "*exo*" position producing the (*S*)-configuration at C-2′ of **11**, **12**, **20**, and **21**. The minor component, formed with **12** in the addition of the relatively planar cyclopentenyl derivative **6**, may have evolved from an "*endo*"-type transition complex corresponding to **A** and, therefore, would have the (*R*)-configuration at C-2′.

In conclusion, the Michael additions of trimethylsilyl enol ethers and of enamines to enuloses open up stereoselective routes to highly functionalized *C*-glycosyl compounds offering opportunities of broad structural variation.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. U.v. spectra were recorded with a Beckman Acta MVI spectrometer, and c.d. spectra with a JASCO J 41C spectral polarimeter. ^{1}H- and ^{13}C-n.m.r. spectra were recorded with (*a*) a Bruker WH-270 (270 MHz-^{1}H–, (*b*) a Bruker WH-90 (90 MHz-^{1}H and 22.63 MHz-^{13}C), or (*c*) a Bruker-AM-400 (400 MHz-^{1}H and 100.6 MHz-^{13}C) spectrometer with tetramethylsilane as the internal standard; the n.m.r. data are reported with arabic numbers for atoms of the residues and arabic numbers with prime for the carbon side-chain atoms. Mass spectra (m.s.) were registered with (*a*) a Varian MAT CH-7A (e.i.), (*b*) a

Varian MAT CH 711 (f.d.), or (*c*) a Finnigan MAT 312 (f.a.b.) spectrometer. Preparative l.c. under elevated pressure was performed with a Waters Prep 500 A equipped with cartouches (500 g silica 10–40), flash chromatography on silica MN 60 (0.04–0.063 mm, Macherey and Nagel), and t.l.c. on Silica gel GF_{254} (E. Merck, Darmstadt).

2,4,6-Tri-*O*-acetyl-1-deoxy-D-*erythro*-hex-1-enopyran-3-ulose (3) and 1-deoxy-2,4,6-tri-*O*-pivaloyl-D-*erythro*-hex-1-enopyran-3-ulose (4) were synthesized from 1,2,4,6-tetra-*O*-acetyl-β-D-glucopyranose (1) and 1,2,4,6-tetra-*O*-pivaloyl-β-D-glucopyranose (2) respectively, as described earlier[12]. Ligroin refers to the fraction of b.p. 45–70°.

General procedure for the preparation of α-*(3,6-di-*O*-acetyl-4-deoxy-*β-D-glycero-*hex-3-enopyranosyl-2-ulose)-carbonyl compounds* **11–16**. — To a solution of **3** (1 g, 3.5 mmol) in dry dichloromethane (10 mL) at −78° was added the corresponding trimethylsilyl enolether **5–10** (4.5 mmol) in dichloromethane (2 mL), followed by $TiCl_4$ (0.72 g, 3.8 mmol). In some reactions (as given in Table I), titanium tetra(2-propanolate) (0.38 mmol) and, after ~2 h, an additional amount of $TiCl_4$ (0.38 mmol) were added. The reaction was indicated by an intensive red or orange coloring of the solution. The mixture was stirred for the time given in Table I, and was then stopped by addition of 2M $KHCO_3$ solution (150 mL) and diethyl ether (80 mL). The aqueous phase was extracted twice with diethyl ether (80 mL), and the collected ether solutions were washed with water and with saturated $NaHCO_3$ solution (40 mL), dried (Na_2SO_4), and evaporated *in vacuo*. The remaining syrupy residue was purified by preparative l.c. under elevated pressure (1:1 ligroin–ethyl acetate). The yields are given in Table I.

*2-(3,6-Di-*O*-4-deoxy-β-D-glycero-hex-3-enopyranosyl-2-ulose)cyclohexanone* (**11**). — M.p. 89°, $[\alpha]_D^{22}$ 39.4° (*c* 1.4, chloroform); λ_{max}^{MeOH} 226 nm; c.d. (methanol): ε + 0.536 (λ = 335 nm); ^{1}H-n.m.r. (*a*, $CDCl_3$): δ 6.56 (d, 1 H, $J_{4,5}$ 4.25 Hz, H-4), 5.08 (d, 1 H, $J_{1,2}$ 2.40 Hz, H-1), 4.82 (ddd, 1 H, $J_{5,6a}$ 6.16, $J_{5,6b}$ 3.40 Hz, H-5), 4.71 (dd, 1 H, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.26 (dd, 1 H, H-6b), and 3.03–3.00 (ddd, 1 H, $J_{2',1}$ 2.40, $J_{2',3'a}$ 7.38, $J_{2',3'b}$ 6.2 Hz, H-2'); ^{13}C-n.m.r. (*b*, C_6D_6): δ 206.5 (C-1'), 189.6 (C-2), 75.5 (C-1), 51.6 (C-2'), and 41.5 (C-6').

Anal. Calc. for $C_{16}H_{20}O_7$ (324.3): C, 59.25; H, 6.21. Found: C, 58.97; H, 6.01.

*2'(S,R)-2-(3,6-Di-*O*-acetyl-4-deoxy-β-D-glycero-hex-3-enopyranosyl-2-ulose) cyclopentanones* (**12**). — The mixture of diastereomers **12** was obtained in 55% yield. The diastereomers were seperated by flash chromatography in 4:1 ligroin–acetone to give probably the 2*S* diastereomer as the main product (see Table I), oil, $[\alpha]_D^{22}$ +10.0° (*c* 0.78, chloroform), R_F 0.52 (2:1 ligroin–acetone); ^{1}H-n.m.r. (*a*, $CDCl_3$): δ 6.55 (d, 1 H, $J_{4,5}$ 4.37 Hz, H-4), 5.07 (d, 1 H, $J_{1,2'}$ 2.33 Hz, H-1), 4.78 (m, 1 H, H-5), 4.63 (dd, 1 H, $J_{6a,5}$ 5.88, $J_{6a,6b}$ 12.1 Hz, H-6a), 4.19 (dd, 1 H, $J_{6b,5}$ 3.40 Hz, H-6b), and 2.85 (m, 1 H, H-2'); ^{13}C-n.m.r. (*b*, $CDCl_3$): δ 217.6 (C-1'), 188.9 (C-2), 75.5 (C-1), 49.7 (C-2'), and 38.3 (C-5'); m.s (*a*): *m/z* 310 (M^+).

Anal. Calc. for $C_{15}H_{18}O_7$ (310.3): C, 57.97; H, 6.12. Found: C, 58.06; H,

5.85.

The minor product is probably the 2*R* diastereomer (yield 7%), oil, $[\alpha]_D^{22}$ −79° (*c* 0.86, chloroform), R_F (2:1 ligroin–acetone) 0.48; ^{1}H-n.m.r. (*b*, $CDCl_3$): δ 6.54 (d, 1 H, $J_{4,5}$ 3.81 Hz, H-4), 4.84 (d, 1 H, $J_{1,2'}$ 3.52 Hz, H-1), 4.82 (m, 1 H, H-5), 4.70 (dd, 1 H, $J_{6a,5}$ 5.28, $J_{6a,6b}$ 11.74 Hz, H-6a), 4.17 (dd, 1 H, $J_{6a,5}$ 2.93 Hz, H-6b), and 2.45 (m, 1 H, H-2′); ^{13}C-n.m.r. (*b*, $CDCl_3$): δ 216.0 (C-1′), 188.3 (C-2), 77.6 (C-1), 50.4 (C-2′), and 38.1 (C-5); m.s (*a*): *m/z* 310 (M^+).

Anal. Calc. for $C_{15}H_{18}O_7 \cdot 0.5\ H_2O$ (319.3): C, 56.42; H, 6.00. Found: C, 56.62; H, 6.14.

*2′-(3,6-Di-*O*-acetyl-4-deoxy-β-*D*-*glycero*-hex-3-enopyranosyl-2-ulose)acetophenone* (**13**). — The compound was purified by flash chromatochraphy in 4:1 ligroin–ethyl acetate, oil $[\alpha]_D^{22}$ −73° (*c* 1.3, chloroform), R_F (2:1 ligroin–ethyl acetone) 0.44; ^{1}H-n.m.r. (*a*, $CDCl_3$): δ 6.55 (d, 1 H, $J_{4'',5''}$ 3.80 Hz, H-4), 5.16 (dd, 1 H, $J_{1,2'a}$ 3.55, $J_{1,2'b}$ 7.33 Hz, H-1), 4.82 (m, 1 H, H-5), 4.63 (dd, 1 H, $J_{6a,5}$ 6.08, $J_{6a,6b}$ 12.07 Hz, H-6a), 4.20 (dd, 1 H, $J_{6b,5}$ 3.51 Hz, H-6b), 3.55 (dd, 1 H, $J_{2'a,2'b}$ 17.34 Hz, H-2′a), and 3.41 (dd, 1 H, H-2′b); ^{13}C-n.m.r. (*b*, $CDCl_3$): δ 197.8 (C-1′), 190.7 (C-2), 137.9 (ipso-C), 75.5 (C-1), and 40.3 [C-2 (ω)]

Anal. Calc. for $C_{18}H_{18}O_7$ (346.3): C, 62.42; H, 5.24. Found: C, 62.49; H, 5.29.

*(3,6-Di-*O*-acetyl-4-deoxy-β-*D*-*glycero*-hex-3-enopyranosyl-2-ulose)propanone* (**14**). — The product crystallized from diethyl ether, m.p. 65°, $[\alpha]_D^{22}$ −98° (*c* 1.2, chloroform), ^{1}H-n.m.r. (*a*, $CDCl_3$): δ 6.52 (d, 1 H, $J_{4,5}$ 3.88 Hz, H-4), 4.94 (dd, 1 H, $J_{1',1'a}$ 4.08, $J_{1,1'b}$ 7.43 Hz, H-1), 4.77 (m, 1 H, H-5), 4.59 (dd, 1 H, $J_{6a,5}$ 6.18, $J_{6a,6b}$ 12.04 Hz, H-6a), 4.17 (dd, 1 H, $J_{6b,5}$ 3.55 Hz, H-6b), 2.97 (dd, $J_{1'a,1'b}$, 17.07 Hz, H-1′a), and 2.84 (dd, 1 H, H-1′b); ^{13}C-n.m.r. (*b*, $CDCl_3$): δ 204.1 (C-2′), 188.6 (C-2), 74.1 (C-1), and 44.0 (C-1′); m.s. (f.a.b.;*c*): *m/z* 285 (M^+ + 1).

Anal. Calc. for $C_{13}H_{16}O_7$ (284.3): C, 54.93; H, 5.67. Found: C, 55.19; H, 5.60.

*2′-(3,6-di-*O*-acetyl-4-deoxy-β-*D*-*glycero*-hex-3-enopyranosyl-2-ulose)isobutyraldehyde* (**15**). — The compound was purified by flash chromatography in 5:2 ligroin–ethyl acetate, oil, $[\alpha]_D^{22}$ −110° (*c* 1.4, chloroform), R_F (1:1 ligroin–ethyl acetate) 0.52; ^{1}H-n.m.r. (*b*,*c*; CD_2Cl_2): δ 9.54 (s, 1 H, CHO), 6.60 (d, 1 H, $J_{4,5}$ 4.12 Hz, H-4), 4.87 (m, 1 H, H-5), 4.71 (s, 1 H, H-1), 4.68 (dd, 1 H, $J_{6a,5}$ 7.19, $J_{6a,6b}$ 12.24 Hz, H-6a), 4.11 (dd, 1 H, $J_{6b,5}$ 3.49 Hz, H-6b), and 1.12 (s, 6 H, CH_3–C); ^{13}C-n.m.r. (*c*, CH_2Cl_2): δ 202.1 (CHO), 188.9 (C-2), 80.5 (C-1), and 50.2 (C-2′); m.s (f.d.; *b*): *m/z* 299 (M^+ + 1, base peak). The product contains small amounts of impurities; therefore, it was transformed into its trimethylene dithioacetal **17**.

tert-*Butyl 2-(3,6-Di-*O*-acetyl-4-deoxy-β-*D*-*glycero*-hex-3-enopyranosyl-2-ulose)acetate* (**16**). — The crude product was purified by flash chromatography in 3:1 ligroin–ethyl acetate, oil $[\alpha]_D^{22}$ −30.1° (*c* 1.6, chloroform), R_F (1:1 ligroin–ethyl acetate) 0.53; ^{1}H-n.m.r. (*a*, $CDCl_3$): δ 6.52 (d, 1 H, $J_{4,5}$ 3.54 Hz, H-4), 4.9–4.8 (m, 2 H, H-5,1), 4.55 (dd, 1 H, $J_{6a,5'}$ 5.92, $J_{6a,6b}$ 12.03 Hz, H-6a), 4.18 (dd, $J_{6b,5}$ 3.62 Hz, H-6b), 2.82 (dd, 1 H, $J_{2'a,1}$ 4.07, $J_{2'a,2'b}$ 17.08 Hz, H-2′a), and

2.69 (dd, 1 H, $J_{2'b,1}$ 7.44 Hz, H-2'b).

Anal. Calc. for $C_{16}H_{22}O_8 \cdot 0.5\ H_2O$ (351.3): C, 54.69; H, 6.60. Found: C, 54.34; H, 6.83.

*2-[2-(3,6-Di-*O*-acetyl-4-deoxy-β-*D*-*glycero*-hex-3-enopyranosyl-2-ulose)-2-propyl]-1,3-dithiane* (**17**). — To a solution of the crude **15** (obtained from 1.75 mmol of **3**) in chloroform (10 mL) was added propane-1,3-dithiol (0.23 g, 2.1 mmol). The mixture was stirred for 3 h at room temperature and then evaporated *in vacuo*. The remaining residue was purified by flash chromatography in 5:2 ligroin–ethyl acetate to give **17** (0.42 g, 62%), pale yellow oil, $[\alpha]_D^{22}$ +69.7° (*c* 1.6, chloroform), R_F (1:1 ligroin–acetate) 0.59; ^{1}H-n.m.r. (*c*, $CDCl_3$): δ 6.45 (d, 1 H, $J_{4,5}$ 4.28 Hz, H-4), 4.82 (m, 1 H, H-5), 4.66 (s, 1 H, H-1), 4.58 (s, 1 H, H-2 dithiane), 4.51 (dd, 1 H, $J_{6a,5}$ 6.41, $J_{6a,6b}$ 12.04 Hz, H-6a), 4.19 (dd, 1 H, $J_{6b,5}$ 3.61 Hz, H-6b), 3.0–2.8 (m, 4 H and H-6 dithiane), 1.20 and 1.14 [2 s, 6 H, $(CH_3)_2C$]; ^{13}C-n.m.r. (*c*, $CDCl_3$): δ 189.0 (C-2), 79.4 (C-1), 58.4 (C-2 dithiane), and 43.5 (Me_2C); m.s (*a*): *m/z* 388 (M^+).

Anal. Calc. for $C_{17}H_{26}O_6S_2$ (388.5): C, 52.56; H, 6.23. Found: C, 52.36; H, 6.16.

*2-(3,6-Di-*O*-pivaloyl-4-deoxy-β-*D*-glycero-hex-3-enopyranosyl-2-ulose) cyclohexanone* (**18**). — To a solution of **4** (0.5 g, 1.21 mmol) and cyclohexenyl trimethylsilyl ether **5** (0.3 g, 1.8 mmol) in dry dichloromethane (10 mL), at −78° was added $TiCl_4$ (0.34 g, 1.8 mmol). The intensively red-colored solution was stirred for 30 min at −78°. The reaction was stopped by the addition of Na_2CO_2) (0.5 g) in water (10 mL). The mixture was processed as described for **11** to give a syrupy product (320 mg) containing a main product, R_F 0.57 (3:1 ligroin–ethyl acetate) and some side products. Preparative l.c. in 6:1 ligroin–ethyl acetate yielded **18** (0.17 g, 34%), colorless oil, $[\alpha]_D^{22}$ −47° (*c* 1.1, chloroform); ^{1}H-n.m.r. (*a*, $CDCl_3$): δ 6.47 (d, 1 H, $J_{4,5}$ 3.97 Hz, H-4), 5.14 (d, 1 H, $J_{1,2'}$ 2.55 Hz, H-1), 4.84 (m, 1 H, H-5), 4.60 (dd, 1 H, $J_{6a,5}$ 5.5, $J_{6a,6b}$ 12.0 Hz, H-6a), and 4.07 (dd, 1 H, $J_{6b,5}$ 3.6 Hz, H-6b).

Anal. Calc. for $C_{22}H_{32}O_7 \cdot H_2O$ (426.5): C, 61.95; H, 8.04. Found: C, 62.24; H, 8.50.

*2-(2,4,6-Tri-*O*-acetyl-β-*D*-ribo-hexopyranosyl-3-ulose)cyclohexanone* (**20**). — A solution of **3** (0.5 g, 1.74 mmol) and 1-(1-cyclohexen-1-yl)pyrrolidine (**19**; 0.28 g, 1.8 mmol) in 1,4-dioxane (7 mL) was stirred at room temp. for 2 days. The mixture was poured into ice (20 g) and aqueous HCl (20 mL). The mixture was extracted five times with diethyl ether (30 mL). The ether solution was washed with sat. $NaHCO_3$ solution (30 mL) and with water, dried (Na_2SO_4), and evaporated *in vacuo*. As monitored by t.l.c. (1:2 ligroin–ethyl acetate), the syrupy residue (0.33 g, 49%) contained only one main product (R_F 0.62) and traces of nonpolar impurities. It was purified by column chromatography on silica (180 g; 1:2 ligroin–ethyl acetate to give **21** (0.13 g, 20%), colorless oil, $[\alpha]_{578}^{22}$ −1.4°, $[\alpha]_{546}^{22}$ −0.9°, $[\alpha]_{436}^{22}$ +5.9°, $[\alpha]_{365}^{22}$ +5.8° (*c* 1.2, chloroform), ^{1}H-n.m.r. ($CDCl_3$): δ 5.26 (d, 1 H, $J_{4,5}$ 10.55 Hz, H-4), 5.21 (d, 1 H, $J_{1,2'}$ 10.88 Hz, H-2), 4.37 (dd, 1 H, $J_{1,2'}$ 1.98, H-1), 4.28 (d, 2 H, $J_{6,5}$ 3.5 Hz, H-6), and 3.93 (dt, 1 H, H-5); f.d.m.s. (*c*): *m/z* 384 (100%, M^+) and 385

(74%, $M^+ + 1$).

Anal. Calc. for $C_{18}H_{24}O_9 \cdot H_2O$ (402.4): C, 53.72; H, 6.51. Found: C, 53.82; H, 6.04.

*2-(2,4,6-Tri-O-pivaloyl-β-*D*-ribo-hexopyranosyl-3-ulose)cyclohexanone* (21). — This compound was obtained from **4** (0.5 g, 1.21 mmol) and **19** (0.2 g) in 1,4-dioxane (7 mL) in a manner analogous to the preparation of **20**. T.l.c. (3:1 ligroin–ethyl acetate) of the crude product indicated a main (R_F 0.75) and a minor component (R_F 0.18). By column chromatography on silica (250 g; 6:1 ligroin–ethyl acetate), **21** (170 mg, 28%) was isolated as a colorless oil, which crystallized during drying *in vacuo*, m.p. 145–146°, $[\alpha]_D^{22}$ +31.8° (*c* 1.5, chloroform); ^{1}H-n.m.r. (*a*, $CDCl_3$): δ 5.23 (d, 1 H, $J_{4,5}$ 10.23 Hz, H-4), 5.18 (d, 1 H, $J_{2,1'}$ 10.88 Hz, H-2), 4.43 (dd, 1 H, $J_{1,2'}$ 2.0 Hz, H-1), 4.33 (dd, 1 H, $J_{6a,5}$ 2.3, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.20 (dd, 1 H, $J_{6b,5}$ 4.62 Hz, H-6b), and 3.90 (ddd, 1 H, H-5); f.d.m.s. (*c*): 510 (75%, M^+) and 511 (19%, $M^+ + 1$).

Anal. Calc. for $C_{27}H_{42}O_9$ (510.6): C, 63.40; H, 8.36. Found: C, 63.53; H, 8.23.

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