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PREPARATION OF METHYL 4,6-*O*-BENZYLIDENE-2-CHLORO- AND -2-BROMO-α- AND β-D-*xylo*-HEXOPYRANOSID-3-ULOSES AND THEIR α-D-*ribo* ISOMERS, AND FORMATION OF GLYCOSID-3-ULOSE HYDRATES FOR THE β-D-*xylo* ISOMERS

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ABSTRACT

The title glycosid-3-uloses were prepared from 3-nitro-β-D-*threo*-hex-2-enopyranoside derivatives. ^{1}H-N.m.r. spectral studies revealed that the 2-bromo- and 2-chloro-β-D-*xylo*-hexopyranosid-3-uloses readily equilibrated with their hydrates, but the remaining glycosid-3-uloses, including the α-D-*xylo* and α- and β-D-*ribo* isomers, were not hydrated under similar conditions.

INTRODUCTION

In general the addition of water to a carbonyl group to form stable, isolable hydrates is unfavorable, except for formaldehyde and compounds having an electronegative group(s) adjacent to the carbonyl function[1], for example chloral. In the carbohydrate realm, glycosid-2-uloses might hydrate similarly, as the vicinal anomeric carbon atom is an electronegative acetal group. However, few examples of hexopyranosid-2-ulose hydrates are known[2] and are limited to the α anomers. The failure to observe the respective β anomers may be explained in terms of the so-called Δ^2-effect[3] (which is actually a manifestation of the more-general anomeric effect). Hydration of the carbonyl group is influenced by the anomeric and exoanomeric effects; formaldehyde hydrate was used as a model compound for investigation of these effects by *ab initio* molecular-orbital calculations[4].

The stability of hexopyranosid-3-ulose hydrates should be affected by several factors, including the Δ^2 effect and exoanomeric effect. For α-D anomers having the $^4C_1$ conformation, 1,3-diaxial repulsion, together with hydrogen bonding between HO-3 (axial) and O-1, are also involved. The exoanomeric effect would make the aglycon of an α-D-pyranosid-3-ulose hydrate having the $^4C_1$ conformation favor the *+sc* conformation. The hydroxyl groups at C-3 would have either the *−sc* or *+sc* orientation (**A** and **B**, respectively), and electrostatic repulsion between one of the lone pairs of electrons of the axial O-3 atom and that of O-1 would make these

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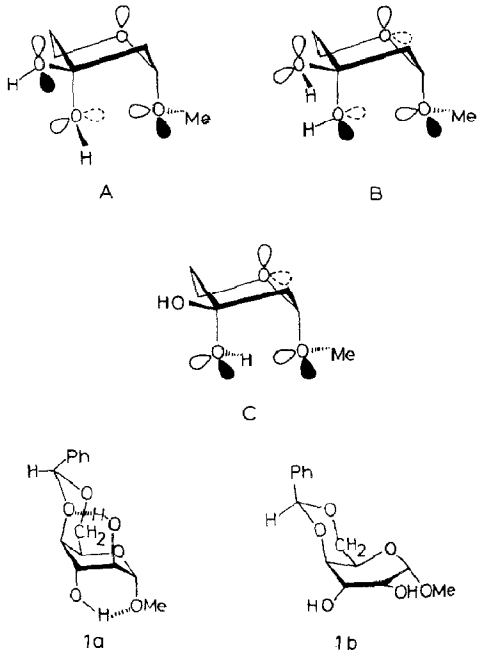


conformations less stable. To overcome this repulsion, the axial 3-OH group should rotate to a position that would allow hydrogen bonding with O-1 (conformation **C**).

In regard to hydrogen bonding, it is noteworthy that methyl 4,6-*O*-benzylidene-α-D-idopyranoside exists in the $^4C_1$ form (**1a**) in chloroform solution, while it adopts the $^OS_2$ conformation (**1b**) in a mixture of dimethyl sulfoxide and deuterium oxide[5]. These solvent effects are explained on the basis that, in chloroform solution, hydrogen bonding between HO-2 and O-4, and HO-3 and O-1, outweigh the 1,3-diaxial repulsion, whereas, on addition of water, intramolecular hydrogen bonding becomes less important[6]. However, judging from the fact that hydration of hexopyranosid-2-uloses is restricted to the α anomers, hydration of the glycosid-3-ulose of the *threo* isomer having the $^4C_1$ conformation should occur more readily than with the respective *erythro* isomer (Fig. 1).

The equilibrium of glycosid-3-ulose derivatives with their hydrates should thus be influenced by many factors and merit detailed study. To the best of our

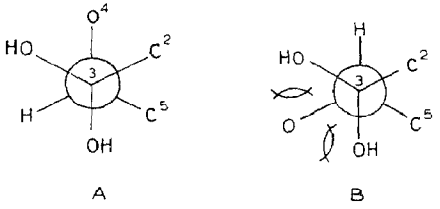
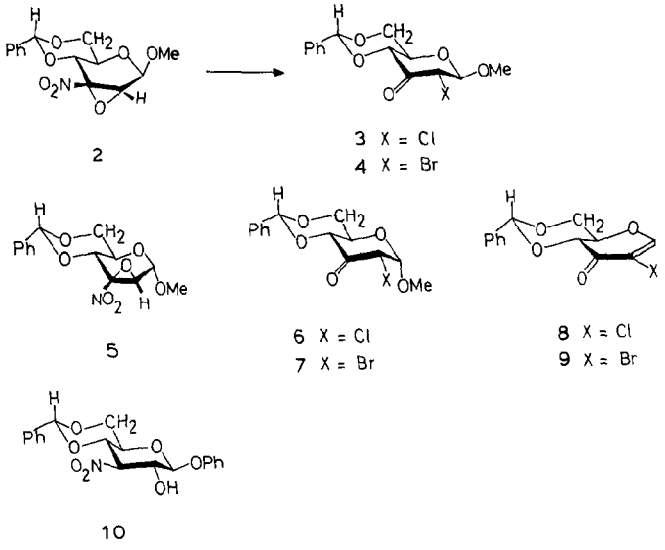


Fig. 1. "Newman" projection along C-3–C-4 (*A*) for compounds **25** and **26**; (*B*) for hydrate of **3** and **4**.

knowledge, the isolation of hexopyranosid-3-ulose hydrates has not been reported. This may be attributed to the instability of the hydrate. We, therefore, decided to introduce an equatorial 2-chloro or 2-bromo group (*a*) to provide electronegative stabilization of the hydrate, and (*b*) because the glycos-3-ulose having a polar C=O bond should be more destabilized than the corresponding hydrate, as the dipole of these bonds (C=O and hydrate) is almost parallel with that of the C–Cl or C–Br bond*. Furthermore, to fix the conformation, the 4,6-*O*-benzylidene derivatives having the α- and β-D-*xylo*, and α- and β-D-*ribo* configurations[8] were prepared, and their hydration behavior examined.

RESULTS AND DISCUSSION

Methyl 4,6-*O*-benzylidene-2-chloro- (**3**) and -2-bromo-2-deoxy-β-D-*ribo*-hexopyranosid-3-uloses (**4**) were prepared by treatment of methyl 2,3-anhydro-4,6-*O*-benzylidene-3-*C*-nitro-β-D-allopyranoside (**2**) with lithium and/or tetrabutylammonium halides[8]. A similar reaction of **5** with lithium bromide in *N,N*-dimethylformamide was much slower than that of **2**, and even after 6 days at room temperature, the reaction proceeded only partially to give the desired glycosidulose **7** in 31% yield†. Compound **7** was alternatively prepared by treatment of 1,5-anhydro-4,6-*O*-benzylidene-2-bromo-2-deoxy-D-*erythro*-hex-1-en-3-ulose[8] (**9**) with meth-

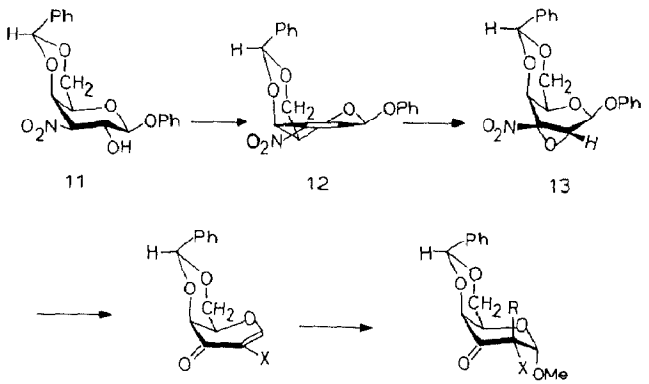


*Such an unfavorable dipole makes the halogen atom tend to occupy the axial disposition rather than the equatorial one; this has been termed the α-halo effect[7].

†A similar difference in the reactivity of **2** and **5** was reported by Baer and Madumelu in the reaction with sodium borohydride[9].

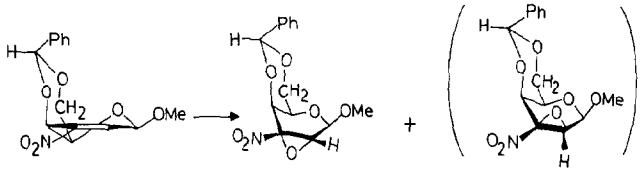
anolic sodium methoxide. In this reaction, methanol smoothly added to the enone **9** to give a 3:1 mixture of the α (**7**) and β (**4**) anomers in high yield. A similar reaction of the 2-chloro analog **8** also afforded the α anomer **6** as the major product and the β anomer **3** as the minor one. Long-range coupling, $J_{2,4}$ 1.2–1.5 Hz, was observed in the α- and β-D-*ribo* isomers, **3, 4, 6,** and **7**.

For preparation of the 4-epimers of these 2-halo derivatives, similar addition reactions were employed for 1,5-anhydro-4,6-*O*-benzylidene-2-deoxy-2-halo-D-*threo*-hex-1-en-3-uloses (**14** and **15**), which were synthesized as follows. Nitromethane cyclization of the dialdehyde[10] obtained from phenyl β-D-glucopyranoside by oxidation with sodium metaperiodate, followed by benzylidenation, afforded the *galacto* isomer **11**, together with the *gluco* one **10**. Compound **11** was converted into the nitro alkene **12** by treatment with methanesulfonyl chloride and triethylamine[11]. Epoxidation of **12** with hydrogen peroxide, according to a method earlier described by our group[8], afforded only the nitro epoxide **13**, as judged from ^{1}H-n.m.r. spectroscopy. Denitration of **13** by tetrabutylammonium chloride and bromide provided the intended enones **14** and **15**, respectively, in low yields. Treatment of the 2-chloro-enone **14** and 2-bromo-enone **15** with methanolic sodium methoxide afforded exclusively the α-D-*xylo* isomers **16** and **18**, respectively, in high yields (Scheme 1). The signals of **16** and **18** were assigned by comparison of their ^{1}H-n.m.r. spectra with those of the respective 2-deuterio derivatives, **17** and **19**; the latter compounds were prepared by use of methanol-*d* instead of methanol. Their i.r. spectra showed carbonyl absorption at 1755 and 1750 cm^{-1}, respectively, suggesting that the halo atom is equatorially disposed[12]. This accords with the fact that no long-range coupling[13] between H-2 and H-4 was observed. These spectral data and small $J_{1,2}$ values indicate that compounds **16** and **18** have the α-D-*xylo* configuration and the $^4C_1$ conformation. The ^{1}H-n.m.r. spectra of all enones thus

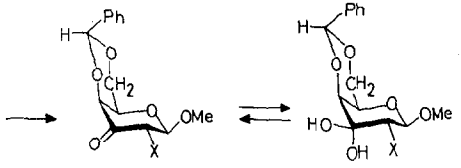


prepared showed no evidence for formation of hydrates in chloroform-*d* and acetone-d_6. No formation of a hydrate was observed upon reinvestigation of the β-D-*ribo* isomers **3** and **4** by ^{1}H-n.m.r. spectroscopy in chloroform-*d* and in dimethyl sulfoxide-d_6.

As the respective β-D anomers were not obtained in the reactions of **14** and **15** with sodium methoxide, we decided to use methyl 2,3-anhydro-4,6-*O*-benzylidene-3-*C*-nitro-β-D-gulopyranoside (**21**) as a precursor. The nitroepoxide **21** has been already synthesized by Baer and Rank[14] by treatment of nitro alkene **20** with hydrogen peroxide in the presence of sodium ethoxide; stereoselectivity was not high and gave a 5:1 mixture of β-D-*gulo* **21** and β-D-*talo* isomers **22**. When compound **20** was treated with *tert*-butyl peroxide in a heterogeneous system (benzene–0.5M sodium hydroxide) in the presence of a phase-transfer catalyst, the nitroepoxide **21** was obtained, almost exclusively. The epoxide **21** thus prepared was treated with tetrabutylammonium chloride to give a complex mixture. After column chromatography, fractions containing the 2-chloro derivatives were combined and evaporated to a syrup, the ^{1}H-n.m.r. spectrum of which suggested that it was a 3:2 mixture of **23** and **25** (Scheme 2). The structure of the crystalline hydrate **25** was determined on the basis of elemental analysis, ^{1}H-n.m.r. (CD_3COCD_3: two hydroxyl groups at δ 5.46 and 5.26) and i.r. spectra (no carbonyl but hydroxyl absorption bands at 3480 and 3376 cm^{-1}). The β configuration of **25** was deduced from the $J_{1,2}$ coupling constant, 8.7 Hz. Although isolation of glucosid-ulose **23** has not yet been accomplished, the glucosid-3-ulose structure for **23** is suggested by the following evidence: (*a*) the anomeric proton resonates at δ 5.24 ($CDCl_3$) as a doublet having a spacing of 9.0 Hz; (*b*) a 1:3 mixture of **23** and **25** became a 2:3 mixture after warming it in chloroform-*d* for 15 min. Similar reaction



20 21 22



23 X = Cl
24 X = Br

25 X = Cl
26 X = Br

of epoxide **21** with tetrabutylammonium bromide also afforded a 3:2 mixture of glycosid-3-ulose **24** and hydrate **26**, from which the latter was isolated.

The hydrates **25** and **26** are free from unfavorable dipole–dipole interaction between the carbonyl function and the equatorial halo atom (α-halo effect). On the basis of dipole–dipole repulsion, formation of the hydrate in the β-D-*ribo* isomer should be more favorable than with the β-D-*xylo* isomer, because the former has additional dipole–dipole interaction between the carbonyl function and the oxygen atom at C-4. However, no evidence for the formation of a hydrate was obtained in the case of the β-D-*ribo* isomers **3** and **4**. This might be because a Δ^2-like destabilization overwhelms the unfavorable dipole–dipole interaction. In the hydrate of the β-D-*ribo* isomers **3** and **4**, the relationship between O-4 and the two hydroxyl groups at C-3 is similar to that between the hydroxyl group at C-2 and both the ring and anomeric oxygen atoms in β-D-mannopyranosides (known as the Δ^2 effect). Regardless of the configurations at C-4, no hydrate was detected in the α anomers. This is understandable, if the 1,3-diaxial repulsion between the hydroxyl group and the anomeric methoxyl group overcomes the stabilization due to hydrogen bonding (which is realized at the cost of the *exo* anomeric effect, as already described) between these groups.

EXPERIMENTAL

General procedures. — All melting points are uncorrected. Optical rotations were determined with a Horiba High Sensitive Polarimeter (SEPA-200). ^{1}H-N.m.r. spectra were recorded at 90 MHz with a JEOL spectrometer (JNM-FX90Q) for solutions in $CDCl_3$ (unless otherwise noted) with Me_4Si as the internal standard. I.r. spectra were recorded for KBr pellets. Solutions were dried over $MgSO_4$ and evaporated under diminished pressure. Column chromatography was conducted on silica gel (Wakogel C-300). The concentration of the methanolic NaOMe used was 2mM.

Phenyl 4,6-O-benzylidene-3-deoxy-3-C-nitro-β-D-gluco- (**10**) *and -galacto-pyranoside* (**11**). — Phenyl 3-deoxy-3-nitro-β-D-glucopyranoside (5.89 g) was obtained by filtration of a reaction mixture formed by nitromethane cyclization of the dialdehyde generated from phenyl β-D-glucopyranoside (12.8 g, 50 mmol)[10]. The remaining filtrate was evaporated and the product benzylidenated with benzaldehyde (25 mL) and anhydrous $ZnCl_2$ (10 g). The mixture was stirred for 24 h at room temperature and then poured into a stirred solution of water (70 mL) and petroleum ether (200 mL), whereby a mixture of **10** and **11** was precipitated. The precipitate (containing **10** and **11** as judged by t.l.c.) was filtered off and washed well with water and petroleum ether (yield 3.8 g). The filtrate was evaporated and chromatographed with benzene as the eluant, to give successively the *gluco* isomer (1.55 g), a mixture of *gluco* and *galacto* isomers (1.6 g), and the *galacto* isomer (745 mg). The *galacto* isomer **11** was recrystallized from EtOH; m.p. 215–216°, $[\alpha]_D^{25}$ −21° (*c* 1.1, Me_2CO); ν_{max} 3420 (broad) and 1565 cm^{-1} (NO_2); ^{1}H-n.m.r.

(CD_3COCD_3): δ 5.22 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.62 (oct, 1 H, $J_{2,3}$ 10.2, $J_{2,OH}$ 4.6 Hz, H-2), 5.09 (q, 1 H, $J_{3,4}$ 3.8 Hz, H-3), 4.91 (dd, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 4.12 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.5 Hz, H-5), 4.30 (d, 2 H, H-6,6'), 5.70 (s, 1 H, PhCH), and 5.55 (d, 1 H, OH).

Anal. Calc. for $C_{19}H_{19}NO_7$: C, 61.12; H, 5.13; N, 3.75. Found: C, 61.06; H, 5.15; N, 3.97.

Phenyl 4,6-O-benzylidene-2,3-dideoxy-3-C-nitro-β-D-threo-hex-2-enopyranoside (**12**). — To an ice-cooled solution of nitro alcohol **11** (795 mg, 2.1 mmol) in tetrahydrofuran (6.2 mL) was successively added MsCl (266 mg, 2.3 mmol) and Et_3N (476 mg, 4.7 mmol). After being stirred for 10 min at room temperature, the mixture was monitored by t.l.c. As the starting alcohol **11** was still present, additional amounts of MsCl (219 mg) and Et_3N (420 mg) were added. After 20 min, the mixture was partitioned between EtOAc and saturated aq. NaCl. The organic layer was washed with water, dried, and evaporated to give nitro alkene **12** in almost quantitative yield, and thus was used without further purification. An analytical sample was prepared by recrystallization from EtOAc–hexane; m.p. 178–178.5°, $[\alpha]_D^{25}$ −80° (*c* 1.0, $CHCl_3$); ν_{max} 1540 and 1535 cm^{-1} (NO_2); ^{1}H-n.m.r.: δ 5.86 (t, 1 H, $J_{1,2} = J_{1,4}$ 1.3 Hz, H-1), 7.15 (t, 1 H, $J_{2,4}$ 1.3 Hz, H-2), 4.97 (t, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 3.60 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.5 Hz, H-5), 4.44 (dd, 1 H, $J_{6,6'}$ 12.8 Hz, H-6), 4.17 (dd, 1 H, H-6'), and 5.61 (s, 1 H, PhCH).

Anal. Calc. for $C_{19}H_{17}NO_6$: C, 64.22; H, 4.82; N, 3.94. Found: C, 64.12; H, 4.82; N, 3.96.

Phenyl 2,3-anhydro-4,6-O-benzylidene-3-C-nitro-β-D-gulopyranoside (**13**). — To a solution of nitro alkene **12** (89 mg, 0.25 mmol) and 30% H_2O_2 (0.25 mL) in tetrahydrofuran (1.5 mL) was added M NaOH (0.25 mL). After being stirred for 30 min, the mixture was partitioned between benzene and water. The organic layer was washed with aq. sodium thiosulfate and water, dried, and evaporated, to afford a single product (90 mg, 97%), as judged from the ^{1}H-n.m.r. spectrum. Without further purification, the crude epoxide was used to the next reaction. An analytical sample was prepared by recrystallization from EtOAc–cyclohexane; m.p. 161.5–162.5°, $[\alpha]_D^{25}$ −124° (*c* 0.5, $CHCl_3$); ν_{max} 1563 and 1557 cm^{-1} (NO_2); ^{1}H-n.m.r.: δ 5.49 (t, 1 H, H-1), 4.51 (s, 1 H, H-2), 4.99 (d, 1 H, $J_{4,5}$ 1.1 Hz, H-4), 3.59 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.0 Hz, H-5), 4.35 (dd, 1 H, $J_{6,6'}$ 12.8 Hz, H-6), 4.08 (dd, 1 H, H-6'), and 5.65 (s, 1 H, PhCH).

Anal. Calc. for $C_{19}H_{17}NO_7$: C, 61.45; H, 4.61; N, 3.77. Found: C, 61.40; H, 4.68; N, 3.47.

Methyl 2,3-anhydro-4,6-O-benzylidene-3-C-nitro-β-D-gulopyranoside (**21**). — A mixture of nitro alkene[15] **20** (88 mg, 0.3 mmol), aq. *tert*-butyl hydroperoxide (0.12 mL, ~70% purity, ~0.8 mmol), tributylhexadecylphosphonium bromide (6 mg), benzene (6 mL), and 0.5M NaOH (0.6 mL) was stirred for 1.5 h at room temperature, and diluted with benzene and water. The organic layer was washed with aq. sodium thiosulfate and water, dried, and evaporated, to give 87.5 mg (94%) of **21**, identical with an authentic specimen[14] by ^{1}H-n.m.r. and i.r. spectra, and used to the next reaction without further purification.

1,5-Anhydro-4,6-O-benzylidene-2-chloro-2-deoxy-D-threo-*hex-1-en-3-ulose* (**14**). — To a stirred solution of crude epoxide **13** (prepared from 349 mg of **12**) in tetrahydrofuran (21 mL) was added Bu_4NCl (576 mg, 2.07 mmol) at room temperature. After 20 h, the mixture was evaporated and the residue was dissolved in EtOAc. The organic layer was washed with water, dried, evaporated, and chromatographed with 10:1 (v/v) benzene–EtOAc as the eluant, to give a fraction (170 mg) containing **14** as the major component. Addition of isopropyl alcohol to the fraction gave 95 mg (36%) of **14** as crystals; m.p. 153–154°, $[\alpha]_D^{25}$ +236° (*c* 1, $CHCl_3$); ν_{max} 1690, 1590 cm^{-1} (O–C=C–CO); ^{1}H-n.m.r.: δ 7.77 (s, 1 H, H-1), 4.43 (d, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 4.32 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.5 Hz, H-5), 4.52 (dd, 1 H, $J_{6,6'}$ 12.8 Hz, H-6), 4.14 (dd, 1 H, H-6'), and 5.62 (s, 1 H, PhCH).

Anal. Calc. for $C_{13}H_{11}ClO_4$: C, 58.55; H, 4.16. Found: C, 58.43; H, 4.04.

1,5-Anhydro-4,6-O-benzylidene-2-bromo-2-deoxy-D-threo-*hex-1-en-3-ulose* (**15**). — As already described for **14**, the crude epoxide **13**, prepared from 361 mg (1.00 mmol) of **12**, was treated with Bu_4NBr (726 mg, 2.25 mmol) for 13 h to give 80 mg (25%) of **15**, together with the unchanged epoxide **13** (35 mg, 9%). An analytical sample was prepared by recrystallization from isopropyl alcohol; m.p. 170–171°, $[\alpha]_D^{25}$ +243° (*c* 0.5, Me_2CO); ν_{max} 1683, 1575 cm^{-1} (O–C=C–CO); ^{1}H-n.m.r.: δ 7.89 (s, 1 H, H-1), 4.51 (d, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 4.38 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.5 Hz, H-5), 4.55 (dd, 1 H, $J_{6,6'}$ 12.8 Hz, H-6), 4.19 (dd, 1 H, dd, H-6'), and 5.67 (s, 1 H, PhCH).

Anal. Calc. for $C_{13}H_{11}BrO_4$: C, 50.19; H, 3.56. Found: C, 50.45; H, 3.56.

Methyl 4,6-O-benzylidene-2-chloro-2-deoxy-α-D-ribo-*hexopyranosid-3-ulose* (**6**). — To methanolic NaOMe (8 mL) was added enone[8] **8** (61.6 mg, 0.23 mmol) at 28°. A precipitate was immediately generated. After being stirred for 10 min, the mixture was diluted with EtOAc and washed with water, dried, and evaporated. The ^{1}H-n.m.r. spectrum of the residue in chloroform-*d* showed that it was a 3:1 mixture of α (**6**) and β (**3**) anomer, as estimated by integration of signals of the benzylidene methine proton. Fractional crystallization from EtOH gave 33.5 mg of **6** as the first crop, a 3:1 mixture (19 mg) of **6** and **3** as the second, and 13 mg of **3** as the third. The β anomer **3** was identical with an authentic sample[8]. The α anomer **6** was recrystallized from EtOH–Me_2CO; m.p. 234° (dec.), $[\alpha]_D^{25}$ +122° (*c* 1, Me_2SO); ν_{max} 1755 cm^{-1} (CO); ^{1}H-n.m.r. (CD_3COCD_3, 50°): δ 5.29 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 5.06 (dd, 1 H, $J_{2,4}$ 1.4 Hz, H-2), 4.66 (m, 1 H, $J_{4,5}$ 8.4 Hz, H-4), 4.45–3.95 (m, 3 H, H-5,6*a*,6*e*), 5.71 (s, 1 H, PhCH), and 3.47 (s, 3 H, OMe).

Anal. Calc. for $C_{14}H_{15}ClO_5$: C, 56.29; H, 5.06. Found: C, 56.30; H, 4.96.

Methyl 4,6-O-benzylidene-2-bromo-2-deoxy-α-D-ribo-*hexopyranosid-3-ulose* (**7**). — (*a*) *From the nitroepoxide* **5**. To a solution of **5** (refs. 8, 14; 309 mg, 1.00 mmol) in *N*,*N*-dimethylformamide (8 mL) was added LiBr (344 mg, 3.96 mmol) at room temperature. After being stirred for 6 days, the mixture was poured into water (100 mL) and the precipitate was filtered off and recrystallized from EtOH–Me_2CO to give 106 mg (31%) of **7**; m.p. 179° (dec.), $[\alpha]_D^{25}$ +123° (*c* 1, Me_2SO); ν_{max} 1740 cm^{-1} (CO); ^{1}H-n.m.r. (CD_3COCD_3): δ 5.33 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1),

5.21 (dd, 1 H, $J_{2,4}$ 1.3 Hz, H-2), 4.73 (m, 1 H, $J_{4,5}$ 8.2 Hz, H-4), 4.40–3.95 (m, 3 H, H-5,6*a*,6*e*), 5.74 (s, 1 H, PhCH), and 3.48 (s, 3 H, OMe).

Anal. Calc. for $C_{14}H_{15}BrO_5$: C, 49.00; H, 4.41. Found: C, 48.75; H, 4.14.

The remaining material consisted mainly of unchanged **5**.

(*b*) *From the enone* **9**. Addition of enone[8] **9** (40 mg, 0.13 mmol) to a stirred methanolic NaOMe solution (4.5 mL) immediately afforded crystalline material. After 10 min, the precipitate was dissolved by addition of acetone and an aliquot of the solution was evaporated below 25°. The ^{1}H-n.m.r. spectrum ($CDCl_3$) of the residue showed a 3:1 mixture of **7** and **4**, as estimated by the integration of signals of the benzylidene methine protons and methoxyl groups. The sample examined by ^{1}H-n.m.r. spectroscopy was added to the remaining solution, which was then evaporated. Fractional crystallization gave 20 mg of **7** as the first crop and a 3:1 mixture of **7** and **4** as the second one.

*Methyl 4,6-O-benzylidene-2-chloro-2-deoxy-α-*D-xylo-*hexopyranosid-3-ulose* (**16**). — Addition of enone **14** (30 mg, 0.11 mmol) to a stirred methanolic NaOMe solution (3.3 mL) immediately afforded a precipitate. After being stirred for 30 min, Me_2CO was added to dissolve the precipitate and the mixture was deionized with cation-exchange resin (Amberlite IR-120, H^+). After removal of the resin, the filtrate was evaporated to give a solid residue in almost quantitative yield. The ^{1}H-n.m.r. spectrum of the residue showed that it was almost pure **16** and no signals for the β anomers **23** and **25** were detected. An analytical sample was prepared by recrystallization from EtOH–Me_2CO; m.p. 159–160°, $[\alpha]_D^{25}$ +162° (*c* 0.9, $CHCl_3$); ν_{max} 1755 cm^{-1} (CO); ^{1}H-n.m.r.: δ 5.22 (s, 2 H, H-1,2), 4.58 (d, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 3.93 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.5 Hz, H-5), 4.40 (dd, 1 H, $J_{6,6'}$ 12.8 Hz, H-6), 4.14 (dd, 1 H, H-6′), 5.61 (s, 1 H, PhCH), and 3.47 (s, 3 H, OMe), ^{1}H-n.m.r. (CD_3COCD_3): δ 5.27 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 5.34 (d, 1 H, H-3), 4.69 (d, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 4.04 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.5 Hz, H-5), 4.33 (dd, 2 H, H-6,6′), 5.77 (s, 1 H, PhCH), and 3.45 (s, 3 H, OMe).

Anal. Calc. for $C_{14}H_{15}ClO_5$: C, 56.28; H, 5.06. Found: C, 56.08; H, 5.03.

Similar treatment of **14** (30 mg) with methanol-*d* in the presence of catalytic amount of NaOMe afforded the 2-deuterio derivative **17**; the signal at δ 5.34 (CD_3COCD_3) almost disappeared and that at δ 5.27 appeared as a singlet.

*Methyl 4,6-O-benzylidene-2-bromo-2-deoxy-α-*D-xylo-*hexopyranosid-3-ulose* (**18**). — Treatment of **15** (104 mg, 0.33 mmol) with methanolic NaOMe (10 mL) as already mentioned gave **18** as a solid residue, the ^{1}H-n.m.r. spectrum of which showed that it was almost pure **18**; no signals for the β anomers **24** and **26** were detected. Addition of EtOH to the residue afforded 90 mg of **18** as crystals. The mother liquor was evaporated and chromatographed with 10:1 (v/v) benzene–EtOAc as eluant to give additional **18** (11.9 mg, total yield 89%). An analytical sample was prepared by recrystallization from EtOH–Me_2CO; m.p. 165.5–167°, $[\alpha]_D^{27}$ +178° (*c* 0.4, Me_2CO); ν_{max} 1750 cm^{-1} (CO); ^{1}H-n.m.r.: δ 5.26 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 5.31 (d, 1 H, H-2), 4.61 (d, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 3.98 (q, 1 H, $J_{5,6}$

= $J_{5,6'}$ 1.5 Hz, H-5), 4.45 (dd, 1 H, $J_{6,6'}$ 12.8 Hz, H-6), 4.17 (dd, 1 H, H-6'), 5.64 (s, 1 H, PhCH), and 3.48 (s, 3 H, OMe).

Anal. Calc. for $C_{14}H_{15}BrO_5$: C, 49.00; H, 4.41. Found: C, 49.12; H, 4.36.

Similar treatment of **15** (30 mg) with methanol-*d* in the presence of catalytic amount of NaOMe afforded the 2-deuterio derivative **19**; the signal at δ 5.31 disappeared and that at δ 5.26 appeared as a singlet.

*Methyl 4,6-O-benzylidene-2-chloro-2-deoxy-α-*D-xylo-*hexopyranosid-3-ulose hydrate* (**25**). — To a solution of **21** (530 mg, 1.71 mmol) in tetrahydrofuran (34 mL) was added Bu_4NCl (1.047 g, 3.77 mmol). After being stirred for 3 days the mixture was evaporated and EtOAc–water was added. The organic layer was washed with water, dried, and evaporated. The residue was chromatographed with 10:1 and 5:1 (v/v) benzene–EtOAc as the eluant to give 203 mg of a solid whose ^{1}H-n.m.r. spectrum indicated that it consisted of 3:2 mixture of glycosidulose **23** and hydrate **25**, as estimated by integration of signals of the benzylidene methine protons (CD_3COCD_3): δ 5.72 for **23** and 5.64 for **25**. In the ^{1}H-n.m.r. spectrum (CD_3COCD_3), the following signals are attributable to **23**: δ 5.72 (s, 1 H, PhCH), 5.24 (d, 1 H, $J_{1,2}$ 9.0 Hz, H-1), 4.52 (d, 1 H, H-2), and 3.36 (s, 3 H, OMe). Recrystallization from isopropyl alcohol–Me_2CO gave 110 mg (20%) crystals of hydrate **25**; m.p. 185–186°, $[\alpha]_D^{25}$ +9° (*c* 1, Me_2SO); ν_{max} 3480, 3376 cm^{-1} (OH); ^{1}H-n.m.r. (CD_3COCD_3): δ 4.55 (d, 1 H, $J_{1,2}$ 8.7 Hz, H-1), 3.96 (d, 1 H, H-2), 4.03 (d, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 3.83 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.5 Hz, H-5), 4.19 (d, 2 H, H-6,6'), 5.46 (bs, 1 H, OH), 5.26 (bs, 1 H, OH), 5.64 (s, 1 H, PhCH), and 3.50 (s, 3 H, OMe).

Anal. Calc. for $C_{14}H_{15}ClO_5 \cdot H_2O$: C, 53.09; H, 5.41. Found: C, 53.19; H, 5.44.

*Methyl 4,6-O-benzylidene-2-bromo-2-deoxy-β-*D-xylo-*hexopyranosid-3-ulose hydrate* (**26**). — Treatment of **21** (630 mg, 2.04 mmol) with Bu_4NBr (1.44 g, 4.47 mmol) in tetrahydrofuran (40 mL) as already noted afforded a residue (360 mg) that was extracted with EtOAc. After chromatographic separation, a 3:2 mixture of glycosidulose **24** and hydrate **26** (as estimated by ^{1}H-n.m.r. spectroscopy by integration of signals for the benzylidene methine protons at δ 5.57 for **26** and at δ 5.62 for **24** in chloroform-*d*) was isolated. (The ratio became 1:1 after dissolving the residue in isopropyl alcohol, followed by evaporation). Crystallization from isopropyl ether–Me_2CO gave the hydrate **26** (85 mg, 12%); m.p. 105.5–106°, $[\alpha]_D^{25}$ +21° (*c* 0.9, Me_2CO); ν_{max} 3480, 3360 cm^{-1} (OH); ^{1}H-n.m.r. (CD_3COCD_3): δ 4.60 (d, 1 H, $J_{1,2}$ 8.7 Hz, H-1), 4.06 (d, 1 H, H-2), 4.04 (d, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 3.84 (q, 1 H, $J_{5,6} = J_{5,6'}$ 1.5 Hz, H-5), 4.18 (m, 2 H, H-6,6'), 5.47 (bs, 1 H, OH), 5.20 (bs, 1 H, OH), 5.63 (s, 1 H, PhCH), and 3.47 (s, 3 H, OMe).

Anal. Calc. for $C_{14}H_{15}BrO_5 \cdot H_2O$: C, 46.56; H, 4.74. Found: C, 46.63; H, 4.74.

From the ^{1}H-n.m.r. spectrum of a mixture of **24** and **26** in chloroform-*d*, the following signals are attributable to **24**: δ 5.62 (s, 1 H, PhCH), 5.01 (s, 1 H, $J_{1,2}$ 8.9 Hz, H-1), 4.51 (d, 1 H, H-2), and 3.65 (s, 3 H, OMe).

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