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DENITRATION OF CARBOHYDRATE α-NITROEPOXIDES BY NUCLEOPHILES

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ABSTRACT

Several nucleophiles were separately treated with methyl and phenyl 2,3-anhydro-4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-allopyranoside, to give 2-substituted aldos-3-ulose derivatives. In the latter case, the subsequent β-elimination of the aglyconic phenyl group always occurred to afford the corresponding glycal. Reaction mechanisms thereof are also discussed.

INTRODUCTION

Sugar derivatives possessing an α-nitroepoxide moiety have versatile utility, because the nitro group is convertible into a carbonyl group under mild conditions[1–3]. We now describe the more-detailed results[1] obtained by the reactions of α-nitroepoxides **10** and **11** with several nucleophiles.

RESULTS AND DISCUSSION

α-Nitroepoxides were synthesized from the corresponding α-nitroalkenes by treatment with hydrogen peroxide[4,5] or *tert*-butyl peroxide[5] in weakly alkaline medium, or with sodium hypochlorite[6], and from 3-deoxy-3-halo-3-nitro sugars[7].

Epoxidation of α-nitroalkenes **1–3** was achieved by treatment with 30% aqueous hydrogen peroxide in the presence of an equimolar amount of M sodium hydroxide in THF, affording the corresponding α-nitroepoxides **10–12**, respectively, in high yields**. Similar treatment of β-glycosides **4** and **5** provided a mixture of a nitroepoxide and a nitro alcohol: compounds **10** and **7**, or **11** and **8**, respectively. Similar treatment of the α anomer **6**, however, gave only the nitro alcohol **9**, reveal-

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Treatment of 3-nitro-hex-2-enopyranoses, including **1 and **3**, with 30% aqueous hydrogen peroxide in ethanolic solution (adjusted to pH 8–9 by addition of sodium hydroxide), afforded almost the same results[4].

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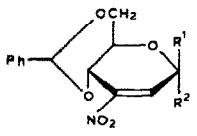
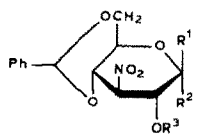
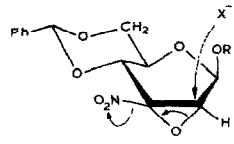


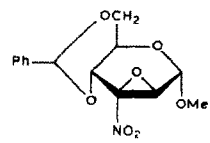
1 R^1 = OMe, R^2 = H
2 R^1 = OPh, R^2 = H
3 R^1 = H, R^2 = OMe



4 R^1 = OMe, R^2 = H, R^3 = Ac
5 R^1 = OPh, R^2 = H, R^3 = Ac
6 R^1 = H, R^2 = OMe, R^3 = Ac
7 R^1 = OMe, R^2 = R^3 = H
8 R^1 = OPh, R^2 = R^3 = H
9 R^1 = R^3 = H, R^2 = OMe



10 R = Me
11 R = Ph



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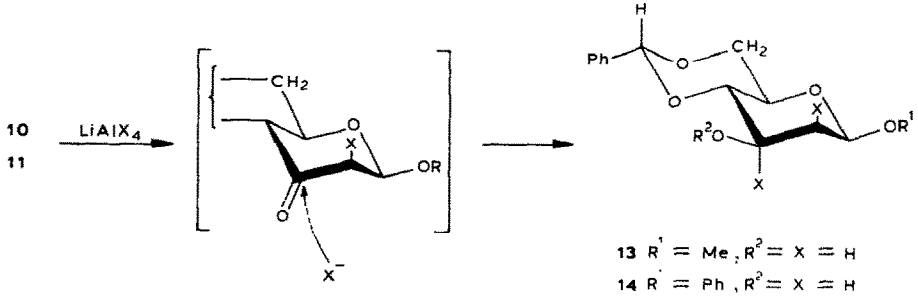
ing that hydrolysis of the 2-*O*-acetyl group occurred preferentially over the elimination of acetic acid.

Treatment of **10** and **11** with lithium aluminum hydride*** afforded 2-deoxy-*β*-D-*arabino*-hexopyranosides **13** and **14**, respectively, in good yields; these were characterized as the 3-acetates **15** and **16**, respectively. Similar treatment of **11** with lithium aluminum deuteride gave the 2(*S*), 3(*R*)-dideuterio derivative **17** in 82% yield; the ^{1}H-n.m.r. spectrum of its 3-acetate **18** showed that the deuterium atoms occupied the axial positions at C-2 and C-3, indicating that the deuteride ion attacked the C-2 atom exclusively from the rear side of the epoxide ring, and then the C-3 atom from the other side (see Scheme 1). Catalytic hydrogenation of **11** in the presence of Pd-C or Raney Ni provided the phenyl 3-deoxy-3-nitro-*β*-D-glucopyranoside derivative **8** in good yield.

Treatment of **10** with concentrated aqueous ammonia in methanol afforded pyrazine derivative **19** in 78% yield. The pyrazine structure of **19** was deduced by elemental analysis, and mass (*m/z* 520, M^+), i.r. (no absorption band due to amino,

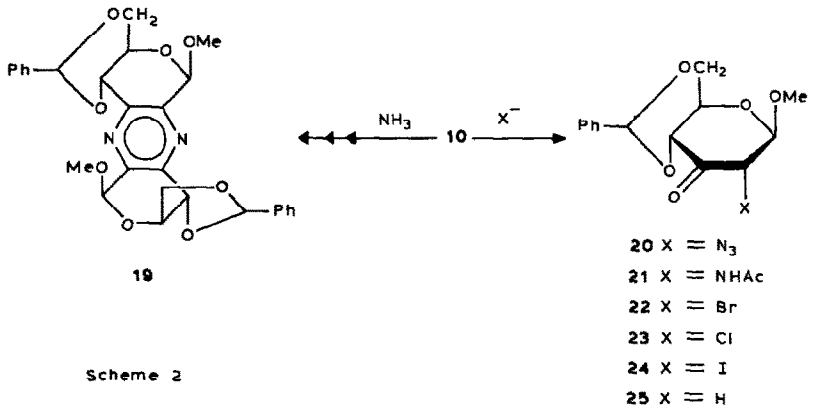


Scheme 1

13 R^1 = Me, R^2 = X = H
14 R^1 = Ph, R^2 = X = H
15 R^1 = Me, R^2 = Ac, X = H
16 R^1 = Ph, R^2 = Ac, X = H
17 R^1 = Ph, R^2 = H, X = D
18 R^1 = Ph, R^2 = Ac, X = D

***Baer and co-workers reported more-detailed studies on reduction of various methyl hexopyranoside derivatives, having an α-nitroepoxide moiety, with sodium borohydride[8] and with palladium- and platinum-catalyzed hydrogenation[9].

nitro, and carbonyl groups), and ^{1}H-n.m.r. spectra (two singlet peaks due to H-1 and benzylidene methine protons, and no signals due to H-2 and H-3). The *erythro* configuration of **19** was deduced from the ^{1}H-n.m.r. spectrum. Apparently, the formation of **19** involves an intermediary 2-amino-2-deoxyaldos-3-ulose produced by attack of ammonia on **10**, followed by successive, inter-bimolecular dehydration and aromatization on air oxidation (see Scheme 2).



19

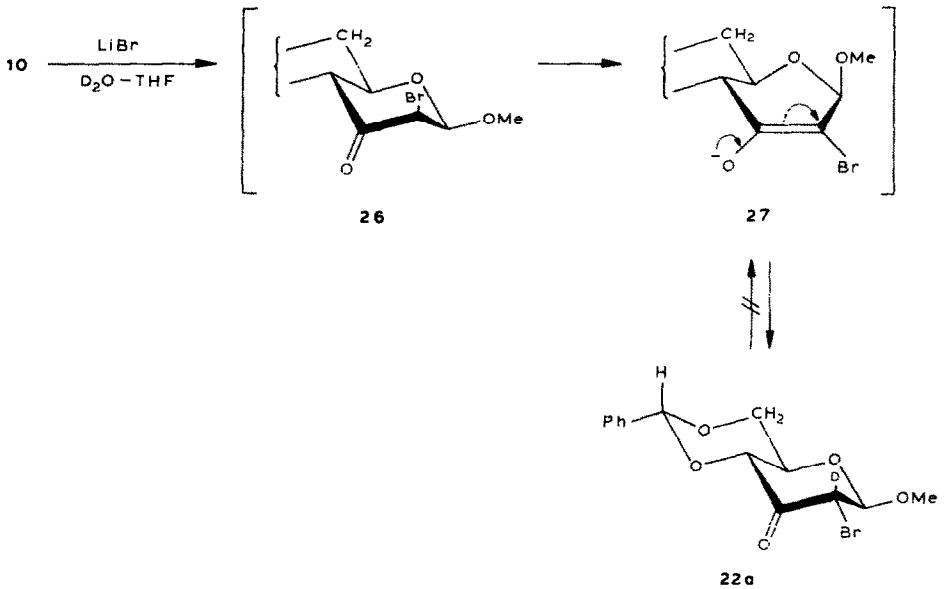
20 X = N_3
21 X = NHAc
22 X = Br
23 X = Cl
24 X = I
25 X = H

Scheme 2

The reaction of **10** with sodium azide afforded the 2-azido derivative **20**, assigned the β-D-*ribo* configuration ($J_{1,2}$ 7.5 Hz), and further characterized as the 2-acetamido derivative **21** by hydrogenation in the presence of Pd-C in 1,4-dioxane-acetic anhydride.

The α-nitroepoxide **10** was treated with lithium bromide monohydrate in THF for 4 h at room temperature, to give the 2-bromo-3-nitro derivative **22** in 75% yield†. The higher carbonyl absorption band (1739 cm^{-1}) suggested the equatorial orientation of the bromine atom, and this deduction was supported by the coupling constants, $J_{1,2}$ 9.0 and $J_{2,4}$ 1.5 Hz. To obtain some information on the stereochemistry of the attack by bromide ion, the following two experiments were carried out: (*i*) treatment of **10** with anhydrous lithium bromide in THF–D_2O afforded the 2-deuterio derivative (**22a**) of **22**; (*ii*) no deuteration was observed by similar treatment of **22** with lithium bromide in the presence of an equimolar amount of lithium nitrite in THF–D_2O. These results indicated (*a*) that the bromide ion also attacks at C-2 from the rear side of the epoxide ring, in SN2′-like fashion, to give the β-D-*arabino* isomer **26** as a primary product that then epimerizes, *via* enolate **27**, to the β-D-*ribo* isomer **22a** through irreversible, keto–enol tautomerism (see Scheme

†An α-nitroepoxide ring-opening with a fluoride ion was accomplished by Szarek and co-workers[3]: reaction of potassium hydrogenfluoride with 1,2-anhydro-3,4:5,6-di-*O*-isopropylidene-1-*C*-nitro-D-mannitol gave a 2-deoxy-2-fluoro-D-glucose derivative.



3); (*b*) the proton at C-2 is not exchangeable under the condition employed; and (*c*) predominance of the so-called Δ^2 effect[10] over the α-halo effect[11].

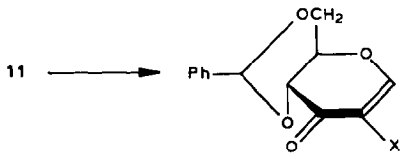
Similar treatment of **10** with lithium chloride gave the 2-chloro derivative **23** in 56% yield. The yield of **23** was raised to 64% by use of DMF instead of THF.

The reaction of **10** with lithium iodide was fairly complex. When compound **10** (0.1 mmol) was treated with lithium iodide (0.4 mmol) in DMF (1 mL) for 14 h at −21°, the product extracted by ethyl acetate or chloroform was almost pure methyl 4,6-*O*-benzylidene-2-deoxy-β-D-*erythro*-hexopyranosid-3-ulose (**25**, 48% yield). If, however, the reaction time was shortened to 15 min, the 2-iodo derivative **24** could be isolated in 26% yield. Therefore, the 2-iodo derivative **24** is presumably a precursor of 2-deoxyglycosid-3-ulose **25**. It was noteworthy that, when the amount of DMF was increased to 2.5 mL from 1 mL, the reductive de-iodination was suppressed, to give a 1.2:1 mixture of **24** and **25**. In comparison with the corresponding chloro and bromo derivatives, 2-iodo derivative **24** is unstable, and should be stored in a freezer. In these halogenations, no β-D-*arabino* isomer was isolated, suggesting that the β-D-*ribo* isomer is thermodynamically more stable than the corresponding β-D-*arabino* isomer.

In contrast to the results with methyl derivative **10**, the reaction of the phenyl analog **11** with the nucleophiles was always accompanied by β-elimination, yielding†† compounds **28**–**32**. Such a difference is reasonable, because a phenoxide is a better leaving-group than a methoxide. For example, the reaction of **11** with sodium

††Baer and Madumelu also reported the formation of glycal-type products by the reactions of **10** and its stereoisomers with dimethylamine[12].

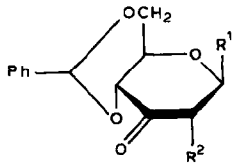
azide gave 2-azido-1-en-3-ulose **28** in 76% yield. The 1-enulose structure of **28** was determined on the basis of its i.r. and ^{1}H-n.m.r. spectra and elemental analysis. Catalytic hydrogenation in the presence of Pd–C in 1,4-dioxane–acetic anhydride



28 X = N_3
29 X = Cl
30 X = Br
31 X = I
32 X = H

gave the 2-acetamido derivative **33**.

Similarly, treatment of **11** with lithium chloride, bromide, and iodide gave the corresponding 2-halo-1-en-3-uloses **29–31** in yields of 73, 77, and 71%, respectively. The 2-iodo-1-enulose **31** gradually decomposed at room temperature, whereas the chloro (**29**) and bromo (**30**) analogs were much more stable. On the other hand, it was expected that the reaction of **11** with lithium iodide under milder conditions might afford an intermediary β-D-*ribo* derivative **34** and/or 1,5-anhydro-4,6-*O*-benzylidene-D-*erythro*-hex-1-en-3-ulose (**32**), the latter derived by reductive deiodination, as observed for the methyl analog. Then, compound **11** was treated with lithium iodide under cooling with ice–water for 10 min, to afford a 1.2:1 mixture of 2-iodo-1-en-3-ulose **31** and unreacted **11**; no evidence for the formation of phenyl 2-iodo-hexopyranosid-3-ulose **34** and 1-en-3-ulose **32** was obtained.



33 R^1 = H, R^2 = NHAc
34 R^1 = OPh, R^2 = I

In addition to these results, the inertness of H-2 of the methyl 2-bromo derivative **22** towards proton exchange, as has already been described, suggests that phenyl 2-deoxy-2-iodo-β-D-*ribo*-hexopyranosid-3-ulose (**34**) is not an intermediate of the corresponding 2-halo-1-enulose. A more reasonable reaction-route is the direct elimination of phenol from the β-D-*arabino* isomer **35**, or enolate **36** (see Scheme 4).

TABLE I

CHEMICAL SHIFTS (δ) AT 100 MHz OF THE PRODUCTS IN DIMETHYL SULFOXIDE-d_6 (Me_4Si AS INTERNAL STANDARD)

Compound	*H-1*	*H-2*	*H-4*	*H-5*	*H-6a*	*H-6e*	*PhCH*	*OMe*
20[a]	4.53	4.13	4.32	3.68	3.94	4.52	5.57	3.66
22	4.85	5.05	4.65	3.8	3.91	4.38	5.72	3.49
23	4.81	4.96	4.65	3.8	3.93	4.40	5.75	3.31
24	4.92	5.19	4.74	3.79	3.94	4.40	5.73	3.49
29	8.17		4.96	4.64	4.08	4.44	5.75	
30	8.15		4.93	4.61	4.07	4.42	5.71	
31	8.15		4.91	4.60	4.06	4.41	5.73	

[a]Recorded in chloroform-*d*.

TABLE II

FIRST-ORDER COUPLING-CONSTANTS (Hz) MEASURED AT 100 MHz FOR THE PRODUCTS IN DIMETHYL SULFOXIDE-d_6

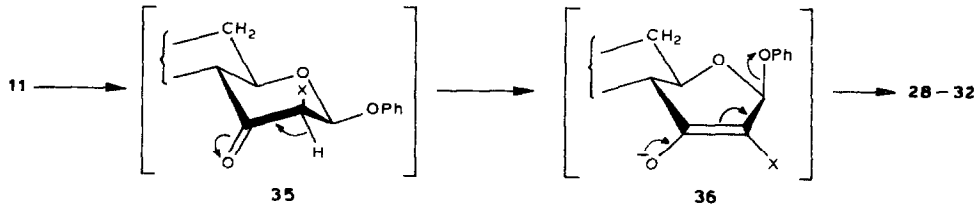
Compound	$J_{1,2}$	$J_{2,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6e}$	$J_{6a,6e}$
20[a]	7.5	1.5	10	10	4.9	10
22	9.0	1.5	10	10	4.0	10
23	8.1	1.3	10	10	4.4	10
24	8.6	1.4	10	10	4.1	10
29			12	10	5.0	10
30			12.5	10	5.0	10
31			12.5	10	5.0	10

[a]Recorded in chloroform-*d*.

Such a facile β-elimination of phenol should be, at least partially, attributable to the instability of the *arabino* isomer due to the Δ^2 effect.

EXPERIMENTAL

Phenyl 2,3-andhydro-4,6-O-benzylidene-3-nitro-β-D-allopyranoside (**11**). — (*a*) *From the nitroalkene* (**2**. To a solution of **2** ref.[13]; 178 mg, 0.5 mmol) and 30% aqueous hydrogen peroxide (0.5 mL) in THF (3 mL) was added M sodium hydro-



xide (0.5 mL). After being stirred for 30 min, the mixture was partitioned between benzene and water. The organic layer was washed successively with aqueous sodium thiosulfate and water, dried ($MgSO_4$), and evaporated to a solid (170 mg, 92%), the t.l.c. and the ^{1}H-n.m.r. spectrum of which showed that it was pure **11**; the product was used for the next reaction. An analytical sample was recrystallized from ethanol; m.p. 175–176°, $[\alpha]_D^{22}$ −149° (*c* 1, chloroform); ν_{max} 1570 cm^{-1} (NO_2); ^{1}H-n.m.r. ($CDCl_3$): δ 5.76 (s, 1 H, PhCH), 5.55 (s, 1 H, H-1), 5.17 (d, 1 H, $J_{4,5}$ 10 Hz, H-4), and 4.06 (s, 1 H, H-2).

Anal. Calc. for $C_{19}H_{17}NO_7$: C, 61.45; H, 4.61; N, 3.77. Found: C, 61.28; H, 4.52; N, 3.93.

Similar epoxidation of **1** (ref.[14]) and **3** (ref.[15]) gave **10** and **12** in 89 and 78% yield, respectively, which were identical with the respective authentic samples[4].

(*b*) *From the 2-acetate* **5**. Similar treatment of **5** (ref.[13]; 208 mg, 0.5 mmol) gave a 1:1 mixture (186 mg) of the epoxide **11** and nitro alcohol **8** (ref.[13]) as judged from ^{1}H-n.m.r. spectrum (in CD_3COCD_3) based on the benzylidene methine proton. Recrystallization from ethanol gave 80 mg (43%) of **11** as a first crop and 41 mg (22%) of **8** (ref.[13]) as a second crop. The residue was chromatographed with 10:1 (v/v) benzene–ethyl acetate, to give an additional 35 mg (19%) of **8**.

Similar treatment of the methyl 2-*O*-acetyl-β-D-glucopyranoside derivative[14] **4** (177 mg, 0.5 mmol) also afforded an ~1:1 mixture (145 mg) of the epoxide **10** and nitro alcohol **7**, as estimated by ^{1}H-n.m.r. spectroscopy.

Similar treatment of the methyl 2-*O*-acetyl-α-D-glucopyranoside derivative[15] **6** (177 mg, 0.5 mmol) afforded the nitro alcohol[15] **9** (151 mg, 97%), but no evidence for the formation of epoxide **12** was obtained by ^{1}H-n.m.r. spectroscopy.

*Phenyl 4,6-O-benzylidene-2-deoxy-β-D-arabino-hexopyranoside (***14**). — To a solution of **11** (742 mg, 2 mmol) in abs. THF (30 mL) was added lithium aluminum hydride (0.5 g), and the mixture was stirred for 2 h. To the mixture were successively added ethyl acetate (15 mL) and water (10 mL); after evaporation, chloroform and conc. sodium hydroxide were added. The organic layer was successively washed with aqueous sodium hydroxide and water, evaporated. Crystallization and recrystallization from ethanol–water gave 550 mg (84%) of **14**; m.p. 175–176°, $[\alpha]_D^{22}$ −60.3° (*c* 1, chloroform); ν_{max} 3330 cm^{-1} (OH).

Anal. Calc. for $C_{19}H_{20}O_5$: C, 69.50; H 6.14. Found: C, 69.72; H, 6.49.

Treatment of **14** (200 mg, 0.61 mmol) with pyridine (5 mL)–acetic anhydride (2 mL) overnight at room temperature gave the acetate **16** in 84% yield (190 mg); m.p. 136–137°, $[\alpha]_D^{22}$ −65.6° (*c* 1, chloroform); ν_{max} 1735 cm^{-1} (OCO); ^{1}H-n.m.r. ($CDCl_3$): δ 5.50 (s, 1 H, PhCH), 5.22 (q, $J_{1,2a}$ 10, $J_{1,2e}$ 2.5 Hz, H-1), 5.15 (m, 1 H, H-3), 4.32 (q, 1 H, $J_{5,6e}$ 4.0, $J_{6a,6e}$ 10 Hz, H-6*e*), 3.79 (t, 1 H, $J_{5,6a}$ 10 Hz, H-6*a*), 3.71 (t, 1 H, $J_{3,4} = J_{4,5}$ 10 Hz, H-4), 3.48 (sex, 1 H, H-5), 2.57 (m, 1 H, $J_{2a,2e}$ 12.5, $J_{2e,3}$ 5.0 Hz, H-2*e*), 2.04 (s, 3 H, OAc), and 1.94 (m, 1 H, $J_{2a,3}$ 10 Hz, H-2*a*).

Anal. Calc. for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99. Found: C, 68.21; H, 6.06.

Similar reduction of **11** (371 mg, 1 mmol) with lithium aluminum deuteride gave the deuterated derivative **17**.

*Methyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-β-*D-arabino-*hexopyranoside* (**15**). — Similar reduction of **10** (618 mg, 2 mmol) with lithium aluminum hydride, followed by acetylation, gave the 3-acetate **15** in 75% yield, after recrystallization from ethanol; m.p. 141–142°, $[\alpha]_D^{22}$ −69.3° (*c* 1, chloroform); ν_{max} 1745 cm^{-1} (OCO); ^{1}H-n.m.r. ($CDCl_3$): δ 5.54 (s, 1 H, PhCH), 5.10 (oct, 1 H, $J_{2a,3}$ 11.6, $J_{2e,3}$ 5.1, $J_{3,4}$ 9.0 Hz, H-3), 4.57 (q, 1 H, $J_{1,2e}$ 2.5, $J_{1,2a}$ 9.6 Hz, H-1), 4.35 (q, 1 H, $J_{5,6e}$ 4.5, $J_{6a,6e}$ 10 Hz, H-6*e*), 3.84 (t, 1 H, $J_{5,6a}$ 10 Hz, H-6*a*), 3.67 (t, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 3.50 (s, 3 H, OMe), 3.44 (sex, 1 H, H-5), 2.44 (oct, 1 H, $J_{2a,2e}$ 12.9 Hz, H-2*e*), 2.06 (s, 3 H, OAc), and 1.65 (oct, 1 H, H-2*a*).

Anal. Calc. for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 62.32; H, 6.68.

*Phenyl 2-O-acetyl-4,6-O-benzylidene-3-deoxy-3-nitro-β-*D-*glucopyranoside* (**5**). — A solution of **11** (371 mg, 1 mmol) in ethyl acetate (50 mL) was hydrogenated in the presence of 5% Pd–C (300 mg). After 8 h, the catalyst was filtered off, and the filtrate was evaporated to a solid, which was acetylated with pyridine (7 mL)–acetic anhydride (3 mL), to give 352 mg (85%) of **5**, identical with an authentic sample[6].

Similar hydrogenation of **11** (1 mmol) in the presence of Raney Ni (300 mg), followed by acetylation, provided **5** in 68% yield.

*2,3:5,6-Bis(methyl 4,6-O-benzylidene-2,3-dideoxy-β-*D-erythro-*hexopyranosido)[2,3-*b.e*]pyrazine* (**19**). — To a solution of **10** (1.546 g, 5 mmol) in methanol (50 mL) was added aqueous ammonia solution (30%, 2 mL). After being stirred for 40 h at room temperature, the mixture was evaporated. Recrystallization from methanol afforded 1.013 g (78%) of **19**; m.p. 248° (dec.), $[\alpha]_D^{22}$ −129° (*c* 1, Me_2SO); ^{1}H-n.m.r. ($CDCl_3$): δ 5.87 (s, 1 H, PhCH), 5.82 (s, 1 H, H-1), 5.08 (d, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 4.47 (q, 1 H, $J_{5,6e,3}$ 5.0, $J_{6a,6e}$ 9.5 Hz, H-6*e*), 4.06 (t, 1 H, $J_{5,6a}$ 9.5 Hz, H-6*a*), 3.99 (sextet, 1 H, H-5), and 3.63 (s, 3 H, OMe).

Anal. Calc. for $C_{28}H_{28}N_2O_8$: C, 64.60; H, 5.42; N, 5.38. Found: C, 64.30; H, 5.68; N, 5.68.

*Methyl 2-acetamido-4,6-O-benzylidene-2-deoxy-β-*D-ribo-*hexopyranosid-3-ulose* (**21**). — To a solution of **10** (309 mg, 1 mmol) in THF (15 mL)–H_2O (1.6 mL) was added sodium azide (97.5 mg, 1.5 mmol), and the mixture was stirred for 7 h and then evaporated below 40°. The residue was partitioned between chloroform and water. The organic layer was dried (Na_2SO_4), and evaporated, to give a solid residue (272 mg), the i.r. spectrum of which showed the presence of an azido (2124 cm^{-1}) and a carbonyl group (1739 cm^{-1}). The residue was hydrogenated in the presence of 5% Pd–C (250 mg) in 1,4-dioxane (30 mL)–acetic anhydride (5 mL). Recrystallization from ethanol–acetone gave 266 mg (83%) of the acetamido derivative **21**; m.p. 204–205° (dec.), $[\alpha]_D^{22}$ −49.8° (*c* 1, Me_2SO); ν_{max} 1744 (CO), 1663, 1634, and 1563 cm^{-1} (NHAc).

Anal. Calc. for $C_{16}H_{19}NO_6$: C, 59.80; H, 5.96; N, 4.36. Found: C, 59.52; H, 5.93; N, 4.35.

*Methyl 2-bromo-4,6-O-benzylidene-2-deoxy-β-*D-ribo-*hexopyranosid-3-ulose* (**22**). — To a solution of **10** (309 mg, 1 mmol) in THF (20 mL) was added lithium

bromide monohydrate (300 mg), and the mixture was stirred for 4 h. After addition of water (30 mL), the organic solvent was evaporated, to yield precipitates, which were recrystallized from ethanol to give 257 mg (75%) of **22**; m.p. 210° (dec.), $[\alpha]_D^{22}$ −131° (*c* 1, chloroform); ν_{max} 1739 cm^{-1} (CO).

Anal. Calc. for $C_{14}H_{15}BrO_5$: C, 49.00; H, 4.41. Found: C, 48.47; H, 4.65.

Similar treatment of **10** (309 mg) with anhydrous lithium bromide (249 mg, 2.86 mmol) in THF (20 mL)–D_2O (0.5 mL) gave the 2-deuterio derivative (**22a**) of **22**).

Treatment of **22** (100 mg, 0.29 mmol) with anhydrous lithium bromide (50 mg, 0.57 mmol) and lithium nitrite (15 mg, 0.29 mmol) in THF (10 mL)–D_2O (0.5 mL) for 4 h at room temperature resulted only in the recovery of **22** (without deuteration), indicating that deuteration at C-2 is not effected by the nitrite ion released from the nitro group of **10**, and therefore, that the transformation of **26** into **22a** is irreversible.

*Methyl 4,6-O-benzylidene-2-chloro-2-deoxy-β-*D-ribo-*hexopyranosid-3-ulose* (**23**). — A mixture of **10** (61.8 mg, 0.2 mmol), lithium chloride (34 mg, 0.8 mmol), and DMF (1 mL) was stirred for 14 h at ~20° and then diluted with ethyl acetate, washed successively with aqueous sodium thiosulfate and water, and then evaporated (~133 Pa). A precipitate caused by addition of water was filtered off, washed with water, and dissolved in ethyl acetate. The solution was washed with water, dried ($MgSO_4$), and evaporated, to give 45 mg of pure **23**. Recrystallization from ethanol gave 38 mg (64%) of **23**; m.p. 180–182°, $[\alpha]_D^{22}$ −25.3° (*c* 1, acetone); ν_{max} 1739 cm^{-1} (CO).

Anal. Calc. for $C_{14}H_{15}ClO_5$: C, 56.29; H, 5.06. Found: C, 56.46; H, 4.92.

*Methyl 4,6-O-benzylidene-2-deoxy-2-iodo-β-*D-ribo-*hexopyranosid-3-ulose* (**24**). — A mixture of **10** (61.8 mg, 0.2 mmol), lithium iodide (108 mg, 0.8 mmol), and DMF (1 mL) was stirred for 15 min at ~20°. Processing as described for the preparation of **23** gave 28 mg (36%) of **24** as almost the sole product extractable by ethyl acetate. Recrystallization from ethanol gave 20 mg (26%) of **24**; m.p. 155° (dec.), $[\alpha]_D^{22}$ +35° (*c* 0.7, acetone); ν_{max} 1732 cm^{-1} (CO).

Anal. Calc. for $C_{14}H_{15}IO_5$: C, 43.10; H, 3.88. Found: C, 42.93; H, 3.91.

*Methyl 4,6-O-benzylidene-2-deoxy-β-*D-erythro-*hexopyranosid-3-ulose* (**25**). — Treatment of **10** (61.8 mg, 0.2 mmol) with lithium iodide as described for the preparation of **23** gave 28 mg (53%) of almost pure **25**. Recrystallization from ethanol gave 25.3 mg (48%) of **25**, identical with an authentic sample[16].

*1,5-Anhydro-2-azido-4,6-O-benzylidene-2-deoxy-*D-erythro-*hex-1-en-3-ulose* (**28**). — To a solution of **11** (1.11 g, 3 mmol) in THF (50 mL)–water (5 mL) was added sodium azide (1.44 g, 22.2 mmol). After stirring for 7 h, water was added, and the organic solvent was evaporated below 40°, to give a precipitate. Crystallization from isopropyl alcohol–acetone provided 620 mg (76%) of **28**, m.p. 96° (dec.), $[\alpha]_D^{22}$ +148° (*c* 0.5, chloroform); ν_{max} 2125, 2104 (N_3), 1689 and 1596 cm^{-1} (C=C–CO); ^{1}H-n.m.r. ($CDCl_3$): δ 7.23 (s, 1 H, H-1), 5.54 (s, 1 H, PhCH), and 2.6–3.8 (m, 4 H, H-4,5,6*a*,6*e*).

Anal. Calc. for $C_{13}H_{11}N_3O_4$: C, 57.14; H, 4.06; N, 15.38. Found: C, 57.37; H, 4.03; N, 14.96.

2-Acetamido-1,5-anhydro-4,6-O-benzylidene-2-deoxy-D-ribo-*3-hexulose* (**33**). — Compound **28** (273 mg, 1 mmol) was hydrogenated in the presence of 10% Pd–C (250 mg) in 1,4-dioxane (30 mL)–acetic anhydride (5 mL), to give 289 mg (almost quantitative yield) of the acetamido derivative **33**; m.p. 242° (dec.), $[\alpha]_D^{22}$ −55.5° (*c* 1, Me_2SO); ν_{max} 1738 (CO), 1717, 1644, and 1550 cm^{-1} (NHAc); ^{1}H-n.m.r. (CD_3SOCD_3): δ 8.10 (d, 1 H, $J_{NH,2}$ 7.5 Hz, NH), 5.65 (s, 1 H, PhCH), 4.8 (m, 1 H, H-2), 4.66 (d, 1 H, $J_{4,5}$ 10 Hz, H-4), 4.29 (q, 1 H, $J_{5,6e}$ 5.0, $J_{6e,6a,3}$ 10 Hz, H-6*e*), 4.19 (q, 1 H, $J_{1a,1e}$ 11.3, $J_{1e,2}$ 7.5 Hz, H-1*e*), 3.84 (t, 1 H, $J_{5,6a}$ 10 Hz, H-6*a*), 3.64 (sex, 1 H, H-5), and 3.45 (t, 1 H, $J_{1a,2}$ 11.3 Hz, H-1*a*).

Anal. Calc. for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.75; H, 5.79; N, 4.81.

1,5-Anhydro-4,6-O-benzylidene-2-chloro-2-deoxy-D-erythro-*hex-1-en-3-ulose* (**29**). — A mixture of **11** (74.2 mg, 0.2 mmol), lithium chloride (34 mg, 0.8 mmol), and THF (4 mL) was stirred for 14 h at ~20°, and then partitioned between benzene and water. The organic layer was washed with water, dried, and evaporated, to give 46 mg (86%) of **29**, which was pure as judged by ^{1}H-n.m.r. spectroscopy. Recrystallization from isopropyl alcohol–acetone gave 39 mg (73%) of **29**; m.p. 176.5–177° (dec.), $[\alpha]_D^{22}$ +190° (*c* 1, acetone); ν_{max} 1712 and 1585 cm^{-1} (O–C=C–CO).

Anal. Calc. for $C_{13}H_{11}ClO_4$: C, 58.56; H, 4.16. Found: C, 58.34; H, 4.16.

1,5-Anhydro-4,6-O-benzylidene-2-bromo-2-deoxy-D-erythro-*hex-1-en-3-ulose* (**30**). — To a solution of **11** (742 mg, 2 mmol) in THF (40 mL) was added lithium bromide monohydrate (500 mg, 4.77 mmol) at room temperature. After stirring for 3 h at room temperature, the mixture was evaporated, and the resulting solid residue was washed with water. Recrystallization from isopropyl alcohol–acetone gave 479 mg (77%) of **30**; m.p. 174–178° (dec.), $[\alpha]_D^{22}$ +213° (*c* 1, chloroform); ν_{max} 1710, 1580, and 1572 cm^{-1} (O–C=C–CO).

Anal. Calc. for $C_{13}H_{11}BrO_4$: C, 50.19; H, 3.56. Found: C, 50.15; H, 3.52.

1,5-Anhydro-4,6-O-benzylidene-2-deoxy-2-iodo-D-erythro-*hex-1-en-3-ulose* (**31**). — To a solution of **11** (74.4 mg, 0.2 mmol) in DMF (1 mL) was added lithium iodide (107 mg, 0.8 mmol). After being stirred for 3 h at ~20°, the mixture was diluted with water, and the resulting precipitate was filtered off; the filtrate was washed with water, dried ($MgSO_4$), and evaporated, to give a solid residue, which was pure **31** as judged from ^{1}H-n.m.r. spectroscopy. Recrystallization from isopropyl alcohol–acetone gave 51 mg (71%) of **31**; m.p. 176° (dec.), $[\alpha]_D^{22}$ +204° (*c* 1, acetone); ν_{max} 1704, 1562, and 1558 cm^{-1} (O–C=C–CO).

Anal. Calc. for $C_{13}H_{11}IO_4$: C, 43.60; H, 3.10. Found: C, 43.82; H, 3.18.

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