Steric and Conformational Effects in the Dehalogenation of 2-Halo Sugar Derivatives with Tributylstannane[1]

Derek Horton,* Waldemar Priebe,† and Marcos L. Sznaidman‡

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

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The stereochemistry of dehalogenation of 2-halo sugars with tributyltin hydride has been investigated in terms of the influence of steric and conformational effects using deuterium-labeling techniques. Detailed analysis of the results (Tables I–III) demonstrates that the size and orientation of the ring substituents are a determining factor in the stereochemical outcome of the reaction. However, some results can only be explained considering reduction of two equilibrating radical conformers.

Introduction

In earlier work,[2,3] directed to synthesis of 2-deoxyglycosides of complex aglycons, we established the preparative utility of alkoxyhalogenation of acylated glycals with NIS[4] (NBS)-ROH, followed by dehalogenation by use of Bu_3SnH. Our previous studies[2] have shown that dehalogenation of some 2′-iododaunorubicin analogs (**1** and **3**) with tributyltin deuteride is highly stereoselective, giving mainly the isomer having deuterium axially disposed at C-2 of the sugar ring (Scheme I). The observed results prompted the present detailed studies on the stereochemistry of this reaction with various model 2-bromo- and 2-iodoglycosides.

Here we present a generalized series of experiments on a stereochemical range of acetylated alkyl 2-deoxy-2-halopento- and hexopyranosides submitted to dehalogenation by (^{2}H)tributylstannane (Bu_3SnD) to afford mixtures of 2-epimeric monodeuterio glycosides whose proportions were determined by ^{1}H-NMR (500 MHz) spectroscopy. Results are presented in Tables I–III.

Results and Discussion

There is substantial evidence that the reduction of alkyl halides by organotin hydrides goes through a radical mechanism.[5] For example, methyl glycoside derivatives **5**, **6**, and **8**, having different halogen substituents and/or configurations at C-2, all undergo dehalogenation with (^{2}H)tributylstannane (Bu_3SnD) to give the isomeric monodeuterated products **7ax** (axial deuterium) and **7eq** (equatorial deuterium) in the same ratio of 4:1. This result indicates that each of these compounds loses the halogen to give a common radical intermediate, which then reacts with Bu_3SnD to afford the observed isomers in the same ratio (Scheme II). The stereochemistry of this reaction is established in the second step.

Scheme I

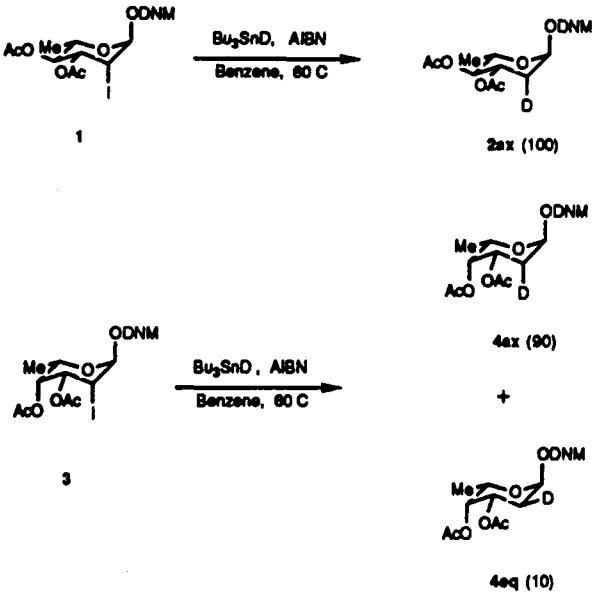
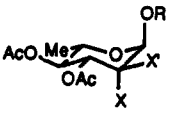
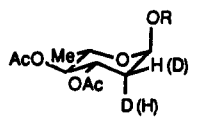
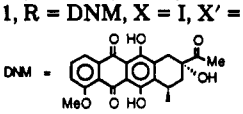


Table I. Product Distribution in the Dehalogenation of Alkyl 3,4-Di-*O*-acetyl-2,6-dideoxy-2-halo-α-L-mannopyranosides with Bu_3SnD

starting material	products
	
5, R = Me, X = I, X′ = H	**7ax** (80 + **7eq** (20)
6, R = Me, X = Br, X′ = H	**7ax** (80) + **7eq** (20)
8, R = Me, X = H, X′ = Br	**7ax** (80) + **7eq** (20)
9, R = Pr^i, X = I, X′ = H	**11ax** (90) + **11eq** (10)
10, R = Pr^i, X = Br, X′ = H	**11ax** (90) + **11eq** (10)
12, R = Bu^t, X = I, X′ = H	**13ax** (95) + **13eq** (5)
1, R = DNM, X = I, X′ = H	**2ax** (100)



Steric Effects. Steric effects play an important role in determining the stereochemistry of tin hydride reductions,[6] with attack by the reductant being favored from the less-hindered side of the intermediate radical. Con-

† Present address: The University of Texas System Cancer Center, M.D. Anderson Hospital and Tumor Institute, 1515 Halcombe Blvd., Houston, TX 77030.

‡ Present address: The University of Virginia, Department of Chemistry, McCormick Rd., Charlottesville, VA 22901.

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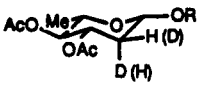
0022-3263/93/1958-1821$04.00/0

Table II. Product Distribution in the Dehalogenation of Alkyl 3,4-Di-*O*-acetyl-2,6-dideoxy-2-halo-β-L-glucopyranosides with Bu_3SnD

starting material	products
	
14, R = Me, X = I	**16ax** (60) + **16eq** (40)
15, R = Me, X = Br	**16ax** (60) + **16eq** (40)
17, R = Pr^i, X = I	**19ax** (60) + **19eq** (40)
18, R = Pr^i, X = Br	**19ax** (60) + **19eq** (40)
20, R = Bu^t, X = I	**21ax** (60) + **21eq** (40)

cordant with this expectation, the present results (Table I) show that, as the steric bulk of the aglycon increases, the proportion of axial deuterium-labeled compound increases. The results show that approach of the reagent from the top side is less favored when the aglycon is *tert*-butyl than when it is methyl, and this difference may be attributed to steric factors.

Table II shows that, when the aglycon lies in the equatorial disposition, the proportion of axial vs equatorial epimers in the product remains the same (60:40) despite the size of the R group. This indicates that there is no detected steric hindrance to the approach of the reagent attributable to the equatorially disposed aglycon.

Literature results on related radical reactions indicate that there is a preference for the tin hydride reagent to approach a radical in a cyclohexane system from the axial side,[7] and this has been interpreted in terms of torsional effects that arise in the transition state. This interpretation explains why a higher proportion of axial deuterium-labeled compound is obtained, even when all of the substituents are equatorial and there is no steric effect for the approach of the reagent from either side of the radical (Table II).

Steric effects are also evident when the orientation of the 4-*O*-acetyl group changes from equatorial to axial (compare entries 1 and 5, 2 and 6, 3 and 7, and 4 and 8 in Table III). The increase in the proportion of equatorial D-labeled product indicates that the presence of an axial group at C-4 prevents to some extent the approach of the reagent from the bottom side of the molecule due to 1,3 steric interactions that might arise in the transition state.

Conformational Effects. When the 5-methyl group is replaced by hydrogen (compare entries 1 and 2, 3 and 4, 5 and 6, and 7 and 8 in Table III), an increase of the equatorial D-labeled isomer is observed in the final ratio of products. These results cannot be explained in terms of steric factors, since the substituent at position 5 is far from the reacting center. Therefore, we propose that rapidly interconverting radical conformers undergo competitive reduction from the axial and equatorial directions (Scheme III). For example, comparison of entries 7 and 8 (Table III) shows that the ratio of transition states **32b**/**32a** will be higher than that of **30b**/**30a** (Scheme III), mainly because the absence of the methyl group at position 5 that would destabilize transition states **30b** more than **32b**. The ratio of approach of the reagent (Bu_3SnD) from the top to the bottom will be higher in transition states **30b** or **32b** than in **30a** or **32a**, respectively, due to steric and torsional factors. In consequence, the higher proportion of **32b**, and its preferential reactivity from the top, would explain the higher proportion of the equatorial deuterium epimer (**33eq**) in the final mixture.

Giese and co-workers[8] have demonstrated by ESR spectroscopy that 2-deoxyhexopyranos-2-yl radicals, exist in a $^4C_1$ (D) conformation. To our knowledge no studies have been carried with 2-deoxypentopyranos-2-yl radicals. It might be the case that the proportion of the $^4C_1$ (L) conformer (**32b**) would be high enough to be detected by ESR.

Conclusions

This comparative study permits a predictive interpretation of dehalogenation of alkyl 2-haloglycopyranosides with $Bu_3SnH(D)$. The general conclusions should be broadly applicable with other free-radical reductions. We have demonstrated that, although steric factors play a key role in determining the stereochemical outcome of these reactions, in some cases reduction of conformationally equilibrating radicals is necessary to explain the observed results. The extent and the factors influencing this conformational equilibrium will be the subject of further studies.

Experimental Section

General Methods. Solvents were dried and redistilled just prior to use. Melting points were determined in open glass capillaries and are uncorrected. ^{1}H-NMR spectra were recorded in $CDCl_3$ at 500 MHz. Evaporations were performed under vacuum. TLC was performed on precoated aluminum sheets (0.2 mm) and glass plates (0.25 mm) coated with Silica-Gel 60F-254 (E. Merck, Darmstadt); components were detected by spraying the plates with 0.1 M ceric sulfate in 2 M sulfuric acid, with subsequent heating. Column chromatography was performed with silica gel 60 (230–400 mesh, E. Merck, Darmstadt). HPLC was performed with an apparatus equipped with a UV absorbance detector.

Glycosides. The alkyl 2-deoxy-2-iodopyranosides **5**, **9**, **12**, **14**, **17**, **20**, **22**, **24**, **26**, **28**, **30**, and **32** were obtained as already described by addition of NIS and MeOH to the appropriate glycal in dry acetonitrile.[3]

Methyl 3,4-Di-*O*-acetyl-2-bromo-2,6-dideoxy-α-L-glucopyranoside (8). 3,4-Di-*O*-acetyl-L-rhamnal (0.6 g, 2.8 mmol) was dissolved in CCl_4 (14 mL) at 0 °C. The flask was protected from light, and bromine was added dropwise until a slight red color persisted. The solution was kept for 10 min at 0 °C and evaporated under diminished pressure to a syrup that was dissolved in dry CH_2Cl_2 (30 mL), and the solution was added to a vigorously stirred suspension of HgO (1.4 g, 6.45 mmol), $HgBr_2$ (0.36 g, 1 mmol), 4-Å molecular sieves (4 g), and dry MeOH (2 mL, 48 mmol) in dry CH_2Cl_2 (60 mL). The mixture was stirred overnight, whereupon TLC (5:1 hexane–EtOAc) showed two spots almost overlapped. The mixture was filtered through Celite, and the filtrate was washed with 10% aqueous KI and water, dried (Na_2SO_4), and evaporated. The resultant mixture was resolved by column chromatography (100 g silica gel, 12:1 hexane–EtOAc) to give two fractions. The faster-migrating fraction (0.59 g, 64%) was a 1:1 mixture of **8** and **6**. The slower-migrating fraction (0.25 g, 27%) was identified as methyl 3,4-di-*O*-acetyl-

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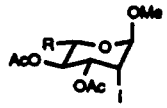
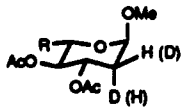
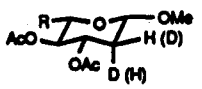
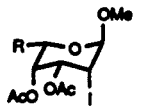
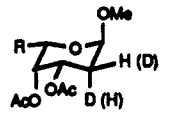
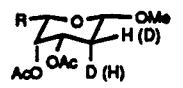
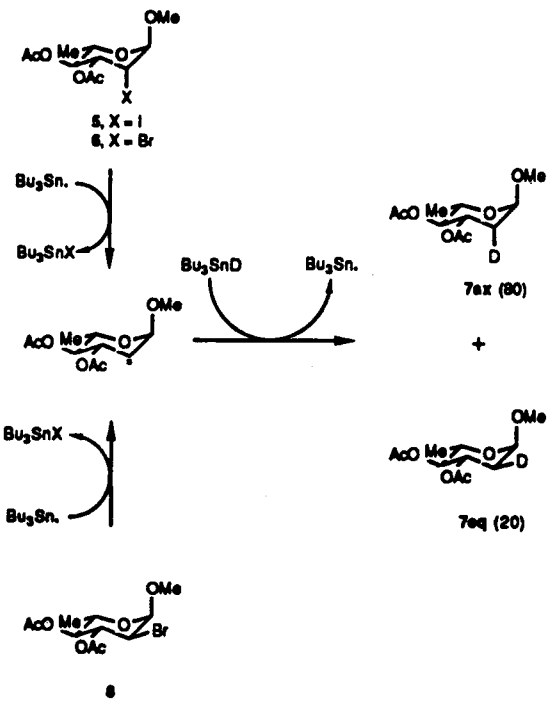
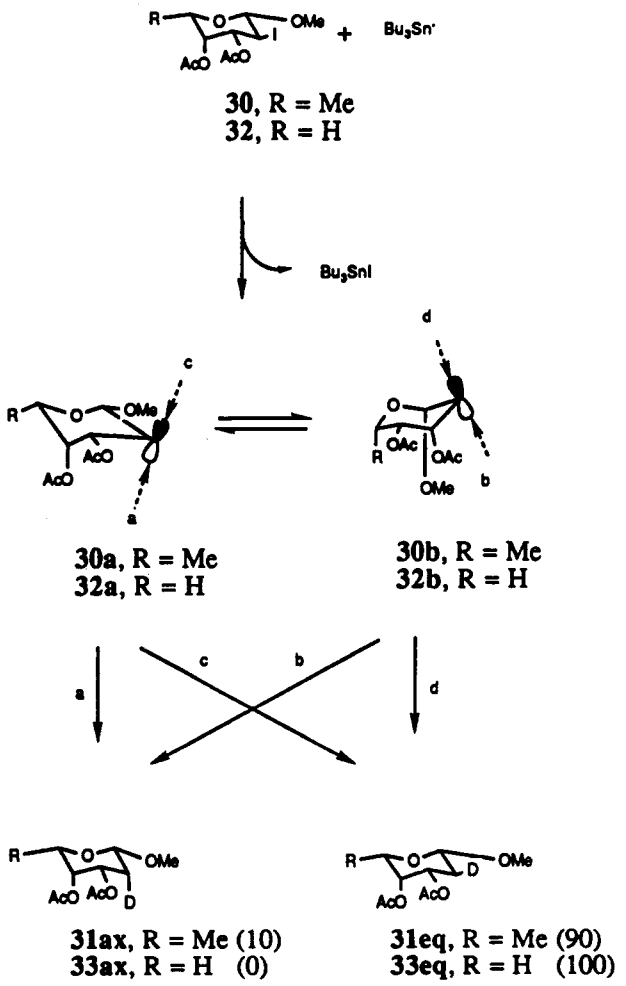
Table III. Product Distribution in the Dehalogenation of 2-Deoxy-2-iodoglycopyranosides

	starting material			products	
entry	structure	no.	R	structure	ratio
1		5	Me		7ax (80) + 7eq (20)
2		22	H		23ax (75) + 23eq (25)
3		14	Me		16ax (60) + 16eq (40)
4		24	H		25ax (40) + 25eq (60)
5		26	Me		27ax (50) + 27eq (50)
6		28	H		29ax (35) + 29eq (65)
7		30	Me		31ax (10) + 31eq (90)
8		32	H		33ax (0) + 33eq (100)

Scheme II



Scheme III



2-bromo-2,6-dideoxy-β-L-glucopyranoside (15). The faster-migrating fraction was quantitatively resolved by HPLC to give the already-described α-L-*manno* isomer 6, along with the α-L-*gluco* isomer 8. Compound 8 (yield 32%) crystallized from ether–hexane with little loss: mp 66–68 °C; $[\alpha]^{20}_D$ −280° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table IV).

Anal. Calcd for $C_{11}H_{17}BrO_6$: C, 40.63; H, 5.27; Br, 24.58. Found: C, 40.71; H, 5.31; Br, 24.52.

Methyl 3,4-Di-*O*-acetyl-2,6-dideoxy-2-bromo-α-L-manno- and -β-L-glucopyranosides (6 and 15). To a solution of 3,4-di-*O*-acetyl-L-rhamnal (1.0 g, 4.7 mmol) in 15 mL of dry acetonitrile was added 0.28 mL (7.0 mmol) of dry methanol followed by 1.0 g (5.6 mmol) of NBS, and the mixture was kept overnight at rt. The mixture was then evaporated to afford a syrup that showed (TLC, 5:1 hexane–EtOAc) two partially resolved spots. Column chromatography (100 g of silica gel, 15:1 hexane–EtOAc) gave two fractions. The faster-moving component, identified as the α-L-*manno* isomer, was isolated as a syrup which crystallized from ether–hexane giving 0.62 g (40%) of pure 6: mp 90–92 °C; $[\alpha]^{20}_D$ −20.4° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table IV).

Anal. Calcd for $C_{11}H_{17}BrO_6$: C, 40.63; H, 5.27; Br, 24.58. Found: C, 40.71; H, 5.29; Br, 24.53.

The slower-moving component, identified as the β-L-*gluco* isomer, was obtained as a syrup, which crystallized from ether–

Table IV. ^{1}H-NMR Parameters of 2-Bromoglycosides 6, 8, 10, 15, and 18

	chemical shifts (δ, ppm) and multiplicities[a]									coupling constants (Hz)					
compd	H-1	H-2	H-3	H-4	H-5	CH_3	OMe	OPr^i	OAc	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	J_{CH,CH_3}
6	4.89 (d)	4.43 (dd)	5.14–5.19 (m)		3.89 (m)	1.24 (d)	3.40 (s)		2.08 (s), 2.05 (s)	1.5	2.3	b	9.3	6.3	
8	4.79 (d)	3.93 (dd)	5.45 (dd)	4.73 (t)	3.95 (m)	1.19 (d)	3.44 (s)		2.06 (s), 2.03 (s)	3.3	11.0	9.2	9.4	6.3	
10	5.07 (d)	4.39 (dd)	5.10–5.20 (m)		3.96 (m)	1.17 (d)		3.91 (m), 1.23 (d), 1.21 (d)	2.07 (s), 2.05 (s)	1.5	3.4	b	9.5	6.2	6.1
15	4.45 (d)	3.75 (dd)	5.24 (dd)	4.72 (t)	3.61 (m)	1.25 (d)	3.57 (s)		2.08 (s), 2.03 (s)	8.6	10.6	9.3	9.5	6.2	
18	4.58 (d)	3.74 (dd)	5.25 (dd)	4.71 (t)	3.59 (m)	c		3.98 (m) and c	2.07 (s), 2.02 (s)	8.6	10.2	9.3	9.5	6.2	6.2

[a] Multiplicities are designated: d = doublet, dd = double doublet, t = triplet, m = multiplet, s = singlet. [b] These coupling constants could not be measured because of overlapping of the signals. [c] These signals are overlapped between 1.20 and 1.30 ppm.

Table V. ^{1}H-NMR Parameters of 2-Deoxyglycosides 7, 11, 13, 16, 19, and 21

	chemical shifts (δ, ppm) and multiplicities[a]									coupling constants (Hz)							
compd	H-1	H-2$_e$	H-2$_a$	H-3	H-4	H-5	CH_3	OMe	OAc	$J_{1,2e}$	$J_{1,2a}$	$J_{2e,2a}$	$J_{2e,3}$	$J_{2a,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$
7	4.75 (d)	2.22 (m)	1.77 (m)	5.24 (m)	4.74 (t)	3.83 (m)	1.18 (d)	3.33 (s)	2.04 (s), 2.00 (s)	1.2	3.7	12.9	5.7	11.7	9.6	9.8	6.3
11[b]	4.97 (d)	2.14 (m)	1.78 (m)	5.29 (m)	4.72 (t)	3.90 (m)	1.12 (d)		2.04 (s), 2.00 (s)	1.3	3.7	12.7	5.4	11.7	9.6	9.7	6.2
13[c]	5.17 (d)	2.04 (m)	1.78 (m)	5.32 (m)	4.70 (t)	4.02 (m)	1.12 (d)		2.05 (s), 2.00 (s)	1.4	3.8	12.2	5.3	11.7	9.6	9.8	6.2
16	4.44 (dd)	2.29 (m)	1.68 (m)	4.98 (m)	4.73 (t)	3.47 (m)	1.23 (d)	3.49 (s)	2.05 (s), 2.02 (s)	2.0	9.6	12.4	5.3	11.9	9.5	9.6	6.2
19[d]	4.61 (dd)	2.23 (m)	1.71 (m)	4.97 (m)	4.73 (t)	3.45 (m)	1.14 (d)		2.04 (s), 2.01 (s)	2.0	9.8	12.5	5.3	11.9	9.4	9.5	6.1
21[e]	4.72 (dd)	2.15 (m)	1.74 (m)	4.98 (m)	4.70 (t)	3.45 (m)	1.20 (d)		2.04 (s), 2.01 (s)	2.1	9.5	12.6	5.3	11.9	9.5	9.6	6.2

[a] Multiplicities are designated: d = doublet, dd = double doublet, m = multiplet, t = triplet, s = singlet. [b] Isopropyl signals appear at δ = 3.85 (m), 1.19 (d, J = 6.1 Hz) and 1.15 (d, J = 6.1 Hz). [c] *tert*-Butyl signal appears at δ = 1.23 (s). [d] Isopropyl signals appear at δ = 3.98 (m), 1.23 (d, J = 6.2 Hz) and 1.22 (d, J = 6.2 Hz). [e] *tert*-Butyl signal appears at δ = 1.25 (s).

hexane to yield 0.16 g (10%) of **15**: mp 83–85 °C; $[\alpha]^{20}_D$ −75.4° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table IV).

Anal. Calcd for $C_{11}H_{17}BrO_6$: C, 40.63; H, 5.27; Br, 24.58. Found: C, 40.54; H, 5.27; Br, 24.61.

Isopropyl 3,4-Di-*O*-acetyl-2,6-dideoxy-2-bromo-α-L-manno- and -β-L-glucopyranosides (10 and 18). The same conditions and same scale as described in the preceding experiment were used, except that 2-propanol was used instead of methanol. Column chromatography gave two compounds, the faster-moving of which was identified as the α-L-*manno* isomer, isolated as a syrup. Distillation at 90 °C (0.04 mmHg) yielded 0.58 g (35%) of syrupy **10**: $[\alpha]^{20}_D$ −41.3° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table IV).

Anal. Calcd for $C_{13}H_{21}BrO_6$: C, 44.20; H, 5.99; Br, 22.62. Found: C, 44.29; H, 6.00; Br, 22.55.

The slower-moving component, identified as the β-L-*gluco* isomer, was isolated as a syrup. Distillation at 90 °C (0.04 mmHg) yielded 0.16 g (9.5%) of syrupy **18**: $[\alpha]_D$ −48.7° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table IV).

Anal. Calcd for $C_{13}H_{21}BrO_6$: C, 44.20; H, 5.99; Br, 22.62. Found: C, 44.13; H, 6.03; Br, 22.57.

Reduction of 2-Deoxy-2-haloglycosides with Bu_3SnH (D). General Procedure for Data Recorded in Tables I–III. To a solution of the 2-halo precursors **5**, **6**, **8**, **9**, **10**, **12**, **14**, **15**, **17**, **18**, **20**, **22**, **24**, **26**, **28**, **30**, or **32** (0.27 mmol) in dry benzene (1 mL), was added Bu_3SnH (0.1 mL, 0.37 mmol) and AIBN (5 mg), and the mixture was kept at 60 °C. After 1 the reaction was complete. The solution was evaporated, the residue dissolved in CH_3CN, and the solution washed four times with hexane (to remove tin compounds).[9] The CH_3CN solution was evaporated to afford a product that was purified either by vacuum distillation and/or crystallization.

Methyl 3,4-Di-*O*-acetyl-2,6-dideoxy-α-L-*arabino*-hexopyranoside (7) and Its 2-Deuterio-α-L-*manno* (7ax) and 2-Deuterio-α-L-*gluco* (7eq) Analogues. The 2-halo precursors **5**, **6**, or **8** were treated with Bu_3SnH as described in the general procedure. The resultant syrups were purified by vacuum distillation (60 °C, 0.04 mmHg) giving compound **7**: $[\alpha]^{20}_D$ −153° (*c* 1.0, $CHCl_3$) (lit.[10] $[\alpha]^{20}_D$ −156.1° and lit.[11] $[\alpha]^{20}_D$ −150°). The ^{1}H-NMR data (see Table V) are in accord with values given in the literature.[10] The final yields of compound **7** were 53 mg (80%) from **5**, 57 mg (85%) from **6**, and 54 mg (81%) from **8**.

When Bu_3SnD was used as the reagent, the final syrup showed, by ^{1}H-NMR analysis, a 80:20 mixture of the axial 2-deuterio derivative **7ax** and the equatorial 2-deuterio isomer **7eq**. The signal for H-2eq (2.22 ppm) integrated for 0.8 proton and had become a double doublet showing $J_{1,2eq}$ = 1.2 Hz and $J_{2eq,3}$ = 5.7 Hz. The signal for H-2ax (1.77 ppm) integrated for 0.2 proton and appeared as a double doublet with $J_{1,2ax}$ = 3.7 Hz and $J_{2ax,3}$ = 11.5 Hz.

Isopropyl 3,4-Di-*O*-acetyl-2,6-dideoxy-α-L-*arabino*-hexopyranoside (11) and Its 2-Deuterio-α-L-*manno* (11ax) and 2-Deuterio-α-L-*gluco* (11eq) Analogues. The 2-halo precursors **9** or **10** were treated with Bu_3SnH as described in the general procedure. The resultant syrups were then purified by vacuum distillation (60 °C, 0.04 mmHg) to give pure **11**: $[\alpha]^{20}_D$ −131° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table V).

Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.09. Found: C, 56.81; H, 8.13. The final yield of compound **11** was 50 mg (68%) from **9** and 56 mg (76%) from **10**.

When Bu_3SnD was used as the reagent, the final syrup showed, by ^{1}H-NMR analysis, a 90:10 mixture of the axial 2-deuterio derivative **11ax** and the equatorial 2-deuterio isomer **11eq**. The signal for H-2eq (2.14 ppm) integrated for 0.9 proton and had become a double doublet showing $J_{1,2eq}$ = 1.3 Hz and $J_{2eq,3}$ = 5.4 Hz. The signal for H-2ax (1.78 ppm) integrated for 0.1 proton and appeared as a double doublet with $J_{1,2ax}$ = 3.7 and $J_{2ax,3}$ = 11.7 Hz.

***tert*-Butyl 3,4-Di-*O*-acetyl-2,6-dideoxy-α-L-*arabino*-hexopyranoside (13) and Its 2-Deuterio-α-L-*manno* (13ax) and 2-Deuterio-α-L-*gluco* (13eq) Analogues.** The 2-iodo compound **12** was treated with Bu_3SnH as described in the general procedure. The syrupy product was then purified by vacuum distillation (60 °C, 0.04 mmHg) to afford 63 mg (81%) of pure **13**; $[\alpha]^{20}_D$ −125° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table V).

Anal. Calcd for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.25; H, 8.43.

When Bu_3SnD was used as the reagent, the final syrup showed, by ^{1}H-NMR analysis, a 95:5 mixture of the axial 2-deuterio (**13ax**) and the equatorial 2-deuterio (**13eq**) derivatives. The signal for H-2eq (2.04 ppm) integrated for 0.95 proton and had become a double doublet showing $J_{1,2eq}$ = 1.4 Hz and $J_{2eq,3}$ = 5.3 Hz. The signal for H-2ax (1.78 ppm) integrated for 0.05 proton and appeared as a double doublet with $J_{1,2ax}$ = 3.8 Hz and $J_{2ax,3}$ = 11.7 Hz.

Methyl 3,4-Di-*O*-acetyl-2,6-dideoxy-β-L-*arabino*-hexopyranoside (16) and Its 2-Deuterio-β-L-*manno* (16ax) and 2-Deuterio-β-L-*gluco* (16eq) Analogues. The 2-halo precursors **14** or **15** were treated with Bu_3SnH as described in the general procedure. The resultant syrups were then purified by vacuum distillation (60 °C, 0.04 mmHg) to give pure **16**: $[\alpha]^{20}_D$ 12.6° (*c*

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1.0, $CHCl_3$) (lit.[10] $[\alpha]^{20}_D$ 13.1° and lit.[11] $[a]^{20}_D$ 13.0°). The ^{1}H-NMR data (see Table V) are in accord with values given in the literature.[10] The final yields of compound **16** were 50 mg (75%) from **14** and 53 mg (80%) from **15**.

When Bu_3SnD was used as the reagent, the final syrup showed, by ^{1}H-NMR analysis, a 60:40 mixture of the axial 2-deuterio derivative **16ax** and the equatorial 2-deuterio isomer **16eq**. The signal for H-2eq (2.29 ppm) integrated for 0.6 proton and had become a double doublet showing $J_{1,2eq}$ = 2.0 Hz and $J_{2eq,3}$ = 5.3 Hz. The signal for H-2ax (1.68 ppm) integrated for 0.4 proton and appeared as a double doublet with $J_{1,2ax}$ = 9.6 Hz and $J_{2ax,3}$ = 11.9 Hz.

Isopropyl 3,4-Di-*O*-acetyl-2,6-dideoxy-β-L-*arabino*-hexopyranoside (19) and Its 2-Deuterio-β-L-*manno* (19ax) and 2-Deuterio-β-L-*gluco* (19eq) Analogues. The 2-halo precursors **17** or **18** were treated with Bu_3SnH as described in the general procedure. The resultant syrups were then purified by vacuum distillation (60 °C, 0.04 mmHg) to afford pure **19**: $[\alpha]^{20}_D$ 35.6° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table V).

Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.09. Found: C, 56.88; H, 8.10. Final yield of compound **19** was 55 mg (74%) from **17** and 51 mg (69%) from **18**.

When Bu_3SnD was used as the reagent, the final syrup showed, by ^{1}H-NMR analysis, a 60:40 mixture of the axial 2-deuterio (**19ax**) and the equatorial 2-deuterio (**19eq**) derivatives. The signal for H-2eq (2.23 ppm) integrated for 0.6 proton and had become a double doublet showing $J_{1,2eq}$ = 2.0 Hz and $J_{2eq,3}$ = 5.3 Hz. The signal for H-2ax (1.71 ppm) integrated for 0.4 proton and appeared as a double doublet with $J_{1,2ax}$ = 9.8 Hz and $J_{2ax,3}$ = 11.9 Hz.

***tert*-Butyl 3,4-Di-*O*-acetyl-2,6-dideoxy-β-L-*arabino*-hexopyranoside (21) and Its 2-Deuterio-β-L-*manno* (21ax) and 2-Deuterio-β-L-*gluco* (21eq) Analogues.** The 2-iodo glycoside **20** was treated with Bu_3SnH as described in the general procedure. The syrupy product was then purified by vacuum distillation (60 °C, 0.04 mmHg) to afford 5 mg (72%) of pure **21**: $[\alpha]^{20}_D$ 9.6° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (see Table V).

Anal. Calcd for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.22; H, 8.40.

When Bu_3SnD was used as the reagent, the final syrup showed, by ^{1}H-NMR analysis, a 60:40 mixture of the axial 2-deuterio (**21ax**) and the equatorial 2-deuterio (**21eq**) derivatives. The signal for H-2eq (2.15 ppm) integrated for 0.6 proton and had become a double doublet showing $J_{1,2eq}$ = 2.1 Hz and $J_{2eq,3}$ = 5.3 Hz. The signal for H-2ax (1.74 ppm) integrated for 0.4 proton and appeared as a double doublet with $J_{1,2ax}$ = 9.5 Hz and $J_{2ax,3}$ = 11.9 Hz.

Methyl 3,4-Di-*O*-acetyl-2-deoxy-α-L-*threo*-pentopyranoside (23) and Its 2-Deuterio-α-L-*lyxo* (23ax) and 2-Deuterio-α-L-*xylo* (23eq) Analogues. Compound **23** was obtained from **22** as described in the general procedure and in a previous paper.[3] For ^{1}H-NMR, see Table VI.

When Bu_3SnD was used as the reagent, the final product showed, by ^{1}H-NMR, a 75:25 mixture of the axial 2-deuterio (**23ax**) and equatorial 2-deuterio (**23eq**) derivatives. The H-2eq signal (2.18 ppm) integrated for 0.75 proton and appeared as a double doublet with $J_{1,2eq}$ = 2.9 Hz and $J_{2eq,3}$ = 5.0 Hz. The H-2ax signal (1.75 ppm) integrated for 0.25 proton and appeared as a double doublet with $J_{1,2ax}$ = 3.1 Hz and $J_{2ax,3}$ = 10.0 Hz.

Methyl 3,4-Di-*O*-acetyl-2-deoxy-β-L-*threo*-pentopyranoside (25) and Its 2-Deuterio-β-L-*lyxo* (25ax) and 2-Deuterio-β-L-*xylo* (25eq) Analogues. Glycoside **24** was treated with Bu_3SnH as described in the general procedure. A syrup was obtained which was then purified by vacuum distillation (60 °C, 0.04 mmHg) to give pure **25** (44 mg, 70%); $[\alpha]^{20}_D$ 107° (*c* 1.0, $CHCl_3$) (lit.[12] $[\alpha]^{20}_D$ −103° for the D enantiomer and lit.[13] $[\alpha]^{20}_D$ −100.6° for the D enantiomer). The ^{1}H-NMR data (see Table VI) coincide with those described for the D enantiomer.[12]

Anal. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.95. Found: C, 51.60; H, 6.97.

Table VI. ^{1}H-NMR Parameters of 2-Deoxyglycosides 23, 25, 27, 29, 31, and 33

	chemical shifts (δ, ppm) and multiplicities[a]									coupling constants (Hz)								
compd	H-1	H-2$_e$	H-2$_a$	H-3	H-4	H-5$_e$	H-5$_a$	Me	OMe	OAc	$J_{1,2e}$	$J_{1,2a}$	$J_{2e,2a}$	$J_{2e,3}$	$J_{2a,3}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{5e,5a}$	$J_{5,6}$
23	4.72 (t)	2.18 (m)	1.75 (m)	5.24 (m)	4.87 (m)	3.78 (dd)	3.64 (dd)		3.36 (s)	2.04 (s), 2.03 (s)	2.9	3.1	13.1	5.0	10.0	8.8	5.0	9.1	11.2	
25	4.54 (dd)	2.23 (m)	1.76 (m)	4.94 (m)	4.83 (m)	4.11 (dd)	3.39 (dd)		3.43 (s)	2.07 (s), 2.06 (s)	3.2	6.3	13.7	4.8	8.3	7.0	4.0	6.8	12.2	
27[b]	4.85 (dd)	1.84 (m)	2.03 (m)	5.26 (m)	5.17 (dd)		4.04 (m)	1.14 (d)	3.34 (s)	2.16 (s), 1.98 (s)	1.2	3.2	12.7	5.1	12.5	3.1		1.5		6.5
29[c]	4.84 (m)	1.87 (m)	2.11 (m)	5.28 (m)	5.16 (s)	3.90 (dd)	3.71 (dd)		3.36 (s)	2.13 (s), 2.01 (s)	1.6	3.8	13.5	4.8	11.8	3.2	1.5	2.7	12.8	
31[d]	4.44 (dd)	1.96 (m)	1.88 (m)	4.98 (m)	5.10 (m)		3.68 (m)	1.22 (d)	3.52 (s)	2.15 (s), 2.00 (s)	2.2	9.6	12.4	5.1	12.4	3.1		1.0		6.5
33	4.43 (t)		−1.99 (m)	5.03 (m)	5.07 (m)	3.56 (dd)	4.06 (d)		3.49 (s)	2.12 (s), 2.04 (s)	3.0	8.0	12.1	4.5	10.5	3.5	1.9	3.8	12.8	

[a] Multiplicities are designated: d = doublet, dd = double doublet, m = multiplet, t = triplet, s = singlet. [b] $J_{2e,4}$ = 1.2 Hz. [c] $J_{2e,4}$ = 1.3 Hz. [d] $J_{2e,4}$ = 0.9 Hz.

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When Bu_3SnD was used as the reagent, the final product showed, by ^1H-NMR, a 40:60 mixture of the axial 2-deuterio (**25ax**) and equatorial 2-deuterio (**25eq**) derivatives. The H-2eq signal (2.23 ppm) integrated for 0.4 proton and appeared as a double doublet with $J_{1,2eq}$ = 3.2 Hz and $J_{2eq,3}$ = 4.8 Hz. The H-2ax signal (1.76 ppm) integrated for 0.6 proton and appeared as a double doublet with $J_{1,2ax}$ = 6.3 Hz and $J_{2ax,3}$ = 8.3 Hz.

Methyl 3,4-Di-*O*-acetyl-2,6-dideoxy-α-L-*lyxo*-hexopyranoside (27) and Its 2-Deuterio-α-L-*talo* (27ax) and 2-Deuterio-α-L-*galacto* (27eq) Analogues. Glycoside **26** was treated with Bu_3SnH as described in the general procedure. A syrup was obtained which was then purified by vacuum distillation (60 °C, 0.04 mmHg) and then crystallized from ethanol–hexane to give **27** (53 mg, 80%) as a solid: mp 66–68 °C (lit.[14] mp 66.6–67.5 °C); $[\alpha]^{20}_D$ −157° (*c* 1.0, $CHCl_3$) (lit.[14] $[\alpha]^{20}_D$ −166°). The ^1H-NMR data (see Table VI) coincide with those described in the literature.[15]

When Bu_3SnD was used as the reagent, the final product showed, by ^1H-NMR, a 50:50 mixture of the axial 2-deuterio (**27ax**) and equatorial 2-deuterio (**27eq**) derivatives. The H-2eq signal (1.84 ppm) integrated for 0.5 proton and appeared as a double triplet with $J_{1,2eq}$ = 1.2 Hz, $J_{2eq,3}$ = 5.1 Hz, and $J_{2eq,4}$ = 1.2 Hz. The H-2ax signal (2.03 ppm) integrated for 0.5 proton and appeared as a double doublet with $J_{1,2ax}$ = 3.2 Hz and $J_{2ax,3}$ = 12.5 Hz.

Methyl 3,4-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentopyranoside (29) and Its 2-Deuterio-β-D-*ribo* (29ax) and 2-Deuterio-β-D-*arabino* (29eq) Analogues. Compound **29** was obtained from **28** as described in the general procedure and in a previous paper.[3] For ^1H-NMR data, see Table VI.

When Bu_3SnD was used as the reagent, the final product showed, by ^1H-NMR analysis, a 35:65 mixture of the axial 2-deuterio (**29ax**) and equatorial 2-deuterio (**29eq**) derivatives. The H-2eq signal (1.87 ppm) integrated for 0.35 proton and appeared as a double triplet with $J_{1,2eq}$ = 1.6 Hz, $J_{2eq,3}$ = 4.8 Hz, and $J_{2eq,4}$ = 1.3 Hz. The H-2ax signal (2.11 ppm) integrated for 0.65 proton and appeared as a double doublet with $J_{1,2ax}$ = 3.8 Hz and $J_{2ax,3}$ = 11.8 Hz.

Methyl 3,4-Di-*O*-acetyl-2,6-dideoxy-β-L-*lyxo*-hexopyranoside (31) and Its 2-Deuterio-β-L-*talo* (31ax) and 2-Deuterio-β-L-*galacto* (31eq) Analogues. Glycoside **30** was treated with Bu_3SnH as described in the general procedure. A syrup was obtained which was then purified by vacuum distillation (60 °C, 0.04 mm) to give pure **31** (48 mg, 72%): $[\alpha]^{20}_D$ 6.1° (*c* 1.0, $CHCl_3$) (lit.[15] $[\alpha]^{20}_D$ 3.5°). The ^1H-NMR data (see Table VI) coincide with those described in the literature.[15]

When Bu_3SnD was used as the reagent, the final product showed, by ^1H-NMR, a 10:90 mixture of the axial 2-deuterio (**31ax**) and equatorial 2-deuterio (**31eq**) derivatives. The H-2eq signal (1.96 ppm) integrated for 0.1 proton and appeared as a double double doublet with $J_{1,2eq}$ = 2.2 Hz, $J_{2eq,3}$ = 5.1 Hz, and $J_{2eq,4}$ = 0.9 Hz. The H-2ax signal (1.88 ppm) integrated for 0.9 proton and appeared as a double doublet with $J_{1,2ax}$ = 9.6 Hz and $J_{2ax,3}$ = 12.4 Hz.

Methyl 3,4-Di-*O*-acetyl-2-deoxy-α-D-*erythro*-pentopyranoside (33) and Its 2-Deuterio-α-D-*ribo* (33ax) and 2-Deuterio-α-D-*xylo* (33eq) Analogues. Glycoside **32** was treated with Bu_3SnH as described in the general procedure. A solid was obtained which was then crystallized from ether–petroleum ether to give **33** (43 mg, 69%): mp 72–73 °C; $[\alpha]^{20}_D$ 14.3° (*c* 1.0, $CHCl_3$) (lit.[16] mp 73–73.5 °C; lit.[16] $[\alpha]^{20}_D$ −11.7° for the L enantiomer). The ^1H-NMR data (see Table VI) coincide with those described for the L enantiomer.[17]

Anal. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.95. Found: C, 51.79; H, 6.97.

When Bu_3SnD was used as the reagent, the final product showed, by ^1H-NMR analysis, equatorial 2-deuterio derivative (**33eq**) as the only isomer. The H-2ax signal (1.99 ppm) appeared as a double doublet with $J_{1,2ax}$ = 8.0 Hz and $J_{2ax,3}$ = 10.5 Hz.

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