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An electrophile-mediated cyclization on the 1,6-anhydro-D-glucopyranose framework

Christine Leteux [a], Alain Veyrières [a,*] and Francis Robert [b]

[a] *Laboratoire de Chimie des Glucides, Université Pierre et Marie Curie, 4 Place Jussieu, 75005 Paris (France)*
[b] *Laboratoire de Chimie des Métaux de Transition, UA 419, Université Pierre et Marie Curie, 4 Place Jussieu, 75005 Paris (France)*

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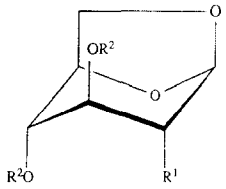
ABSTRACT

Iodocyclization of *O*-tributylstannyl-D-glucal with iodine in acetonitrile gave 1,6-anhydro-2-deoxy-2-iodo-β-D-glucopyranose (**1**) in high yield. The 3,4-di-*O*-acetyl derivative of **1** could be converted into the corresponding 2-deoxy compound and into the 2-*C*-allyl-2-deoxy branched sugar (**5**) by treatment with tributylstannane and allyltributylstannane, respectively. Controlled alkaline hydrolysis of **5** gave the 4-monoacetyl derivative. Complete hydrolysis of **5** gave the 3,4-diol, which underwent a 5-*exo* cyclization by treatment with *N*-bromosuccinimide. ^{1}H NMR spectroscopy and X-ray analysis showed that the cyclized product has the $B_{3,O}$ conformation in its pyranose ring, which is *trans*-fused to the newly formed tetrahydrofuran ring.

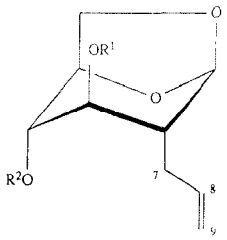
INTRODUCTION

1,6-Anhydro-β-D-glucopyranose (levoglucosan), a readily available compound, has been shown[1–3] to be a convenient starting material for the synthesis of complex natural products. The bicyclic structure of 1,6-anhydro sugars is usually rigid enough to ensure good regio- and stereo-chemical control in reactions such as the opening of epoxides leading to *trans*-diaxial products[4]. Thus, treatment of 1,6:2,3-dianhydro-4-*O*-benzyl-β-D-mannopyranose ("Cerny epoxide") with an ethynyl alane[2], a vinyl lithium[2], or a Grignard reagent[3] allows the fully regioselective introduction of an axial unsaturated branch at C-2 of the D-glucopyranose framework held in the $^1C_4$ conformation. Chelation of the incoming carbon nucleophile with the axial oxygen atom at C-4 was postulated in these stereodirected reactions[4].

* Corresponding author (present address): Université d'Orléans, UFR-Faculté des Sciences, Laboratoire de Biochimie Structurale, URA 499, 45067 Orléans (France).



	R^1	R^2
1	I	H
2	I	Ac
3	H	Ac
4	H	H



	R^1	R^2
5	Ac	Ac
6	H	H
7	H	Ac

We recently reported[5] a fast preparation of 1,6-anhydro-2-deoxy-2-iodo-β-D-glucopyranose (**1**) by iodocyclization of *O*-tributylstannyl-D-glucal. While a 2,3-*manno* epoxide could certainly be obtained from **1** by alkaline treatment[2], the presence of an iodine atom suggests a free radical methodology[6] for carbon–carbon bond formation at C-2.

RESULTS AND DISCUSSION

O-Stannylation of D-glucal was conducted in refluxing acetonitrile with 0.8 molar equivalent of bis(tributyltin) oxide in the presence of molecular sieves. Addition of iodine to the mixture gave the iodo compound **1** (80% isolated yield). The decreased amount of tin reagent avoided the formation of the *manno*-isomer[5] and made the extraction of **1** much easier *. Conventional *O*-acetylation of **1** gave the diacetate **2**, now obtainable on a 2–5 g scale.

Treatment of **2** with tributylstannane and α,α′-azobisisobutyronitrile in refluxing benzene gave 3,4-di-*O*-acetyl-1,6-anhydro-2-deoxy-β-D-*arabino*-hexopyranose (**3**) quantitatively, which could be *O*-deacetylated to the known diol **4**, usually prepared by a much longer route[7].

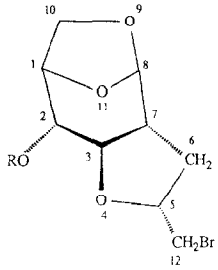
Keck's pioneering work[8] demonstrated the efficacy of allylstannanes for making carbon–carbon bonds by free radical S_H2' reactions. *C*-Allyl branches have thus been introduced at various positions of monosaccharides[8–10] or nucleosides[11], the allylstannanes usually adding preferentially to the less hindered face of the carbon-centered radical. However, in conformationally locked six-membered rings having an oxygen substituent adjacent to the radical center, the allylstannane showed some tendency to enter in an orientation *syn* to the β oxygen atom[8]. In the present work, when the iodo derivative **2** was treated with allyltributylstannane and α,α′-azobisisobutyronitrile in boiling benzene the axially branched *C*-allyl product

* We are indebted to Dr. J.-M. Beau (Université d'Orléans) for communicating this spectacular improvement of our published[5] procedure.

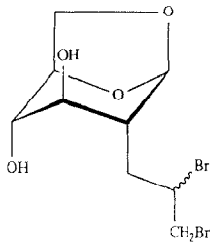
5 was isolated in 65% yield, with no trace of the *manno*-isomer. Transfer of allylic hydrogen from the reagent to the carbon-centered radical gave some reduced product (**3**). As far as stereoselectivity is concerned, preferential addition of allylstannane to the convex face of **2** therefore parallels the *trans*-diaxial heterolytic opening of 1,6:2,3-dianhydro *manno* derivatives. The ^{1}H NMR spectrum of **5** shows small vicinal coupling constants, $J_{2,3}$ and $J_{3,4} \leq 1$ Hz, indicating the *gluco* configuration and the $^1C_4$ conformation of the pyranose ring.

O-Deacetylation of **5** with 10:10:1 methanol–water–triethylamine at room temperature afforded the diol **6**, which is also in the $^1C_4$ conformation as shown by its ^{1}H NMR spectrum in $(CD_3)_2SO$ containing D_2O. When the reaction was conducted at 5°C, the monoacetate **7** could be isolated in 36% yield. The location of the acetyl group at O-4 was demonstrated by ^{1}H NMR spectroscopy as follows: Irradiation of the signal at δ 4.54 (br dd, H-5) modified the signals of H-6*endo* (δ 4.07) and H-6*exo* (δ 3.80), and also a low-field signal at δ 4.65 (d, $J_{3,4}$ 1.5 Hz after irradiation), therefore attributed to H-4. A signal at much higher field (δ 2.87, br dd, $J_{3,OH}$ 6.9 Hz) corresponds therefore to H-3. The small values of $J_{2,3}$ and $J_{3,4}$($\leq$ 1.5 Hz) indicate again the $^1C_4$ conformation for the pyranose ring in **7**. The acyl group at C-3 of peracylated 1,6-anhydro-β-D-glucopyranoses has already been reported[12] to be the most labile in alkaline hydrolysis. In the $^1C_4$ conformation the oxygen atom of the 1,6-anhydro bridge is close to the acyl group at C-3, and formation of a hydrogen bond between the formed hydroxyl group at C-3 and this oxygen may facilitate the splitting of the negatively charge tetrahedral intermediate in a base-catalyzed hydrolysis.

Electrophile-mediated intramolecular cyclizations[13] were then attempted upon the diol **6**. Whereas rotation about the C-7–C-8 vinylic bond, which varies the relative orientations of the internal nucleophiles (OH-3 and OH-4) and the double bond, is not constrained by the ring system, the rigid bicyclic structure will certainly not facilitate nucleophilic closure in accordance with Baldwin's rules[14]. However, when **6** was treated with *N*-bromosuccinimide in 99:1 dichloromethane–ethanol at room temperature, a tricyclic product (**8**) resulting from a cyclization via the 5-*exo* mode was isolated in 54% yield. Molecular bromine was also formed, and it added nonstereoselectively to the double bond to give a mixture of dibromides (**10**). These were characterized by mass spectrometry; the 1:2:1 distribution of peaks of mass P, P + 2, and P + 4 is typical of molecules containing two bromine atoms. Allylic bromination also occurred to a small extent, leading to **11**. In pure dichloromethane the reaction became very sluggish, whereas in 4:1 tetrahydrofuran–water at 0°C a fast cyclization was accompanied by the formation of a mixture of bromohydrins. In *N*,*N*-dimethylformamide[15] the dibromo compounds **10** and the cyclization product **8** were formed in nearly equal amounts. Bromine in 99:1 dichloromethane–ethanol containing sodium hydrogencarbonate gave mostly **10**. Iodine, *N*-iodosuccinimide in various solvents, and mercuric trifluoroacetate in tetrahydrofuran gave no reaction. From these results it can be concluded that the cyclization of **6** requires a strong electrophile (Br^+)



8 R = H
9 R = Ac



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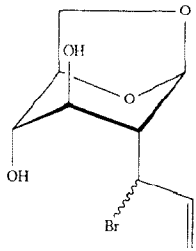

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without a nucleophilic counter-anion, and a protic medium to solvate the anionic part (succinimide anion) of the activated complex[16]. Water and aliphatic alcohols are known[17] to release bromine from *N*-bromosuccinimide, hence the concomitant formation of the dibromo products **10** could not be completely avoided.

Compound **8** was *O*-acetylated in pyridine and acetic anhydride to provide crystalline **9**. This gave a ^{1}H NMR spectrum exhibiting large vicinal coupling constants, $J_{2,3}$ (8.6 Hz) and $J_{3,7}$ (11.2 Hz), indicating a $B_{3,O}$ conformation for the pyranose ring. The relatively small magnitude of $J_{2,3}$ is caused by the electronega-

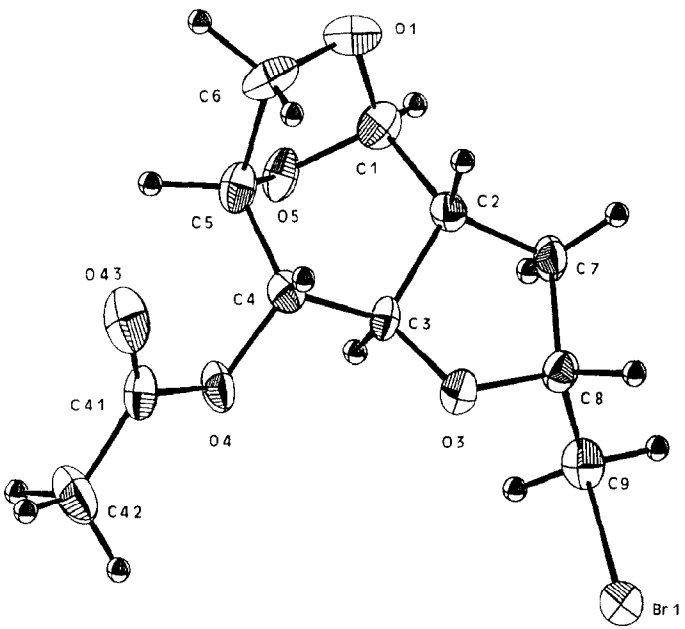


Fig. 1. A view of the molecule of (1*R*,2*S*,3*R*,5*R*,7*R*,8*R*)-2-acetoxy-5-bromomethyl-4,9,11-trioxatricyclo-[6.2.1.0^{3,7}]undecane (**9**).

TABLE I

Crystal data and experimental conditions for the X-ray analysis of **9**

Formula	$C_{11}H_{15}O_5Br$	Crystal dimensions (mm)	0.22×0.30×0.38
Mol wt	307.14	Systematic absences	0K0 K = 2n+1
Crystal system	monoclinic	Diffractometer	Enraf-Nonius CAD-4
Space group	$P2_1$	Radiation (graphite	
Cell parameters		monochromator)	Mo$K\alpha$ (λ = 0.71069 Å)
a (Å)	6.403(3)	Linear absorption coefficient (cm^{-1})	33.22
b (Å)	8.230(2)	Scan type	$\theta/2\theta$
c (Å)	12.022(3)	Scan range (deg)	0.8+0.345 tan θ
β (deg)	75.50(2)	θ limits (deg)	1–25
V (Å^3)	613(4)	Octants collected	−7.7; 0.9; 0.14
Z	2	No. of data collected	1275
ρ(calcd) ($g.cm^{-3}$)	1.66	No. of unique data collected	1164
		No. of unique data used	731 $(F_o)^2 > 3\sigma(F_o^2)$
		Decay (%)	<1
		$R = \Sigma(\|\|F_o\| - \|F_c\|\|)/\Sigma\|F_o\|$	0.036
		$R_w = [\Sigma w(\|F_o\| - \|F_c\|)^2/\Sigma wF_o^2]^{1/2}$	0.037

tivity of the oxygen at C-3. An upfield shift of 0.29 ppm is observed for H-10*endo* when going from **5** in the $^1C_4$ conformation to **9** in the $B_{3,O}$ conformation, where the oxygen atom at C-3 does not exert any Van der Waals effect[18].

X-ray analysis (Fig. 1 and Tables I–IV) confirms the $B_{3,O}$ conformation of the pyranose ring (dihedral angles of 164 and 165° are found for H-2,3 and H-3,7, respectively) and also establishes the *R* configuration of the new asymmetric center at C-5. The new tetrahydrofuran ring is nearly in the E_3 envelope conformation, with C-3 out of the O-4, C-5,6,7 plane.

Most derivatives of 1,6-anhydro-D-glucopyranose adopt the $^1C_4$ conformation for the pyranose ring. However, 3-amino-3-deoxy[18], 2,4-diadeninyl-2,4-dideoxy[19], and 2,4-bis(diphenylphosphino)-2,4-dideoxy derivatives[20], 2,4-diammonium-2,4-dideoxy salts[21], and 1,6-anhydrolactose[22] are mixtures of $^1C_4$ and $B_{3,O}$ conformers,

TABLE II

Interatomic distances for **9** with esd's in parentheses.

Atoms	Distance (Å)	Atoms	Distance (Å)
Br-1–C-9	1.95(1)	O-1–C-1	1.40(1)
O-1–C-6	1.47(2)	O-3–C-3	1.43(1)
O-3–C-8	1.45(2)	O-4–C-4	1.45(1)
O-4–C-41	1.35(2)	O-5–C-1	1.42(1)
O-5–C-5	1.44(1)	O-43–C-41	1.20(1)
C-1–C-2	1.54(1)	C-2–C-3	1.53(2)
C-2–C-7	1.52(2)	C-3–C-4	1.51(1)
C-4–C-5	1.55(1)	C-5–C-6	1.54(2)
C-7–C-8	1.56(2)	C-8–C-9	1.52(1)
C-41–C-42	1.50(2)		

TABLE III

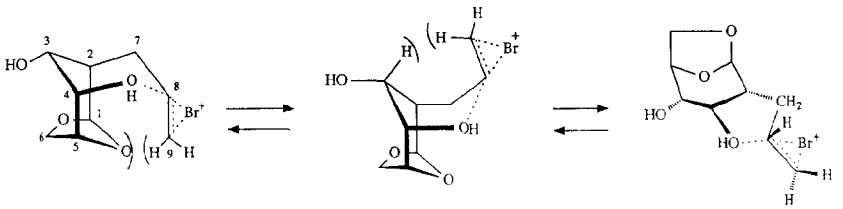
Bond angles for **9** with esd's in parentheses.

Atoms	Angles (°)	Atoms	Angles (°)
C-6–O-1–C-1	104.6(9)	C-8–O-3–C-3	105.6(8)
C-41–O-4–C-4	114.9(8)	C-5–O-5–C-1	102.1(8)
O-5–C-1–O-1	103.6(10)	C-2–C-1–O-1	110.4(9)
C-2–C-1–O-5	107.7(9)	C-3–C-2–C-1	109.5(9)
C-7–C-2–C-1	122.4(13)	C-7–C-2–C-3	99.8(7)
C-2–C-3–O-3	103.1(7)	C-4–C-3–O-3	114.7(8)
C-4–C-3–C-2	108.5(8)	C-3–C-4–O-4	107.2(8)
C-5–C-4–O-4	110.3(8)	C-5–C-4–C-3	105.4(9)
C-4–C-5–O-5	109.9(8)	C-6–C-5–O-5	101.4(9)
C-6–C-5–C-4	112.8(9)	C-5–C-6–O-1	104.2(9)
C-8–C-7–C-2	101.5(10)	C-7–C-8–O-3	106.9(7)
C-9–C-8–O-3	110.0(8)	C-9–C-8–C-7	107.8(10)
C-8–C-9–Br-1	112.3(8)	O-43–C-41–O-4	122.5(13)
C-42–C-41–O-4	111.1(11)	C-42–C-41–O-43	126.4(17)

TABLE IV

Torsion angles for **9**

Angle	Magnitude (°)
C-6–O-1–C-1–O-5	38.80
C-6–O-1–C-1–C-2	−76.24
O-5–C-1–C-2–C-7	115.99
O-5–C-1–C-2–C-3	0.02
C-1–C-2–C-3–O-3	178.15
C-1–C-2–C-3–C-4	−59.86
C-7–C-2–C-3–O-3	48.56
C-7–C-2–C-3–C-4	170.55
C-2–C-3–C-4–O-4	165.83
C-2–C-3–C-4–C-5	48.32
C-7–C-3–C-4–O-4	177.16
C-7–C-3–C-4–C-5	59.65
C-3–C-4–C-5–O-5	17.49
C-3–C-4–C-5–C-6	−94.77
O-4–C-4–C-5–O-5	−97.86
O-4–C-4–C-5–C-6	149.87
C-4–C-5–C-6–O-1	100.60
O-5–C-5–C-6–O-1	−16.80
C-4–C-5–O-5–C-1	−79.42
C-6–C-5–O-5–C-1	40.06
O-1–C-1–O-5–C-5	−50.59
C-2–C-1–O-5–C-5	66.41
C-1–C-2–C-7–C-8	−156.95
C-3–C-2–C-7–C-8	−36.25
C-2–C-7–C-8–O-3	13.82
C-2–C-7–C-8–C-9	132.04
C-3–O-3–C-8–C-9	−100.24
C-3–O-3–C-8–C-7	16.57
C-8–O-3–C-3–C-4	−158.32
C-8–O-3–C-3–C-2	−40.56



Scheme 1. Transition states for the bromonium ion-mediated cyclization of **6**.

or adopt a flattened $B_{3,O}$ conformation. A *trans*-fused δ-lactam ring was also recently reported [23] to confer the $B_{3,O}$ conformation on the pyranose ring of 1,6-anhydroglucose. Dreiding models (Scheme 1) show that a 6-*exo* cyclization of **6** (expected if **6** retains the $^1C_4$ conformation) would involve transition states with severe steric constraints in order to have O-4 and one C–Br bond of a symmetric bromonium ion in a nearly colinear relationship[14,24]. Attack of Br^+ at the *si* face of the double bond leads to a chair-like intermediate with an axial bromonium appendage, and attack at the *re* face gives a boat-like transition state. On the other hand, MM2 calculations have shown[25] that the $^1C_4$ conformer of 1,6-anhydro-β-D-glucopyranose is favored by only 1.4 kcal/mol over the $B_{3,O}$ conformer. Moreover, the C-2 branch in **6** will decrease this difference in free energies since the HO-4–O-2 hydrogen bond stabilizing the $^1C_4$ conformer is now suppressed[22]. The 5-*exo* cyclization of **6** with the $B_{3,O}$ conformation would then suffer less constraint, provided that Br^+ attacks the double bond at the *re* face. A *trans*-fused tetrahydrofuran ring is thus formed with the *R* configuration at the carbon atom undergoing the ring closure.

The monoacetyl derivative **7** could not be cyclized with *N*-bromosuccinimide in various solvents. So even a slight deactivation of OH-3 by a vicinal electroattracting substituent is enough to impede the electrophile-mediated cyclization on the bicyclic framework.

In conclusion, the existence of a chair–boat equilibrium in 1,6-anhydro-β-D-glucopyranose derivatives, which has already been proposed[25] as part of the mechanism of acid-catalyzed alcoholysis, shows that these bicyclic synthons are less rigid than is often assumed, and may lead to interesting intramolecular reactions.

EXPERIMENTAL

General methods.—Melting points were determined on a Thomas–Hoover apparatus and are uncorrected. Optical rotations were measured at 22 ± 2°C on a Perkin–Elmer 141 polarimeter. ^1H NMR spectra (internal Me_4Si) were recorded with a Bruker AM-250 (250 MHz) spectrometer. Desorption CI(ammonia) mass spectra were recorded with a Nermag R10-10 spectrometer. All solvents and reagents were purified and dried according to standard procedures[26]. TLC was

performed on Silica Gel 60-F_{254} (Merck) with detection by charring with 10:1 EtOH–H_2SO_4. Products were purified by flash-column chromatography on Silica Gel 60 (Merck, 230–400 mesh). Elemental analyses were performed at the Service de Microanalyse de l'Université Pierre et Marie Curie, Paris.

*1,6-Anhydro-2-deoxy-2-iodo-β-*D*-glucopyranose* (**1**).—A solution of tri-*O*-acetyl-D-glucal (2.72 g, 10 mmol; Aldrich) in 10:10:1 MeOH–H_2O–Et_3N (125 mL) was stirred for 5 h at room temperature, then concentrated. The residue was dried by repeated evaporations with EtOH, then kept overnight under vacuum in the presence of P_2O_5. The syrupy D-glucal (1.41 g, 98%) was treated with bis(tributyltin) oxide (4.77 g, 8 mmol) and activated, powdered 3A molecular sieves (4 g) in refluxing dry acetonitrile (100 mL) for 3 h. The mixture was cooled to 5°C under Ar, and iodine (3.8 g, 15 mmol) was added in one portion. The dark-brown mixture was stirred for 15 min at 5°C, then for 2 h at room temperature. TLC (1:1 toluene–acetone) showed the complete conversion of D-glucal (R_f 0.14) into **1** (R_f 0.45). The mixture was filtered through Celite and concentrated. To the residue were added satd aq sodium thiosulfate (50 mL) and hexane (50 mL), and the biphasic mixture was vigorously stirred for 3 h. The aqueous phase was then continuously extracted with EtOAc for 8 h. The extract was concentrated to give **1** (2.18 g, 80%). A sample for analysis was crystallized from EtOH–hexane; mp 101–103°C; $[\alpha]_D$ +10° (*c* 1, MeOH). ^{1}H NMR [$(CD_3)_2SO$]: δ 5.61 (s, 1 H, H-1), 5.52 (d, 1 H, $J_{3,OH}$ 4.2 Hz, OH-3), 5.20 (d, 1 H, $J_{4,OH}$ 4.1 Hz, O*H*-4), 4.42 (m, 1 H, H-5), 4.01 (d, 1 H, $J_{6endo,6exo}$ 6.9 Hz, H-6*endo*), 3.94 (m, 1 H, H-3), 3.83 (m, 1 H, H-2), 3.52 (dd, 1 H, $J_{5,6exo}$ 6.4 Hz, H-6*exo*), and 3.45 (m, 1 H, H-4). *Anal.* Calcd for $C_6H_9IO_4$: C, 26.49; H, 3.32. Found: C, 26.66; H, 3.41.

*3,4-Di-*O*-acetyl-1,6-anhydro-2-deoxy-2-iodo-β-*D*-glucopyranose* (**2**).—Crude **1** (2 g) was treated overnight at room temperature with pyridine (6 mL) and Ac_2O (4 mL). The mixture was cooled to 5°C, then treated with MeOH (10 mL), and concentrated. Column chromatography (7:3 petroleum ether–EtOAc) of the residue gave **2** (2.2 g, 84%); mp 95°C; $[\alpha]_D$ +39° (*c* 1, $CHCl_3$); lit.[27] mp 95°C; $[\alpha]_D$ +38° (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$); δ 5.70 (s, 1 H, H-1), 5.14 (m, 1 H, H-3), 4.72 (m, 1 H, H-4), 4.65 (m, 1 H, H-5), 4.23 (dd, 1 H, $J_{5,6endo}$ 0.8, $J_{6endo,6exo}$ 7.7 Hz, H-6*endo*), 3.94 (m, 1 H, H-2), 3.82 (dd, 1 H, $J_{5,6exo}$ 5.8 Hz, H-6*exo*), 2.21, and 2.12 (2 s, 6 H, 2 OAc).

*3,4-Di-*O*-acetyl-1,6-anhydro-2-deoxy-β-*D*-*arabino*-hexopyranose* (**3**).—A solution of **2** (356 mg, 1 mmol) and α,α'-azobisisobutyronitrile (27 mg, 0.16 mmol) in dry benzene (20 mL) was degassed with Ar for 15 min. Tributylstannane (582 mg, 2 mmol) was added under Ar and the mixture was heated under reflux for 2 h. TLC (3:2 petroleum ether–EtOAc) showed complete conversion of **2** (R_f 0.40) into **3** (R_f 0.30). The mixture was concentrated and a solution of the residue in acetonitrile (10 mL) was washed with petroleum ether (10 mL), then evaporated. Column chromatography (7:3 petroleum ether–EtOAc) gave **3** (193 mg, 84%); $[\alpha]_D$ −122° (*c* 1.26, $CHCl_3$); lit.[28] $[\alpha]_D$ −103° (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.57 (s, 1 H, H-1), 4.86 (ddd, 1 H, $J_{2ax,3}$ 6 Hz, H-3), 4.69 (s, 1 H, H-4), 4.58 (m, 1 H, H-5), 4.19

(dd, 1 H, $J_{5,6endo}$ 0.8 Hz, H-6*endo*), 3.78 (dd, 1 H, $J_{5,6exo}$ 5.8, $J_{6endo,6exo}$ 7.5 Hz, H-6*exo*), 2.2-2.1 (m, 1 H, H-2*ax*), 2.14 and 2.08 (2 s, 6 H, 2 OAc), and 1.82 (d, 1 H, $J_{2ax,2eq}$ 15.2 Hz, H-2*eq*). *Anal.* Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.33; H, 6.13.

3,4-Di-O-acetyl-1,6-anhydro-2-deoxy-2-C-(2-propenyl)-β-D-glucopyranose (**5**).—A solution of **2** (1.07 g, 3 mmol) and α,α′-azobisisobutyronitrile (82 mg, 0.5 mmol) in dry benzene (50 mL) was degassed with Ar for 15 min. Allyltributylstannane (2 g, 6 mmol) was added under Ar and the mixture was heated under reflux for 3 h. TLC (7:3 petroleum ether–EtOAc) showed the complete conversion of **2** (R_f 0.31) into **5** (R_f 0.37), a small amount of **3** (R_f 0.22), and some polar products ($R_f \leq 0.1$). The solvent was evaporated, and a solution of the residue in acetonitrile (25 mL) was washed with petroleum ether (25 mL), then concentrated. Column chromatography (7:3 petroleum ether–EtOAc) gave **5** (527 mg, 65%) isolated as a syrup; $[\alpha]_D$ −66° (*c* 1.13, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 5.82 (m, 1 H, H-8), 5.41 (s, 1 H, H-1), 5.15 (m, 1 H, H-9*trans*), 5.10 (m, 1 H, H-9*cis*), 4.69 (m, 1 H, H-3), 4.67 (m, 1 H, H-4), 4.57 (m, 1 H, H-5), 4.16 (d, 1 H, $J_{6endo,6exo}$ 7.6 Hz, H-6*endo*), 3.79 (dd, 1 H, $J_{5,6exo}$ 5.9 Hz, H-6*exo*), 2.32 (m, 2 H, H-7a, 7b), 2.15 and 2.09 (2 s, 6 H, 2 OAc), and 1.82 (t, 1 H, $J_{2,7a} = J_{2,7b} = 7.8$ Hz, H-2); MS: *m/z* 288 ($M^+ + 18$), 271 ($M^+ + 1$). *Anal.* Calcd for $C_{13}H_{18}O_6$: C, 57.76; H, 6.71. Found: C, 58.01; H, 6.71.

1,6-Anhydro-2-deoxy-2-C-(2-propenyl)-β-D-glucopyranose (**6**).—A solution of **5** (270 mg, 1 mmol) in 10:10:1 MeOH–H_2O–Et_3N (20 mL) was left for 4 h at room temperature and then concentrated. The residue was dried by repeated additions and evaporations of EtOH to give **6** (177 mg, 95%). An analytical sample, obtained by column chromatography (3:2 petroleum ether–acetone), had $[\alpha]_D$ −52° (*c* 1.3, MeOH). ^1H NMR [$(CD_3)_2SO$]: δ 5.80 (m, 1 H, H-8), 5.20 (s, 1 H, H-1), 5.08–5.01 (m, 3 H, H-9*cis* and *trans*, O*H*), 4.72 (d, 1 H, *J* 3.8 Hz, O*H*), 4.33 (m, 1 H, H-5), 3.98 (d, 1 H, $J_{6endo,6exo}$ 6.7 Hz, H-6*endo*), 3.50 (dd, 1 H, $J_{5,6exo}$ 6 Hz, H-6*exo*), 3.40 and 3.33 (2 H, 2 s, overlapped by H_2O signal but appeared when D_2O was added, H-3,4), 2.16 (m, 2 H, H-7a,7b), and 1.53 (t, 1 H, $J_{2,7a} = J_{2,7b} = 7.3$ Hz, H-2). *Anal.* Calcd for $C_9H_{14}O_{14} \cdot 0.33\ H_2O$: C, 56.24; H, 7.69. Found: C, 56.21; H, 7.54.

4-O-Acetyl-1,6-anhydro-2-deoxy-2-C-(2-propenyl)-β-D-glucopyranose (**7**).—To an ice-cooled solution of **5** (270 mg, 1 mmol) in MeOH (20 mL) were added water (5 mL) and Et_3N (1 mL). The mixture was stirred for 4 h at 5°C and then brought to pH 5 by addition of glacial acetic acid (2 mL). TLC (1:1 toluene–acetone) showed traces of **5** (R_f 0.81), the monoacetate **7** (R_f 0.61), and the diol **6** (R_f 0.53). The solution was evaporated and the residue dried by repeated additions and evaporations of EtOH. Column chromatography (7:3 petroleum ether–acetone) gave fractions containing pure syrupy **7** (83 mg, 36%); $[\alpha]_D$ −49° (*c* 1.25, MeOH). ^1H NMR ($CDCl_3$): δ 5.82 (m, 1 H, H-8), 5.41 (s, 1 H, H-1), 5.18–5.10 (m, 2 H, H-9*cis* and *trans*), 4.65 (m, 1 H, H-4), 4.54 (m, 1 H, H-5), 4.07 (dd, 1 H, $J_{5,6endo}$ 1.0, $J_{6endo,6exo}$ 7.5 Hz, H-6*endo*), 3.80 (dd, 1 H, $J_{5,6exo}$ 5.9 Hz, H-6*exo*), 3.61 (d, 1 H, $J_{3,OH}$ 5.9 Hz, O*H*-3), 2.87 (d, 1 H, H-3), 2.34 (m, 2 H, H-7a, 7b), and 1.81 (m, 1 H, H-2). *Anal.* Calcd for $C_{11}H_6O_5$: C, 57.44; H, 7.06. Found: C, 57.21; H, 7.10.

(1R,2S,3R,5R,7R,8R)-2-Acetoxy-5-bromomethyl-4,9,11-trioxatricyclo-[6.2.1.0^{3,7}]undecane (**9**).—To an ice-cooled solution of **6** (186 mg, 1 mmol) in 99:1 CH_2Cl_2–EtOH was added *N*-bromosuccinimide (214 mg, 1.2 mmol, freshly crystallized from boiling water and thoroughly dried under vacuum). The mixture was stirred for 2 h at room temperature. TLC (1:1 petroleum ether–acetone) then showed the complete conversion of **6** (R_f 0.38) into **8** (R_f 0.57) and **10** (R_f 0.45). A trace of a brick red product **11** was also visible at R_f 0.61. The solution was washed with satd aq sodium thiosulfate and then concentrated. Column chromatography (7:3 petroleum ether–acetone) of the residue gave first **11** (13 mg, 5%). MS: *m/z* 282 (M^+ + 18, 100%), 284 (M^+ + 18, 98%), and 185 (M^+ − Br).

The tricyclic product **8** was eluted next (144 mg, 54%). MS: *m/z* 282 (M^+ + 18, 100%), 284 (M^+ + 18, 98%), and 185 (M^+ − Br). Compound **8** was treated with 2:1 pyridine–Ac_2O (15 mL) overnight at room temperature. Methanol (10 mL) was added and the mixture was concentrated to dryness to give **9** (158 mg, 95%). Column chromatography (7:3 petroleum ether–EtOAc) gave an analytical sample; mp 111–112°C (from EtOH); $[\alpha]_D$ −29° (*c* 1.17, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.54 (d, 1 H, $J_{7,8}$ 1.4 Hz, H-8), 4.59 (dd, 1 H, $J_{1,2} \leq 1.0$, $J_{2,3}$ 8.6 Hz, H-2), 4.46–4.40 (m, 2 H, H-1,5), 3.99 (dd, 1 H, $J_{1,10exo}$ 6.8, $J_{10exo,10endo}$ 8.5 Hz, H-10*exo*), 3.86 (dd, 1 H, $J_{1,10endo}$ 2.2 Hz, H-10*endo*), 3.80 (dd, 1 H, $J_{3,7}$ 11.2 Hz, H-3), 3.53 (dd, 1 H, $J_{5,12a}$ 5.0, $J_{12a,12b}$ 10.3 Hz, H-12a), 3.44 (dd, 1 H, $J_{5,12b}$ 6.9 Hz, H-12b), 2.40 (m, 1 H, H-6a), 2.15 (s, 3 H, OAc), and 1.87–1.72 (m, 2 H, H-6b,7). *Anal.* Calcd for $C_{11}H_{15}BrO_5$: C, 43.01; H, 4.92. Found: C, 42.93; H, 4.88.

The mixture of dibromo compounds **10** was eluted last (38 mg, 11%). MS: *m/z* 362 (M^+ + 18, 100%), 364 (M^+ + 18, 200%), and 366 (M^+ + 18, 95%).

TABLE V

Fractional atomic coordinates

Atom	*x/a*	*y/b*	*z/c*	U_{eq}
Br-1	0.0103(2)	0.0111(4)	0.06883(9)	0.0548
O-1	1.1274(9)	0.019(2)	−0.3378(6)	0.0609
O-3	0.475(1)	0.142(1)	−0.1056(6)	0.0362
O-4	0.540(1)	0.356(1)	−0.3201(7)	0.0449
O-5	0.839(1)	0.037(1)	−0.4084(5)	0.0467
O-43	0.757(1)	0.5737(9)	−0.3440(7)	0.0554
C-1	0.920(2)	−0.046(1)	−0.3241(9)	0.0464
C-2	0.775(1)	−0.001(2)	−0.2055(8)	0.0340
C-3	0.598(1)	0.116(1)	−0.2205(8)	0.0343
C-4	0.704(2)	0.267(1)	−0.2814(9)	0.0399
C-5	0.880(2)	0.205(1)	−0.3858(9)	0.0447
C-6	1.104(2)	0.192(2)	−0.361(1)	0.0520
C-7	0.638(2)	−0.125(1)	−0.1267(9)	0.0436
C-8	0.461(2)	−0.015(2)	−0.0499(8)	0.0385
C-9	0.244(2)	−0.092(1)	−0.045(1)	0.0479
C-41	0.586(2)	0.514(2)	−0.3452(7)	0.0446
C-42	0.404(2)	0.597(2)	−0.380(1)	0.0693

TABLE VI

Anisotropic thermal parameters

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br-1	0.0521(5)	0.0576(7)	0.0553(7)	0.004(1)	−0.0134(4)	0.003(1)
O-1	0.043(4)	0.068(5)	0.079(5)	−0.02(1)	−0.010(3)	0.007(9)
O-3	0.054(5)	0.025(4)	0.034(4)	−0.006(3)	−0.004(3)	0.001(4)
O-4	0.054(5)	0.044(5)	0.061(5)	0.024(4)	−0.028(4)	−0.015(4)
O-5	0.070(4)	0.049(6)	0.031(4)	−0.000(5)	−0.010(3)	−0.013(5)
O-43	0.098(6)	0.032(5)	0.089(7)	0.013(4)	−0.043(5)	−0.028(5)
C-1	0.058(7)	0.052(8)	0.035(7)	−0.012(5)	−0.008(5)	−0.001(5)
C-2	0.045(5)	0.025(6)	0.036(5)	−0.004(7)	−0.008(4)	0.008(8)
C-3	0.044(6)	0.034(6)	0.031(6)	0.009(5)	−0.008(4)	−0.010(5)
C-4	0.041(6)	0.039(6)	0.044(7)	−0.002(6)	−0.017(5)	−0.003(5)
C-5	0.059(7)	0.043(7)	0.042(7)	0.004(6)	−0.014(5)	−0.018(6)
C-6	0.041(6)	0.059(9)	0.068(8)	−0.023(7)	0.009(6)	−0.012(6)
C-7	0.058(7)	0.037(7)	0.041(7)	0.010(6)	−0.008(5)	0.006(6)
C-8	0.044(5)	0.04(1)	0.033(6)	−0.000(6)	−0.004(4)	0.001(6)
C-9	0.064(7)	0.031(7)	0.057(8)	−0.005(6)	−0.016(6)	−0.002(6)
C-41	0.072(6)	0.045(6)	0.031(5)	0.01(1)	−0.018(5)	−0.01(1)
C-42	0.091(9)	0.057(9)	0.09(1)	0.024(8)	−0.041(8)	0.006(8)

X-ray analysis of **9**.—The structure was solved by direct methods using SHELXS86 (ref 29). Data reduction and structure refinement were performed using the CRYSTALS package[30]. The positional and anisotropic thermal parameters (Tables V, VI) of all nonhydrogen atoms were refined by full matrix least squares. The hydrogen atoms were located on difference-Fourier maps and introduced in the last least squares cycles as fixed contributions. The intensities were corrected for absorption (using DIFABS[31]) and for secondary extinction.

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