The Use of Grignard Reagents in the Synthesis of Carbohydrates. I.[1] The Synthesis of Deoxy and Branched-chain Deoxy Sugars

Masajiro KAWANA* and Sakae EMOTO

The Institute of Physical and Chemical Research, Wako-shi, Saitama 351

(Received July 2, 1979)

Two branched-chain deoxy sugars, methyl 5,6-*O*-cyclohexylidene-3-deoxy-2-*C*-methyl-β-D-*arabino*-hexofuranoside and its α-D-*ribo* isomer, were easily prepared by the one-step reaction of methyl 5,6-*O*-cyclohexylidene-3-*O*-mesyl-β-D-allofuranoside (**3a**) with methylmagnesium iodide. Similarly, the corresponding α-mesylate (**4a**) gave methyl 5,6-*O*-cyclohexylidene-3-deoxy-2-*C*-methyl-α-D-*ribo*-hexofuranoside. It was demonstrated that these reactions involved 1,2-hydride shifts. The reaction of **3a** and **4a** with *t*-butylmagnesium bromide yielded two deoxy sugars, methyl 5,6-*O*-cyclohexylidene-3-deoxy-β-D-*arabino*-hexofuranoside and the corresponding α-D-*ribo* isomer, respectively. Under certain reaction conditions with the Grignard reagents, the sulfonate (**3a**) afforded dimeric compounds, in which two furanose rings were directly bound with a carbon–carbon bond. A convenient method for the preparation of the sulfonates (**3a** and **4a**) is also reported.

The synthesis of deoxy and branched-chain sugars has recently received increased attention because these sugars are found in nature as glycoside-components of an important class of antibiotics.[2] We would like to describe here the details of a new method previously reported in only preliminary form[3] for the one-step synthesis of deoxy and branched-chain deoxy sugars starting from sugar sulfonates with Grignard reagents; we will also report some observations made during this work.

The starting point for the present work was our finding of a convenient method for the preparation of the starting sulfonates, methyl 5,6-*O*-cyclohexylidene-3-*O*-mesyl-β-D-allofuranoside (**3a**) and the corresponding α-anomer (**4a**), in good yields. Thus, a methanolic solution of a 3-*O*-mesyl derivative (**2** in Fig. 1) prepared from 1,2:5,6-di-*O*-cyclohexylidene-α-D-allofuranose[4a] (**1**) was refluxed in the presence of an acid, after which the mixture was diluted with benzene. In order to complete this reaction, a large amount of the methanol was evaporated to give a mixture (92%) of **3a** and **4a** in a ratio of 2:1; those anomers were easily separated by fractional crystallization.

The structures of both mesylates were established by means of their elemental analyses and spectrocsopic data (see Experimental). Their mass spectra showed strong peaks at *m/e* 141 characteristic of the dioxolane ring at C-4, thus indicating the furanose structures of these mesylates.[5]

The branched-chain deoxy sugars were obtained very easily when these mesylates were treated with an excess of methylmagnesium iodide (MeMgI). Thus **3a** was added to an ethereal solution of a 3-molar excess of MeMgI to give, in one step, methyl 5,6-*O*-cyclohexylidene-3-deoxy-2-*C*-methyl-β-D-*arabino*-hexofuranoside (**6a**) and the corresponding *ribo* isomer

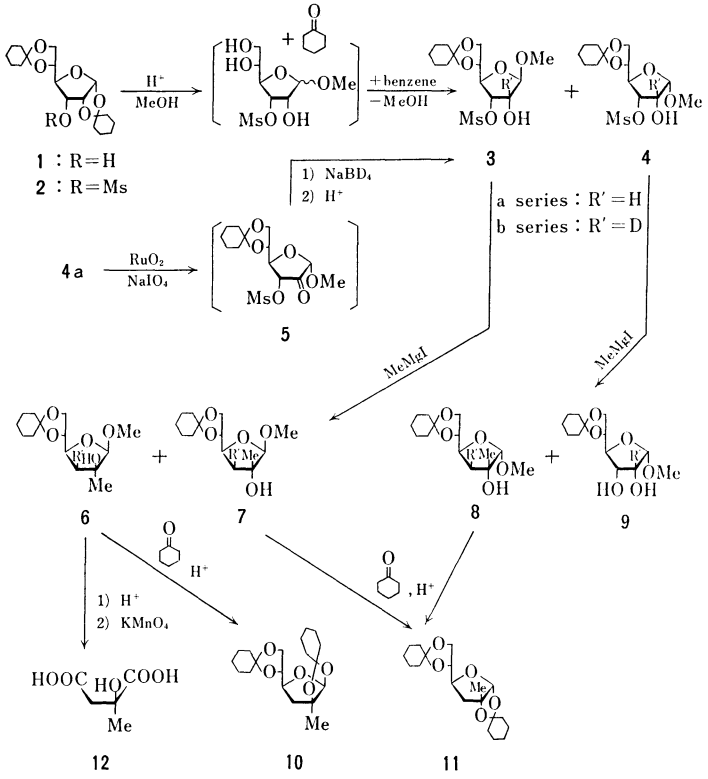

Fig. 1.

(**7a**) in 86 and 4% yields respectively. When **4a** was treated with MeMgI, methyl 5,6-*O*-cyclohexylidene-3-deoxy-2-*C*-methyl-α-D-*ribo*-hexofuranoside (**8a**) was obtained in a 29% yield, besides methyl 5,6-*O*-cyclohexylidene-α-D-allofuranoside (**9a**) in a 37% yield, the cleavage of the mesyl group in **4a** being predominant in this case.

The structures of the newly synthesized branched-chain deoxy sugars were established on the basis of their analytical and spectroscopic data and the chemical conversion. The ^{1}H NMR spectrum of each sugar derivative (**6a**—**8a**) showed a singlet due to the anomeric proton and a pair of quartets characteristic of the AB parts of an ABX system; these phenomena were assignable to H_{3a} (A), H_{3b} (B), and H_4 (X).[6] The relatively large values (8.6—6.4 Hz) of the coupling constants for H_{3a}–H_4 and H_{3b}–H_4 in **6a**—**8a** suggested that these sugars most probably existed in C_3-*endo* conformations.[7] For example, the C_3-*endo* conformation of **6a** can be depicted as in Fig. 2, in which H_{3a} and the methyl group at C-2 as well as H_{3a} and H_4 consititute an axial-quasi axial pair. Spin-spin decoupling experiments demonstrated that the methyl protons in the former pair were coupled to H_{3a} (J=0.8 Hz) because of their W-shaped arrangement.

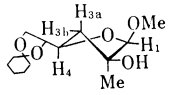

Fig. 2. C_3-*endo* conformation of **6a**.

The ^{13}C NMR spectra of **6a**—**8a** were also taken (Table 1). The signal due to the methyl carbon at C-2 of **7a** appeared at fields higher by 2.7 and 4.6 ppm than those for **6a** and **8a** respectively. This indicated that the methyl group at C-2 in **7a** was located vicinal to the methoxyl group at C-1 in a *cis* manner.[8] These ^{1}H and ^{13}C NMR spectral data are consistent with the proposed structures for **6a**, **7a**, and **8a**.

Both compounds, **7a** and **8a**, gave 1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-2-*C*-methyl-α-D-*ribo*-hexofuranose (**11**) when they were treated with cyclohexanone in the presence of an acid. Similarly, the corresponding β-D-*arabino* isomer (**10**) could be obtained from **6a**. The mass spectra of **10** and **11** showed strong peaks at *m/e* 141 attributable to the dioxolane ring at C-4, thus indicating the furanose structures of these compounds.[5] Their anomeric configurations were also assigned on the basis of the sign of the optical rotation; **10** had a negative sign, whereas **11** had a positive one.[9] From these results, it was concluded that **7a** and **8a** were a pair of anomers, and that the configurations at C-2 for these anomers were different from that for **6a**.

Furthermore, the absolute configuration of the branching point at the C-2 position of **6a** was determined by chemical degradation. Thus, **6a** was treated with an acid to hydrolyze the acetal protecting group and the glycoside, after which the resulting free sugar was oxidized with potassium permanganate to yield the known 2-methylmalic acid (**12**), which had the *S* configuration at its asymmetric center.[10a]

Salaün and Conia[11] have reported that when 2-tosyloxycyclobutanone was treated with MeMgI, the resulting Grignard adduct, 1-methyl-2-*O*-tosyl-1,2-cyclobutanediol, underwent a skeletal rearrengement of the cyclobutane ring to give cyclopropyl methyl ketone. Sasaki *et al.*[12] have obtained 3-deoxy-2-keto sugar-nucleosides by the reaction of 3′-*O*-sulfonates of nucleosides with sodium benzoate in *N*,*N*-dimethylformamide; they assumed that these reactions proceeded *via* the 1,2-elimination of the sulfonyloxyl group at C-3′ and of the proton at C-2′. In the present reactions, it was considered that the 3-deoxy-2-keto sugars (**B** in Fig. 3) were formed as intermediates from **3a** and **4a** by the elimination of the mesyloxyl groups at C-3 concomitant with the 1,2-hydride shifts from C-2 to C-3.

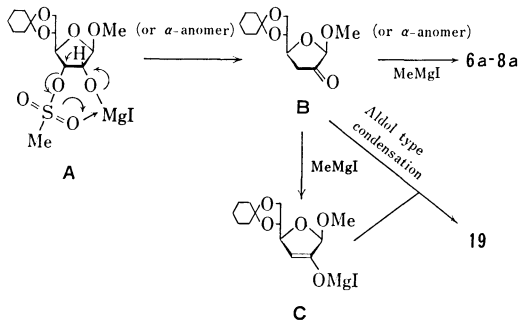

Fig. 3.

In order to demonstrate the hydride shifts in our case, the C-2 deuterated analogs of **3a** and **4a** were prepared. The oxidation of **4a** with ruthenium dioxide-sodium metaperiodate gave an ulose (**5**), which, without purification, was then reduced with sodium borodeuteride to give the C-2 deuterated analog (**4b**). The corresponding β-anomer (**3b**) was obtained by the anomerization of **4b** with an acid.

The deuterated analogs (**3b** and **4b**) thus obtained were subjected to the same Grignard reactions to give the corresponding deuterated products (**6b**—**8b**). The mass spectra of these products showed that the deuterium contents of the starting materials were almost entirely retained in the products. Their ^{1}H NMR spectra indicated that the deuteriums at C-2 in the starting materials had been transferred to the C-3 position of the products. As the ^{1}H NMR analysis distinguished between H_{3a} and H_{3b} in **6a**, the *S* configuration could be assigned to the C-3 position of **6b**. Therefore, the 1,2-deuteride shift in **3b** occurred stereoselectively by way of the intramolecular S_N2 displacement of the mesyloxyl group at C-3.

On the basis of these observations it can be assumed that the present Grignard reactions proceed through a postulated intermediate (**A** in Fig. 3) in which the oxygen atom of the sulfone moiety is coordinated to the magnesium atom to form a cyclic seven-membered ring. The formation of the keto group, the 1,2-hydride shift, and the elimination of the mesyloxyl group then occurs in a concerted manner to give the 3-deoxy-2-keto sugar (**B**), which, in turn, reacts with another MeMgI, mainly from the opposite side of the methoxyl group at C-1, to yield the branched-chain deoxy sugars.

TABLE 1. THE ^{13}C NMR CHEMICAL SHIFTS OF DEOXY AND BRANCHED-CHAIN DEOXY SUGARS[a]

Product	Carbon positions[b]											
	C_1	C_2	C_3	C_4	C_5	C_6	C-Me	O-Me	$C_{1'}$	$C_{2',6'}$	$C_{3',4',6'}$	
6a	106.56	77.60	41.18	78.66[c]	78.78[c]	66.72	23.80	54.90	109.88	34.84 36.51	23.80 24.00	25.14
7a	109.81	80.51	41.39	79.87	79.05	67.20	21.10	54.54	109.81	34.98 36.52	23.86 24.02	25.16
8a	107.38	77.51	40.66	78.00	76.94	66.72	25.73	55.43	110.06	34.74 36.20	23.78 23.94	25.16
13a	101.82	72.33	35.02	78.08[c]	78.59[c]	66.65	—	54.86	109.67	34.78 36.42	23.77 23.97	25.09
14a	102.56	71.69	33.60	77.03[c]	77.69[c]	66.43	—	55.24	110.13	34.62 36.17	23.74 23.98	25.14

a) The spectra were run in $CDCl_3$ and were completely decoupled. The shifts are given in parts per million relative to the internal tetramethylsilane. b) C_1–C_6 refer to the carbon atoms of the sugars, while $C_{1'}$–$C_{6'}$ refer to the cyclohexylidene carbon atoms. c) The assignment of the signals to C_4 and C_5 may be reversed.

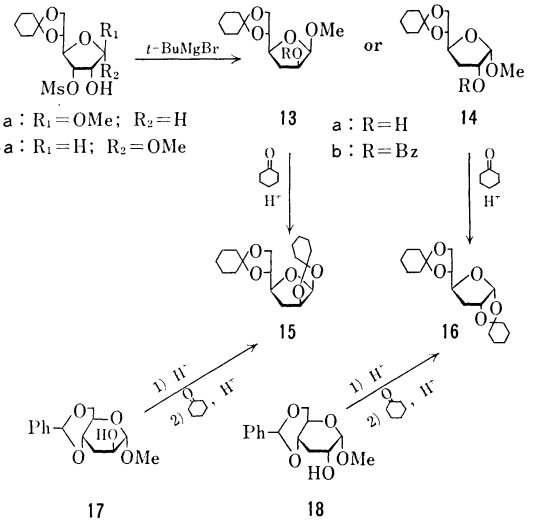

Fig. 4.

With the hope of obtaining exclusively the 3-deoxy-2-keto sugars in the present reactions, we attempted to use sterically bulky *t*-butylmagnesium bromide (*t*-BuMgBr) instead of MeMgI. However, the reaction of **3a** or **4a** with *t*-BuMgBr did not stop at the stage of the formation of the desired sugar derivative, but proceeded further to afford methyl 5,6-*O*-cyclohexylidene-3-deoxy-β-D-*arabino*-hexofuranoside (**13a**) or the corresponding α-D-*ribo* isomer (**14a**) in an 87 or 75% yield respectively after column chromatography (Fig. 4). The Grignard reduction by *t*-BuMgBr was effective in this case. An attempt to reduce 1,2:5,6-di-*O*-cyclohexylidene-α-D-*ribo*-hexofuranos-3-ulose[4b] with *t*-BuMgBr under similar conditions gave a mixture (91:9) of the corresponding *allo*- and *gluco*-furanose in a 78% yield.

The structures of **13a** and **14a** as well as their monobenzoates (**13b** and **14b**) were characterized by their elemental analyses and spectroscopic data, including the ^{13}C NMR spectra (Table 1). Furthermore, the treatment of **13a** and **14a** with cyclohexanone in the presence of an acid gave 1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-β-D-*arabino*-hexofuranose (**15**) and the corresponding α-D-*ribo* isomer (**16**) respectively, their furanose

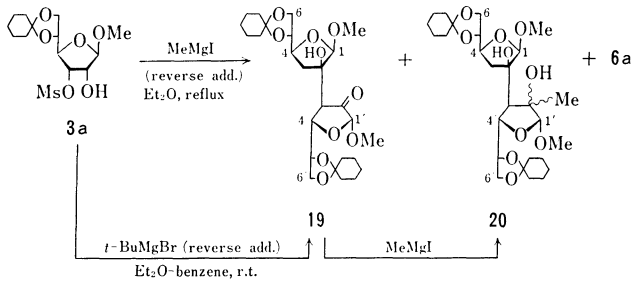

Fig. 5.

structures being tentatively assigned. However, the physical properties of **15** and **16** were identical with those of the specimens prepared from known compounds, methyl 4,6-*O*-benzylidene-3-deoxy-α-D-*arabino*-hexopyoranoside[13] (**17**) and the corresponding α-D-*ribo* isomer[14] (**18**) respectively.

When an ethereal solution of MeMgI was very gradually added to a refluxing solution of **3a** in ether, it gave two dimeric compounds, **19** and **20**, in 3 and 44% yields respectively, besides **6a** (29%)(Fig. 5). Using *t*-BuMgBr, we obtained **19** in a moderate yield, upon subsequent treatment with MeMgI, this gave **20**.

The structures and the stereochemistry of the binding sites of the two furanose rings for **19** and **20** were deduced to be as is shown in the scheme on the basis of their spectral data as well as an inspection of the CPK molecular model, but the configuration of the methyl and hydroxyl groups in **20** is not clear at this time. These reactions are considered to be Aldol-type condensations of the ketone (**B**, β-anomer) and its enolate (**C**) (Fig. 3); the slow addition of MeMgI to a solution of **3a** would result in the survival of a relatively large amount of unreacted ketone (**B**), some of which would be isomerized with MeMgI to **C**. Similar reactions have been reported by Horton and Just[15a] and others.[15b,c]

Experimental

The boiling and melting points are uncorrected. The optical rotations were measured with a Perkin-Elmer Model 141 polarimeter. The IR spectra were recorded on a Shimadzu IR-27 instrument. The mass spectra were obtained

with a Japan Optics Lab. Model JMS-01SG instrument. The ^{1}H NMR spectra were recorded on a Varian HA-100D apparatus, with tetramethylsilane as the internal standard. The proton noise-decoupling ^{13}C NMR spectra were obtained on a JEOL FX-60 FT.

Merck silica gel 60 (0.063—0.20 mm) was used for the column chromatography, and silica gel GF_{254} was used for the analytical TLC; visualization was effected by the use of a methanol–sulfuric acid–*p*-methoxybenzaldehyde (85:10:5, v/v) spray, followed by heating. The elemental analyses were performed by this Institute. The sodium borodeuteride (98% min deuterium content) was purchased from Merck.

*1,2:5,6-Di-*O*-Cyclohexylidene-3-*O*-mesyl-α-*D*-allofuranose (**2**).* Mesyl chloride (5.5 ml) was added to a stirred solution of I[4a] (17 g, 0.05 mol) in a mixture of dry pyridine (30 ml) and benzene (30 ml) at 0—5 °C (bath temperature). The mixture was then stirred at room temperature overnight. After cooling, iced water was added and the mixture was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and concentrated. The pyridine was removed by co-evaporation with xylene. The residue was diluted with methanol to give **2** (88%) as crystals. An analytically pure sample was obtained by recrystallization from methanol: mp 119.5—121.5 °C; $[\alpha]_D^{23}$ +82.2° (*c* 1.3, $CHCl_3$). IR (KBr): 1358 (S=O), 1179 (S=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.0—2.0 (20H, m, CH_2 of the cyclohexylidene groups), 3.8—4.4 (4H, m), 4.7—4.9 (2H, m), 5.82 (1H, dd, J=3.8 Hz, J=0.8 Hz, H-3).

Found: C, 54.68; H, 6.98; S, 7.67%. Calcd for $C_{19}H_{30}O_8S$: C, 54.53; H, 7.23; S, 7.66%.

*Methyl 5,6-*O*-Cyclohexylidene-3-*O*-mesyl-β-*D*-allofuranoside (**3a**) and Its α-Anomer (**4a**).* A mixture of **2** (16.8 g, 0.04 mol) and concd sulfuric acid (0.2 ml) in dry methanol (120 ml) was stirred at 75—80 °C (bath temperature) for 3 h. The methanol was then removed below 35 °C *in vacuo* until crystals appeared. Dry benzene (60 ml) was added, and the mixture was concentrated to *ca.* 30 ml. This procedure (the addition of benzene and the concentration of the mixture) was repeated once again. Calcium hydroxide (4 g) was then added, and the mixture was diluted with chloroform. After the crystalline materials had been removed by filtration, the chloroform solution was washed successively with aqueous sodium hydrogencarbonate and water, and dried ($MgSO_4$). The removal of the solvent gave crude products, the ^{1}H NMR spectrum of which showed that the ratio of **3a** and **4a** was approximately 2:1. The products were triturated with hot hexane (80 ml). After the mixture had been cooled, the crystalline compounds were collected and washed with hexane. Recrystallization from benzene–diisopropyl ether gave **3a** (8.1 g, 57%). The mother liquor was concentrated, and the residue was submitted to fractional crystallization from diisopropyl ether, giving **4a** (3.95 g, 28%) and another crop of **3a** (0.98 g, 7%).

The recrystallization of the crude **3a** from methanol gave an analytically pure sample as needles: mp 138—140 °C; $[\alpha]_D^{24}$ −44.6° (*c* 1, $CHCl_3$). IR (KBr): 3470 (OH), 1353 (S=O), 1173 (S=O) cm^{-1}. MS: *m/e* 352 (M^+), 141 (the dioxolane ring at C-4). ^{1}H NMR ($CDCl_3$): δ 1.2—1.8 (10H, m, CH_2 of the cyclohexylidene groups), 2.50 (1H, br s, OH), 3.16 (3H, s, SCH_3), 3.35 (3H, s, OCH_3), 3.9—4.2 (4H, m), 4.31 (1H, dd, $J_{1,2}$=1.4 Hz, $J_{2,3}$=4.6 Hz, H-2), 4.87 (1H, d, $J_{1,2}$=1.4 Hz, H-1), 5.10 (1H, m, H-3).

Found: C, 47.73; H, 6.84; S, 9.00%. Calcd for $C_{14}H_{24}O_8S$: C, 47.72; H, 6.78; S, 9.10%.

The recrystallization of the crude **4a** from benzene–diisopropyl ether gave an analytically pure sample as prisms: mp 118—119 °C; $[\alpha]_D^{22}$ +97.7° (*c* 1, $CHCl_3$). IR (KBr): 3500 (OH), 1353 (S=O), 1172 (S=O) cm^{-1}. MS: *m/e* 352 (M^+), 141 (the dioxolane ring at C-4). ^{1}H NMR ($CDCl_3$): δ 1.2—2.0 (10H, m, CH_2 of the cyclohexylidene groups), 3.12 (3H, s, SCH_3), 3.47 (3H, s, OCH_3), 3.7—4.4 (5H, m) 4.93 (1H, d, $J_{1,2}$=4.8 Hz, H-1), 5.0 (1H, m, H-3).

Found: C, 47.53; H, 6.83; S, 9.13%. Calcd for $C_{14}H_{24}O_8S$: C, 47.72; H, 6.87; S, 9.10%.

*Methyl 5,6-*O*-Cyclohexylidene-3-*O*-mesyl-β-*D*-allofuranoside-2-*d (**3b**) and Its α-Anomer (**4b**).* A mixture of **4a** (2.27 g, 6.45 mmol), sodium metaperiodate (6.8 g), ruthenium dioxide (400 mg), and potassium carbonate (720 mg) in alcohol-free chloroform (80 ml) and water (80 ml) was vigorously stirred at room temperature for 8 h.[16] After the excess of ruthenium tetraoxide had then been decomposed with 2-propanol, the undissolved materials were filtered through a Celite pad and washed with chloroform. The filtrate was dried ($MgSO_4$) and concentrated to give a syrupy ketone (**5**, 1.85 g) which was almost pure, judging from its TLC analysis, and IR and ^{1}H NMR spectral data; this product was found to be converted to almost pure **4a** by reduction with sodium borohydride under conditions similar to those described below.

Sodium borodeuteride (200 mg) was added to a stirred solution of this crude **5** (1.75 g) in methanol (15 ml) at 0—5 °C (bath temperature) over a period of 5 min. After 1 h, the mixture was diluted with ether, and the solution was washed with water and dried ($MgSO_4$). The evaporation of the solvent gave a crystalline product, which was triturated with hot diisopropyl ether to give **4b** (1.48 g, 69% from **4a**); the deuterium content was found to be 91% on the basis of the mass spectrometric analysis. MS: *m/e* 353 (M^+). ^{1}H NMR ($CDCl_3$): δ 1.1—1.8 (10H, m, CH_2 of the cyclohexylidene group), 3.11 (3H, s, SCH_3), 3.46 (3H, s, OCH_3), 3.9—4.3 (4, 1H, m), 4.92 (1H, s, H-1), 4.97 (1H, m, H-3).

A stirred mixture of **4b** (1.3 g) and concd sulfuric acid (0.03 ml) was refluxed at 80—85 °C (bath temperature) for 3 h. The solution was treated in a manner to that described for the synthesis of **3a** to give a mixture (1.2 g) of **3b** and **4b** in a ratio of 2:1, from which **3b** (500 mg, 38%) was isolated. Recrystallization from benzene–diisopropyl ether gave **3b**; the deuterium content was found to be 87% on the basis of the mass spectrometric analysis. MS: *m/e* 353 (M^+). ^{1}H NMR ($CDCl_3$): δ 1.1—1.9 (10H, m, CH_2 of the cyclohexylidene group), 3.16 (3H, s, SCH_3), 3.36 (3H, s, OCH_3), 3.8—4.2 (4H, m), 4.3 (0.1H, m, H-2), 4.87 (1H, s, H-1), 5.1 (1H, m, H-3).

*Methyl 5,6-*O*-Cyclohexylidene-3-deoxy-2-*C*-methyl-β-*D*-arabino-hexofuranoside (**6a**) and Methyl 5,6-*O*-Cyclohexylidene-3-deoxy-2-*C*-methyl-β-*D*-ribo-hexofuranoside (**7a**).* To a stirred solution of MeMgI (6 mmol) in ether (20 ml) we added **3a** (705 mg, 2 mmol) at 0—5 °C (bath temperature) under a dry nitrogen atmosphere over a period of 5 min, after which the mixture was stirred at room temperature for 2 h. After the mixture had been cooled, aqueous ammonium chloride was added. The mixture was then extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to give crystalline products, which were recrystallized from water–ethanol on seeding to afford **6a** (262 mg, 48%): mp 69—70 °C; $[\alpha]_D^{25}$ −69.4° (*c* 1, $CHCl_3$). IR (KBr): 3500 (OH) cm^{-1}. MS: *m/e* 272 (M^+). ^{1}H NMR[6] ($CDCl_3$): δ 1.2—1.7 (10H, m, CH_2 of the cyclohexylidene group), 1.32 (3H, d, $J_{3a,Me}$=0.8 Hz, C-CH_3), 1.88 (1H, q, $J_{3a,3b}$=11.5 Hz, $J_{3a,4}$=8.0 Hz, H-3a), 2.09 (1H, q, $J_{3a,3b}$=11.5 Hz, $J_{3b,4}$=6.5 Hz, H-3b), 2.72 (1H, br s, OH), 3.40 (3H, s, OCH_3), 3.7—4.2 (4H, m), 4.35 (1H, s, H-1).

Found: C, 62.00; H, 8.70%. Calcd for $C_{14}H_{24}O_5$: C,

61.74; H, 8.88%.

The mother liquor was concentrated, and the residue was chromatographed on a silica-gel column with hexane–ether (2:1) to give a ketonic compound (11 mg) which was not characterized, another crop of **6a** (209 mg, 38%), and the C-2 epimer (**7a**, 22 mg, 4%) as crystals: mp 90—92 °C; $[\alpha]_D^{20}$ −80.2° (*c* 0.3, $CHCl_3$). IR (KBr): 3280 (OH) cm^{-1}. MS: *m/e* 272 (M^+). ^1H NMR[6] ($CDCl_3$): δ 1.1—1.7 (10H, m, CH_2 of the cyclohexylidene group), 1.36 (3H, s, C-CH_3), 1.91 (1H, q, $J_{3a,3b}$=13.1 Hz, $J_{3a,4}$=8.6 Hz, H-3a), 2.09 (1H, q, $J_{3a,3b}$=13.1 Hz, $J_{3b,4}$=6.6 Hz, H-3b), 2.23 (1H, br s, OH), 3.32 (3H, s, OCH_3), 3.8—4.4 (4H, m), 4.51 (1H, s, H-1).

Found: C, 61.96; H, 8.97%. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88%.

*Methyl 5,6-O-Cyclohexylidene-3-deoxy-2-C-methyl-α-D-ribo-hexofuranoside (**8a**) and Methyl 5,6-O-Cyclohexylidene-α-D-allofuranoside (**9a**).* A solution of MeMgI (18 mmol) in ether (15 ml) was gradually added to a stirred suspension of powdered **4a** (1.06 g, 3 mmol) in ether (20 ml) at −3—0 °C (bath temperature) under a dry nitrogen atmosphere over a period of 30 min; when powdered **4a** was added to the solution of MeMgI under conditions similar to those described for the synthesis of **6a**, gummy materials were formed to decrease the yield of **8a**. After the mixture had then been stirred at room temperature for 7 h, it was poured into a cold solution of ammonium chloride (1 g) in water (30 ml) and extracted with ether (250 ml). The extract was washed with water (40 ml×8), dried ($MgSO_4$), and concentrated. The residue was chromatographed on a silica-gel column with hexane–ether to give **8a** (240 mg, 29%) as a syrup. An analytically pure sample was obtained by distillation: bp 128—130 °C (bath temperature)/2 mmHg; $[\alpha]_D^{21}$ +75.2° (*c* 1, $CHCl_3$). IR (neat): 3530 (OH) cm^{-1}. MS: *m/e* 272 (M^+). ^1H NMR[6] ($CDCl_3$): δ 1.2—1.7 (10H, m, CH_2 of the cyclohexylidene group), 1.37 (3H, s, C-CH_3), 1.93 (1H, q, $J_{3a,3b}$=12.4 Hz, $J_{3a,4}$=6.4 Hz, H-3a), 2.11 (1H, q, $J_{3a,3b}$=12.4 Hz, $J_{3b,4}$=7.0 Hz, H-3b), 2.74 (1H, br s, OH), 3.47 (3H, s, OCH_3), 3.8 (1H, m), 3.9—4.3 (3H, m), 4.53 (1H, s, H-1).

Found: C, 61.86; 8.89%. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88%.

The aqueous ammonium chloride and washings were combined and concentrated. The residue was triturated with chloroform, and the undissolved materials were removed by filtration. The chloroform was evaporated to give a syrup, which was then chromatographed on a silica-gel column with chloroform–methanol (98:2) to afford **9a** (304 mg, 37%) as a syrup: $[\alpha]_D^{21}$ +100° (*c* 1, $CHCl_3$). IR (neat): 3450 (OH) cm^{-1}. MS: *m/e* 274 (M^+). ^1H NMR ($CDCl_3$): δ 1.1—2.0 (10H, m, CH_2 of the cyclohexylidene group), 2.85 (2H, s, two hydroxyl protons), 3.48 (3H, s, OCH_3), 3.7—4.3 (6H, m), 4.9 (1H, m, H-1); (benzene-d_6) δ 3.11 (3H, s, OCH_3), 4.60 (1H, d, $J_{1,2}$=4.2 Hz, H-1).

Found: C, 56.90; H, 7.95%. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08%.

*Methyl 5,6-O-Cyclohexylidene-3-deoxy-2-C-methyl-β-D-arabino-hexofuranoside-3-d (**6b**) and Its C-2 Epimer (**7b**).* The deuterated analog (**3b**, 300 mg, 0.85 mmol) was treated with MeMgI (5.1 mmol) in a manner similar to that described for the synthesis of **6a** to give, after chromatography, **6b** (192 mg, 83%) and **7b** (5 mg, 2.2%). The mass spectra of these products indicated that their deuterium contents were 87%.

6b. MS: *m/e* 273 (M^+). ^1H NMR[6] ($CDCl_3$): δ 1.34 (3H, s, C-CH_3), 1.2—1.8 (10H, m, CH_2 of the cyclohexylidene group), 1.9 (0.15H, m, H-3a), 2.1 (1H, m, H-3b), 2.79 (1H, s, OH), 3.42 (3H, s, OCH_3), 3.8—4.2 (4H, m), 4.36 (1H, s, H-1).

7b. MS: *m/e* 273 (M^+). ^1H NMR[6] ($CDCl_3$): δ 1.1—1.8 (10H, m, CH_2 of the cyclohexylidene group), 1.34 (3H, s, C-CH_3), 1.9 (0.15H, m, H-3a), 2.1 (1H, m, H-3b), 3.30 (3H, s, OCH_3), 3.8—4.3 (4H, m), 4.50 (1H, s, H-1).

*Methyl 5,6-O-Cyclohexylidene-3-deoxy-2-C-methyl-α-D-ribo-hexofuranoside-3-d (**8b**) and Methyl 5,6-O-Cyclohexylidene-α-D-allofuranoside-2-d (**9b**).* The deuterated analog (**4b**, 282 mg, 0.8 mmol) was treated with MeMgI (4.8 mmol) in a manner similar to that described for the synthesis of **8a**. After the reaction had been completed, a small amount of cold aqueous ammonium chloride was added to the cooled reaction mixture and the products were extracted with ether and dried ($MgSO_4$). The residue was chromatographed on a silica-gel column with hexane–ether (1:1) to give **8b** (63 mg, 29%) and **9b** (59 mg, 27%). The mass spectra of **8b** and **9b** indicated that their deuterium contents were 86 and 90% respectively.

8b. MS: *m/e* 273 (M^+). ^1H NMR[6] ($CDCl_3$): δ 1.2—1.8 (10H, m, CH_2 of the cyclohexylidene group), 1.36 (3H, s, C-CH_3), 1.9 (0.15H, m, H-3a), 2.1 (1H, m, H-3b), 2.94 (1H, s, OH), 3.46 (3H, s, OCH_3), 3.7—3.9 (1H, m), 4.0—4.2 (3H, m), 4.52 (1H, s, H-1).

9b. MS: *m/e* 257 (M^+). ^1H NMR ($CDCl_3$): δ 1.1—1.8 (10H, m, CH_2 of the cyclohexylidene group), 2.79 (1H, br d, *J*=7.4 Hz, OH at C-3), 3.01 (1H, br s, OH at C-2), 3.47 (3H, s, OCH_3), 3.7—4.3 (5.1H, m), 4.91 (1H, s, H-1).

*1,2:5,6-Di-O-cyclohexylidene-3-deoxy-2-C-methyl-β-D-arabino-hexofuranose (**10**).* A mixture of **6a**, cyclohexanone (0.4 ml), and concd sulfuric acid (*ca.* 40 mg) in dry benzene (2 ml) was vigorously stirred at room temperature for 30 h. During this reaction time, the following procedure was repeated several times: the mixture was concentrated below 30 °C *in vacuo*, followed by the addition of dry benzene in order to remove the methanol and water produced. The mixture was then diluted with dry benzene and neutralized with calcium hydroxide. The undissolved material was filtered and washed with chloroform. The chloroform solution was washed successively with aqueous sodium hydrogencarbonate and water, and then dried ($MgSO_4$). The subsequent evaporation of the solvent gave a syrup, which was chromatographed on a silica-gel column with hexane–ether (8:2) to give **10** (180 mg, 58%). An analytically pure sample was obtained by distillation: bp 167—170 °C (bath temperature)/1 mmHg; $[\alpha]_D^{23}$ −21.0° (*c* 1, $CHCl_3$). IR (neat): no OH absorption. MS: *m/e* 338 (M^+), 141 (the dioxolane ring at C-4). ^1H NMR[6] ($CDCl_3$): δ 1.1—1.9 (10H, m, CH_2 of the cyclohexylidene group), 1.48 (3H, s, C-CH_3), 2.09 (1H, q, $J_{3a,3b}$=13.8 Hz, $J_{3a,4}$=7.8 Hz, H-3a), 2.34 (1H, q, $J_{3a,3b}$=13.8 Hz, $J_{3b,4}$=6.8 Hz, H-3b), 3.6—4.4 (4H, m), 5.35 (1H, s, H-1).

Found: C, 67.59; H, 8.70%. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.94%.

*1,2:5,6-Di-O-cyclohexylidene-3-deoxy-2-C-methyl-α-D-ribo-hexofuranose (**11**).* *From **8a***: A mixture of **8a** (130 mg, 0.48 mmol), cyclohexanone (0.4 ml), and concd sulfuric acid (*ca.* 40 mg) in dry benzene (2 ml) was vigorously stirred at room temperature for 2.5 h; the benzene was then removed below 30 °C *in vacuo*. The residue was treated in a manner similar to that described for the synthesis of **10** to afford, after column chromatography, **11** (140 mg, 86%). An analytically pure sample was obtained by distillation: bp 173—175 °C (bath temperature)/1.5 mmHg; $[\alpha]_D^{23}$ +10.3° (*c* 1, $CHCl_3$). IR (neat): no OH absorption. MS: *m/e* 338 (M^+), 141 (the dioxolane ring at C-4). ^1H NMR ($CDCl_3$): δ 1.1—1.9 (10H, m, CH_2 of the cyclohexylidene group),

1.50 (3H, s, C-CH_3), 2.1—2.5 (2H, m, H-3a and H-3b), 3.7—4.3 (4H, m), 5.48 (1H, s, H-1).

Found: C, 67.63; H, 8.75%. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.94%.

From **7a**. The compound (**7a**, 5 mg, 0.018 mmol) was treated with cyclohexanone in a manner similar to that described for the synthesis of **11** from **8a**, giving a syrupy **11** (5 mg, 82%). The physical properties (IR, ^1H NMR, and the specific rotation) of this material were identical with those of the specimen prepared from **8a**.

*(S)-(+)-2-Methylmalic Acid (**12**).* Dowex 50W-X8 (H^+ form, 6 ml) was added to a solution of **6a** (1.32 g, 4.85 mmol) in a mixture of dioxane (10 ml) and water (16 ml), after which was stirred at 90 °C (bath temperature) for 1 h. The resin was removed by filtration and washed with water. The combined filtrate and washings were concentrated. The residue was chromatographed on a silica-gel column with chloroform–methanol (8:2) to give a syrupy product (740 mg). To a solution of this syrup (350 mg) and potassium hydroxide (200 mg) in water (50 ml), there was added powdered potassium permanganate (1.3 g) at 4—5 °C over a period of 1 h. After the mixture had been stirred at this temperature for another 1 h, 15% hydrogen peroxide (*ca.* 5 ml) was added to decompose the excess potassium permanganate. The mixture was then diluted with water and treated with charcoal. The undissolved materials were removed by filtration through a Celite pad and washed with water. The combined filtrate and washings were acidified with Dowex 50W-X8 (H^+ form). After the removal of the resin, the solution was concentrated. The residue was chromatographed on a column of Dowex-X8 (H^+ form, 100—200 mesh, 300 ml, 2.8×66 cm) with water; a 6-ml fraction was thus collected. Fractions No. 31—38 were combined and concentrated to give a syrup, which was taken up in ethyl acetate. A small amount of the undissolved material was filtered, and the filtrate was concentrated. The water which remained in the residue was removed by repeated co-evaporation with ethyl acetate–benzene to give, after drying (P_2O_5) at 57 °C *in vacuo* for 4 h, **12** as a syrup (190 mg, 56% from **6a**): $[\alpha]_D^{27}$ +21.2° (*c* 1.2, H_2O) [lit,[10b] $[\alpha]_D^{22}$ +23° (*c* 6.316, H_2O)]; $[\alpha]_D^{37}$ +1300° [*c* 0.1, in a mixture of H_2O (2.5 ml), 0.25 M sodium citrate (2.5 ml), 29% ammonium molybdate (4.5 ml), and acetic acid (0.5 ml)] [lit,[10c] $[\alpha]_D^{18}$ −1335°: This optical rotation was measured in a mixture of 0.01 M (−)-2-methylmalic acid (2.5 ml), 0.25 M sodium citrate (2.5 ml), 29% ammonium molybdate (4.5 ml), and acetic acid (0.5 ml)]. The ^1H NMR spectrum of **12** was completely identical with that of an authentic sample of racemic **12**.

A solution of the syrupy **12** (47 mg) and brucine (136 mg) in water (0.3 ml) was allowed to stand at 3 °C overnight to give an analytically pure brucine salt of **12** as crystals (67 mg, 41%): mp 216—217 °C (dec under rapid heating) [lit,[10b] 222 °C (dec)]; $[\alpha]_D^{26}$ −7.3° (*c* 0.44, 50% MeOH). The IR spectrum of this salt was completely identical with that of an authentic sample.

*Methyl 5,6-O-Cyclohexylidene-3-deoxy-β-*D*-arabino-hexofuranoside (**13a**).* Into a solution of *t*-BuMgBr (24 mmol) in a mixuter of ether (20 ml) and benzene (10 ml) we stirred **3a** (704 mg, 2 mmol) at room temperature under a dry nitrogen atmosphere over a period of 30 min. The mixture was stirred for another 30 min and then cooled to 5 °C. Cold aqueous ammonium chloride was added, and the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and then concentrated. The residue was chromatographed on a silica-gel column with benzene–ethyl acetate (9:1) to give **13a** (447 mg, 87%) as a syrup: $[\alpha]_D^{25}$ −86.0° (*c* 0.8, $CHCl_3$). IR (neat): 3480 (OH) cm^{-1}. MS: *m/e* 258 (M^+). ^1H NMR ($CDCl_3$): δ 1.2—1.9 (10H, m, CH_2 of the cyclohexylidene group), 2.2—2.6 (2H, m, H-3a and H-3b), 3.39 (3H, s, OCH_3), 3.8—4.4 (5H, m), 4.71 (1H, d, $J_{1,2}$=4.3 Hz, H-1).

Found: C, 60.27; H, 8.55%. Calcd for $C_{13}H_{22}O_5$: C, 60.44; H, 8.59%.

*Methyl 5,6-O-Cyclohexylidene-3-deoxy-α-*D*-ribo-hexofuranoside (**14a**).* To a stirred solution of *t*-BuMgBr (24 mmol) in a mixture of ether (20 ml) and benzene (10 ml) we added **4a** (704 mg, 2 mmol) at 60—65 °C (bath temperature) under a dry nitrogen atmosphere over a period of 15 min. The stirring was continued at this temperature for another 25 min. The usual work-up gave a syrupy product, which was chromatographed on a silica-gel column with hexane–ether (6:4) to give **14a** (387 mg, 75%) as a syrup: $[\alpha]_D^{25}$ +93.6° (*c* 1, $CHCl_3$). IR (neat): 3500 (OH) cm^{-1}. MS: *m/e* 258 (M^+). ^1H NMR ($CDCl_3$): δ 1.1—1.9 (10H, m, CH_2 of the cyclohexylidene group), 1.7—2.4 (2H m, H-3a and H-3b), 2.46 (1H, d, J=8.6 Hz, OH), 3.43 (3H, s, OCH_3), 3.72 (1H, m), 3.9—4.5 (4H, m), 4.83 (1H, d, $J_{1,2}$=4.5 Hz, H-1).

Found: C, 60.48; H, 8.55%. Calcd for $C_{13}H_{22}O_5$: C, 60.44; H, 8.59%.

*Methyl 2-O-Benzoyl-5,6-O-cyclohexylidene-3-deoxy-β-*D*-arabino-hexofuranoside (**13b**).* Benzoyl chloride (0.3 ml) was stirred into a cold (0—5 °C) solution of **13a** (147 mg, 0.57 mmol) in dry pyridine (1.5 ml). The mixture was stirred at room temperature for 10 min and then cooled. Iced water was added, and the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and then concentrated to give a syrup, which was chromatographed on a silica-gel column with benzene–ethyl acetate (9:1) to give **13b** as crystals in a quantitative yield: mp 86.0—86.5 °C; $[\alpha]_D^{25}$ −88.4° (*c* 1.2, $CHCl_3$). IR (KBr): 1724 (C=O) cm^{-1}. MS: *m/e* 362 (M^+). ^1H NMR ($CDCl_3$): δ 1.1—1.9 (10H, m, CH_2 of the cyclohexylidene group), 2.0—2.8 (2H, m, H-3a and H-3b), 3.32 (3H, s, OCH_3), 3.8—4.3 (4H, m), 5.0—5.3 (2H, m, H-1 and H-2), 7.2—7.7 (3H, m, the phenyl protons), 7.9—8.2 (2H, m, the phenyl protons).

Found: C, 66.38; H, 7.17%. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23%.

*Methyl 2-O-Benzoyl-5,6-O-cyclohexylidene-3-deoxy-α-*D*-ribo-hexofuranoside (**14b**).* Benzoyl chloride (0.3 ml) was stirred into a cold (0—5 °C) solution of **14a** (160 mg, 0.62 mmol) in dry pyridine (1.5 ml). The mixture was then stirred at room temperature for 10 min. The usual work-up gave a syrup, which was subsequently chromatographed on a silica-gel column with hexane–ether (8:2) to afford **14b** (185 mg, 83%) as a syrup: $[\alpha]_D^{25}$ +96.0° (*c* 1, $CHCl_3$). IR (neat): 1721 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.2—1.8 (10H, m, CH_2 of the cyclohexylidene group), 2.2—2.5 (2H, m, H-3a and H-3b), 3.36 (3H, s, OCH_3), 3.78 (1H, m), 4.0—4.3 (3H, m), 5.1—5.3 (2H, m, H-1 and H-2), 7.2—7.7 (3H, m, the phenyl protons), 7.9—8.2 (2H, m, the phenyl protons).

Found: C, 66.30; H, 7.27%. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23%.

*The Reaction of 1,2:5,6-Di-O-cyclohexylidene-α-*D*-ribo-hexofuranos-3-ulose with* t*-BuMgBr.* To a stirred solution of *t*-BuMgBr (6 mmol) in ether (8 ml) and benzene (4 ml), there was added a solution of the title compound[4b] (172 mg, 0.51 mmol) at room temperature under a dry nitrogen atmosphere over a period of 5 min. The mixture was then stirred for 15 min. The usual work-up gave crystalline products, which were recrystallized from ligroin to give a mixture (154 mg, 89%) of 1,2:5,6-di-*O*-cyclohexylidene-α-D-allofuranose and the corresponding gluco isomer in a ratio of approximately 91:9, judging from the ^1H NMR

spectroscopy.

*1,2:5,6-Di-O-cyclohexylidene-3-deoxy-β-D-arabino-hexofuranose (**15**).* *From **13a***: A mixutre of **13a** (100 mg, 0.39 mmol), cyclohexanone (0.3 ml), and concd sulfuric acid (*ca.* 40 mg) in dry benzene (1.5 ml) was stirred at room temperature for 4 h. Calcium hydroxide was then added, and the undissolved material was filtered off and washed with methanol. The combined filtrate and washings were treated with sodium borohydride at 0—5 °C (bath temperature) to reduce the excess cyclohexanone. The mixture was then extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to give a syrup, which was subsequently chromatographed on a silica-gel column with hexane–ether (9:1) to afford **15** (80 mg, 63%) as a syrup: $[\alpha]_D^{24}$ +6.1° (*c* 1.4, $CHCl_3$). IR (neat): no OH absorption. MS: *m/e* 324 (M^+). ^1H NMR ($CDCl_3$): δ 1.2—1.9 (20H, m, CH_2 of the cyclohexylidene groups), 2.0—2.5 (2H, m, H-3a and H-3b), 3.7—4.5 (4H, m), 4.72 (1H, m), 5.75 (1H, d, $J_{1,2}$=4.0 Hz, H-1).

Found: C, 66.58; H, 8.59%. Calcd for $C_{18}H_{28}O_5$: C, 66.64; H, 8.70%.

*From **17***: A mixture of **17**[13] (500 mg, 1.9 mmol) and Dowex 50W-X8 (H^+ form, 4 ml) in dioxane (10 ml) and water (4 ml) was stirred at room temperature for 23 h. The resin was removed by filtration through a Celite pad, and washed successively with dioxane and water. The combined filtrate and washings were concentrated. The residue was chromatographed on a silica-gel column with chloroform–methanol (9:2) to give a syrupy product (350 mg). A stirred mixture of this product (100 mg), cyclohexanone (0.35 ml), and concd sulfuric acid (*ca.* 80 mg) was heated at 65—70 °C (bath temperature) for 30 min. After cooling, calcium hydroxide was added, and the undissolved material was removed by filtration and washed with methanol (6 ml). The combined filtrate and washings were cooled (0—5 °C) and treated with sodium borohydride (230 mg) for 5 min to reduce the excess of cyclohexanone. The mixture was then diluted with ether. The solution was washed with water, dried ($MgSO_4$), and concentrated to give syrup, which was subsequently chromatographed on a silica-gel column with hexane–ether (9:1), thus affording **15** (74 mg, 41% from **17**). An analytically pure sample was obtained by distillation: bp 172—175 °C (bath temperature)/1 mmHg. This product was identical in all respects (IR, ^1H NMR, and the specific rotation) with a specimen prepared from **13a**.

*1,2:5,6-Di-O-cyclohexylidene-3-deoxy-α-D-ribo-hexofuranose (**16**).* *From **14a***: A mixture of **14a** (63 mg, 0.24 mmol), cyclohexanone (0.3 ml), and concd sulfuric acid (*ca.* 40 mg) in dry benzene (1.5 ml) was stirred at room temperature for 1.5 h and then treated in a manner similar to that described for the synthesis of **15** from **13a**, thus giving **16** (75 mg, 95%) as a syrup: $[\alpha]_D^{26}$ +1.4° (*c* 1.2, $CHCl_3$). IR (neat): no OH absorption. MS: *m/e* 324 (M^+). ^1H NMR ($CDCl_3$): δ 1.1—2.0 (20H, m, CH_2 of the cyclohexylidene groups), 2.0—2.4 (2H, m, H-3a and H-3b), 3.6—4.3 (4H, m), 4.72 (1H, m) 5.80 (1H, d, $J_{1,2}$=3.7 Hz, H-1).

Found: C, 66.64; H, 8.67%. Calcd for $C_{18}H_{28}O_5$: C, 66.64; H, 8.70%.

*From **18a***: The sugar derivative (**18**,[14] 500 mg, 2 mmol) was treated with Dowex 50W-X8 (H^+ form, 4 ml) at room temperature for 20 h in a manner similar to that described for the synthesis of **15** from **17** to yield a syrupy product (300 mg) after chromatography. This product (100 mg) was treated with cyclohexanone (0.35 ml) in dry benzene (1.5 ml) in the persence of concd sulfuric acid at 70 °C (bath temperature) for 5 min. Subsequent reduction with sodium borohydride, followed by column chromatography, gave analyticaly pure **16** (104 mg, 49% from **18**). The physical properties (IR, ^1H NMR, and the specific rotation) of this product were identical with those of a specimen prepared from **14a**.

*The Dimer (**19**).* To a stirred solution of **3a** (352 mg, 1 mmol) in a mixture of ether (10 ml) and benzene (10 ml) we added, drop by drop, a solution of *t*-BuMgBr (6 mmol) in a mixture of ether (10 ml) and benzene (5 ml) at room temperature under a dry nitrogen atmosphere over a period of 1 h; the mixture was then stirred for another 1 h. After cooling, cold aqueous ammonium chloride was added and the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was chromatographed on a silica-gel column with hexane–ether (6:4) to give **19** (143 mg, 56%) as crystals. An analytically pure sample was obtained by recrystallization from hexane–benzene: mp 151—153 °C; $[\alpha]_D^{20}$ −49.6° (*c* 0.8, $CHCl_3$). IR (KBr): 3480 (OH), 1773 (C=O) cm^{-1}. MS: *m/e* 512 (M^+). ^1H NMR ($CDCl_3$): δ 1.1—1.9 (20H, m, CH_2 of the cyclohexylidene groups), 1.90 (1H, m, H-3a), 2.53 (1H, m, H-3b), 2.65 (1H, d, $J_{3',4'}$=3.0 Hz, H-3′), 2.83 (1H, br s, OH), 3.41 and 3.43 (each 3H, s, OCH_3), 3.6—4.3 (7H, m), 4.3—4.6 (1H, m, H-4′), 4.68 and 5.31 (each 1H, s, H-1 and H-1′).

Found: C, 61.08; H, 7.71%. Calcd for $C_{26}H_{40}O_5$: C, 60.92; H, 7.87%.

*The Dimer (**20**).* *From **3a***: To a refluxing suspension of **3a** (1.06 mg, 3 mmol) in ether (25 ml) we added, drop by drop, a solution of MeMgI (12 mmol) in ether (20 ml) under a dry nitrogen atmosphere over a period of 1 h. The mixture was further refluxed for another 10 min and then treated with aqueous ammonium chloride and extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and concentrated. The resulting crystalline products were triturated with a small amount of hexane. The undissolved crystals were collected by filtration, washed with cold hexane, and dried.

The hexane-insoluble crystals were recrystallized from benzene to give **20** (350 mg. 44%) as crystals. An analytically pure sample was obtained by silica-gel column chromatography with chloroform–ether (9:1): mp 155—156 °C; $[\alpha]_D^{25}$ −83.2° (*c* 1, $CHCl_3$). IR (KBr): 3460 (OH) cm^{-1}. MS: *m/e* 528 (M^+). ^1H NMR ($CDCl_3$): δ 1.2—1.9 (20H, m, CH_2 of the cyclohexylidene groups), 1.36 (3H, s, C–CH_3), 1.76 (1H, q, $J_{3a,3b}$=12.0 Hz, $J_{3a,4}$=7.8 Hz, H-3a), 2.22 (1H, d, $J_{3a',4'}$=4.0 Hz, H-3a′), 2.92 (1H, q, $J_{3a,3b}$=12 Hz, $J_{3b,4}$=6.4 Hz, H-3b), 3.30 and 3.44 (each 3H, s, OCH_3), 3.8—4.5 (8H, m), 4.58 and 5.10 (each 1H, s, H-1 and H-1′).

Found: C, 61.53; H, 8.19%. Calcd for $C_{27}H_{44}O_{10}$: C, 61.34; H, 8.39%.

The mother liquor, from which **20** had been isolated, was concentrated, and the residue was chromatographed on a silica-gel column with chloroform–ether (9:1), thus giving **19** (26 mg, 3%).

The hexane-soluble material was chromatographed on a silica-gel column with hexane–ether (4:6) to afford **6a** (240 mg, 29%).

*From **19**.* The dimer (**19**, 50 mg, 0.098 mmol) was added to a stirred solution of MeMgI (1 mmol) in ether (4 ml) at room temperature under a dry nitrogen atmosphere, after which the mixture was stirred for 30 min. After cooling, cold aqueous ammonium chloride was added, and the mixture was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was chromatographed on a silica-gel column with chloroform–methanol (99.5:0.5) to give **20** (45 mg, 87%). The

IR spectrum of this material was completely identical with that of a sample prepared from **3a**.

We wish to thank Dr. Haruo Homma and his staff for the elemental analyses, Dr. Jun Uzawa and Mrs. Tamiko Chijimatsu for measuring the NMR spectra, and Mr. Yasuaki Ezumi and Miss Kyoko Sugita for their measurment of the mass spectra. We are also grateful to Drs. Hiroyoshi Kuzuhara and Hiroshi Ohrui for their valuable discussions.

References

1) Portions of this work have been reported at (a) the 32nd National Meeting of the Chemical Society of Japan, Tokyo, April 1975, Abstr. III., p. 1724, and (b) the 9th International Symposium of Carbohydrate Chemistry, London, April 1978, Abstr. p. 111.

2) F. Shafizadeh, "Advances in Carbohydrate Chemistry," ed by M. L. Wolfrom and R. S. Tipson, Academic Press, New York (1956), Vol. 11, p. 263; S. Hanessian, *ibid.*, (1966), Vol. 21, p. 143; J. S. Brimacombe, *Angew. Chem.*, **81**, 415 (1969).

3) M. Kawana and S. Emoto, *Tetrahedron Lett.*, **1975**, 3395; M. Kawana and S. Emoto, *Chem. Lett.*, **1977**, 597.

4) (a) M. Kawana, H. Ohrui, and S. Emoto, *Bull. Chem. Soc. Jpn.*, **41**, 2199 (1968); (b) K. James, A. R. Tatchell, and P. K. Ray, *J. Chem. Soc., C*, **1967**, 2681.

5) A. N. de Belder, "Advances in Carbohydrate Chemistry and Biochemistry," ed by R. S. Tipson and D. Horton, Academic Press, New York (1977), Vol 34, p. 179.

6) The configurational relations among H_{3a}, H_{3b}, and H_4 in the sugars obtained are the same as those among the corresponding protons in Fig. 2.

7) C. D. Jardetzky, *J. Am. Chem. Soc.*, **84**, 62 (1962).

8) M. Christle, H. J. Reich, and J. D. Roberts, *J. Am. Chem. Soc.*, **93**, 3463 (1971); H. Ohrui, G. H. Jones, J. G. Moffatt, M. L. Maddox, A. T. Christensen, and S. K. Byram, *ibid.*, **97**, 4602 (1975), and the references cited therein,

9) C. S. Hudson, *J. Am. Chem. Soc.*, **31**, 66 (1909); E.L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., New York (1962), p. 110.

10) (a) P. A. Stadler, A. J. Frey, and A. Hofmann, *Helv. Chim. Acta*, **46**, 2300 (1963); they quote the results of G. Settimy, H. Weber, and D. Arigoni; (b) E. B. Abbot, E.A. Kidney, and A. McKenzie, *Chem. Ber.*, **71**, 1210 (1938); (c) H. A. Krebs and L. V. Eggleston, *Biochem. J.*, **37**, 334 (1943).

11) J. Salaün and J. M. Conia, *Chem. Commun.*, **1970**, 1358.

12) T. Sasaki, K Minamoto, and K. Hattori, *Tetrahedron*, **30**, 2689 (1974), and the references cited therein; Y. Mizuno, Y. Watanabe, K. Ikeda, and J. A. McCloskey, *Chem. Pharm. Bull.*, **23**, 1411 (1975).

13) D. A. Prins, *J. Am. Chem. Soc.*, **70**, 3955 (1948).

14) E. Vis and P. Karrer, *Helv. Chim. Acta*, **37**, 378 (1954).

15) (a) D. Horton and E. K. Just, *Carbohydr. Res.*, **9**, 129 (1969); (b) J. M. J. Tronchet and M. J. Tronchet, *Helv. Chim. Acta*, **53**, 1174 (1970); (c) P. M. Collins and R. Iyer, *Carbohydr. Res.*, **46**, 277 (1976).

16) D. C. Baker, D. Horton, and C. G. Tindall, Jr., *Carbohydr. Res.*, **24**, 192 (1972).