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Note

Efficient synthesis of pyruvic acetals of carbohydrate vicinal diols: 3,4-*O*-(1-methoxycarbonyl)ethylidene-D-galactopyranoside and 5,6-*O*-(1-methoxycarbonyl)ethylidene-D-galactofuranoside, via 1-hydroxy-2-propanone acetals

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Pyruvic acetals of carbohydrates are often found in bacterial lipopolysaccharides [1] and capsular polysaccharides [1], and also in glycolipids of fish nerve fibers [2]. In addition to the most common 4,6-acetals of hexose residues [3,4], acetals of vicinal diols in the pyranose [5–8] and furanose [9] structures are known. Although several efficient methods have been reported for preparation of the 4,6-pyruvic acetals [10–16], the acetalation of vicinal diols has scarcely been examined [17]. We now report effective syntheses of 3,4- and 5,6-pyruvic acetals linked to methyl α-D-galactopyranoside and methyl β-D-galactofuranoside, respectively, by a modification of the classical method using 1-acetoxy-2-propanone as reported by Gorin and Ishikawa [18]. The novel coupling reaction of alkyl pyruvates with silylated diols in the presence of trimethylsilyl triflate (Me_3SiOTf) [16] proved ineffective for preparation of these vicinal diols.

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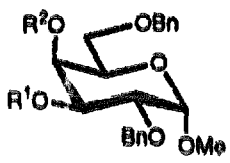
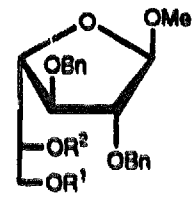
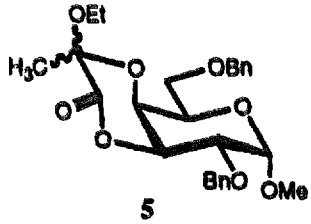
Methyl 2,6-di-*O*-benzyl-3,4-di-*O*-(trimethylsilyl)-α-D-galactopyranoside **2** was obtained in 91% yield by treatment of the diol **1** [19] with 1,1,1,3,3,3-hexamethyldisilazane in the presence of trifluoroacetic acid in dichloromethane. Compound **2** (1 mmol) was coupled, in the same manner as reported [16], with ethyl pyruvate (2 mmol) in the presence of Me_3SiOTf (0.4 mmol) and triflic acid (TfOH, 0.02 mmol) in ether for 2 days at −20 °C and for 1 day at −5 °C, to give two main products, i.e., 3,4-acetal **3** and an unexpected bicyclic lactone **5** [16], in 13 and 14% yields, respectively, after purification by silica-gel column chromatography. The acetal **3** was obtained as a mixture of (*R*)- and (*S*)-acetals, whose ^1H NMR data are in good agreement with those of the corresponding methyl esters **10R** and **10S** synthesized below. Further, **3** was reduced with lithium aluminum hydride in tetrahydrofuran to give a 2:1 mixture of **9R** and **9S**. The structure of the lactone **5** was deduced by the following facts. The ^{13}C NMR chemical shift of the quaternary acetal carbon (98.02 ppm) suggested a six-membered ring [20], the ^1H NMR chemical shift of the methylene protons in the ethoxyl group was at a higher field (3.51 ppm) and is clearly distinguished from that of the ethyl ester (ca. 4.2 ppm). Further, the lactone structure was supported by ^1H-detected heteronuclear multiple-bond correlation (HMBC) measurements, which confirmed the correlation between H-3 and the carbonyl carbon of the lactone. Although the configuration at the acetal carbon could not be determined, ^1H and ^{13}C NMR spectral data indicated a single isomer.



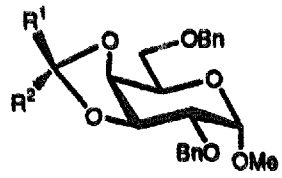
1 $R^1 = R^2 = H$
2 $R^1 = R^2 =$ TMS
3 $R^1, R^2 =$ 
4 $R^1, R^2 =$ 

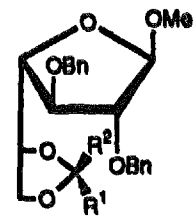


6 $R^1 = R^2 = H$
7 $R^1 = R^2 =$ TMS
8 



5





9R	$R^1 = CH_2OH, R^2 = CH_3$	**11R**
9S	$R^1 = CH_3, R^2 = CH_2OH$	**11S**
10R	$R^1 =$ COOMe, $R^2 = CH_3$	**12R**
10S	$R^1 = CH_3, R^2 =$ COOMe	**12S**

Methyl 2,3-di-*O*-benzyl-5,6-di-*O*-(trimethylsilyl)-β-D-galactofuranoside (**7**), was also prepared from 5,6-diol derivative **6** [21], and was coupled with ethyl pyruvate as just described for 1 day at −20 °C. TLC of the reaction mixture, however, gave many spots. Thus, the coupling of pyruvate with a silylated vicinal diol does not seem to be suitable

Table 1
Chemical shifts (δ ppm) of acetal methyl protons and carbons for pyruvic acetals of D-galactosides in $CDCl_3$ [a]

Pyruvic acetal	$^1H(C-CH_3)$		$^{13}C(C-CH_3)$		$^{13}C(C-CH_3)$	
	R	*S*	*R*	*S*	*R*	*S*
Pyranoside 3,4-acetal						
10 (methyl pyruvate)	1.55	1.52	23.47	23.43	105.50	105.12
methyl pyruvate [b]	–	–	23.60	23.49	106.47	106.06
pyruvic acid [c]	1.94	2.04	24.53	24.06	107.24	107.44
Furanoside 5,6-acetal						
12 (methyl pyruvate) [d]	1.58	1.59	22.68	22.01	106.09	106.02

[a] At 270 MHz for ^1H NMR and 67.5 MHz for ^{13}C NMR.
[b] Methyl 3,4-*O*-(1-methoxycarbonylethylidene)-β-D-galactopyranoside [24].
[c] Methyl 3,4-*O*-(1-carboxylethylidene)-β-D-galactopyranoside [24].
[d] ^{13}C NMR data of pyruvic acid acetal in *Klebsiella* capsular polysaccharides K12 in D_2O are as follows: 22.1 and 22.8 for C-CH_3, 108.5, 108.8, 108.9 for C-CH_3 [9].

for synthesis of the corresponding acetal. In order to prevent lactone formation, a classical method using 1-hydroxy-2-propanone acetal was applied but improving both the acetalation as well as the oxidation steps.

The silylated diol **2** was condensed with 1-acetoxy-2-propanone in the presence of Me_3SiOTf and TfOH to give the 3,4-*O*-1-(acetoxymethyl)ethylidene derivative **4** in excellent yield (97%) as a mixture of (*R*)- and (*S*)-acetals, which were separated after *O*-deacetylation to give the (*R*)-isomer **9R** and (*S*)-isomer **9S** of the 3,4-*O*-1-(hydroxymethyl)ethylidene derivative (*R*:*S* = 0.4–1.8:1). 3,4-*O*-1-(Hydroxymethyl)ethylidene derivatives **9R** and **9S** were oxidized in two steps, namely by Swern oxidation followed by bromine oxidation [22] to give the corresponding pyruvic acetals **10R** and **10S** in 65 and 49% yields, respectively. In each case, the oxidation with bromine afforded the 6-*O*-debenzylated derivative as a byproduct in ~ 10% yield.

The 3,4-acetals **9R** and **9S** were further identified as the known *O*-debenzylated derivatives [23], whose acetal configurations were determined by X-ray analysis, by comparing ^1H and ^{13}C NMR chemical shifts of acetal methyl groups. The ^1H and ^{13}C NMR signals for the acetal methyl group show a trend, in that those for the exo-oriented methyl group resonate at lower field for both pyruvic and pyruvate acetals, as shown in Table 1.

The improved synthetic method just described was also applied to prepare 5,6-pyruvic acetals. Silylated diol **7** was condensed with 1-acetoxy-2-propanone in the presence of Me_3SiOTf and TfOH to give the 5,6-*O*-1-(acetoxymethyl)ethylidene derivative **8** in 96% yield. After *O*-deacetylation of **8**, both diastereomers were separated by column chromatography and each isomer was converted into the pyruvic acetals in the same manner, giving **12R** and **12S** in 70 and 76% yields, respectively. *O*-Debenzylation was not observed in this case.

In the case of the five-membered pyruvic acetal, no remarkable difference was found between the chemical shifts of the two isomers, as shown in Table 1. The configurations of the acetal carbons of 5,6-*O*-1-(hydroxymethyl)ethylidene derivatives **11R** and **11S**

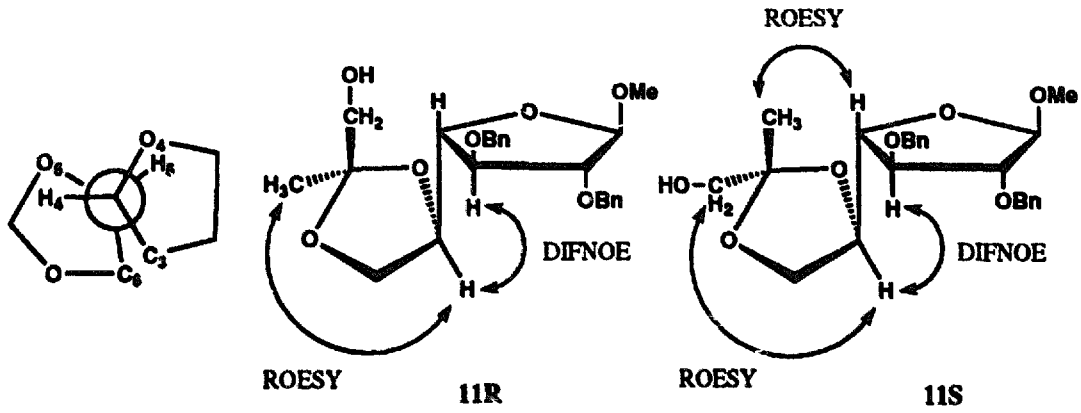


Fig. 1. Observed NOE for the 5,6-acetals **11R** and **11S**.

were determined by NOE experiments. Both the coupling constants of vicinal protons and the 1D difference-NOE observed between H-3 and H-5 suggested a near-eclipsed conformation between C-4 and C-5 substituents, as depicted in Fig. 1. In a 1D ROESY experiment with the (*R*)-isomer **11R**, a NOE from H-5 to the acetalic methyl group, and with the (*S*)-isomer, NOEs from H-5 to the acetalic hydroxymethyl group and from H-4 to the acetalic methyl group, were observed. These results agree well with the proposed acetal configurations for **11R** and **11S**.

The modified pyruvic acetal preparation described here is thus highly effective for preparing 3,4- and 5,6-pyruvic acetals linked to methyl α-D-galactopyranoside and β-D-galactofuranoside, respectively.

1. Experimental

General methods.—Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Dried solvents were used for all reactions. Solutions were evaporated under diminished pressure at a bath temperature not exceeding 50 °C. Optical rotations were measured in a 0.5 dm tube with a Jasco DIP-4 polarimeter, using $CHCl_3$ as the solvent, unless stated otherwise. IR spectra were recorded with a Hitachi model EPI-G2 spectrometer and a Shimadzu IR-408 spectrometer. ^1H NMR (270 MHz) and ^{13}C NMR (67.5 MHz) spectra were recorded with a JEOL EX-270 spectrometer for solutions in $CDCl_3$, unless stated otherwise, using Me_4Si as the internal standard. Column chromatography was performed on silica gel (Merck Kieselgel 60).

Methyl 2,6-di-O-benzyl-3,4-di-O-trimethylsilyl-α-D-galactopyranoside (**2**).—To a stirred solution of methyl 2,6-di-*O*-benzyl-α-D-galactopyranoside [19] (967 mg, 2.58 mmol) and 1,1,1,3,3,3-hexamethyldisilazane (1.06 mL, 5.16 mmol) in CH_2Cl_2 (10 mL) were added 3 drops of trifluoroacetic acid. After 7 h, the mixture was concentrated and the residue was purified on a column of silica gel with 10:1 hexane–EtOAc to give **2** (1.21 g, 91%); $[\alpha]_D$ +44.5° (*c* 0.7, $CHCl_3$); ^1H NMR: δ 7.40–7.21 (m, 10 H, 2 Ph), 4.73, 4.56 (ABq, *J* 12.5 Hz, PhCH_2), 4.58 (d, $J_{1,2}$ 3.6 Hz, H-1), 4.55, 4.50 (ABq, *J* 12.2 Hz, PhCH_2), 3.96 (dd, $J_{2,3}$ 9.9, $J_{3,4}$ 2.3 Hz, H-3), 3.89 (d, H-4), 3.87 (t, H-5),

3.68 (dd, H-2), 3.56 (dd, $J_{5,6a}$ 6.9, J_{gem} 9.2 Hz, H-6a), 3.49 (dd, $J_{5,6b}$ 5.9 Hz, H-6b), 3.34 (s, 3 H, OMe), 0.17, 0.12 (each s, 18 H, 2 $SiMe_3$); ^{13}C NMR: δ 138.60, 138.10, 129.52–127.66 (2 Ph), 98.94 (C-1), 75.58, 73.59, 73.37, 73.30, 72.90, 72.97, 70.82, 69.36, 69.34, 55.24 (OMe), 0.67, 0.52 (2 $SiMe_3$). Anal. Calcd for $C_{27}H_{42}O_6Si_2$: C, 62.51; H, 8.16. Found: C, 62.22; H, 8.09.

Pyruvate acetalation of **2**.—Thoroughly dried di-*O*-silylated diol **2** (641 mg, 1.24 mmol) and ethyl pyruvate (0.27 mL, 2.47 mmol) were dissolved in diethyl ether (1.2 mL). To this solution was added a mixture of Me_3SiOTf (110 mg, 0.50 mmol) and TfOH (3.7 mg, 0.025 mmol) in diethyl ether (0.1 mL) at −20 °C, and the solution was kept at the same temperature for 2 days and at −5 °C for 1 day. Pyridine (1 mL) was added to this solution. The mixture was poured into cold aq $NaHCO_3$ (15 mL) and extracted with $CHCl_3$ (15 mL × 3). The extract was washed with water, dried over anhyd Na_2SO_4, and evaporated. The residue was subjected to column chromatography with 7:1 hexane–EtOAc to give a mixture of **3R** and **3S** and a bicyclic lactone **5**.

5: Yield 14%; mp 96–98 °C (EtOH); $[\alpha]_D$ +3.5° (*c* 0.56, $CHCl_3$); IR: ν_{max} (NaCl) 1767 cm^{-1} (lactone); ^1H NMR: δ 7.42–7.25 (m, 10 H, 2 Ph), 4.83, 4.70 (ABq, *J* 12.3 Hz, PhCH_2), 4.73 (dd, $J_{2,3}$ 9.9, $J_{3,4}$ 3.1 Hz, H-3), 4.69 (d, $J_{1,2}$ 3.6 Hz, H-1), 4.54 (s, 2 H, PhCH_2), 4.58–4.51 (m, 1 H, H-4), 4.09 (ddd, $J_{4,5}$ 1.5, $J_{5,6a}$ 7.3, $J_{5,6b}$ 5.9 Hz, H-5), 3.79 (dd, H-2), 3.69 (dd, J_{gem} 9.6 Hz, H-6a), 3.59 (dd, H-6b), 3.51 (dddd, OCH_2), 3.40 (s, 3 H, OMe), 1.47 (s, 3 H, CMe), 1.09 (t, *J* 7.1 Hz, CH_2*Me*); ^{13}C NMR: δ 165.50 (C=O), 137.50, 137.23 (2 Ph), 128.50–127.53 (2 Ph), 98.49 (C-1), 98.02 (acetal), 78.33 (C-3), 74.28 (C-2), 73.50, 73.24 (PhCH_2), 67.60 (C-6), 66.69 (C-5), 64.10 (C-4), 56.77 (OCH_2), 55.56 (OMe), 21.08 (C*Me*), 14.94 (CH_2*Me*). Anal. Calcd for $C_{26}H_{32}O_8$: C, 66.08; H, 6.83. Found: C, 66.19; H, 6.59.

3R: ^1H NMR: δ 3.36 (s, 3 H, OMe), 1.56 (s, 3 H, CMe), 1.27 (t, *J* 7.3 Hz, CH_2*Me*); ^{13}C NMR: δ 169.60 (C=O), 105.54 (acetal), 98.44 (C-1), 23.45 (C*Me*), 14.07 (CH_2*Me*).

3S: ^1H NMR: δ 3.41 (s, 3 H, OMe), 1.52 (s, 3 H, CMe), 1.27 (t, *J* 7.3 Hz, CH_2*Me*); ^{13}C NMR: δ 169.74 (C=O), 105.18 (acetal), 98.13 (C-1), 23.38 (C*Me*), 14.07 (CH_2*Me*).

*Methyl 2,3-di-*O*-benzyl-5,6-di-*O*-trimethylsilyl-β-*D*-galactofuranoside* (**7**).—Trimethylsilylation of methyl 2,3-di-*O*-benzyl-β-D-galactofuranoside [21] (738 mg, 1.97 mmol) was carried out in the same manner as described for **2**. The crude **7** was purified on a column with 10:1 hexane–EtOAc to give **7** (870 mg, 85%); $[\alpha]_D$ −48.2° (*c* 1.1, $CHCl_3$); ^1H NMR: δ 7.39–7.23 (m, 10 H, 2 Ph), 4.96 (s, 1 H, H-1), 4.59, 4.49 (ABq, *J* 11.9 Hz, PhCH_2), 4.56, 4.46 (ABq, *J* 11.9 Hz, PhCH_2), 4.11–4.04 (m, 1 H, H-4), 4.02–3.96 (m, 2 H, H-2,3), 3.87 (ddd, $J_{4,5}$ 2.3, $J_{5,6a}$ 5.6, $J_{5,6b}$ 7.1 Hz, H-5), 3.66 (dd, J_{gem} 10.2 Hz, H-6a), 3.54 (dd, H-6b), 3.36 (s, 3 H, OMe), 0.10 (s, 18 H, 2 $SiMe_3$); ^{13}C NMR: δ 137.93, 137.66 (2 Ph), 128.35–127.75 (2 Ph), 107.03 (C-1), 88.25, 82.50, 80.90, 72.11, 71.95, 71.77, 63.76, 54.83 (OMe), 0.40, −0.63 (2 $SiMe_3$). Anal. Calcd for $C_{27}H_{42}O_6Si_2$: C, 62.51; H, 8.16. Found: C, 62.01; H, 8.44.

*Methyl 2,6-di-*O*-benzyl-3,4-O-[(*R*)- and (*S*)-1-(hydroxymethyl)ethylidene]-α-*D*-galactopyranoside* (**9R** *and* **9S**).—Thoroughly dried di-*O*-silylated diol **2** (496 mg, 0.96 mmol) and 1-acetoxy-2-propane (0.21 mL, 1.95 mmol) were dissolved in diethyl ether (1 mL). To this solution was added a mixture of Me_3SiOTf (85 mg, 0.38 mmol) and

TfOH (2.9 mg, 0.025 mmol) in diethyl ether (0.1 mL) at −20 °C, and the solution was kept at the same temperature for 2 days. The mixture was worked up in the same manner as described for pyruvate acetalation of **2** and the crude acetal was purified on a column of silica gel to give the 1-(acetoxymethyl)ethylidene derivative **4** (439 mg, 97%). To a solution of **4** in MeOH (9 mL) was added water (3 mL) and Et_3N (1.4 mL), and the mixture was kept at room temperature overnight. The mixture was concentrated and the residue was purified on a column of silica gel with 3:2 hexane–EtOAc to give the 1-(hydroxymethyl)ethylidene derivative **9R** and **9S** (*R*:*S* = 0.4–0.8:1) quantitatively.

(*R*)-Isomer **9R**: *Rf* 0.32 (2:1 hexane–EtOAc); $[\alpha]_D$ +54.2° (*c* 2.1, $CHCl_3$); ^1H NMR: δ 7.41–7.22 (m, 10 H, 2 Ph), 4.74 (s, 2 H, PhCH_2), 4.69 (d, $J_{1,2}$ 3.6 Hz, H-1), 4.65, 4.53 (ABq, *J* 12.2 Hz, PhCH_2), 4.39 (dd, $J_{2,3}$ 13.7, $J_{3,4}$ 6.2 Hz, H-3), 4.27 (dd, $J_{4,5}$ 2.3 Hz, H-4), 4.19 (ddd, $J_{5,6a}$ 5.3, $J_{5,6b}$ 6.9 Hz, H-5), 3.74 (dd, J_{gem} 10.2 Hz, H-6a), 3.70 (dd, H-2), 3.68 (dd, H-6b), 3.46 (d, *J* 6.6 Hz, CH_2OH), 3.40 (s, 3 H, OMe), 1.29 (s, 3 H, CMe); ^{13}C NMR: δ 138.36, 138.20 (2 Ph), 128.39–127.58 (2 Ph), 109.54 (acetal), 98.27 (C-1), 76.22, 75.95, 73.89, 73.46, 72.59, 69.34, 67.01, 66.58, 55.58 (OMe), 23.89 (C*Me*). Anal. Calcd for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02. Found: C, 66.48; H, 6.82.

(*S*)-Isomer **9S**: *Rf* 0.21 (2:1 hexane–EtOAc); $[\alpha]_D$ +52.2° (*c* 1.1, $CHCl_3$); ^1H NMR: δ 7.40–7.20 (m, 10 H, 2 Ph), 4.82, 4.72 (ABq, *J* 13.0 Hz, PhCH_2), 4.69 (d, $J_{1,2}$ 3.5 Hz, H-1), 4.65, 4.52 (ABq, *J* 12.2 Hz, PhCH_2), 4.40 (dd, $J_{2,3}$ 7.8, $J_{3,4}$ 5.8 Hz, H-3), 4.30 (dd, $J_{4,5}$ 2.5 Hz, H-4), 4.11 (ddd, $J_{5,6a}$ 5.3, $J_{5,6b}$ 7.3 Hz, H-5), 3.75 (dd, J_{gem} 10.2 Hz, H-6a), 3.69 (dd, H-6b), 3.53 (dd, H-2), 3.49, 3.40 (ABq, *J* 11.6 Hz, CH_2OH), 3.40 (s, 3 H, OMe), 1.33 (s, 3 H, CMe); ^{13}C NMR: δ 138.09 (2 Ph), 128.39–127.58 (2 Ph), 109.32 (acetal), 98.16 (C-1), 76.60, 74.87, 73.51, 72.43, 69.45, 67.01, 66.47, 55.53 (OMe), 23.30 (C*Me*). Anal. Calcd for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02. Found: C, 66.86; H, 6.95.

Methyl 2,3-di-O-benzyl-5,6-O-[(R)- and (S)-1-(hydroxymethyl)ethylidene]-β-D-galactofuranoside (**11R** *and* **11S**).—Acetalation of 1-acetoxy-2-propanone with di-*O*-Me_3Si derivative **7** was carried out in the same manner as described for **9**, followed by *O*-deacetylation, to give a 1:1 mixture of **11R** and **11S** quantitatively, which were separated on a column of silica gel with 3:2 hexane–EtOAc.

(*R*)-Isomer **11R**: *Rf* 0.29 (2:1 hexane–EtOAc); $[\alpha]_D$ −78.6° (*c* 1.1, $CHCl_3$); ^1H NMR: δ 7.40–7.22 (m, 10 H, 2 Ph), 4.96 (s, 1 H, H-1), 4.58, 4.50 (ABq, *J* 11.9 Hz, PhCH_2), 4.57, 4.47 (ABq, *J* 11.9 Hz, PhCH_2), 4.31 (td, $J_{4,5}$ 3.5, $J_{5,6a} = J_{5,6b}$ = 7.0 Hz, H-5), 4.04–4.02 (m, 3 H, H-3,6a,6b), 4.00 (dd, $J_{3,4}$ 6.1 Hz, H-4), 3.98 (dd, $J_{1,2}$ 0.9, $J_{2,3}$ 2.4 Hz, H-2), 3.57 (dd, 1 H, $J_{H,OH}$ 7.9, J_{gem} 11.9 Hz, CH_2OH), 3.48 (dd, 1 H, $J_{H,OH}$ 5.3 Hz, CH_2OH), 3.37 (s, 3 H, OMe), 2.75 (dd, 1 H, OH), 1.52 (s, 3 H, CMe). Anal. Calcd for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02. Found: C, 67.17; H, 6.88.

(*S*)-Isomer **11S**: *Rf* 0.20 (2:1 hexane–EtOAc); $[\alpha]_D$ −65.4° (*c* 1.3, $CHCl_3$); ^1H NMR: δ 7.40–7.22 (m, 10 H, 2 Ph), 4.96 (s, 1 H, H-1), 4.60, 4.50 (ABq, *J* 11.9 Hz, PhCH_2), 4.58, 4.42 (ABq, *J* 11.9 Hz, PhCH_2), 4.23 (dt, $J_{4,5} = J_{5,6a}$ = 6.7, $J_{5,6b}$ 7.3 Hz, H-5), 4.01 (t, $J_{3,4}$ 6.4 Hz, H-4), 4.00 (dd, $J_{1,2}$ 0.9, $J_{2,3}$ 2.4 Hz, H-2), 3.91 (dd, J_{gem} 8.6 Hz, H-6a), 3.84 (dd, H-6b), 3.72 (dd, H-3), 3.50 (d, 2 H, $J_{H,OH}$ 6.7 Hz, CH_2OH), 3.40 (s, 3 H, OMe), 1.82 (t, 1 H, OH), 1.37 (s, 3 H, CMe). Anal. Calcd for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02. Found: C, 66.66; H, 6.93.

Conversion of 1-hydroxy-2-propanone acetal to pyruvate acetal.—To a stirred solution of oxalyl chloride (202 mg, 1.59 mmol, 5.6 equiv) in CH_2Cl_2 (1 mL) was added a solution of Me_2SO (0.26 mL, 3.68 mmol, 13 equiv) in CH_2Cl_2 (2 mL) during 10 min under an Ar atmosphere at −78 °C and, after 15 min, a solution of 1-hydroxy-2-propanone acetal (122 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 10 min, followed by, after 90 min, Et_3N (0.95 mL, 6.82 mmol, 24 equiv). The mixture was kept at the same temperature for 30 min and then warmed to room temperature. After 90 min the mixture was poured into water and extracted with $CHCl_3$. The extract was washed with 1 M HCl, aq $NaHCO_3$, and water, dried over anhyd Na_2SO_4, and evaporated to give crude aldehyde. To a ~0.4 M solution of the aldehyde in 9:1 MeOH–water was added $NaHCO_3$ (477 mg, 5.7 mmol, 20 equiv) followed by 2 M bromine (0.5 mL) in 90% aq MeOH. After being stirred at room temperature overnight, the mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with aq $Na_2S_2O_3$ and water, dried over anhyd Na_2SO_4, and evaporated to give crude pyruvate acetal, which was purified on a column of silica gel with 6:1–5:1 hexane–EtOAc.

Methyl 2,6-di-O-benzyl-3,4-O-[(R)-1-(methoxycarbonyl)ethylidene]-α-D-galacto-pyranoside (**10R**).—The 1-hydroxy-2-propanone acetal **9R** was oxidized in the same manner as just described to give the pyruvic acetal **10R** in 65% yield; $[\alpha]_D$ +22.5° (*c* 0.8, $CHCl_3$); ^1H NMR: δ 7.42–7.19 (m, 10 H, 2 Ph), 4.88, 4.68 (ABq, *J* 12.4 Hz, PhCH_2), 4.64, 4.53 (ABq, *J* 12.0 Hz, PhCH_2), 4.59 (d, $J_{1,2}$ 3.6 Hz, H-1), 4.50 (dd, $J_{2,3}$ 7.9, $J_{3,4}$ 5.3 Hz, H-3), 4.23 (dd, $J_{4,5}$ 2.3 Hz, H-4), 4.15 (ddd, $J_{5,6a}$ 5.3, $J_{5,6b}$ 7.3 Hz, H-5), 3.78 (dd, J_{gem} 10.0 Hz, H-6a), 3.75 (dd, H-2), 3.72 (dd, H-6b), 3.70 (s, 3 H, OMe), 3.36 (s, 3 H, OMe), 1.55 (s, 3 H, CMe); ^{13}C NMR: δ 170.00 (C=O), 138.56, 138.13 (2 Ph), 128.32–127.51 (2 Ph), 105.50 (acetal), 98.44 (C-1), 77.58, 75.31, 74.70, 66.09, 55.55, 52.58 (C-2,3,4,5, OMe, OMe), 73.42, 72.85, 69.35 (2 PhCH_2, C-6), 23.47 (C*Me*). Anal. Calcd for $C_{25}H_{30}O_8$: C, 65.50; H, 6.60. Found: C, 65.19; H, 6.72.

Methyl 2,6-O-di-benzyl-3,4-O-[(S)-1-(methoxycarbonyl)ethylidene]-α-D-galacto-pyranoside (**10S**).—The 1-hydroxy-2-propanone acetal **9S** was oxidized in the same manner as just described to give the pyruvic acetal **10S** in 49% yield; $[\alpha]_D$ +60.0° (*c* 0.8, $CHCl_3$); IR: ν_{max} (NaCl) 1750 cm^{-1} (ester); ^1H NMR: δ 7.44–7.20 (m, 10 H, 2 Ph), 4.82, 4.73 (ABq, *J* 13.3 Hz, PhCH_2), 4.70 (d, $J_{1,2}$ 3.6 Hz, H-1), 4.64, 4.55 (ABq, *J* 12.0 Hz, PhCH_2), 4.47 (dd, $J_{2,3}$ 7.6, $J_{3,4}$ 5.8 Hz, H-3), 4.40 (dd, $J_{4,5}$ 2.6 Hz, H-4), 4.16 (ddd, $J_{5,6a}$ 5.3, $J_{5,6b}$ 7.3 Hz, H-5), 3.79 (dd, J_{gem} 10.4 Hz, H-6a), 3.74 (s, 3 H, OMe), 3.73 (dd, H-6b), 3.46 (dd, H-2), 3.41 (s, 3 H, OMe), 1.52 (s, 3 H, CMe); ^{13}C NMR: δ 170.15 (C=O), 138.14, 137.81 (2 Ph), 128.32–127.46 (2 Ph), 105.12 (acetal), 98.06 (C-1), 76.64, 76.05, 75.81, 66.22, 55.53, 52.45 (C-2,3,4,5, OMe, OMe), 73.39, 72.31, 69.24 (2PhCH_2, C-6), 23.43 (C*Me*). Anal. Calcd for $C_{25}H_{30}O_8$: C, 65.50; H, 6.60. Found: C, 65.64; H, 6.49.

Methyl 2,3-di-O-benzyl-5,6-O-[(R)-1-(methoxycarbonyl)ethylidene]-β-D-galacto-furanoside (**12R**).—The 1-hydroxy-2-propanone acetal **11R** was oxidized in the same manner as already described to give the pyruvic acetal **12R** in 70% yield; $[\alpha]_D$ −57.8° (*c* 0.45, $CHCl_3$); ^1H NMR: δ 7.43–7.20 (m, 10 H, 2 Ph), 4.92 (s, 1 H, H-1), 4.59, 4.49 (ABq, *J* 11.9 Hz, PhCH_2), 4.58, 4.42 (ABq, *J* 11.9 Hz, PhCH_2), 4.22 (dt, $J_{4,5}$ 6.6, $J_{5,6a}$ 6.6, $J_{5,6b}$ 8.3 Hz, H-5), 4.06 (t, $J_{3,4}$ 6.6 Hz, H-4), 3.99 (dd, $J_{1,2}$ 1.2, $J_{2,3}$ 3.0 Hz,

H-2), 3.95 (dd, J_{gem} 12.2 Hz, H-6a), 3.92 (dd, H-6b), 3.78 (dd, H-3), 3.72 (s, 3 H, OMe), 3.39 (s, 3 H, OMe), 1.58 (s, 3 H, CMe); ^{13}C NMR: δ 170.44 (C=O), 137.32 (s, 2 Ph), 128.46–127.92 (2 Ph), 107.21 (C-1), 106.09 (acetal), 87.76, 83.61, 80.92, 77.68, 55.02, 52.31 (C-2,3,4,5, OMe, OMe), 72.18, 72.08, 67.15 (2 PhCH_2, C-6), 22.68 (C*Me*). Anal. Calcd for $C_{25}H_{30}O_8$: C, 65.50; H, 6.60. Found: C, 65.64; H, 6.49.

*Methyl 2,3-di-*O*-benzyl-5,6-*O*-[(S)-1-(methoxycarbonyl)ethylidene]-β-*D*-galacto-furanoside* (**12S**).—The 1-hydroxy-2-propanone acetal **11S** was oxidized in the same manner as already described to give the pyruvic acetal **12S** in 76% yield; $[\alpha]_D$ −63.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR: δ 7.41–7.22 (m, 10 H, 2 Ph), 4.96 (s, 1 H, H-1), 4.57, 4.49 (ABq, *J* 11.4 Hz, PhCH_2), 4.53, 4.45 (ABq, *J* 11.4 Hz, PhCH_2), 4.46 (dt, $J_{4,5} = J_{5,6b} = 5.9$, $J_{5,6a}$ 7.9 Hz, H-5), 4.07 (t, $J_{3,4}$ 5.9 Hz, H-4), 4.01 (t, J_{gem} 7.9 Hz, H-6a), 4.00 (dd, $J_{1,2}$ 0.8, $J_{2,3}$ 2.3 Hz, H-2), 3.96 (dd, H-6b), 3.82 (dd, H-3), 3.74 (s, 3 H, OMe), 3.39 (s, 3 H, OMe), 1.59 (s, 3 H, CMe); ^{13}C NMR: δ 170.31 (C=O), 137.27 (2 Ph), 128.45–127.89 (2 Ph), 107.12 (C-1), 106.02 (acetal), 87.44, 83.38, 82.00, 77.11, 54.95, 52.27 (C-2,3,4,5, OMe, OMe), 72.13, 71.93, 66.72 (2 PhCH_2, C-6), 22.01 (C*Me*). Anal. Calcd for $C_{25}H_{30}O_8$: C, 65.50; H, 6.60. Found: C, 65.26; H, 6.79.

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