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α-Hydrogen elimination in some carbohydrate triflates

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Abstract

Treatment of 1,2;5,6-di-*O*-isopropylidene-3-*O*-triflyl-D-gluco- and D-allo-furanoses (**2** and **6**) with MeLi (or BuLi) in diethyl ether afforded different products; the former gave a 3,4-unsaturated product (**4**), the latter a 3-methyl(or butyl)-D-allofuranose derivative (**7**, **8**). Similar treatment of the 2-triflates (**27**, **30**) of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α- and -β-D-gluco-pyranosides gave the corresponding 2-*C*-alkyl derivatives. The 3- and 4-triflates of similar pyranoside structures examined gave, in most cases, the corresponding unsaturated compounds. Both of the reactions (unsaturation and *C*-alkylation) are explained, in most cases, on the basis of α-elimination, that is, the reactions commenced with abstraction of the hydrogen attached to the carbon bearing a triflyloxy group, this fact being confirmed by studies with deuterated analogs. Transition states for these reactions were also studied by computer calculations. © 1996 Elsevier Science Ltd.

Keywords: Branched-chain sugars; Unsaturation; Triflate; Methyllithium; Butyllithium; Deuterated compound; Carbanion; Transition state; Proton 1,2-shift; Carbene

1. Introduction

Substitution reactions utilizing triflates are widely used [1] in carbohydrate chemistry, because of the effectiveness of the triflyloxy group as a leaving group, as demonstrated by the reactivity ratio for mesylate, tosylate, and triflate being 1.00:0.70:56,000 [2], and by the acetolysis ratio of 1:30,000 for TsOEt and CF_3SO_3Et [3]. In 1,2;5,6-di-*O*-isopropylidene-3-*O*-triflyl-α-D-allofuranose [4] (**6**), for example, a variety of substituents (NH_2, NHC_6H_5, F, Cl, Br, I, SCN, etc.) are readily introduced [1,5–7], giving the

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corresponding D-glucofuranoses. In the case of 1,2;5,6-di-*O*-isopropylidene-3-*O*-triflyl-α-D-glucofuranose [4] (**2**), both substitution to give the 3-halo (Cl, Br, I)-D-allofuranoses [5] and 3,4-unsaturation [7] to give 3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose [8] (**4**) by TASF [9] occurred. When, however, **2** and **6** were treated with base (DBU, $KOCMe_3$), **2** gave **4** readily and **6** resisted this reaction, giving **4** (by $KOCMe_3$) only under more-drastic conditions [10]. When, however, **6** was treated with butyllithium (BuLi) in diethyl ether, the major product was an unknown compound which was neither the S_N2 displacement product of 3-deoxy-3-*C*-butyl-D-*gluco* constitution nor an unsaturated compound [11]. Here we describe the details of this new reaction, together with other similar examples, and discuss the reaction mechanism, which was found to be closely related to that of the elimination reaction.

2. Results

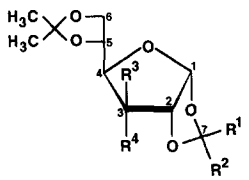
The structure of the unknown compound produced from **6** was found to be 1,2;5,6-di-*O*-isopropylidene-3-*C*-butyl-α-D-allofuranose (**8**), a branched-chain sugar having a butyl and a hydroxyl group at C-3. This result indicates that the reaction does not proceed through an S_N2 process. Actually, this compound is identical with that obtained [12] by the reaction of 1,2;5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**9**) with BuLi.

To increase the yield of **8**, several commonly used solvents were examined, and diethyl ether was found to be the best. Similar treatment of **6** with methyllithium (MeLi) in diethyl ether also gave the expected product **7** [13]. Thus it was decided to use diethyl ether throughout the experiments.

Synthesis of triflates.—A number of triflates besides **6** have been prepared. In this reaction, the *endo* methyl of the 1,2-*O*-isopropylidene group in **6** was thought to have an effect due to its close proximity to C-3, so *endo* and *exo* phenyl analogs (**18** and **19**) of **6** were prepared as probes. Treatment of D-glucose with C_6H_5CHO in the presence of H_3PO_4 gave a diastereoisomeric mixture of 1,2;5,6-di-*O*-benzylidene-α-D-glucofuranoses. Partial acid-catalyzed hydrolysis in MeOH followed by chromatography gave a mixture of 1,2-*O*-benzylidene-α-D-glucofuranoses (24%). Treatment of the mixture with 2,2-dimethoxypropane, followed by chromatography of the resulting 5,6-*O*-isopropylidene derivatives, gave the *endo* phenyl **10** and *exo* phenyl derivatives **11** in a ratio of 2:3. Their structures were determined by NOESY measurements: in **10**, cross peaks were observed between H-1–*H*CPh, H-2–*H*CPh, and H-4–Ph (the *ortho* protons), and in **11**, between H-4–*H*CPh (strong), indicating that **11** has the *exo* phenyl structure. Oxidation of **10** and **11** with Me_2SO–Ac_2O followed by reduction with $NaBH_4$ gave the corresponding D-allo derivatives **16** and **17**, respectively, and successive triflation gave the desired 3-triflates **18** and **19**. The triflated phenyl analogs (**12** and **13**) of **2** were likewise prepared from **10** and **11**, respectively.

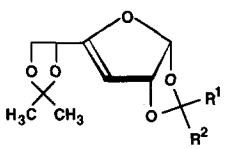
In order to add another furanose-type triflate in this series, the 2-triflate **25** of methyl 3,5-di-*O*-benzyl-6-bromo-6-deoxy-β-D-glucofuranoside (**24**) was prepared (**24** was required for another synthetic purpose). Bromination of methyl 3,5-di-*O*-benzyl-β-D-glucofuranoside [14] (**23**) followed by triflation gave **25**.

Materials

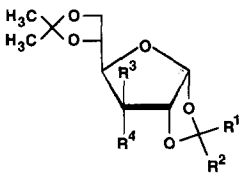


	R^1	R^2	R^3	R^4
1	CH_3	CH_3	OH	H
2	CH_3	CH_3	OTfl	H
3	CH_3	CH_3	OMs	H
5	CH_3	CH_3	H	OH
6	CH_3	CH_3	H	OTfl
9	CH_3	CH_3	=O	
10	H	C_6H_5	OH	H
11	C_6H_5	H	OH	H
12	H	C_6H_5	OTfl	H
13	C_6H_5	H	OTfl	H
16	H	C_6H_5	H	OH
17	C_6H_5	H	H	OH
18	H	C_6H_5	H	OTfl
19	C_6H_5	H	H	OTfl

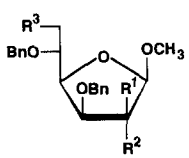
Products



	R^1	R^2
4	CH_3	CH_3
14	H	C_6H_5
15	C_6H_5	H



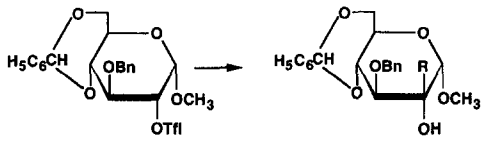
	R^1	R^2	R^3	R^4
7	CH_3	CH_3	CH_3	OH
8	CH_3	CH_3	C_4H_9	OH
20	H	C_6H_5	CH_3	OH
21	C_6H_5	H	CH_3	OH
22	C_6H_5	H	OH	CH_3



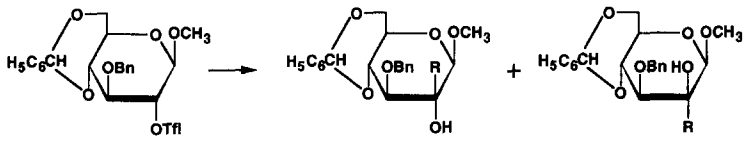
	R^1	R^2	R^3
23	H	OH	OH
24	H	OH	Br
25	H	OTfl	Br
26	OH	C_4H_9	Br

Several pyranoside-type triflates were also prepared. Thus, the 2-triflates **27** [15–17] and **30** [16] were obtained from methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α- and -β-D-glucopyranosides [18], and the 3-triflates **35**, **38**, and **41** were prepared from methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α- and -β-D-gluco- and -α-D-allo-pyranosides [18,19]; in the case of **41**, the precursor alcohol **40** was prepared by oxidation of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside [18,19] followed by reduction with $NaBH_4$. The 4-triflates **42** [20] and **44** [7] were also prepared from the corresponding precursors;

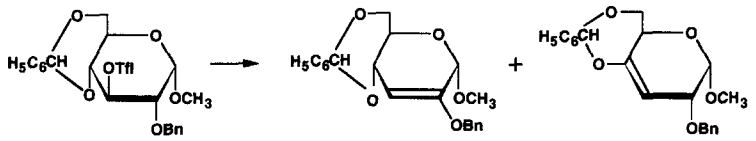
in the synthesis of **44**, however, prolonged triflation in pyridine gave rise to the corresponding 4-deoxy-4-(pyridinium-1-yl)-D-gluco derivative **45** as the major product.



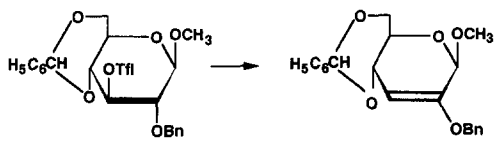
27 **28** R= CH_3 **29** R= C_4H_9



30 **31** R= CH_3 **33** R= C_4H_9 **32** R= CH_3 **34** R= C_4H_9



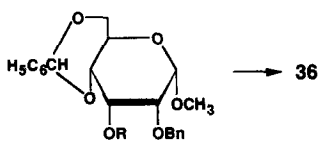
35 **36** **37**



38 **39**

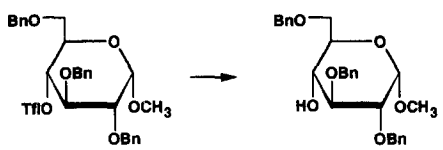
Reactions of the triflates with MeLi or BuLi.—At first the 3-*O*-triflyl-D-glucofuranose diacetone derivative **2** was treated with MeLi or BuLi under the aforementioned conditions and the 3,4-unsaturated derivative **4** was obtained as the major product. This result was as expected, because **2** is known to give **4** under strongly basic conditions [10]. Application of the reaction to the *endo* and *exo* phenyl analogs (**12** and **13**) also gave the corresponding 3,4-unsaturated derivatives, **14** and **15**. This result indicates that the reactions are not influenced by steric crowding in the *endo* space of C-3. In the case of the 3-*O*-triflyl-D-allofuranosides **18** and **19**, on the other hand, treatment with MeLi

gave the 3-*C*-methyl-D-allofuranose **20** from the *endo* phenyl derivative **18**, and a mixture of 3-*C*-methyl-D-gluco- (**22**) and -D-allo-furanoses (**21**) from the *exo* phenyl derivative **19**. The structures of the products were confirmed by NOE measurements (see Experimental section). Production of the two compounds having opposite configurations at C-3 from **19** again suggests that the reactions occur through the 3-oxo intermediates, as exemplified by the reaction of **6**; MeLi may approach the C-3-carbonyl generated in **19** from both faces, owing to the absence of the bulky *endo* phenyl group. The 2-*O*-triflyl-β-D-glucofuranoside **25** was next examined with BuLi; the 2-*C*-butyl-β-D-mannofuranoside **26** was produced without formation of any unsaturated derivative. The structure was confirmed by NOE experiments: irradiation of H-4 caused signal increase of the α-CH_2 (3.4%) of the butyl group [$-CH_2(CH_2)_2CH_3$] in addition to H-3 (8.9%), and irradiation of H-1 caused an increase of the β-CH_2 (2.2%) of the butyl in addition to OCH_3 (5.6%) (see Fig. 1). The butyl group was thus concluded to be introduced from the less-hindered, lower side of the 2-oxo intermediate.

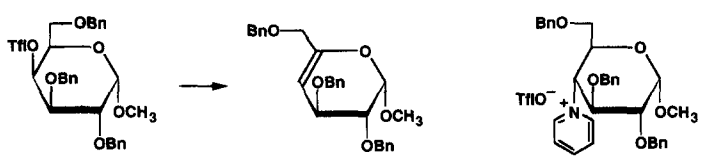


36

40 R= H
41 R= Tfl

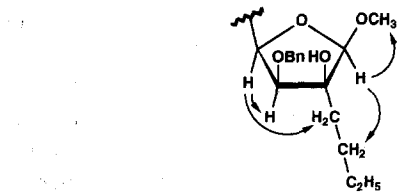


42 **43**

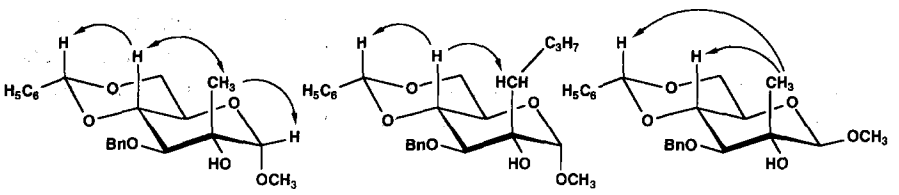


44 **46** **45**

Reactions of 2-*O*-triflyl-α- and -β-D-glucopyranosides (**27** and **30**) were examined next. In this context we briefly describe the reactivity of 2-*O*-triflylglycopyranosides to nucleophiles. Ishido and Sakairi [21] reported that **27** gave, in treatment with several nucleophiles (BzO^-, N_3^-, MeS^-, PhS^-, and MeO^-), the corresponding α-D-man-



26



28 29 31

Fig. 1. NOE's observed in **26**, **28**, **29**, and **31** (see text).

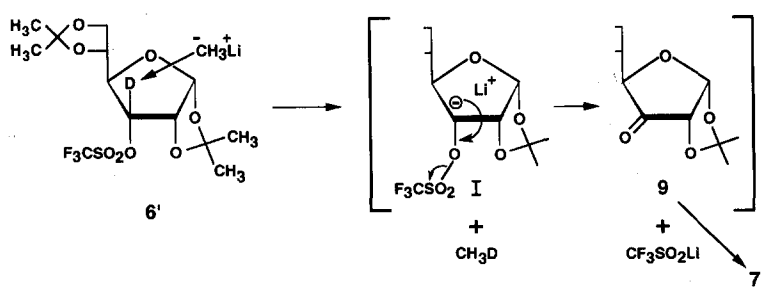
nopyranosides in high yields under reaction conditions where 2-*O*-mesyl or -tosylglycopyranosides are generally reluctant to give products. Some other 2-*O*-triflyl-α-D-glucopyranosides also gave similar results [16,22–25], and 2-*O*-triflyl-β-D-glucopyranosides gave the expected products more readily [7,16,26]. Other types of 2-*O*-triflylglycopyranosides (α- and β-D-manno [7,27–29], β-D-talo [30], α- and β-D-ido [25,31], and others [25,32,33]) also gave the corresponding inverted products at C-2 in moderate to good yields, although in some cases [7,29,30,33] 2,3-unsaturated compounds were produced. In the case of 6-deoxy-2-*O*-triflyl-α- and -β-L-galactopyranosides [34] and 3-azido-3,4-dideoxy-α-DL-*threo*-pentopyranoside [32], treatment with sodium benzoate, for example, gave the corresponding 2,5-anhydro compounds via ring contraction. In our compounds **27** and **30**, however, treatment with MeLi (or BuLi) gave neither the substituted, unsaturated, nor ring-contracted products but 2-*C*-methyl(butyl) derivatives readily (at room temperature for 2 h) in high yields: **27** gave the 2-*C*-methyl(or -butyl)-D-gluco derivatives (**28** and **29**), and **30** gave both the D-gluco (**31** and **33**) and D-manno derivatives (**32** and **34**). Their structures were confirmed by NOE experiments (Fig. 1). In **28**, irradiation of CH_3-2 caused signal increases of both H-1 (2.7%) and H-4 (3.2%), and irradiation of H-4 caused signal increases of both CH_3-2 (7.9%) and C*H*Ph (14.7%). These results indicate that an upward facing CH_3-2 is present. In **29**, irradiation of H-4 caused signal increases at δ 1.52–1.61 (10.9%; the region contains one of the α-CH_2 of Bu) and of the singlet for C*H*Ph (14.7%), indicating the presence of upward facing Bu-2. Likewise, in **31** (measured in pyridine-d_5), irradiation of CH_3-2 caused increases of H-4 (3.1%) and C*H*Ph (3.7%; this may occur through mediation of the resonance of H-4), indicating the upward orientation of CH_3-2. In **32**, irradiation of CH_3-2 caused increases of both H-1 (1.8%) and H-3 (2.1%), indicating the downward orientation of CH_3-2.

The 3-triflates **35**, **38**, and **41** were examined next. Treatment of the 3-*O*-triflyl-α-D-glucopyranoside **35** with BuLi did not give the expected *C*-butyl derivative, but 2,3-(**36**) and 3,4-unsaturated compounds (**37**) in good overall yield in a ratio of 2:1. Similar treatment of the β anomer **38** with MeLi gave the 2,3-unsaturated derivative **39** in low yield (36%), along with unknown by-products; in the mixture, however, no *C*-methyl product was observed (as revealed by the ^{1}H NMR spectrum). As the configuration at C-3 was considered to be an important factor in determining the direction of the reaction as concerns *C*-alkylation or unsaturation, as observed for **2** and **6**, the 3-*O*-triflyl-α-D-allopyranoside **41** was also treated with MeLi. However, the same unsaturated product **36** was obtained in high yield, and no relation with the C-3 configuration was apparent.

Two 4-triflates having 2,3,6-tri-*O*-benzyl-α-D-gluco (**42**) and -D-galacto (**44**) structures were treated next with MeLi. In the latter reaction, the 4,5-unsaturated derivative **46** was produced in moderate yield (45%), along with unknown products lacking a *C*-methyl group. This result was in accordance with our expectations, because **44** has diaxial OTfl-4 and H-5 substituents. In the case of **42**, neither *C*-methyl nor unsaturated compounds were produced, and only the detriflated product **43** [20,35] was formed.

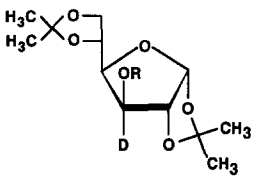
3. Discussion

Indications thus far suggest that *C*-alkyl compounds are produced from the corresponding oxo intermediates, and, therefore, isolation of any of these intermediates would facilitate the mechanistic study. First attempts to obtain the oxo compound **9** by treatment of **6** with a limited amount of MeLi gave the starting compound **6** and the *C*-methyl compound **7**, without formation of any of the desired **9**. This indicates that the reaction between **9** and MeLi is considerably faster than its production. Therefore, the bulky *tert*- and *iso*-butyllithium, as well as LDA were tried as reagents, with the expectation that they would react less rapidly with **9**. However, no reaction was observed and in all cases only the starting **6** was recovered. Raising the temperature gave only decomposed products along with **6**, and no *C*-alkyl compounds (as revealed by the ^{1}H NMR spectrum). These results suggest that MeLi abstracts H-3 of **6** (which the bulky reagents are unable to do), and formation of **9** follows. If this assumption is true, the 3-deuterio analog (**6′**) of **6** should afford, on treatment with MeLi, **7** together with CH_3D and CF_3SO_2Li (Scheme 1). Therefore, **6′** was prepared by triflation of 1,2;5,6-di-*O*-isopropylidene-α-D-(3-^{2}H)allofuranose [36,37] (**5′**) and subjected to reac-

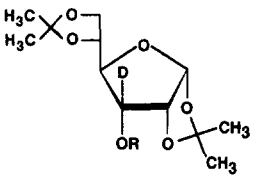


Scheme 1.

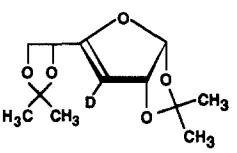
tion with MeLi. The volatile substances generated during the reaction were collected in a cold trap containing $CDCl_3$, and the resulting $CDCl_3$ solution was analyzed by ^1H NMR spectroscopy. It did indeed contain CH_3D, detected as a triplet (J 2 Hz) of equal strength [38] 0.015 ppm upfield from the CH_4 singlet, which inevitably accompanied it (no other signals were observed in this region). Formation of CF_3SO_2Li was verified from the residue obtained after distillation of all volatile substances from the reaction mixture. The salt was identified, in its ^{19}F NMR spectrum (D_2O), by a singlet at δ −88.3 ppm (see Experimental section).



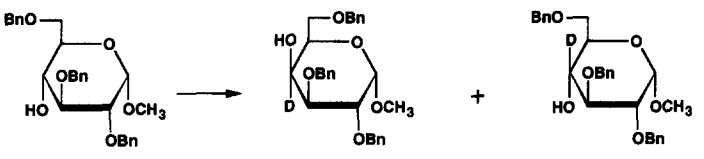
1' R=H
2' R=Tfl



5' R=H
6' R=Tfl

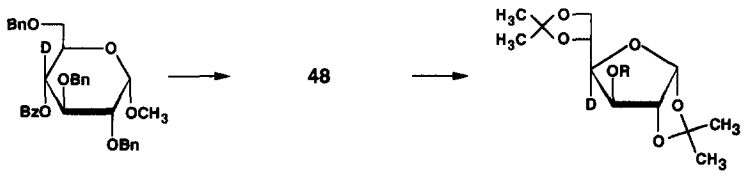


4'



43 47 48

50 49



51 48 52 R=H
2" R=Tfl

These results strongly support the aforementioned assumption. Since a CF_3SO_2O group is strongly electron-withdrawing, it would be reasonable to assume that the

hydrogen (H-3 of **6**) attached to the carbon bearing it is eliminated at the first stage of the reaction as a proton, in the presence of strong base (MeLi or BuLi). However, if this is the case, H-3 of **2** would also be eliminated under the same reaction conditions, although **2** gave an unsaturated compound (**4**). Formation of **4** from **2** in the presence of base is well known [10] and has been accepted [1] as occurring via β-elimination, that is, H-4 (not H-3) is initially abstracted and 3,4-unsaturation follows (typical E2 reaction [39]). To clarify the real mechanism, namely, whether by α- or β-elimination, the 3- (**2′**) and 4-deuterio analogs (**2″**) of **2** were prepared.

Compound **2′** was prepared by triflation of 1,2;5,6-di-*O*-isopropylidene-α-D-(3-^{2}H)glucofuranose [36] (**1′**). The 4-deuterio analog **2″** was prepared by the following route: methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside [20] (**43**) was oxidized with Me_2SO–Ac_2O and the resulting 4-oxo derivative was reduced with $NaBD_4$ giving a 6:1 mixture of D-(4-^{2}H)-galacto (**47**) and -gluco (**48**) derivatives (Gabriel [40] reported the preparation of the 4-^{3}H isomers of **47** and **48** through a similar route). In order to facilitate separation of **47** and **48** (both have the same chromatographic mobility), benzoylation with C_6H_5COCl in 1:1 pyridine–CH_2Cl_2 was attempted, whereby, and contrary to expectation, **47** was preferentially benzoylated to give **49**, with **48** and a small amount of **47** remaining unreacted. After chromatographic separation, **49** was successively debenzoylated to generate **47**, triflated to give **50**, and converted into the 4-*O*-benzoyl-D-gluco derivative **51** by treatment with NaOBz. After debenzoylation, the resulting **48** was debenzylated catalytically, the deblocked 4-deuterio glucoside was hydrolyzed in an acidic medium, and finally the product was acetonated to give the 4-deuterio derivative **52**. Triflation of **52** gave the 4-deuterio analog (**2″**) of **2**.

When the 3-deuterio analog (**2′**) of **2** was treated with MeLi, compound **4** having no deuterium was obtained. When, however, **2″** was treated similarly, the 3-deuterio analog **4′** was produced without contamination by any **4**. The structure of **4′** was confirmed by the ^{1}H and ^{13}C NMR spectra; in the former, the lack of H-3 was observed while the other proton-shifts remained the same with those for **4**, and in the latter, C-3 appeared as a triplet by C-D coupling (see Experimental section).

These results suggest that the α-hydrogen is first eliminated to give the C-3 carbanion II, and II is converted into **4** (**4′**) with a 4 → 3 hydrogen (deuterium) shift. The fact that analog [41] (**3**) with the much weaker electron-withdrawing mesyl substituent did not react also supports the foregoing interpretation. The reaction mechanism, however, remains ambiguous. One possibility is that II is first transformed into C-4 carbanion III by 4 → 3 proton (deuteron) shift, and then III degenerates into **4** (**4′**) by sharing the H-4-electron pair into C-3 under release of the $CF_3SO_3^-$ anion, the pathway for conventional β-elimination. Another possibility is that II is first transformed into C-3 carbene IV under release of a $CF_3SO_3^-$ group, and then IV migrates into **4** (**4′**) along with 4 → 3 hydrogen shift.

To clarify the mechanism, we chose the simplified systems 1,2-*O*-isopropylidene-5-*O*-methyl-3-*O*-triflyl-α-D-xylo (**A**) and -ribopentofuranoses (**C**) as substitutes for **2** and **6**, respectively, and tried to find the respective transition state giving 3-deoxy-1,2-*O*-isopropylidene-5-*O*-methyl-α-D-*glycero*-pent-3-enofuranose (**B**) and 1,2-*O*-isopropylidene-5-*O*-methyl-α-D-*erythro*-pentofuranos-3-ulose (**D**) by computation with MOPAC93/PM3.

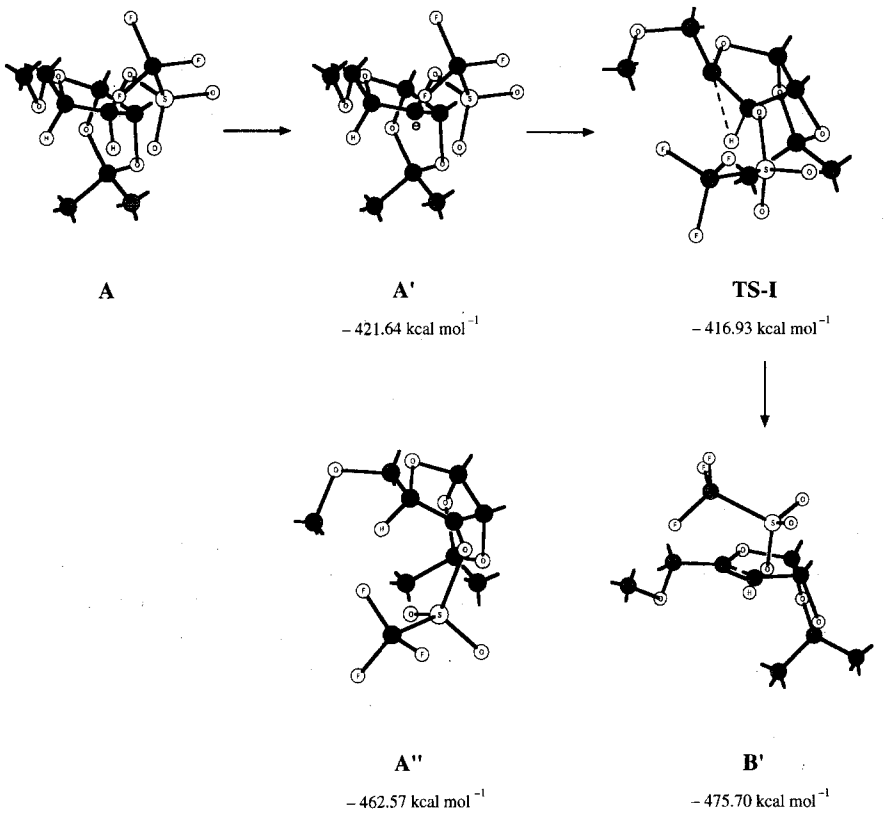


Fig. 2. Optimized structures other than A′ for the species in the **A** → **B** reaction (energy: heat of formation).

As reaction **A** + MeLi → **B** is thought to commence with the formation of C-3 carbanion **A′** (see Fig. 2), geometry-optimized **A** obtained by eigenvector following (EF) was transformed into **A′** by removing the H-3 as a proton while fixing the remaining structure. Successive energy-minimization by EF of the resulting **A′** gave **A″**, which was chosen as the starting compound for this reaction. Choosing **A″** instead of **A** + MeLi avoids the complexity caused by computation for a two-molecule combination. As regards **B**, in order to eliminate the computational difficulty caused by the discrepancy between **A″** and **B** in the number of atoms involved and the electronic charge, several substitutes for **B**, including $TflO^-$, placed near the C-3–H-3 bond, were arbitrarily prepared, and these were respectively optimized to give the best energy-minimized **B′**, which was chosen as the 'product' of this reaction.

The transition state for **A″** → **B′** was searched next by PM3 routines. The saddle structure incipiently obtained was optimized with PM3/TS to give TS-I, which was characterized by a single imaginary vibration, and by reversal into **A″** and **B′** by IRC calculation (see Experimental section). The TS-I obtained was, respectively, 46 and 4.6 kcal mol^{-1} higher in energy than **A″** and **A′**. These large and small energy differences suggest that **B′** must be brought from **A′** through TS-I, and not from the low-energy **A″**.

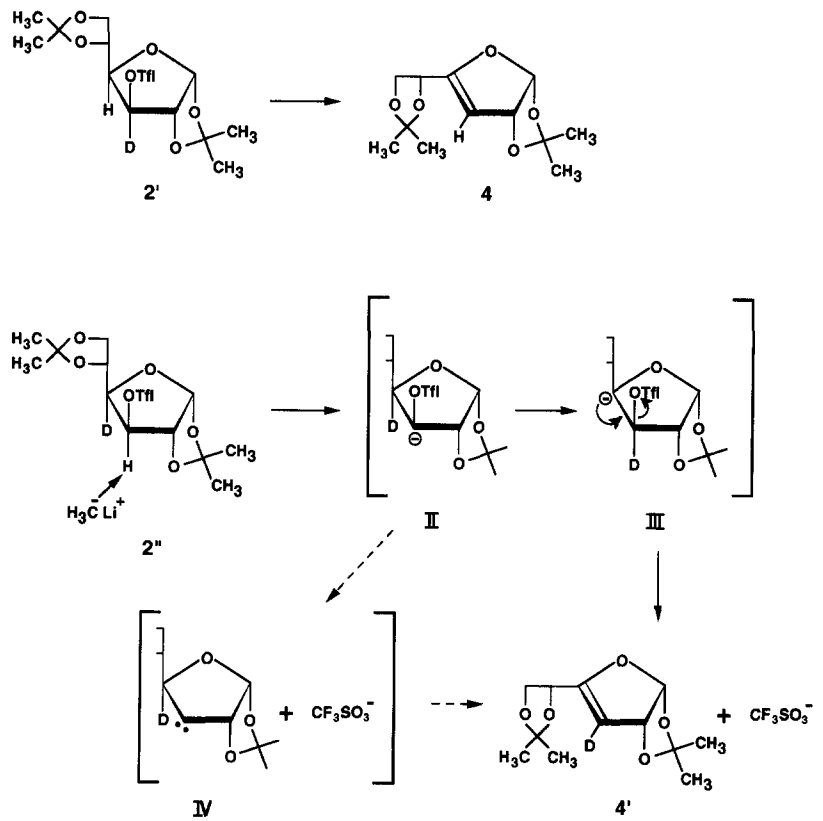
Table 1
Interatomic bond lengths and charge distribution for optimized molecular species in the reaction of **A** → **B** and **C** → **D**

Species	Bond length (Å)						Charge distribution [a]						
	C-3–H-3	C-3–O-3	O-3–S	C-3–H-4	C-3–C-4	C-4–H-4	C-3	H-3	O-3	S	C-4	H-4	S–O_2 [b]
A	1.12	1.42	1.69	2.18	1.56	1.13	0.09	0.10	−0.58	2.38	0.04	0.08	1.40
A′		1.42	1.69		1.56	1.13	−0.42		−0.46	2.26	0.11	0.06	1.40
A″		1.25	1.87		1.52	1.13	−0.11		−0.19	1.45	0.03	0.09	1.52
TS-I		1.48	1.67	1.13	1.44	2.14	0.21		−0.59	2.17	−0.52	0.04	1.45
B′	1.12	3.69	1.45		1.35		−0.25	0.23	−0.91	2.38	−0.01		1.46
B	1.09				1.35		−0.27	0.15			0.04		
C	1.12	1.41	1.69		1.56	1.12	0.09	0.07	−0.56	2.37	0.03	0.11	1.41
C′		1.41	1.69		1.56	1.12	−0.48		−0.46	2.30	0.11	0.04	1.41
C″		1.24	1.88		1.52	1.12	−0.07		−0.19	1.41	0.07	0.08	1.52
TS-II		1.22	2.20		1.53	1.11	0.10		−0.19	1.22	0.03	0.09	1.53
D′		1.21	5.16		1.53	1.11	0.27		−0.28	1.13	0.01	0.09	1.54
D		1.21			1.53	1.12	0.23		−0.25		0.00	0.11	

[a] The sum total of the atomic charge was confirmed as zero for **A**, **B**, **C**, and **D** and that for the other species as −1.
[b] Averaged value of two oxygens.

This assumption was partly supported by the fact that another calculated transition state, based on **A′** and **B′**, gave the same TS-I, albeit it gave **A″** and **B′** on IRC calculation. The structure of TS-I is shown in Fig. 2 (see also Table 1). This structure indicates that H-4 is almost separated from C-4 (C-4–H-4, 2.14 Å) and a new C-3–H-4 bond (1.13 Å) is almost complete despite the fact that the C-3–OTfl bond still exits. The shifts in charge from **A′** to TS-I at C-3, C-4, and H-4 (−0.42, 0.11, 0.06 → 0.21, −0.52, 0.04; see Table 1) are also supportive of this conclusion (the sum total of the atomic charge distributed in **A′** and TS-I is −1, respectively). A large negative-charge transfer from C-3 to C-4 is clear, and this would be brought about by a 4 → 3 proton shift as has already been suggested, and this may neutralize the negative charge at C-3 with concomitant creation of a negative charge of similar-magnitude at C-4. This kind of proton 1,2-shift has not been reported before, to the best of our knowledge. Alternatively, the foregoing result could be explained by negative-charge (at C-3) transfer to C-4 through the C-3–C-4 bond along with an H-4 hydride shift. However, we favoured the former mechanism. It must be mentioned in any event that accumulation of a large negative charge at C-4 is a necessary condition to form a 3,4-double bond, as in the case of β-elimination.

At this stage the possibility of a carbene as a transient in this reaction must be taken into account. If a C-3 carbanion that forms immediately releases the TflO group as an anion, the resulting species should be a true carbene (IV in Scheme 2). Generally, when a simple singlet-state carbene, a neutral species, rearranges [42] into the corresponding alkene, a 1,2-shift of hydrogen [43–46] occurs through a transition state that is higher in energy by only 0–5 kcal mol^{-1} than the parent carbene [43,45–48] and has a well-balanced triangular structure composed of the migrating hydrogen and two carbons,



Scheme 2.

the triangle being roughly perpendicular to the main frame to which it is attached [44]. Our TS-I has an energy (in terms of the heat of formation) close to that of C-3 carbanion **A'**, but in structure, it has an ill-balanced triangle (C-3–C-4 1.44, C-3–H-4 1.13, and C-4–H-4 2.14 Å; see Table 1 and Fig. 2), and this is ascribed to the biased negative-charge distribution in TS-I (the problem of a carbene is discussed again later).

The reaction **C** + MeLi → **D** is discussed next (Fig. 3). In this case the C-3 carbanion initially formed is destined to be converted into **D**. Applying a similar procedure to that described for **A''**, geometry-optimized **C** was transformed into the corresponding C-3 carbanion **C'** by eliminating H-3 as a proton, and it was optimized to give **C''**. For product **D**, as it has no Tfl^- group, a Tfl^- was placed near the C=O bond, and the arbitrarily prepared structures were optimized, to give the best energy-minimized **D'**, which was chosen as the 'product'. Then the transition state TS-II for **C''** → **D'** was searched. The TS-II obtained were 20 and only 3.0 kcal mol^{-1} higher in energy than those for **D'** and **C''**, respectively. This is in sharp contrast with the result of TS-I, in that the energy level is close to that of the higher-energy C-3 carbanion **A'**, and far from that of the optimized **A''**. Other characteristic features are that (*a*) **A'** and **C'**, and **A''** and **C''**, respectively, have almost the same geometry, bond lengths (between atoms in an

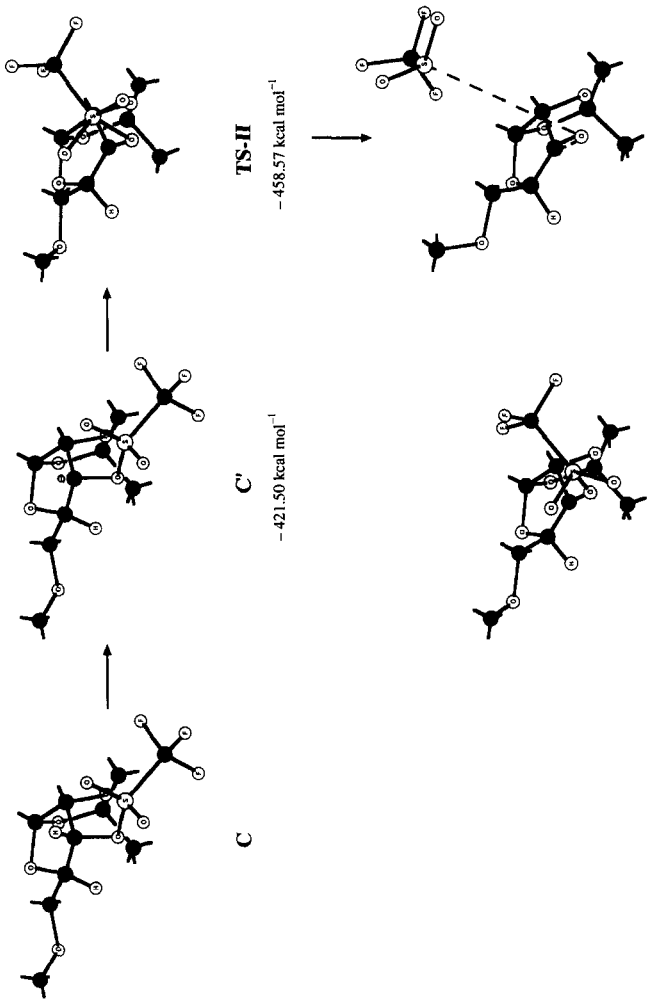
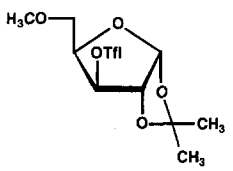


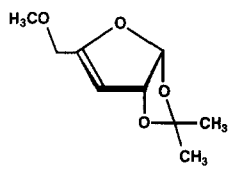
Fig. 3. Optimized structures other than **C'** for the species in the **C** → **D** reaction (energy: heat of formation).

equivalent situation), charge distribution, and energy levels as each other (Figs. 2 and 3 and Table 1) and (*b*) **A″** and **C″** have, respectively, shorter C-3–O-3 bond lengths than those for **A′** and **C′** by 0.17 Å. This suggests that both **A″** and **C″** have a structure close to that of the 3-oxo compound **D**, rather than a structure releasing the TflO group giving alkene **B**. This suggests that both carbanions **A′** and **C′** give the same **D**, irrespective of the C-3 configuration, when they undergo degeneration.

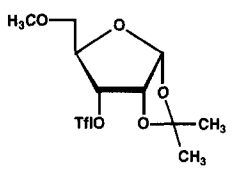
If, as described above, **A′** gives a carbene by releasing the $TflO^-$ group, **C′**, which closely resembles **A′** in energy and geometry, it should also give the same carbene, giving **B** as the final product. From the structural viewpoint, however, a sharp difference exists between **A** (**A′** or **2**) and **C** (**C′** or **6**) in the disposition of H-4 relative to TflO-3. In **A′**, the anionic lone-pair (at C-3) is located, if not epimerized, on the same face as H-4, but in **C′**, H-4 is located on the opposite face, and H-2 must take the role. However, formation of a 2,3-unsaturated compound is not favoured because of the high steric strain associated with placing O-2 into the plane of the double bond. Therefore **C′** can not yield the alkene, but instead degenerates spontaneously into **D** through TS-II.



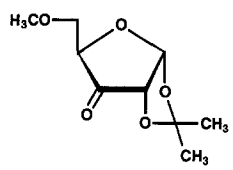
A



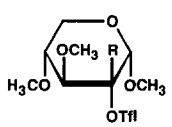
B



C

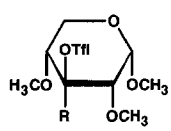


D



R= H **E**

R=⊖ **E'**



R= H **F**

R=⊖ **F'**

Summarizing the above, it is concluded that, in **A**, a 4 → 3 hydrogen shift occurs at a stage when removal of the TflO group is not complete, and 3,4-unsaturation follows

Table 2
Bond lengths, charge distribution, and energy levels (E, by heats of formation) of the optimized structures for the **E** and **F** series of compounds

		E	**F**	**E′**	**F′**	**E″**	**F″**
Bond length (Å)	C-2–O-2	1.42		1.42		1.26	
	O-2–S-2	1.68		1.68		1.86	
	C-3–O-3		1.42		1.42		1.25
	O-3–S-3		1.68		1.68		1.88
Charge distribution	H-2	0.08					
	C-2	0.10		−0.44		−0.16	
	O-2	−0.57		−0.44		−0.21	
	S-2	2.38		2.25		1.47	
	H-3		0.09				
	C-3		0.13		−0.39		−0.05
	O-3		−0.60		−0.48		−0.19
	S-3		2.39		2.27		1.41
Energy (kcal mol^{-1})	E	−401.8	−398.7	−410.5	−400.6	−448.9	−440.6

without passing through a carbene. On the other hand, in **C**, we consider that spontaneous degeneration occurs, affording the oxo compound because of a particular feature of a carbanion bearing a TflO group.

In the pyranosides studied, the reaction mechanisms giving the oxo compounds or alkenes may not necessarily be the same as those for the furanoside series, and detailed studies will be required to clarify them, so we discuss the problem here only briefly by introducing two simple molecular models. As all of the 2-triflates examined are assumed to give the corresponding 2-oxo compounds as the initial products, and the 3- and 4-triflates give alkenes in most cases, there must be a serious difference between them. Thus methyl 3,4-di-*O*-methyl-2-*O*-triflyl-α-D-xylopyranoside (**E**) and 2,4-di-*O*-methyl-3-*O*-triflyl-α-D-xylopyranoside (**F**) were introduced as model compounds for the 2- and 3-triflates and, after geometry-optimization, the H-2 and H-3 hydrogens were abstracted, respectively, as a proton to give the corresponding C-2 (**E′**) and C-3 carbanions (**F′**). Further optimization gave **E″** and **F″**. The results obtained (Table 2) show that no substantial differences exist between **E** and **F**, and between **E′** and **F′** in interatomic distances for C-2(or 3)–O, O–S, and S–O_2, respectively, but slight charge differences are observed between **E′** at C-2 (−0.44) and **F′** at C-3 (−0.39), and between **E″** at C-2 (−0.16) and **F″** at C-3 (−0.05). However, there is a great difference between the energy-differences $\Delta\Delta = \Delta_{E'-E}$ (−8.74 kcal mol^{-1}) − $\Delta_{F'-F}$ (−1.93 kcal mol^{-1}) [it should be noted that the absolute values (Δ's) have no fundamental meaning because of the inaccordance between **E** and **E′** (and **F** and **F′**) in the number of atoms and formal charge]. Although Δ_{E-F} (−3.09 kcal mol^{-1}) is small, the $\Delta\Delta$ magnitude (−6.81 kcal mol^{-1}) leads to the conclusion that the C-2 carbanion **E′** is more stable than the C-3 carbanion **F′**, and this may be attributed to the presence of a vicinal, electron-withdrawing glycosyl (acetal) group. The stabilized nature of **E′** relative to **F′** would produce bound electrons, as illustrated by the enhanced negative-charge (as already described) at C-2 in **E′** and **E″**, relative to that at C-3 in **F′** and **F″**, respectively, facilitating formation

of the 2-oxo compound. On the other hand, the unstable **F′**, with higher-energy electrons at C-3, would tend to stabilize itself either by abstracting a vicinal hydrogen as a proton, rapidly dispersing a part of its negative charge into the surroundings, or releasing the $TflO^-$ group giving a carbene (conversion of **35** into alkenes, for example, would take place [1]).

In summary, we have shown that, in some carbohydrate triflates, α-hydrogen elimination occurs on treatment with MeLi or BuLi in diethyl ether, and that the resulting α-carbanion is either transformed into ketone or induces unsaturation, depending on the particular structure.

4. Experimental

General methods.—Optical rotations were determined with a Perkin–Elmer 241 polarimeter. Mass spectra were measured by the fast-atom-bombardment method with a Jeol SX-102 spectrometer. NMR spectra (^1H at 250 and 500 MHz, ^{13}C at 125.8 MHz, and ^{19}F at 235.35 MHz) were recorded with Bruker AC-250P and AMX-500 spectrometers, using Me_4Si and $CFCl_3$ (for ^{19}F) as the internal and external references, respectively. TLC was performed on Silica Gel 60 F_{254} (Merck 5715 and 5717), and detected by charring with aq 50% H_2SO_4. Column chromatography was performed on Wakogel C-200.

General procedure to prepare the triflates.—To an ice-cold solution of the starting alcohol (1 M equiv) in pyridine (~ 15 v/w for the alcohol) was added $(CF_3SO_2)_2O$ (1.3 M equiv), and the solution was kept for several h in the cold. After the addition of water (~ 10 M equiv), the solution was concentrated in vacuo at room temperature and the residue was extracted with $CHCl_3$. The solution was washed with water, dried (Na_2SO_4), and concentrated to give the product. The triflates were chromatographically homogeneous although some of them were slightly unstable, and were used without purification.

General procedure for the reaction of the triflates and MeLi (or BuLi).—To a cold (−50 °C) solution of a triflate (1 M equiv) in dry ether (~ 20 v/w for the triflate) was added 4 M equiv of MeLi (by use of commercial 1.4 M MeLi in ether) or BuLi (commercial 2.5 M BuLi in hexane) and the solution was kept for 1–4 h at room temperature. When the reaction was complete (monitored by TLC with 2–4:1 hexane–EtOAc, unless otherwise stated), aq 2 M NH_4Cl was stirred in and the organic layer separated was washed with water, dried (Na_2SO_4), and concentrated. The residue was chromatographed with 3–4:1 hexane–EtOAc (unless otherwise stated), to give the final product.

Computation.—All calculations were performed on Sun SPARC Station 2 with Materia Version 3.1 (Teijin System Technology, Ltd., Japan) using semiempirical MOPAC93/PM3 (J.J.P. Stewart and Fujitsu Ltd., Tokyo). Geometry optimization was performed by the eigenvector following (EF) method. Transition states were searched initially by SADDLE (to give the saddle points) and the incipient structures were

[1] Details will be reported in the near future.

optimized by the TS routine. The transient structures were confirmed by frequency analysis to give a single imaginary vibration. To ascertain the TS structures further, they were reversed to the corresponding starting and end structures by Intrinsic Reaction Coordinate (IRC) calculation.

*1,2;5,6-Di-*O*-isopropylidene-3-*O*-triflyl-α-*D*-glucofuranose* (**2**).—Preparation from 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) in the usual manner to give a crystalline solid, mp 71–72 °C (lit. [4] 70 °C), $[\alpha]_D^{21}$ −37° (*c* 2.5, $CHCl_3$) {lit. [4] $[\alpha]_D^{25}$ −35° (*c* 2, acetone)}; ^{1}H NMR ($CDCl_3$): δ 1.33, 1.34, 1.43, and 1.52 [each s of 3 H, 2 $C(CH_3)_2$], 3.97 (m, 1 H, H-6), 4.1–4.26 (m, 3 H, H-4,5,6′), 4.76 (d, 1 H, H-2), 5.26 (unresolved d, 1 H, H-3), 5.99 (d, 1 H, H-1); $J_{1,2}$ 3.5, $J_{2,3}$ 0, $J_{3,4}$ ~ 2 Hz. Complex signals for H-4, 5, 6, and 6′, respectively, originated from virtual coupling between H-4 and 6′ due to the close shifts of H-4, 5, 6′.

Reaction of **2** *with MeLi to form 3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-*D*-erythro-hex-3-enofuranose* (**4**).—Treatment of **2** [4] (1.00 g) with MeLi according to the general procedure gave **4** as a solid (312 mg, 51%) along with **1** (163 mg, 25%). Compound **4**, mp 49–50 °C (lit. [9] 50 °C), $[\alpha]_D^{23}$ +28° (*c* 2.7, $CHCl_3$); *m/z* 243.20 [$M^+ + 1$]; Calcd for $C_{12}H_{18}O_5$: *m/z* 242.12 for M^+; ^{1}H NMR ($CDCl_3$): δ 1.39, 1.45, and 1.47 [s of 3, 3, and 6 H, respectively, 2 $C(CH_3)_2$], 3.97 (dd, 1 H, H-6), 4.15 (dd, 1 H, H-6′), 4.59 (ddd, 1 H, H-5), 5.25 (slightly deformed dd, 1 H, H-3), 5.30 (ddd, 1 H, H-2), 6.08 (d, 1 H, H-1); $J_{1,2}$ 5.2, $J_{2,3}$ 2.5, $J_{2,5}$ 1.2, $J_{3,5}$ ~ 1, $J_{5,6}$ 6.0, $J_{5,6'}$ 7.0, $J_{6,6'}$ 8.5 Hz. ^{13}C NMR ($CDCl_3$) (shifts were confirmed by the C–H COSY): δ 25.54, 26.24, 27.94, and 28.26 [2 (CH_3)$_2$C] 66.99 (C-6), 71.31 (C-5), 83.41 (C-2), 98.98 (C-3), 106.61 (C-1), 110.36 and 112.34 [2 (CH_3)$_2$*C*], 160.06 (C-4).

Reaction of **2** *with BuLi to form* **4**.—Treatment of **2** (1.00 g) with BuLi according to the general procedure gave **4** (440 mg, 71%) along with **1** (46 mg, 7%).

*1,2;5,6-Di-*O*-isopropylidene-3-*O*-triflyl-α-*D*-(3-*^{2}*H)glucofuranose* (**2′**).—Prepared from 1,2;5,6-di-*O*-isopropylidene-α-D-[3-^{2}H]glucofuranose [37] (**1′**, 60 mg) in the usual manner, as a solid (86 mg, 95%), mp 74 °C, $[\alpha]_D^{21}$ −39° (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.33, 1.34, 1.43, and 1.52 [each s of 3 H, 2 $C(CH_3)$], 3.97 (m, 1 H, H-6), 4.1–4.26 (m, 3 H, H-4,5,6′), 4.76 (d, 1 H, H-2), 5.99 (d, 1 H, H-1); $J_{1,2}$ 3.5 Hz.

Reaction of **2′** *with MeLi*.—Treatment of **2′** (50 mg) with MeLi (0.5 mmol) as described for **4** gave the authentic **4** (20 mg, 65%) along with **1′** (8 mg, 24%).

*1,2;5,6-Di-*O*-isopropylidene-3-*O*-triflyl-α-*D*-(4-*^{2}*H)glucofuranose* (**2″**).—Prepared from **52** (200 mg) in a usual manner to give a crystalline solid (260 mg, 86%), mp 73 °C, $[\alpha]_D^{21}$ −38° (*c* 3, $CHCl_3$); *m/z* 378.04 [$M^+ - CH_3$], 394.09 [$M^+ + 1$]; Calcd for $C_{13}H_{18}DF_3O_8S$: *m/z* 393.08 for M^+; ^{1}H NMR ($CDCl_3$): δ 1.33, 1.34, 1.43, and 1.52 [each s of 3 H, 2 $C(CH_3)_2$], 3.97 (dd, 1 H, H-6), 4.15 (dd, 1 H, H-6′), 4.21 (dd, 1 H H-5), 4.76 (d, 1 H, H-2), 5.26 (s, 1 H, H-3), 5.99 (d, 1 H, H-1); $J_{1,2}$ 3.5, $J_{2,3}$ ~ 0, $J_{5,6}$ 4.5, $J_{5,6'}$ 6.0, $J_{6,6'}$ 9.0 Hz.

Reaction of **2″** *with MeLi to form 3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-*D*-erythro-hex-3-eno-(3-*^{2}*H)furanose* (**4′**).—Treatment of **2″** (30 mg, 0.08 mmol) with MeLi (0.31 mmol) as described for **4** gave the 3-deuterio isomer (**4′**) of **4** as a solid (11 mg, 59%) together with **52** (4 mg, 20%); compound **4′**, mp 48–50 °C, $[\alpha]_D^{21}$ +27° (*c* 1.6, $CHCl_3$); *m/z* 242.36 [$M^+ - 1$]; Calcd for $C_{12}H_{17}DO_5$: *m/z* 243.12 for M^+; ^{1}H NMR ($CDCl_3$): δ 1.39, 1.45, and 1.47 [s of 3, 3 and 6 H, respectively, 2 $C(CH_3)_2$], 3.97 (dd, 1 H, H-6),

4.15 (dd, 1 H, H-6′), 4.59 (dt, 1 H, H-5), 5.30 (dd, 1 H, H-2), 6.08 (d, 1 H, H-1); $J_{1,2}$ 5.2, $J_{2,5}$ 1.3, $J_{5,6}$ 6.0, $J_{5,6'}$ 7.0, $J_{6,6'}$ 8.5 Hz. ^{13}C NMR ($CDCl_3$): δ 25.54, 26.24, 27.94, and 28.26 [2 (CH_3)$_2$C], 66.99 (C-6), 71.30 (C-5), 83.34 (C-2), 98.74 (t, $J_{C,D}$ 27.6 Hz, C-3), 106.62 (C-1), 110.36 and 112.34 [2 (CH_3)$_2$*C*], 160.00 (C-4).

*(7*R *And 7*S*)-1,2-*O*-benzylidene-5,6-*O*-isopropylidene-α-*D*-glucofuranose* (**10** *and* **11**).—A mixture of D-glucose (10.0 g, 55.5 mmol), PhCHO (80 mL), $ZnCl_2$ (12 g), and H_3PO_4 (2 mL) was stirred for 3 days at room temperature, poured in small portions into an ice-cold aq 0.5 M NaOH (1 L), and the products (dibenzylidene derivatives) were extracted with $CHCl_3$. The organic solution was washed with water, dried (Na_2SO_4), and concentrated. To the residue (~ 6.1 g) in MeOH (200 mL), was added 1% H_2SO_4 in MeOH (24 mL) and the solution was kept overnight at room temperature. Neutralization with M NaOH in MeOH, followed by evaporation of the solvent gave a residue, which was chromatographed (20:1 $CHCl_3$–MeOH) to give a mixture of 1,2-*O*-benzylidene-D-glucofuranoses (3.61 g, 24% based on D-glucose). To a solution of the mixture (3.2 g) in DMF (30 mL) were added 2,2-dimethoxypropane (3 mL) and pyridinium *p*-tolouenesulfonate (1.5 g), and the solution was kept for 2 days at room temperature, poured into aq Na_2CO_3 (saturated), and the products were extracted with $CHCl_3$. Chromatography (2:1 petroleum ether–EtOAc) of the products gave **11** (from the faster-moving fractions) as a crystalline solid (1.62 g, 44%) and **10** (from the slower-moving fractions) as a syrup (1.14 g, 30%). **10**: $[\alpha]_D^{24}$ +25° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.36 and 1.41 [each s of 3 H, C(CH_3)$_2$], 2.66 (d, 1 H, OH), 3.97 (dd, 1 H, H-6), 4.11 (dd, 1 H, H-4), 4.17 (dd, 1 H, H-6′), 4.36 (ddd, 1 H, H-5), 4.43 (t, 1 H, H-3), 4.61 (d, 1 H, H-2), 5.89 (s, 1 H, C*H*Ph), 6.10 (d, 1 H, H-1), 7.40 (m, 3 H, *m*- and *p*-H of Ph), 7.49 (m, 2 H, *o*-H of Ph); $J_{1,2}$ 4, $J_{2,3}$ 0, $J_{3,4}$ 3, $J_{3,OH}$ 3.5, $J_{4,5}$ 7.5, $J_{5,6}$ 5.5, $J_{5,6'}$ 6, $J_{6,6'}$ 9 Hz. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 62.06; H, 6.39.

11: mp 120–121 °C, $[\alpha]_D^{24}$ +1° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.38 and 1.47 [each s of 3 H, C(CH_3)$_2$], 2.56 (d, 1 H, OH), 4.08 (dd, 1 H, H-6), 4.12 (dd, 1 H, H-4), 4.19 (dd, 1 H, H-6′), 4.30 (ddd, 1 H, H-5), 4.50 (t, 1 H, H-3), 4.68 (d, 1 H, H-2), 6.09 (s, 1 H, C*H*Ph), 6.12 (d, 1 H, H-1), 7.37–7.47 (m, 5 H, Ph); $J_{1,2}$ 3.5, $J_{2,3}$ 0, $J_{3,4}$ 3, $J_{3,OH}$ 3.5, $J_{4,5}$ 7.8, $J_{5,6}$ 5, $J_{5,6'}$ 6, $J_{6,6'}$ 9 Hz. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 62.49; H, 6.42.

*(7*R*)-1,2-*O*-Benzylidene-5,6-*O*-isopropylidene-3-*O*-triflyl-α-*D*-glucofuranose* (**12**).—Prepared from **10** (300 mg) as a syrup (388 mg, 91%). An analytical sample was prepared by passing it through a Silica Gel column with 5:1 hexane–EtOAc to give a solid, mp 54–55 °C, $[\alpha]_D^{24}$ +4.5° (*c* 2, $CHCl_3$); *m/z* 441.16 [M^+ + 1]; Calcd for $C_{17}H_{19}F_3O_8S$: *m/z* 440.08 for M^+; ^{1}H NMR ($CDCl_3$): δ 1.32 and 1.36 [each s of 3 H, C(CH_3)$_2$], 3.92 (dd, 1 H, H-6), 4.14 (dd, 1 H, H-6′), 4.15–4.27 (m, 2 H, H-4,5), 4.87 (d, 1 H, H-2), 5.34 (sl. br d, 1 H, H-3), 5.97 (s, 1 H, C*H*Ph), 6.15 (d, 1 H, H-1); $J_{1,2}$ 4, $J_{3,4}$ 2.5 Hz. Anal. Calcd for $C_{17}H_{19}F_3O_8S$: C, 46.36; H, 4.35; S, 7.28. Found: C, 46.71; H, 4.51; S, 7.40.

Reaction of **12** with BuLi to form (7R)-1,2-O-benzylidene-3-deoxy-5,6-O-isopropylidene-α-D-erythro-*hex-3-enofuranose* (**14**).—Preparation from **12** (300 mg) and BuLi gave a crystalline solid (141 mg, 71%), mp 103–104 °C, $[\alpha]_D^{24}$ +12° (*c* 3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.27 and 1.31 [each s of 3 H, C(CH_3)$_2$], 2.97 (dd, 1 H, H-6), 3.84 (dd, 1 H, H-6′), 4.31 (dddd, 1 H, H-5), 5.09 (dd, 1 H, H-3), 5.40 (ddd, 1 H, H-2), 6.18

(d, 1 H, H-1), 6.31 (s, 1 H, C*H*Ph); 7.34 (3 H) and 7.45 (2 H) (each m, C_6H_5); $J_{1,2}$ 5, $J_{2,3}$ 2, $J_{2,5} \approx J_{3,5} \sim 1.5$, $J_{5,6}$ 6.5, $J_{5,6'}$ 6.8, $J_{6,6'}$ 8.5 Hz. Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 65.85; H, 6.07.

(7S)-1,2-O-Benzylidene-5,6-O-isopropylidene-3-O-triflyl-α-D-glucofuranose (**13**).—Prepared from **11** (500 mg) as a solid (707 mg, 99%). An analytical sample was prepared as described for **2**, mp 79–80 °C (decomp.), $[\alpha]_D^{24}$ −17° (*c* 3, $CHCl_3$); *m/z* 441.13 [$M^+ + 1$]; Calcd for $C_{17}H_{19}F_3O_8S$: *m/z* 440.08 for M^+; ^{1}H NMR ($CDCl_3$): δ 1.35 and 1.46 [each s of 3 H, $C(CH_3)_2$]; 4.03–4.11 (1 H) and 4.16–4.28 (3 H) (each unresolved m derived from virtual couplings; H-4,5,6,6′), 4.92 (d, 1 H, H-2), 5.44 (sl. br d, 1 H, H-3), 6.14 (s, 1 H, C*H*Ph), 6.16 (d, 1 H, H-1); $J_{1,2}$ 4, $J_{3,4}$ 2.5 Hz. Anal. Calcd for $C_{17}H_{19}F_3O_8S$: C, 46.36; H, 4.35; S, 7.28. Found: C, 46.45; H, 4.71; S, 7.35.

Reaction of **13** with BuLi to form (7S)-1,2-O-benzylidene-3-deoxy-5,6-O-isopropylidene-α-D-erythro-*hex-3-enofuranose* (**15**).—Preparation from **13** (200 mg) and BuLi (1.36 mmol) gave a syrup (102 mg, 77%), $[\alpha]_D^{23}$ +28° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.42 and 1.51 [each s of 3 H, $C(CH_3)_2$], 4.02 (dd, 1 H, H-6), 4.23 (dd, 1 H, H-6′), 4.66 (dddd, 1 H, H-5), 5.12 (dd, 1 H, H-3), 5.60 (ddd, 1 H, H-2), 5.87 (s, 1 H, C*H*Ph), 6.18 (d, 1 H, H-1), 7.40 (3 H) and 7.50 (2 H) (each m, C_6H_5); $J_{1,2}$ 5, $J_{2,3}$ 2.5, $J_{2,5} \approx J_{3,5}$ 1.5, $J_{5,6}$ 6, $J_{5,6'}$ 7, $J_{6,6'}$ 8.5 Hz. Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.05; H, 6.25.

1,2;5,6-Di-O-isopropylidene-3-O-triflyl-α-D-allofuranose (**6**).—Mp 41 °C (lit. [4] 40 °C), $[\alpha]_D^{21}$ +62° (*c* 3, $CHCl_3$) {lit. [4] $[\alpha]_D^{25}$ +64° (acetone)}; ^{1}H NMR ($CDCl_3$): δ 1.35, 1.39, 1.45, and 1.59 [each s of 3 H, 2 $C(CH_3)_2$], 3.91 (m, 1 H, H-6), 4.08–4.25 (m, 3 H, H-4,5,6′), 4.77 (dd, 1 H, H-2), 4.91 (dd, 1 H, H-3), 5.84 (d, 1 H, H-1); $J_{1,2}$ 3.7, $J_{2,3}$ 5.0, $J_{3,4}$ 7.0 Hz.

Reaction of **6** *with MeLi to form 1,2;5,6-di-O-isopropylidene-3-C-methyl-α-D-allofuranose* (**7**).—Treatment of **6** [4] (600 mg, 1.53 mmol) with MeLi (6.12 mmol) for 4 h as described for the general procedure gave a crude mixture [TLC with 1:1 hexane–EtOAc: R_f 0.42 (slight, **6**), 0.38 (**7**), and 0], which was chromatographed with 1:1 hexane–EtOAc to give **7** as a crystalline solid (203 mg, 48%) together with 1,2;5,6-di-*O*-isopropylidene-D-allofuranose [49] (**5**, slowest moving product, 99 mg, 25%). Compound **7**: mp 99–100 °C (lit. [13] 105–107 °C), $[\alpha]_D^{24}$ +19° (*c* 1.5, $CHCl_3$) [lit. [13] +22° (*c* 1, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 3 H, H_3C-3), 1.35, 1.36, 1.45, and 1.59 [each s of 3 H, 2 $C(CH_3)_2$], 2.67 (br s, 1 H, OH), 3.78 (1 H, H-4), 3.93 (1 H, H-6), 4.10 (m, 2 H, H-5,6′), 4.17 (d, 1 H, H-2), 5.70 (d, 1 H, H-1); $J_{1,2}$ 4, $J_{4,5} \sim 6$ Hz. Signals for H-4, 5, 6, and 6′ were all deformed by virtual couplings brought about by close shifts of H-5 and 6′.

Reaction of **6** *with BuLi to form 3-C-butyl-1,2;5,6-di-O-isopropylidene-α-D-allofuranose* (**8**).—Treatment of **6** [4] (1.00 g, 2.55 mmol) with BuLi (10.2 mmol) for 4 h as described for the general procedure gave a crude mixture [TLC with 10:1 toluene–EtOAc: R_f 0.5 (slight, **6**), 0.25 (**8**), and 0.05 (**5**)], which was chromatographed (10:1 toluene–EtOAc) to give **5** (165 mg, 25%) and **8** as a crystalline solid (503 mg, 62%), mp 102–103 °C (lit. [12] 132–133 °C), $[\alpha]_D^{21}$ +11° (*c* 2, $CHCl_3$) {lit. [12] $[\alpha]_D^{25}$ +23.9° (*c* 1, MeOH)}; ^{1}H NMR ($CDCl_3$): δ 0.94 [t, 3 H, $CH_3(CH_2)_3$], 1.3–1.43 [m, 4 H, $CH_3(CH_2)_2CH_2$], 1.36, 1.37, 1.45, and 1.59 [each s of 3 H, 2 $C(CH_3)_2$], 1.62 and 1.75 [each m of 1 H, $CH_3(CH_2)_2CH_2$], 2.56 (s, 1 H, OH), 3.80 (d, 1 H, H-4), 3.91 (dd, 1 H,

H-6), 4.09 (dd, 1 H, H-6′), 4.13 (ddd, 1 H, H-5), 4.36 (d, 1 H, H-2), 5.69 (d, 1 H, H-1); $J_{1,2}$ 4, $J_{4,5}$ 8, $J_{5,6} \approx J_{5,6'}$ 6, $J_{6,6'}$ 8 Hz.

Reaction of **9** *with BuLi to form* **8**.—Compound **9** [49] (120 mg) was treated with BuLi (1.38 mmol) for 30 min as described above to give **8** (79 mg, 54%), identical in all respects to the specimen obtained from **6**.

1,2;5,6-Di-O-isopropylidene-3-O-triflyl-α-D-(3-^{2}H)allofuranose (**6′**).—Triflation of 1,2;5,6-di-*O*-isopropylidene-α-D-(3-^{2}H)allofuranose [37,38] (**5′**, 450 mg) in a usual manner gave **6′** as a solid (582 mg, 86%), mp 42–43 °C, $[\alpha]_D^{20}$ +66° (*c* 2.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.35, 1.39, 1.45, and 1.59 [each s of 3 H, 2 $C(CH_3)_2$], 3.91 (dd, 1 H, H-6), 4.11 (dd, 1 H, H-6′), 4.18 (d, 1 H, H-4), 4.20 (dt, 1 H, H-5), 4.77 (dd, 1 H, H-2), 5.84 (d, 1 H, H-1); $J_{1,2}$ 3.7, $J_{4,5}$ 6.0, $J_{5,6}$ 4.5, $J_{5,6'}$ 6.0, $J_{6,6'}$ 8.5 Hz. ^{13}C NMR ($CDCl_3$) (shifts were confirmed by C–H COSY): δ 24.85, 26.29, 26.55, and 26.92 [2 (CH_3)$_2$C], 66.36 (C-6), 75.26 (C-4), 77.69 (C-2), 77.90 (C-5); 82.46, 82.65, and 82.84 (t, $^1J_{C,D}$ 24.0 Hz, C-3), 104.26 (C-1), 110.36 (1,2-di-*O*-*C*Me_2), 114.47 (5,6-di-*O*-*C*Me_2), 114.65, 117.19, 119.73, and 122.27 (q, $J_{C,F}$ 319.5 Hz).

Reaction of **6′** *with MeLi*.—A vessel containing a solution of **6′** (400 mg, 102 mmol) in dry ether (5 mL) was cooled to −50 °C (dry ice–acetone) and connected to a cold (−50 °C) tube containing $CDCl_3$ (0.5 mL). A solution of 1.4 M MeLi in ether (2.6 mL) in a funnel was added dropwise (~30 min) into the reaction vessel under a slight pressure (a thin rubber-balloon containing N_2 was used). The temperature was allowed to rise, and the reaction was continued for 2 h at room temperature. The $CDCl_3$ tube was disconnected and the ^{1}H NMR spectrum was measured at room temperature (see text). The separated reaction vessel was heated (100 °C) and the volatile substances were all distilled off under vacuum. The residue dissolved in D_2O was filtered, and the solution was examined by ^{19}F NMR. In the spectrum, a singlet (−88.3 ppm from external $CFCl_3$) appeared, among other unassigned signals; the singlet had the same shift value as that of CF_3SO_2Li prepared by reduction of CF_3SO_2Cl with Zn [50], followed by conversion of the resulting $(CF_3SO_2)_2Zn$ to CF_3SO_2Li by passing it through a column of Dowex 50W resin (Li^+ form) with water.

(7R)-1,2-O-Benzylidene-5,6-O-isopropylidene-α-D-allofuranose (**16**).—A solution of **10** (1.00 g) in 3:5 Ac_2O–Me_2SO (15 mL) was kept for 2 days at room temperature, and then poured into an ice-cold mixture of $CHCl_3$ (150 mL) and aq Na_2CO_3 (saturated, 100 mL) under stirring, and the organic solution that separated was washed with water (30 mL × 2) and concentrated. To the residue (TLC with 1:1 hexane–EtOAc, R_f 0.5; cf. **10**: R_f 0.4) in MeOH (20 mL) was added $NaBH_4$ (250 mg), and for 2 h, dry ice was added and the mixture concentrated. The residue was chromatographed (1:1 hexane–EtOAc) to give **16** as a semi-crystalline solid (714 mg, 71%), $[\alpha]_D^{24}$ +47° (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.39 and 1.45 [each s of 3 H, $C(CH_3)_2$], 2.52 (d, 1 H, OH), 3.89 (dd, 1 H, H-4), 4.01 (dd, 1 H, H-6), 4.08 (dd, 1 H, H-6′), 4.15 (dt, 1 H, H-3), 4.35 (dt, 1 H, H-5), 4.67 (dd, 1 H, H-2), 5.97 (d, 1 H, H-1), 6.01 (s, 1 H, C*H*Ph); $J_{1,2}$ 4, $J_{2,3}$ 5, $J_{3,OH}$ 9, $J_{3,4}$ 9, $J_{4,5}$ 4.5, $J_{5,6} \approx J_{5,6'}$ 6.5, $J_{6,6'}$ 9 Hz. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 61.96; H, 6.33.

(7S)-1,2-O-Benzylidene-5,6-O-isopropylidene-α-D-allofuranose (**17**).—Compound **11** (1.00 g) was treated as described for **16** to give **17** as crystals (726 mg, 73%), mp 100–101 °C, $[\alpha]_D^{24}$ +30° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.39 and 1.48 [each s of 3

H, $C(CH_3)_2$], 2.72 (d, 1 H, OH), 3.90 (dd, 1 H, H-4), 4.03 (dd, 1 H, H-6), 4.11 (dd, 1 H, H-6′), 4.18 (br q, 1 H, H-3), 4.27 (dt, 1 H, H-5), 4.76 (dd, 1 H, H-2), 5.97 (d, 1 H, H-1), 6.17 (s, 1 H, C*H*Ph); $J_{1,2}$ 4, $J_{2,3}$ 6, $J_{3,OH}$ 7, $J_{3,4}$ 8, $J_{4,5}$ 4.5, $J_{5,6} \approx J_{5,6'}$ 6, $J_{6,6'}$ 9 Hz. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 62.19; H, 6.34.

(7R)-1,2-O-Benzylidene-5,6-O-isopropylidene-3-O-triflyl-α-D-allofuranose (**18**).—Prepared from **16** (140 mg) as a solid (196 mg, 98%). An analytical sample was prepared by passing the crude product through a Silica Gel column with 4:1 hexane–EtOAc, mp 68–69 °C, $[\alpha]_D^{24}$ +16° (*c* 2.5, $CHCl_3$); *m/z* 441.13 [M^+ + 1]; Calcd for $C_{17}H_{19}F_3O_8S$: *m/z* 440.08 for M^+; ^1H NMR ($CDCl_3$): δ 1.34 and 1.41 [each s of 3 H, $C(CH_3)_2$], 3.85 (dd, 1 H, H-6), 4.06 (dd, 1 H, H-4), 4.08 (dd, 1 H, H-6′), 4.21 (dt, 1 H, H-5), 4.86 (dd, 1 H, H-2), 4.99 (dd, 1 H, H-3), 5.99 (d, 1 H, H-1), 6.11 (s, 1 H, C*H*Ph); $J_{1,2}$ 4, $J_{2,3}$ 5, $J_{3,4}$ 8, $J_{4,5}$ 6, $J_{5,6}$ 5, $J_{5,6'}$ 7, $J_{6,6'}$ 9 Hz. Anal. Calcd for $C_{17}H_{19}F_3O_8S$: C, 46.36; H, 4.35; S, 7.28. Found: C, 46.14; H, 4.23; S, 7.35.

Reaction of **18** *with MeLi to form (7R)-1,2-O-benzylidene-5,6-O-isopropylidene-3-C-methyl-α-D-allofuranose* (**20**).—Prepared from **18** (71 mg) and MeLi as a syrup (46 mg, 89%), $[\alpha]_D^{24}$ +43 ° (*c* 2.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.33 (s, 3 H, CH_3-3), 1.36 and 1.41 [each s of 3 H, CMe_2], 2.65 (s, 1 H, OH), 3.84 (complex m, 1 H, H-4), 3.92 (complex m, 1 H, H-6), ~4.12 (2 H, H-5,6′), 4.22 (d, 1 H, H-2), 5.86 (d, 1 H, H-1), 5.98 (s, 1 H, C*H*Ph); $J_{1,2}$ 4 Hz. Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.14; H, 6.74.

(7S)-1,2-O-Benzylidene-5,6-O-isopropylidene-3-O-triflyl-α-D-allofuranose (**19**).—Prepared from **17** (340 mg) as a crystalline solid (needles, 479 mg, 99%). An analytical sample was prepared as described for **18**, mp 81–82 °C, $[\alpha]_D^{24}$ +62° (*c* 4, $CHCl_3$); *m/z* 441.16 [M^+ + 1]; Calcd for $C_{17}H_{19}F_3O_8S$: *m/z* 440.08 for M^+; ^1H NMR ($CDCl_3$): δ 1.36 and 1.47 [each s of 3 H, $C(CH_3)_2$], 3.93 (1 H, H-6), ~4.17 (2 H, H-5,6′), 4.27 (t, 1 H, H-4), 4.98 (dd, 1 H, H-2), 5.14 (t, 1 H, H-3), 6.00 (d, 1 H, H-1), 6.14 (s, 1 H, C*H*Ph); $J_{1,2}$ 4, $J_{2,3} \approx J_{3,4} \approx J_{4,5}$ 6 Hz. Anal. Calcd for $C_{17}H_{19}F_3O_8S$: C, 46.36; H, 4.35; S, 7.28. Found: C, 46.63; H, 4.42; S, 7.40.

Reaction of **19** *with MeLi*.—Treatment of **19** (140 mg, 0.32 mmol) with MeLi (1.27 mmol) according to the general procedure (chromatography: 2:1 ether–hexane) gave a 2.5:1 mixture of **21** and **22** (they had the same mobility) as a solid (70 mg, 69%), $[\alpha]_D^{24}$ +18° (*c* 1, $CHCl_3$); *m/z* 323.25 [M^+ + 1]; Calcd for $C_{17}H_{22}O_6$: *m/z* 322.14 for M^+; ^1H NMR ($CDCl_3$), δ values of **21** and **22** confirmed by ^1H–^1H COSY are shown in this order: 1.34, 1.56 (s, CH_3-3), 1.38, 1.48 and 1.37, 1.47 [each s, $C(CH_3)_2$], 2.80 (s, 1 H, OH), 3.85, 3.83 (d, *J* 8.0 Hz, H-4), 4.02, 4.08 (dd, *J* 5.0 and 8.0 Hz, H-6), 4.10, 4.27 (m, H-5), 4.14, 4.17 (dd, *J* 6.0 and 8.0 Hz, H-6′), 4.28, 4.41 (d, $J_{1,2}$ 3.5 Hz, H-2), 5.89, 6.05 (d, H-1), 6.29, 6.055 (s, C*H*Ph). NOE study: irradiation of H-2 of **21** (major) caused increases of both CH_3-3 (δ 1.34, 3.9%) and H-1 (δ 5.89, 4.2%), and irradiation of H-2 of **22** (minor) caused increase of H-1 (δ 6.05, 4.5%).

Methyl 3,5-di-O-benzyl-6-bromo-6-deoxy-β-D-glucofuranoside (**24**).—To an ice-cold solution of **23** [14] (400 mg, 1.07 mmol) and $P(C_6H_5)_3$ (560 mg, 2.13 mmol) in pyridine (10 mL), was added dropwise CBr_4 (390 mg, 1.18 mmol) in pyridine (3 mL), and the solution was heated for 15 min at 60 °C. After addition of MeOH (3 mL) the solution was concentrated, and the residue was chromatographed (2:1 hexane–EtOAc) to give **24** as needles (587 mg, 90%), mp 97–98 °C, $[\alpha]_D^{24}$ −100° (*c* 1, $CHCl_3$); ^1H NMR

($CDCl_3$): δ 3.72 (dd, 1 H, H-6), 3.81 (dd, 1 H, H-6′), 3.95 (dd, 1 H, H-3), 4.05 (ddd, 1 H, H-5), 4.19 (sl. br s, 1 H, H-2), 4.37 (dd, 1 H, H-4), 4.47 and 4.68 (each d of 1 H, CH_2Ph), 4.53 and 4.62 (each d of 1 H, CH_2Ph), 4.81 (s, 1 H, H-1); $J_{1,2}$ ~ 0, $J_{2,3}$ 1.5, $J_{3,4}$ 5.0, $J_{4,5}$ 8.5, $J_{5,6}$ 4.0, $J_{5,6'}$ 3.0, $J_{6,6'}$ 11.0 Hz. Anal. Calcd for $C_{21}H_{25}BrO_5$: C, 57.67; H, 5.76; Br 18.27. Found: C, 57.38; H, 5.64; Br, 18.60.

*Methyl 3,5-di-*O*-benzyl-6-bromo-6-deoxy-2-*O*-triflyl-β-*D*-glucofuranoside* (**25**).—Prepared from **24** (200 mg) similarly as described for the general procedure, as a solid (232 mg, 94%). An analytical sample was prepared as described for **18**, mp 62–63 °C, $[\alpha]_D^{23}$ −38° (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.44 (s, 3 H, OCH_3), 3.69 (dd, 1 H, H-6), 3.80 (dd, 1 H, H-6′), 4.04 (dt, 1 H, H-5), 4.25 (d, 1 H, H-3), 4.38 (dd, 1 H, H-4), 4.41 and 4.67 (each d of 1 H, *J* 11 Hz, CH_2Ph), 4.55 and 4.68 (each d of 1 H, *J* 11.5 Hz, CH_2Ph), 5.08 (s, 1 H, H-1), 5.13 (sl. br s, H-2); $J_{1,2} \approx J_{2,3}$ ~ 0, $J_{3,4}$ 5, $J_{4,5}$ 8.5, $J_{5,6}$ 3.2, $J_{5,6'}$ 2.8, $J_{6,6'}$ 11 Hz. Anal. Calcd for $C_{22}H_{24}BrF_3O_7S$: C, 46.40; H, 4.25; Br, 14.03; S, 5.63. Found: C, 46.38; H, 4.15; Br, 14.11; S, 5.74.

Reaction of **25** *with BuLi to form methyl 3,5-di-*O*-benzyl-6-bromo-2-*C*-butyl-6-deoxy-β-*D*-mannofuranoside* (**26**).—Treatment of **25** (83 mg, 0.15 mmol) with BuLi (0.45 mmol) as described for the general procedure (chromatography: 3:1 hexane–EtOAc) gave **26** as a syrup (41 mg, 64%), $[\alpha]_D^{24}$ −75° (*c* 1, $CHCl_3$); *m/z* 493.27 and 495.27 [$M^+ + 1$]; Calcd for $C_{25}H_{33}BrO_5$: *m/z* 492.15 and 494.15 for M^+; ^{1}H NMR ($CDCl_3$): δ 0.91 [t, 3 H, $CH_3(CH_2)_3$]; 1.28–1.36 (m, 2 H) and 1.36–1.46 (m, 2 H) [$CH_3(CH_2)_2CH_2$]; 1.47–1.61 [m, 2 H, $CH_3(CH_2)_2CH_2$], 3.32 (s, 1 H, OH), 3.41 (s, 3 H, OCH_3), 3.74 (d, 1 H, H-3), 3.77 (dd, 1 H, H-6), 3.87 (dd, 1 H, H-6′), 3.99 (dt, 1 H, H-5), 4.24 (dd, 1 H, H-4), 4.46 (s, 1 H, H-1), 4.35 and 4.65 (each d of 1 H, *J* 11 Hz, CH_2Ph), 4.58 and 4.75 (each d of 1 H, *J* 11.5 Hz, CH_2Ph); $J_{3,4}$ 5.5, $J_{4,5}$ 8.5, $J_{5,6}$ 2.8, $J_{5,6'}$ 2.5, $J_{6,6'}$ 11 Hz.

Reaction of **27** *with MeLi to form methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-methyl-α-*D*-glucopyranoside* (**28**).—Treatment of **27** [15–17] (500 mg, 0.99 mmol) with MeLi (3.96 mmol) as described for the general procedure (chromatography: 4:1 hexane–EtOAc) gave **28** as a syrup (347 mg, 91%), $[\alpha]_D^{23}$ +50° (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.37 (s, 3 H, H_3C-2), 2.55 (s, 1 H, OH), 3.43 (s, 3 H, OCH_3), 3.65 (t, 1 H, H-4), 3.77 (t, 1 H, H-6), 3.81 (d, 1 H, H-3), 3.85 (m, 1 H, H-5), 4.28 (dd, 1 H, H-6′), 4.43 (s, 1 H, H-1), 4.88 (ABq, 2 H, CH_2Ph), 5.56 (s, 1 H, C*H*Ph); $J_{3,4} \approx J_{4,5} \approx J_{5,6} \approx J_{6,6'}$ 9.5, $J_{5,6'}$ 4 Hz. Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.37; H, 6.78. Found: C, 68.65; H, 6.74.

Reaction of **27** *with BuLi to form methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-butyl-α-*D*-glucopyranoside* (**29**).—Prepared conventionally from **27** (400 mg, 0.79 mmol) and BuLi (2.37 mmol) (chromatography: 20:1 toluene–EtOAc) gave a syrup (263 mg, 77%), $[\alpha]_D^{24}$ +31° (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.93 [t, 3 H, $CH_3(CH_2)_3$]; 1.24–1.4 (m, 3 H) and 1.52–1.61 (m, 2 H) [5 H of $CH_3(CH_2)_3$], 2.04 [m, 1 H, one of the $CH_3(CH_2)_2CH_2$ groups], 2.40 (s, 1 H, OH), 3.43 (s, 3 H, OCH_3), 3.72 (t, 1 H, H-4), 3.78 (t, 1 H, H-6), 3.82 (dt, 1 H, H-5), 3.85 (d, 1 H, H-3), 4.27 (dd, 1 H, H-6′), 4.60 (s, 1 H, H-1), 4.86 (ABq, 2 H, CH_2Ph), 5.56 (s, 1 H, C*H*Ph); $J_{3,4} \approx J_{4,5} \approx J_{5,6} \approx J_{6,6'}$ 9.5, $J_{5,6'}$ 3.5 Hz. Anal. Calcd for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C, 70.07; H, 7.29.

*Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-triflyl-β-*D*-glucopyranoside* (**30**).—Prepared conventionally by triflation of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside [18] (700 mg), it was a slightly unstable solid (897 mg, 95%), mp 109–110

°C (decomp.) (lit. [16] 110–111 °C), $[\alpha]_D^{21}$ −51° (*c* 1.2 $CHCl_3$) {lit. [16] $[\alpha]_D$ −39.7° (*c* 0.6, $CHCl_3$)}; *m/z* 505.17 [$M^+ + 1$]; Calcd for $C_{22}H_{23}F_3O_8S$: *m/z* 504.11 for M^+; ^1H NMR ($CDCl_3$): δ 3.45 (dt, 1 H, H-5), 3.56 (s, 3 H, OCH_3), 3.74 (t, 1 H, H-4), 3.79 (t, 1 H, H-6), 3.87 (t, 1 H, H-3), 4.38 (dd, 1 H, H-6′), 4.50 (d, 1 H, H-1), 4.61 (t, 1 H, H-2), 4.84 (ABq, 2 H, CH_2Ph), 5.56 (s, 1 H, CHPh); $J_{1,2}$ 8, $J_{2,3} \approx J_{3,4} \approx J_{4,5}$ 9, $J_{5,6} \approx J_{6,6'}$ 10, $J_{5,6'}$ 5 Hz.

Reaction of **30** *with MeLi to form methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-methyl-β-*D*-glucopyranoside* (**31**) *and methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-methyl-β-*D*-mannopyranoside* (**32**).—Treatment of **30** (200 mg, 0.41 mmol) with MeLi (1.58 mmol) as before gave, after chromatography (3:2 hexane–EtOAc), **31** (from the faster-moving fractions) as a syrup (59 mg, 39%), $[\alpha]_D^{24}$ −43° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.32 (s, 3 H, H_3C-2), 2.12 (s, 1 H, OH), 3.48 (m, 1 H, H-5), 3.56 (s, 3 H, OCH_3), 3.6–3.7 (m, 2 H, H-3,4), 3.81 (t, 1 H, H-6), 4.27 (s, 1 H, H-1), 4.36 (dd, 1 H, H-6′), 4.87 (ABq, 2 H, CH_2Ph), 5.57 (s, 1 H, CHPh). ^1H NMR (pyridine-d_5): δ 1.73 (s, 3 H, H_3C-2), 3.55 (s, 3 H, OCH_3), 3.71 (dt, 1 H, H-5), 3.94 (t, 1 H, H-6), 3.97 (t, 1 H, H-4), 4.04 (d, 1 H, H-3), 4.49 (dd, 1 H, H-6′), 4.63 (s, 1 H, H-1), 5.20 (s, 2 H, CH_2Ph), 5.78 (s, 1 H, CHPh); $J_{3,4} \approx J_{4,5}$ 9.5, $J_{5,6} \approx J_{6,6'}$ 10.5, $J_{5,6'}$ 5 Hz. Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.37; H, 6.78. Found: C, 68.25; H, 6.55.

From the slower-moving fractions, **32** was obtained as a solid (79 mg, 52%), $[\alpha]_D^{24}$ −35° (*c* 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.25 (s, 3 H, CH_3), 2.31 (s, 1 H, OH), 3.38 (d, 1 H, H-3), 3.39 (dt, 1 H, H-5), 3.55 (s, 3 H, OCH_3), 3.91 (t, 1 H, H-6), 4.41 (t, 1 H, H-4), 4.19 (s, 1 H, H-1), 4.35 (dd, 1 H, H-6′), 4.87 (ABq, 2 H, CH_2Ph), 5.62 (s, 1 H, CHPh); $J_{3,4} \approx J_{4,5}$ 9.5, $J_{5,6} \approx J_{6,6'}$ 10.5, $J_{5,6'}$ 5 Hz. Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.37; H, 6.78. Found: C, 68.38; H, 6.48.

Reaction of **30** *with BuLi to form methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-butyl-β-*D*-glucopyranoside* (**33**) *and methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-butyl-β-*D*-mannopyranoside* (**34**).—Treatment of **30** (200 mg, 0.40 mmol) and BuLi (1.19 mmol) as before gave, after chromatography (3:2 hexane–EtOAc), **33** (from the faster-moving fractions) as a syrup (31 mg, 18%), $[\alpha]_D^{24}$ −47° (*c* 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.92 [t, *J* 7 Hz, 3 H, $CH_3(CH_2)_3$–], 1.33 and 1.56 [each m of 2 H, $CH_3(CH_2)_2CH_2$–], 1.77 and 1.84 [mirror-imaged two multiplets, $CH_3(CH_2)_2CH_2$–], 2.22 (s, 1 H, OH), 3.47 (dt, 1 H, H-5), 3.53 (s, 3 H, OCH_3), 3.63 (d, 1 H, H-3), 3.73 (t, 1 H, H-4), 3.81 (t, 1 H, H-6), 4.25 (s, 1 H, H-1), 4.35 (dd, 1 H, H-6′), 4.85 (ABq, 2 H, CH_2Ph), 5.57 (s, 1 H, CHPh); $J_{3,4} \approx J_{4,5}$ 9.5, $J_{5,6} \approx J_{6,6'}$ 10.5, $J_{5,6'}$ 4.5 Hz. Anal. Calcd for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C,69.89; H, 7.31.

From the slower-moving fractions **34** was obtained as a syrup (100 mg, 59%), $[\alpha]_D^{24}$ +5° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.83 [t, 3 H, $CH_3(CH_2)_3$–], 0.90 [m, 1 H, one of the $CH_3(CH_2)_2CH_2$–], 1.04–1.26 [m, 3 H, three of the $CH_3(CH_2)_2CH_2$–], 1.62 and 1.78 [each dt of 1 H, *J* 4, 13, 13 Hz, $CH_3(CH_2)_2CH_2$–], 2.27 (s, 1 H, OH), 3.37 (dt, 1 H, H-5), 3.53 (s, 3 H, OCH_3), 3.58 (d, 1 H, H-3), 3.90 (t, 1 H, H-6), 4.20 (t, 1 H, H-4), 4.31 (s, 1 H, H-1), 4.34 (dd, 1 H, H-6′), 4.86 (ABq, 2 H, CH_2Ph), 5.63 (s, 1 H, CHPh); $J_{3,4} \approx J_{4,5}$ 9.5, $J_{5,6} \approx J_{6,6'}$, 10.5, $J_{5,6'}$ 5.0 Hz. Anal. Calcd for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C, 70.34; H, 7.35.

*Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-*D*-glucopyranoside* (**35**).—Prepared by triflation of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside [18,19]

(410 mg) in the standard manner; it was a slightly unstable solid (516 mg, 93%), mp 96–97 °C (decomp.; from MeOH), $[\alpha]_D^{24}$ −0.5° (*c* 3, $CHCl_3$); *m/z* 505.17 [M^+ + 1]; Calcd for $C_{22}H_{23}F_3O_8S$: *m/z* 504.11 for M^+; ^1H NMR ($CDCl_3$): δ 3.34 (s, 3 H, OCH_3), 3.64 (dd, 1 H, H-2), 3.70 (t, 1 H, H-4), 3.72 (t, 1 H, H-6), 3.83 (dt, 1 H, H-5), 4.29 (dd, 1 H, H-6′), 4.55 (d, 1 H, H-1), 4.57 and 4.83 (each d of 1 H, *J* 12 Hz, CH_2Ph), 5.21 (t, 1 H, H-3), 5.54 (s, 1 H, C*H*Ph); $J_{1,2}$ 4, $J_{2,3} \approx J_{3,4} \approx J_{4,5}$ 9.5, $J_{5,6} \approx J_{6,6'}$ 10, $J_{5,6'}$ 4.5 Hz. Anal. Calcd for $C_{22}H_{23}F_3O_8S$: C, 52.38; H, 4.59; S, 6.36. Found: C, 52.55; H, 4.60; S, 6.38.

Reaction of **35** *with BuLi to form methyl* 2-O-*benzyl-4,6-*O-*benzylidene-3-deoxy-α-*D-erythro-*hex-2-enopyranoside* (**36**) *and methyl* 2-O-*benzyl-4,6-*O-*benzylidene-3-deoxy-α-*D-erythro-*hex-3-enopyranoside* (**37**).—Treatment of **35** (500 mg, 0.99 mmol) with BuLi (2.97 mmol) as described in the general procedure (chromatography: 4:1 hexane–EtOAc) gave **36** (from the faster-moving fractions) as needles (178 mg, 51%), mp 133–134 °C, $[\alpha]_D^{22}$ +21° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.50 (s, 3 H, OCH_3), 3.82 (t, 1 H, H-6), 4.00 (ddd, 1 H, H-5), 4.28 (dd, 1 H, H-4), 4.30 (dd, 1 H, H-6′), 4.81 (s, 1 H, H-1), 4.83 (ABq, 2 H, CH_2Ph), 5.07 (d, 1 H, H-3), 5.57 (s, 1 H, C*H*Ph); $J_{3,4}$ 1.5, $J_{4,5}$ 9, $J_{5,6} \approx J_{6,6'}$ 10, $J_{5,6'}$ 4.5 Hz. ^{13}C NMR ($CDCl_3$): δ 56.16 (OCH_3), 65.05 (C-5), 69.13 (C-6), 69.74 (*C*H_2Ph), 76.08 (C-4), 96.80 (C-1), 98.36 (C-3), 101.99 (*C*HPh); 126.34 (2 C), 127.54 (2 C), 128.07, 128.36 (2 C), 128.53 (2 C), and 129.16 [2 (*C*H)$_5$C of Ph]; 136.14 and 137.45 [2 (CH)$_5$*C* of Ph; no C–H coupling], 152.98 (C-2; no C–H coupling). Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 70.88; H, 6.33.

From the slower-moving fractions **37** was obtained as needles (82 mg, 23%), mp 108–109 °C, $[\alpha]_D^{22}$ +51° (*c* 2.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.51 (s, 3 H, OCH_3), 3.70 (t, 1 H, H-6), 4.30 (dd, 1 H, H-6′), 4.33 (m, 1 H, H-2), 4.37 (m, 1 H, H-5), 4.64 (ABq, *J* 12.5 Hz, 2 H, CH_2Ph), 4.80 (dd, 1 H, H-1), 5.34 (small range m, 1 H, H-3), 5.54 (s, 1 H, C*H*Ph); $J_{1,2}$ 4.5, $J_{1,3} \sim 0.5$, $J_{2,3} \approx J_{3,5}$ 2, $J_{5,6} \approx J_{6,6'}$ 10.5, $J_{5,6'}$ 6.5 Hz. ^{13}C NMR ($CDCl_3$): δ 55.99 (OCH_3), 60.47 (C-5), 69.70 (C-6), 71.07 (*C*H_2Ph), 71.45 (C-2), 96.75 (C-1), 103.25 (C-3 and *C*HPh); 120.27 (2 C), 127.84, 127.94 (2 C), 128.40 (2 C), 128.46 (2 C), and 129.49 [2 (*C*H)$_5$C of Ph]; 136.60 and 138.14 [2 (CH)$_5$*C* of Ph; no C-H coupling], 152.16 (C-4; no C–H coupling). Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 70.90; H, 6.12.

Methyl 2-O-*benzyl-4,6-*O-*benzylidene-3-*O-*triflyl-β-*D-*glucopyranoside* (**38**).—Prepared from methyl 2-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside [18] (700 mg) in the standard manner; it was a slightly unstable solid (918 mg, 97%). An analytical sample was prepared as described for **18**, mp 85–86 °C (decomp.), $[\alpha]_D^{25}$ −33° (*c* 0.5, $CHCl_3$); *m/z* 505.20 [M^+ + 1]; Calcd for $C_{22}H_{23}F_3O_8S$: *m/z* 504.11 for M^+; ^1H NMR ($CDCl_3$): δ 3.44 (dt, 1 H, H-5), 3.57 (dd, 1 H, H-2), 3.59 (s, 3 H, OCH_3), 3.78 (t, 1 H, H-4), 3.81 (t, 1 H, H-6), 4.41 (dd, 1 H, H-6′), 4.48 (d, 1 H, H-1), 4.82 (ABq, *J* 10.5 Hz, 2 H, CH_2Ph), 4.95 (t, 1 H, H-3), 5.56 (s, 1 H, C*H*Ph); $J_{1,2}$ 7.8, $J_{2,3} \approx J_{3,4} \approx J_{4,5}$ 9.5, $J_{5,6} \approx J_{6,6'}$ 10, $J_{5,6'}$ 5.0 Hz. Anal. Calcd for $C_{22}H_{23}F_3O_8S$: C, 52.38; H, 4.59; S, 6.36. Found: C, 52.19; H, 4.81; S, 6.07.

Reaction of **38** *with MeLi to form methyl* 2-O-*benzyl-4,6-*O-*benzylidene-3-deoxy-β-*D-erythro-*hex-2-enopyranoside* (**39**).—Treatment of **38** (82 mg, 0.16 mmol) with MeLi (0.64 mmol) as described in the general procedure (chromatography: 4:1 hexane–EtOAc) gave **39** as a syrup (21 mg, 36%) along with a mixture of unknown products (14 mg)

which included no *C*-methyl compound (as checked by the ^{1}H NMR), $[\alpha]_D^{24}$ −38° (*c* 0.6, $CHCl_3$); *m/z* 355.25 [M^+ + 1]; Calcd for $C_{21}H_{22}O_5$: *m/z* 354.15 for M^+; ^{1}H NMR ($CDCl_3$): δ 3.48 (s, 3 H, OCH_3), 3.67 (ddd, 1 H, H-5), 3.89 (t, 1 H, H-6), 4.32 (dd, 1 H, H-6′), 4.39 (dt, 1 H, H-4), 4.84 (s, 2 H, CH_2Ph), 5.21 (sl, br s, 1 H, H-3), 5.30 (d, 1 H, H-1), 5.61 (s, 1 H, C*H*Ph); $J_{1,4}$ ~ 1, $J_{3,4}$ 1.8, $J_{4,5}$ 8.5, $J_{5,6} \approx J_{6,6'}$ 10.3, $J_{5,6'}$ 5.0 Hz.

*Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-allopyranoside* (**40**).—To a cold (−78 °C) solution of oxalyl chloride (0.41 g) in CH_2Cl_2 (20 mL), Me_2SO (0.5 g) was added, and after 15 min, methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside [18,19] (1.00 g, 2.68 mmol) in CH_2Cl_2 (10 mL) was added gradually in the cold and the mixture was stirred for 30 min. After addition of Et_3N (1.36 g), the mixture was warmed to room temperature and kept for 30 min. Water (30 mL) was added, and the organic layer separated was washed with water, dried (Na_2SO_4), and concentrated. The resulting crystalline residue was dissolved in 1:2 CH_2Cl_2–MeOH (100 mL) and $NaBH_4$ (203 mg) was added. After 1 h, dry ice was added, and the solvent was evaporated to give a residue, which was chromatographed with 2:1 hexane–EtOAc to give **40** as needles (921 mg, 92%), mp 73 °C, $[\alpha]_D^{25}$ +5° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.19 (d, 1 H, OH), 3.42 (dd, 1 H, H-4), 3.46 (s, 3 H, OCH_3), 3.51 (t, 1 H, H-2), 3.71 (t, 1 H, H-6), 4.16 (dt, 1 H, H-5), 4.35 (dd, 1 H, H-6′), 4.45 (dt, 1 H, H-3), 4.70 (ABq, 2 H, CH_2Ph), 4.76 (d, 1 H, H-1), 5.53 (s, 1 H, C*H*Ph); $J_{1,2} \approx J_{2,3}$ 3.5, $J_{3,OH}$ 7, $J_{3,4}$ 3, $J_{4,5} \approx J_{5,6} \approx J_{6,6'}$ ~ 10, $J_{5,6'}$ 5.0 Hz. Anal. Calcd for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.39; H, 6.21.

*Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-*D*-allopyranoside* (**41**).—Prepared from **40** (500 mg) in the standard manner; it was a slightly unstable solid (612 mg, 90%). An analytical sample was prepared by passing it through a Silica Gel column with 2:1 hexane–EtOAc, mp 87–89 °C (decomp.), $[\alpha]_D^{23}$ −3° (*c* 3, $CHCl_3$); *m/z* 505.17 [M^+ + 1]; Calcd for $C_{22}H_{23}F_3O_8S$: *m/z* 504.11 for M^+; ^{1}H NMR ($CDCl_3$): δ 3.45 (s, 3 H, OCH_3), 3.58 (t, 1 H, H-2), 3.61 (dd, 1 H, H-4), 3.68 (t, 1 H, H-6), 4.18 (dt, 1 H, H-5), 4.33 (dd, 1 H, H-6′), 4.70 (d, 1 H, H-1), 4.71 (ABq, 2 H, CH_2Ph), 5.43 (t, 1 H, H-3), 5.52 (s, 1 H, C*H*Ph); $J_{1,2} \approx J_{2,3}$ 3.5, $J_{3,4}$ 2.5, $J_{4,5} \approx J_{5,6} \approx J_{6,6'}$ ~ 10, $J_{5,6'}$ 5.0 Hz. Anal. Calcd for $C_{22}H_{23}F_3O_8S$: C, 52.38; H, 4.59; S, 6.36. Found: C, 52.38; H, 4.68; S, 6.66.

Reaction of **41** *with MeLi.*—Treatment of **41** (113 mg, 0.22 mmol) with MeLi (0.88 mmol) as described for **36** gave a solid (72 mg, 91%) identical with **36** obtained from **35** in all respects.

Reaction of **42** *with MeLi.*—Treatment of **42** [35] (450 mg, 0.75 mmol) with MeLi (3 mmol) as described in the general procedure (chromatography: 2:1 hexane–EtOAc) gave the detriflated product **43** as a syrup (281 mg, 80%), $[\alpha]_D^{24}$ +13° (*c* 2, $CHCl_3$) (lit. [20] +13° in $CHCl_3$).

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-triflyl-α-*D*-galactopyranoside* (**44**) *[7] and methyl 4-deoxy-2,3,6-tri-*O*-benzyl-4-(pyridinium-1-yl)-α-*D*-glucopyranoside triflate* (**45**).—*Method A.* To a cold (−30 °C) solution of methyl 2,3,6-tri-*O*-benzyl-α-D-galactopyranoside [51] (500 mg, 1.07 mmol) in dry pyridine (7 mL) was added $(CF_3SO_2)_2O$ (400 mg 1.4 mmol) and the solution was kept for 4 h at −10 °C. Water (20 mL) and $CHCl_3$ (100 mL) were added, and, after shaking for a while, the organic solution separated was washed successively with aq M HCl (50 mL × 3), aq $NaHCO_3$ (saturated), and water, dried (Na_2SO_4), and concentrated to give **44** as an unstable syrup (551 mg, 86%), TLC

(5:1 hexane–EtOAc): R_f 0.25, $[\alpha]_D^{23}$ +28° (*c* 3, $CHCl_3$) (lit. [7] no data reported); *m/z* 595.22 [$M^+ - 1$]; Calcd for $C_{29}H_{31}F_3O_8S$: *m/z* 596.17 for M^+; ^1H NMR ($CDCl_3$): δ 3.36 (s, 3 H, OCH_3), 3.55 (dd, 1 H, H-6), 3.60 (dd, 1 H, H-6′), 3.78 (dd, 1 H, H-2), 3.98 (dd, 1 H, H-3), 4.07 (dd, 1 H, H-5), 4.62 (d, 1 H, H-1), 5.40 (d, 1 H, H-4); $J_{1,2}$ 3.5, $J_{2,3}$ 10, $J_{3,4}$ 3, $J_{4,5}$ ~ 0, $J_{5,6}$ 8.0, $J_{5,6'}$ 6.0, $J_{6,6'}$ 9.2 Hz.

Method B. To a cold (−30 °C) solution of the same 4-hydroxy precursor (500 mg, 1.07 mmol) in pyridine (7 mL) was added $(CF_3SO_2)_2O$ (400 mg, 1.4 mmol) and the solution was kept for 1 h at room temperature. Water (1 mL) was added, and the excess solvent was evaporated under diminished pressure at 35 °C (bath temperature). The $CHCl_3$ solution of the residue was washed with water, dried (Na_2SO_4), and concentrated. The residue was chromatographed (5:1 hexane–EtOAc) to give **44** as a syrup (95 mg, 15%) and subsequent elution with 5:1 $CHCl_3$–CH_3OH gave **45** as a syrup (487 mg, 67%), TLC (5:1 $CHCl_3$–CH_3OH): R_f 0.45, $[\alpha]_D^{23}$ 0° (*c* 4.5, $CHCl_3$); *m/z* 526.27 [M^+]; Calcd for $C_{33}H_{36}NO_5$: *m/z* 526.26; ^1H NMR ($CDCl_3$): δ 3.22 (dd, 1 H, H-6), 3.47 (s, 3 H, OCH_3), 3.64 (dd, 1 H, H-6′), 3.74 (dd, 1 H, H-2); 4.14 (1 H), 4.37 (2 H), 4.67 (1 H), 4.71 (1 H), and 4.81 (1 H) (each d of *J* 12.0 Hz, 3 CH_2Ph), 4.30 (dd, 1 H, H-3), 4.42 (dt, 1 H, H-5), 4.50 (dd, 1 H, H-4), 4.75 (d, 1 H, H-1); 6.79 (2 H), 7.11 (5 H), 7.26 (3 H), 7.39 (5 H) (each m, 3 CH_2Ph); 7.63 (2 H), 8.16 (1 H), 8.38 (2 H) (each m, C_5H_5N); $J_{1,2}$ 3.2, $J_{2,3}$ 8.8, $J_{3,4}$ 10, $J_{4,5}$ 10.5, $J_{5,6}$ 3.0, $J_{5,6'}$ 3.5, $J_{6,6'}$ 11.2 Hz. ^{19}F NMR ($CDCl_3$): δ −78.64 (s, CF_3SO_3; identical with the shift of pyridinium trifluoromethanesulfonate in $CDCl_3$).

Reaction of **44** *with MeLi to form methyl 2,3,6-tri-*O*-benzyl-4-deoxy-β-*L*-threo-hex-4-enopyranoside* (**46**).—Treatment of **44** (61 mg, 0.1 mmol) with MeLi (0.41 mmol) as described in the general procedure (chromatography: 3:1 hexane–EtOAc) gave **46** as a syrup (20 mg, 45%) together with unknown compound(s), $[\alpha]_D^{22}$ +78° (*c* 1, $CHCl_3$); *m/z* 447.32 [$M^+ + 1$]; Calcd for $C_{28}H_{30}O_5$: *m/z* 446.21 for M^+; ^1H NMR ($CDCl_3$): δ 3.49 (s, 3 H, OCH_3), 3.78 (dd, 1 H, H-2), 3.92 (sl. br s, 2 H, H-6,6′), 4.23 (ddt, 1 H, H-3), 4.54 (ABq, 2 H, CH_2Ph), 4.63 (s, 2 H, CH_2Ph), 4.77 (ABq, 2 H, CH_2Ph), 4.85 (d, 1 H, H-1), 5.04 (d, 1 H, H-4); $J_{1,2}$ 2.5, $J_{2,3}$ 7, $J_{3,4}$ 3, $J_{3,6} \approx J_{3,6'}$ ~ 1 Hz.

*Methyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-α-*D*-(4-^{2}H)galactopyranoside* (**49**).—A solution of **43** [18] (11.0 g, 23.7 mmol) in 3:2 Me_2SO–Ac_2O (200 mL) was kept for 48 h at room temperature. Aq 2 M Na_2CO_3 (500 mL) was added and the mixture was extracted with $CHCl_3$ (200 mL × 2). The organic solution was washed with water (100 mL × 3), dried (Na_2SO_4), and concentrated to give a yellow syrup. To an ice-cold solution of the syrup in MeOH (100 mL), $NaBD_4$ (1.98 g, 47.4 mmol) was added, and the solution was kept for 30 min at room temperature. Excess CO_2 (dry ice) was added, and the solution was concentrated. The resulting residue was chromatographed (20:1 $CHCl_3$–Et_2O) to give a ~ 6:1 mixture (checked by ^1H NMR) of **47** and **48** (9.23 g, 84%) with the same mobility. To an ice-cold solution of the mixture (9.00 g, 19.3 mmol) in 1:1 pyridine–CH_2Cl_2 (150 mL), B_zCl (1.12 mL, 9.7 mmol) was added dropwise, and the solution was kept for 24 h at room temperature. Water (1 mL) was added, and the solution was concentrated to give a residue, which was chromatographed (4:1 hexane–EtOAc) to give **49** as a syrup (5.23 g, 47% based on the starting mixture) together with a mixture of **47** and **48** (rich in **48**). Compound **49**, $[\alpha]_D^{21}$ +31° (*c* 2.7, $CHCl_3$); *m/z* 538.32 [$M^+ -$ OMe],

570.30 [$M^+ + 1$]; Calcd for $C_{35}H_{35}DO_7$: *m/z* 569.25 for M^+; ^1H NMR ($CDCl_3$): δ 3.43 (s, 3 H, OCH_3), 3.54 (d, 2 H, H-6,6'), 3.91 (dd, 1 H, H-2), 4.07 (d, 1 H, H-3), 4.15 (t, 1 H, H-5), 4.45 (ABq, 2 H, CH_2Ph), 4.59 and 4.835 (each d of 1 H, CH_2Ph), 4.66 and 4.83 (each d of 1 H, CH_2Ph), 4.76 (d, 1 H, H-1); $J_{1,2}$ 3.5, $J_{2,3}$ 10, $J_{5,6} \approx J_{5,6'}$ 6.3 Hz.

*Methyl 2,3,6-tri-*O*-benzyl-α-*D*-(4-^{2}H)galactopyranoside* (**47**).—Zemplén debenzoylation of **49** (5.0 g, 8.78 mmol) in MeOH (50 mL) gave **47** as a syrup (4.08 g, quant.), $[\alpha]_D^{21}$ +32° (*c* 1.6, $CHCl_3$) (compare non-deuterated isomer [51,52] of **47**: $[\alpha]_D^{22}$ +35° (*c* 1, $CHCl_3$) [52]); *m/z* 434.27 [$M^+ - OCH_3$], 464.27 [$M^+ - 1$], 466.27 [$M^+ + 1$]; Calcd for $C_{28}H_{31}DO_6$: *m/z* 465.23 for M^+.

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-triflyl-α-*D*-(4-^{2}H)galactopyranoside* (**50**).—Triflation of **47** (3.50 g) was carried out in a manner as described for **44** (Method A) to give **50** as a syrup (4.15 g, 92%), $[\alpha]_D^{22}$ +30° (*c* 1, $CHCl_3$) (cf. **44**: $[\alpha]_D^{23}$ +28°); *m/z* 506.19 [$M^+ - CH_2C_6H_5$], 596.22 [$M^+ - 1$]; Calcd for $C_{29}H_{30}DF_3O_8S$: *m/z* 597.18 for M^+; ^1H NMR ($CDCl_3$): δ 3.37 (s, 3 H, OCH_3), 3.55 (dd, 1 H, H-6), 3.60 (dd, 1 H, H-6'), 3.78 (dd, 1 H, H-2), 3.98 (d, 1 H, H-3), 4.07 (dd, 1 H, H-5), 4.62 (d, 1 H, H-1); $J_{1,2}$ 3.5, $J_{2,3}$ 10, $J_{5,6}$ 8.0, $J_{5,6'}$ 6.0, $J_{6,6'}$ 9.0 Hz.

*Methyl 4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-α-*D*-(4-^{2}H)glucopyranoside* (**51**).—A mixture of **50** (4.00 g, 6.69 mmol) and dried $C_6H_5CO_2Na$ (1.93 g, 13.4 mmol) in DMF (20 mL) was heated for 3 h at 70 °C. After addition of water (50 mL), the mixture was extracted with $CHCl_3$ (70 mL × 3) and the organic solution was washed with water, dried (Na_2SO_4), and concentrated. Chromatography (4:1 hexane–EtOAc) of the residue gave **51** as a syrup (3.47 g, 91%), $[\alpha]_D^{22}$ −10° (*c* 2.7, $CHCl_3$); *m/z* 538.25 [$M^+ - OCH_3$], 568.22 [$M^+ - 1$], 570.22 [$M^+ + 1$]; Calcd for $C_{35}H_{35}DO_7$: *m/z* 569.25 for M^+.

*Methyl 2,3,6-tri-*O*-benzyl-α-*D*-(4-^{2}H)glucopyranoside* (**48**).—Zemplén debenzoylation of **51** (3.20 g) gave **48** as a syrup (2.51 g, 96%), $[\alpha]_D^{22}$ +12° (*c* 1.3, $CHCl_3$) (cf. **43**: $[\alpha]_D^{24}$ +13°); *m/z* 434.22 [$M^+ - OCH_3$], 464.21 [$M^+ - 1$]; Calcd for $C_{28}H_{31}DO_6$: *m/z* 465.23 for M^+.

*1,2;5,6-Di-*O*-isopropylidene-α-*D*-(4-^{2}H)glucofuranose* (**52**).—A solution of **48** (2.40 g, 5.15 mmol) in 5:1:1 EtOH–H_2O–AcOH (70 mL) was shaken in the presence of Pd-black under 3 atm pressure of H_2 for 5 h at room temperature. After filtration, the solution was concentrated. A solution of the residue in 1:1 CF_3CO_2H–aq 35% HCl was refluxed for 5 h, concentrated under intermittent additions of water, and the residue obtained was dried well, which was dissolved in acetone (30 mL) containing $ZnCl_2$ (3 g) and H_3PO_4 (0.2 mL) and the mixture was stirred for 30 h at room temperature. Aq 20% NaOH was added until the solution became slightly alkaline, and the clarified solution was concentrated. The residue was extracted with $CHCl_3$ and the soluble material was chromatographed (2:1 toluene–EtOAc) to give **52** as crystals (673 mg, 50%), mp 106–108 °C (cf. **1**: mp 105–109 °C [53]), $[\alpha]_D^{22}$ −8.3° (*c* 1.8, $CHCl_3$) (cf. **1**: $[\alpha]_D^{20}$ −13.5° [53]); *m/z* 246.17 [$M^+ - CH_3$], 262.18 [$M^+ + 1$]; Calcd for $C_{12}H_{19}DO_6$: *m/z* 261.13 for M^+; ^1H NMR ($CDCl_3$): δ 1.32, 1.37, 1.45, and 1.50 [each s of 3 H, 2 $C(CH_3)_2$], 2.64 (br d, 1 H, OH), 3.99 (dd, 1 H, H-6), 4.17 (dd, 1 H, H-6'), 4.30–4.37 (m, 2 H, H-3,5), 4.54 (d, 1 H, H-2), 5.95 (d, 1 H, H-1); $J_{1,2}$ 3.5, $J_{5,6}$ 5.3, $J_{5,6'}$ 6.0, $J_{6,6'}$ 8.5 Hz.

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