ELSEVIER

Carbohydrate Research 303 (1997) 267–281

CARBOHYDRATE RESEARCH

α- And β-hydrogen eliminations in the reactions of some 3-*O*-triflylglycosides with ^{t}BuOK and pyridine

Ahmed El Nemr, Tsutomu Tsuchiya *

Institute of Bioorganic Chemistry, 3-34-17 Ida, Nakahara-ku, Kawasaki 211, Japan

Received 25 February 1997; accepted in revised form 30 May 1997

Abstract

Previous papers [10–12] reported new reactions that occur when some carbohydrate triflates are treated with MeLi (or BuLi) in Et_2O to give the *C*-methyl(butyl) or unsaturated compounds through elimination of the CH-hydrogen bearing a CF_3SO_3 group (α-elimination) as a proton. This paper extends the previous work and describes the reactions for some 3-*O*-triflyl-D-gluco- and -allo-furanosides and -pyranosides with ^{t}BuOK and pyridine [instead of Me(Bu)Li], utilizing the corresponding 2- and 3-deuterated analogs. It was found that, when ^{t}BuOK was used, the 3-*O*-triflyl-D-glucopyranosides gave 2,3- and 3,4-unsaturated compounds through α-hydrogen elimination (α-elimination) followed by (possibly) C-3 carbene formation, while the 3-*O*-triflyl-D-allopyranosides gave mainly 2,3-unsaturated compounds through β-elimination. When pyridine was used, most of the compounds gave the corresponding 3-pyridinium derivatives through an SN2 process. © 1997 Elsevier Science Ltd.

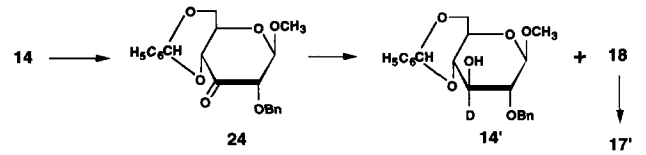
Keywords: Triflate; Unsaturation; ^{t}BuOK; Pyridine; Deuterated compound; α-Elimination; β-Elimination; Carbene; 1 → 2 Proton-shift

1. Introduction

Trifluoromethanesulfonylation (triflation) of hydroxyl groups in carbohydrates is widely used in substitution reactions [1] in view of the effective electron-withdrawing character of the trifluoromethyl group [2,3]. Other reactions sometimes encountered with triflates are elimination, ring-contraction [4–8], and ring-opening reactions [9], all of which take place through loss of a CF_3SO_3H fragment. However, we recently discovered [10,11] that, when 1,2;5,6-di-*O*-isopropylidene-3-*O*-triflyl-α-D-allofuranoside was treated with MeLi (or BuLi) in diethyl ether, a compound produced by neither substitution, elimination, nor ring-contraction was formed by loss of a CF_3SO_2H fragment; this compound was proved to be a 3-*C*-methyl(or butyl)-α-D-allofuranoside initiated via elimination of H-3. The structurally related 1,2;5,6-di-*O*-isopropylidene-3-*O*-triflyl-α-D-glucofuranoside, treated similarly, gave a 3-eno compound, although the reaction also proceeded through the H-3-hydrogen elimination. This difference in prod-

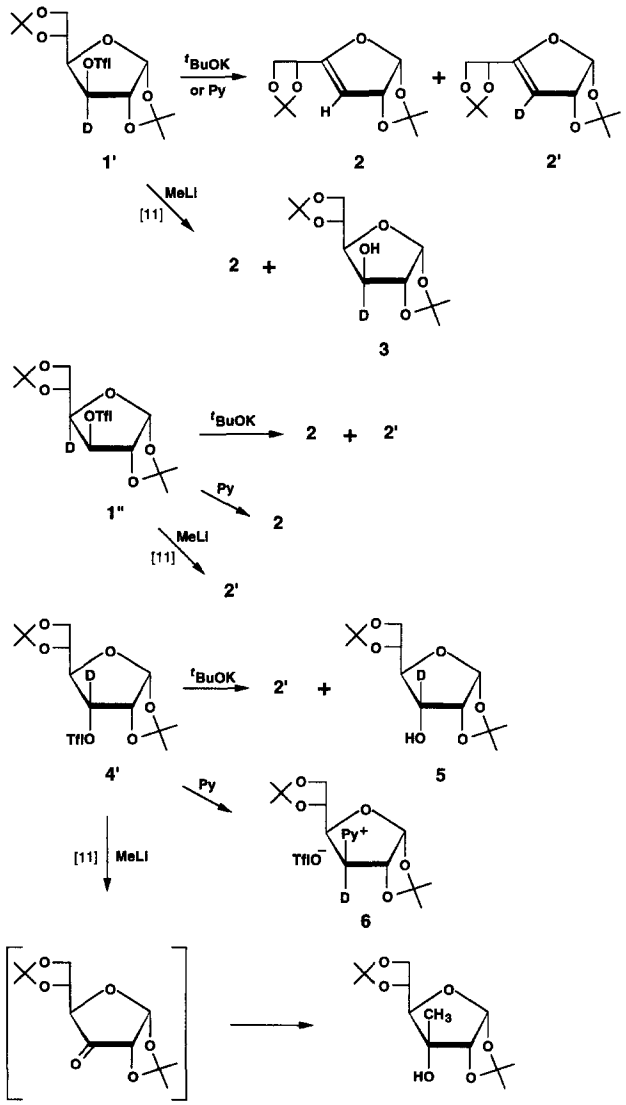
* Corresponding author.

PII S0008-6215(97)00168-7



Scheme 1.

ucts initiated from the same H-3 elimination (α-elimination) was explained on the basis of the difference in relative positions (cis or trans) between the lone-pair electrons and a vicinal hydrogen [11] in the C-3 carbanion formed. Our work then progressed to investigation of several 2-, 3-, and 4-triflates of glycopyranosides, and it was found that the 2-triflates gave the corresponding 2-*C*-alkyl derivatives, whereas the 3- and 4-triflates gave the 2,3-, 3,4-, or 4,5-unsaturated compounds. The difference in products between the 2- and 3-(or 4-)triflates was explained on the basis of the difference in stability of the transition states [11]. The mechanism of the reactions of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-D-gluco- and -allo-pyranosides was subsequently studied in detail [12] utilizing some deuterated analogs, and it was concluded that the former compounds gave 2,3- and 3,4-unsaturated compounds through α-hydrogen (H-3) elimination (to give the C-3 carbanion) with subsequent formation of C-3 carbene, while the latter compounds gave a 2,3-unsaturated compound through α- or β-hydrogen elimination (to give the C-3 and C-2 carbanions, respectively) with subsequent migration, for the α-elimination, of the H-2-hydrogen to C-3 as a proton (that is, a $1 \rightarrow 2$ proton-shift). The present study describes the reactions of the 3-triflates



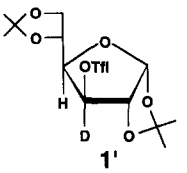
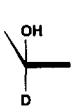
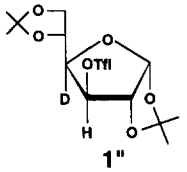
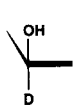
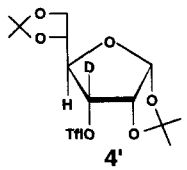
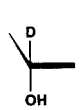
Scheme 2.

mainly used in the previous papers [10–12], with ^{t}BuOK or pyridine chosen as typical strong and weak bases, respectively, using several deuterated analogs, to clarify the difference in chemical behavior resulting from changing the reagent from MeLi (BuLi) to the foregoing two bases.

2. Results and discussion

Synthesis of deuterated triflates.—The 3- and 4-deuterated analogs (**1′** and **1″**) of 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranoside (**1**) and the 3-deuterated analog **4′** of 1,2;5,6-di-*O*-isopropylidene-α-D-allofuranoside (**4**) were prepared according to the procedure described in ref. [11]. The 2- and 3-deuterated analogs (**7″** and **7′**) of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-D-glucopyranoside (**7**) and the 2- and 3-deuterated analogs (**15″** and **15′**) of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-D-allopyranoside (**15**) were prepared according to the procedure reported [12]. The 3-deuterated analog **11′** of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-β-D-glucopyranoside (**11**) was prepared by triflation of the corresponding 3-hydroxy precursor [12]. The 3-deuterated analog **17′** of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-β-D-allopyranoside (**17**) was prepared by a series of reactions including Swern oxidation of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**14**) [13,14] giving the 3-oxo derivative **24** (see Scheme 1), reduction of **24** with $NaBD_4$ giving a mixture of 3-deuterated D-gluco (**14′**) and D-allo compounds (**18**, major), and finally triflation of **18**.

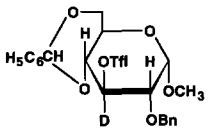
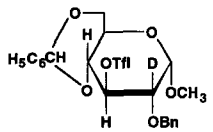
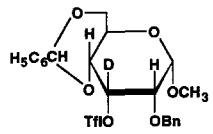
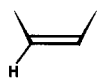
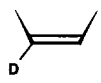
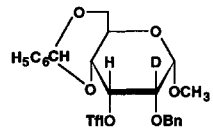
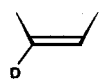
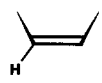
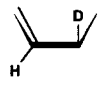
Table 1
The product yields[a] for comparison of the reactions of **1′**, **1″**, and **4′** with MeLi, ^{t}BuOK, pyridine, and NaOMe

Starting material	Products			Reference
	α-elim.	β-elim.	3-ol	
 **1′**	 **2**	 **2′**	 **3**	
MeLi	65		24	[11]
^{t}BuOK	7	67		
pyridine	13	55		
NaOMe		13	84	
 **1″**	 **2′**	 **2**	 **3**	
MeLi	59		20	[11]
^{t}BuOK	7	61		
pyridine		63		
 **4′**	 **2**	 **2′**	 **5**	
MeLi				[11]
^{t}BuOK	0	52	18	
pyridine **6**				

[a] Isolated yields; as **2** and **2′** could not be separated, their yields were calculated based on the intensity of the H-3 peak of **2** in the ^{1}H NMR spectra.

Reactions of undeuterated and deuterated 3-triflates with ^{t}BuOK, pyridine, or NaOMe.—At first the 3-deuterio- (**1′**) and 4-deuterio-3-triflates **1″** having the furanoside structure were treated with ^{t}BuOK in diethyl ether, whereupon each of them gave a mixture of unlabeled (**2**) and 3-labeled 3,4-unsaturated compounds **2′** in a ratio of 1:9 (for **1′**) and 9:1 (for **1″**) (see Scheme 2). This indicates that the ratio of α-/β-hydrogen elimination is not affected by the positions of deuterium, and the β-elimination is strongly preponderant. This result was, however, different from that obtained with MeLi (BuLi), when only α-elimination was observed. When, however, the 3-deuterio-3-triflate **4′** of allo structure was treated with ^{t}BuOK, the labeled 3,4-unsaturated compound **2′** was produced (52%) by β-elimination as the only unsaturated compound, together with the detriflyl 3-ol (**5**, 18%). This is in sharp contrast with the result obtained with MeLi, when a 3-oxo compound was formed as the key intermediate (Table 1).

Table 2
The product yields[a] for comparison of the reactions of **7′**, **7″**, **15′**, and **15″** with MeLi, BuLi, and ^{t}BuOK

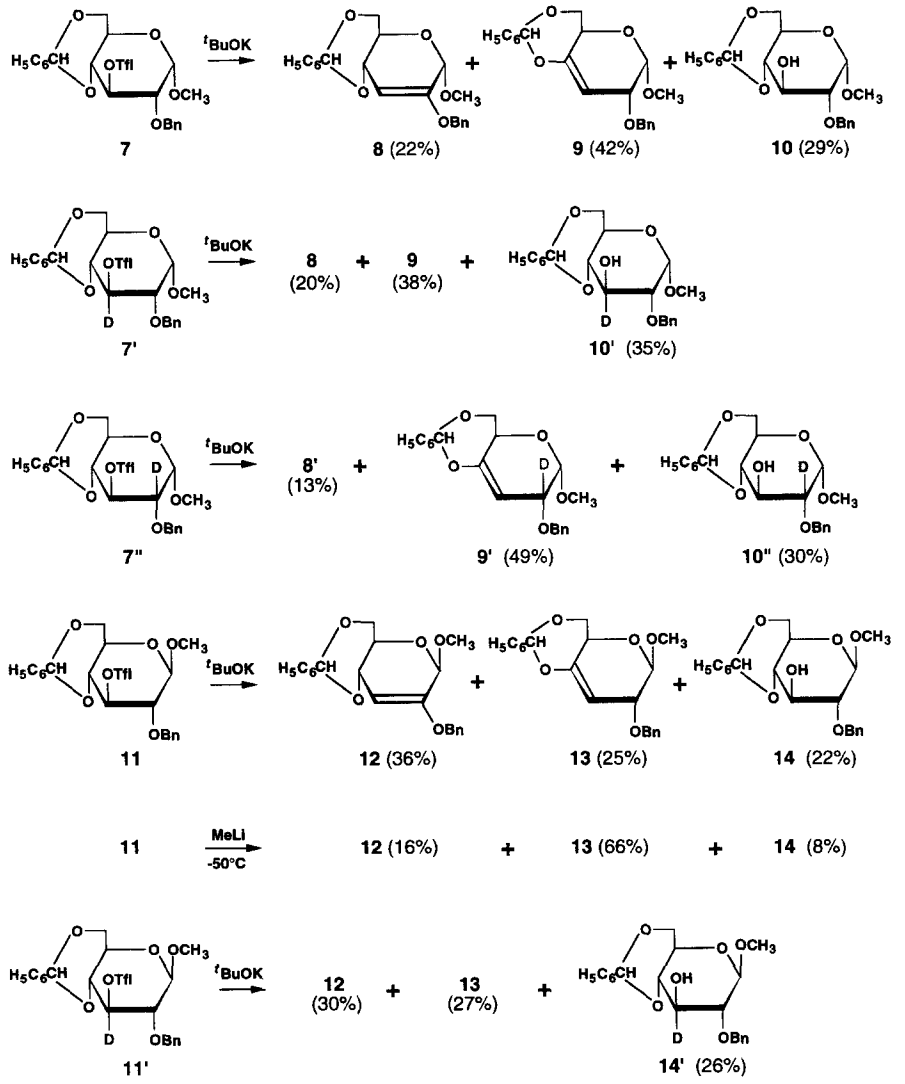
Starting material	Products				Reference
	α-elim.	β-elim.	α-elim.	3-ol	
					
7′	**8**	**8′**	**9**	**10′**	
MeLi	50 (49)	0 (0)	37 (35)	t	[12]
BuLi	42 (40)	1 (1)	27 (25)	15 (19)	[12]
^{t}BuOK	20	1.5	38	35	
					
7″	**8′**	**8**	**9′**	**10″**	
MeLi	43 (39)	0 (0)	35 (30)	t	[12]
BuLi	42 (40)	0 (0)	19 (16)	18 (22)	[12]
^{t}BuOK	13	0	49	30	
					
15′	**8**	**8′**		**16′**	
MeLi	32	48			[12]
BuLi	55	20			[12]
^{t}BuOK	1.5	86		6	
			β-elim.[b] 		
15″	**8′**	**8**	**9′**	**16″**	
MeLi	81	1			[12]
BuLi	71	1			[12]
^{t}BuOK	0	82	4	9	

[a] Isolated yields; as **8** and **8′** could not be separated, their yields were calculated based on the intensity of the H-3 peak of **8** in the ^{1}H NMR spectra. However, the deuterated triflates prepared from the corresponding deuterated alcohol were contaminated with the non-deuterated analog (mostly ~ 5%) owing to the imperfect purity of the deuteration reagents (D_2O or $NaBD_4$) preparing the alcohol. The content of **8** (and also that of **8′**) was corrected based on the degree of contamination of the triflates (measured by the H-3 or H-2 intensity). The values in parenthesis are for the second runs.

[b] It is not possible theoretically to decide that compound **9′** is produced by α- or β-elimination, but judging from the relative difficulty in elimination of D-2 (compared to H-2), **9′** may be produced by β-(H-4) elimination.

The 3-deuterio-3-triflate **1′** was next heated in pyridine (70 °C, 10 h), and a mixture of compound **2** formed by α-elimination and compound **2′** formed by β-elimination was obtained in a ratio of ~ 1:4 in 68% yield. Similar treatment of the 4-deuterio analog **1″** gave only compound **2** (64%) by β-elimination. These results are analogous to those obtained from ^{t}BuOK, with the predominance of β-elimination. Compound **1′** was further treated with NaOMe in methanol, whereupon the detriflyl 3-ol **3** was formed in high yield, along with the 3-labeled compound **2′** (β-elimination). Again, no α-elimination was observed. When, however, compound **4′** (allo) was heated in pyridine, no unsaturated compound was produced, and 3-deoxy-1,2;5,6-di-*O*-isopropylidene-3-(pyridinium-1-yl)-α-D-(3-^{2}H)glucofuranoside (**6**) was obtained in 90% yield, by an SN2 process. This result indicates that the chemical behavior of **1′** and **4′** with pyridine is fundamentally different.

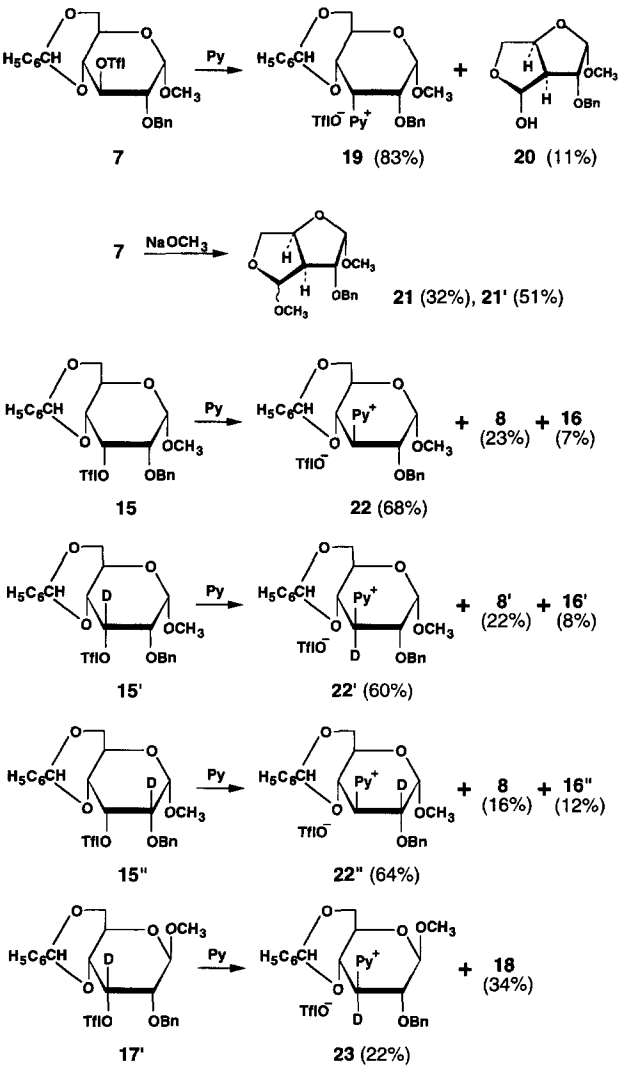
Our search then proceeded into reactions with glycopyranosides (Table 2). At first, unlabeled methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-D-glucopyranoside (**7**) was treated with ^{t}BuOK, whereupon a mixture of 2,3- (**8**, 22%) and 3,4-unsaturated compounds (**9**, 42%) was obtained, together with the detriflyl 3-ol (**10**, 29%) (see Scheme 3). The 3-deuterated analog (**7′**) of **7** was then treated similarly with ^{t}BuOK, whereupon a mixture of unlabeled 2,3-unsaturated (**8**, 20%) and unlabeled 3,4-unsaturated compounds (**9**, 38%) was obtained together with the detriflyl 3-ol **10′** (35%) and a small proportion (~ 1.5%) of 3-labeled 2,3-unsaturated compound (**8′**). The essential absence of deuterium in these unsaturated products indicates that the reaction advanced



Scheme 3.

mainly through α-elimination, as experienced in the reactions with MeLi. The fact that the yield of 3-ol **10′** is slightly higher than the 3-ol (**10**) produced from **7** suggests that the abstraction of D-3 by ^{t}BuOK is slightly more difficult than that of H-3, increasing, as a result, the yield of detriflyl product. This means that ^{t}BuOK can attack the sulfur atom of the TflO-3 group producing an alcohol **10** or **10′**. The 2-deuterated analog (**7″**) of **7** was then treated similarly, whereupon the 3-labeled 2,3-unsaturated compound **8′** was formed (13%), together with the 2-labeled 3,4-unsaturated compound **9′** (49%). Detriflyl compound **10″** was produced in 30% yield. Examining this result, it is clear that the 2,3- and 3,4-unsaturated compounds are produced through α-elimination. In addition, the fact that the yield of **8′** from **7″** is less than that of **8** from **7** or **7′**, and that the yield of the 3,4-unsaturated product **9′** from **7″** is higher than that of **9** derived from **7** or **7′**, indicates that the migration of D-2 to C-3, which occurs accompanied by α-elimination, is more difficult than that of H-2. However, the magnitude of the product-ratio of 2,3:3,4-unsaturated compounds is very different from that obtained from MeLi (or BuLi) (Table 2); this point is discussed later.

Unlabeled compound **7** was next heated in pyridine. In this reaction, no unsaturated compound was produced, and a 3-pyridinium compound **19** (83%) with the D-allo structure was obtained as the major product by an SN2 process, accompanied by a small amount (11%) of ring-contracted product **20** [8] (see Scheme 4). The structure of **20** was confirmed by ^{1}H NMR and NOESY spectroscopy. The result indicates that pyridine is a very weak base in causing elimination of either H-3 (α-elimination) or H-2 (β-elimination), and rather acts as a nucleophile, as in the case of **4′** (to give **6**). When **7** was treated with the non-nucleophilic 2,6-di-*t*-butyl-4-methylpyridine in ether, neither **20** nor a substituted product was produced, and only **7** was recovered. Compound **7** was additionally treated with NaOMe in methanol, and only ring-contracted products **21** (32%) and **21′** (51%) were produced. The mechanism of reaction is presumably substantially the same as that reported [5] in the solvolysis of methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-trifluoroacetamido-3-*O*-triflyl-α-D-glucopyranoside in MeOH, when (1*S*,3*S*,4*R*,5*R*,6*R*)-3,6-diethoxy-4-trifluoroacetamido-2,7-dioxabicyclo[3,3,0]-octane was obtained in good yield; the coupling constants for the corresponding protons of the foregoing octane and **21′** (as well as **20**) were almost identical. These results suggest that, in a polar protic solvent



Scheme 4.

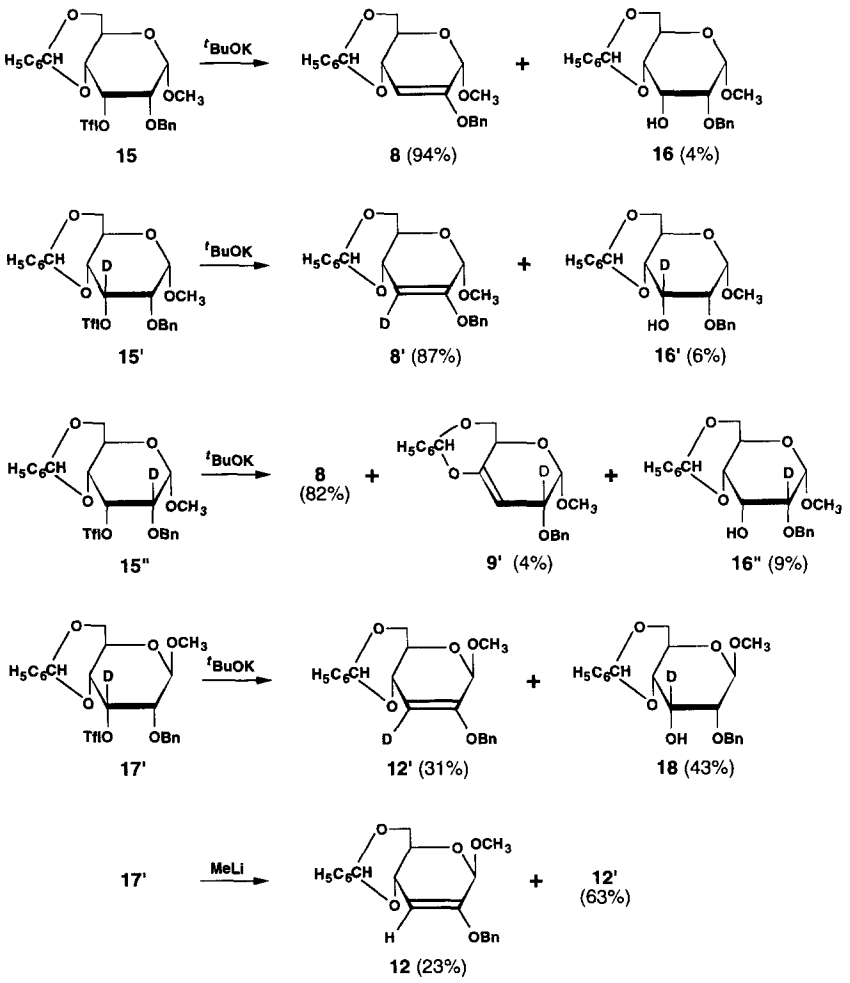
(MeOH), the 3-*O*-triflyl-α-D-glucopyranosides degenerate into ring-contracted products by attack of the C-4–C-5 bond-electrons to C-3 with concomitant departure of the CF_3SO_3 group, which will be facilitated by the antiparallel, coplanar relationship [15] of the leaving CF_3SO_3 and migrating groups.

To examine the influence of the anomeric MeO group on the aforementioned reactions, 3-*O*-triflyl-β-D-glucopyranoside **11** was treated with ^{t}BuOK, whereupon a mixture of 2,3- (**12**, 36%) and 3,4-unsaturated compounds (**13**, 25%) were produced, together with the detriflyl 3-ol (**14**, 22%). Similar treatment of the 3-deuterated analog (**11′**) of **11** gave a mixture of unlabeled **12** (30%) and **13** (25%), together with the detriflyl 3-ol (**14′**, 26%). This result indicates that the unsaturation also occurred through α-elimination in the β-D compounds. It should be noted that the 2,3-/3,4-unsaturation ratios between

the β- (**11** and **11′**) and α-glycosides (**7**, **7′**, and **7″**) are reversed.

Next, unlabeled 3-*O*-triflyl-α-D-allopyranoside **15** was treated with ^{t}BuOK, when a pure 2,3-unsaturated **8**, not contaminated with the 3,4-unsaturated compound, was obtained in high yield (94%) along with the detriflyl 3-ol **16** (4%) (see Scheme 5). Similar treatment of the 3-deuterated analog (**15′**) of **15** gave the 3-labeled 2,3-unsaturated compound **8′** in high yield (87%) together with the 3-deuterio-3-ol **16′** (6%). These facts indicate that the reactions proceed through β-hydrogen (H-2) elimination, which is in sharp contrast to the α-elimination in the α-D-gluco structure (**7′** and **7″**). Similar treatment of the 2-deuterated analog (**15″**) of **15** also gave a comparable result, that is, unlabeled 2,3-unsaturated compound **8** arising from β-elimination was mainly produced together with the 3,4-unsaturated (**9′**, 4%) and detriflyl compounds **16″**. Formation of the 3,4-unsaturated compound **9′**, not observed in the reaction for **15** or **15′**, suggests again that deuterium-abstraction (D-2 in this case) by ^{t}BuO^{-} is more difficult than hydrogen-abstraction.

Compound **15** was next treated with pyridine, when an SN2 product, methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-3-(pyridinium-1-yl)-α-D-glucopyranoside (**22**), was the main product together with the 2,3-unsaturated (**8**, 23%) and detriflyl compounds **16** (7%). Treatment of **15** with 2,6-di-*t*-butyl-4-methylpyridine in ether gave no reaction product; only **15** was recovered, as observed for **7**. When, however, **15** was heated in *N*,*N*-dimethylformamide in the presence of $NaOB_z$, compound **8** was the main product (65%). The 3- and 2-deuterated analogs (**15′** and **15″**) of **15** were also treated similarly with pyridine, whereupon the expected 3-pyridinium compounds (**22′** and **22″**) were produced, together with the 2,3-unsaturated (**8′** and **8**) and 3-hydroxy compounds (**16′** and **16″**) in comparable yields to those for **15**, respectively. It is noteworthy that the yield (16%) of **8** from



Scheme 5.

15″ is less than that from **15** or **15′**, indicating again that the abstraction of D-2 is more difficult than that of H-2.

A β-D-allopyranoside was also examined. When 3-deuterated 3-*O*-triflyl-β-D-allopyranoside **17′** was treated with ^{t}BuOK, a 3-labeled 2,3-unsaturated compound **12′** (31%) was produced by β-elimination, together with the detriflyl 3-ol **18** (43%). It is noteworthy that, in this reaction, the detriflyl compound was mainly produced, in contrast to the case for the α-D isomer **15′**. This may be explained if we assume that CH_3O-1 group has an effect as follows: In the α-D-allopyranosides (e.g. **15′**), H-2 and the electron-withdrawing CH_3O-1*ax* are in antiperiplanar positions, and when an anionic species (^{t}BuO$^-$) approaches H-2, the CH_3O-1 withdraws the C-1–O bond-electrons more strongly than when the CH_3O-1 is in an equatorial position, lowering, as a the result, the transition state energy for formation of the C-2-anion into a comparative extent, facilitating the production of the 2,3-unsaturated compound. For the CH_3O-1*eq* in **17′**, this kind of electron-withdrawing effects not expected. The mechanism, however, is not applicable to the combination of **7** (α-D) and **11** (β-D), where the H-3 (not H-2) is eliminated, producing the 3-ols in comparative yields. Incidentally, it seems certain that the hydrogen-abstraction by the reagent is not so strongly influenced, as compared to an SN2 reaction, by the steric and electronic repulsions operating between an approaching species (^{t}BuO$^-$) and nearby groups in the molecule, because of the greater distance between them.

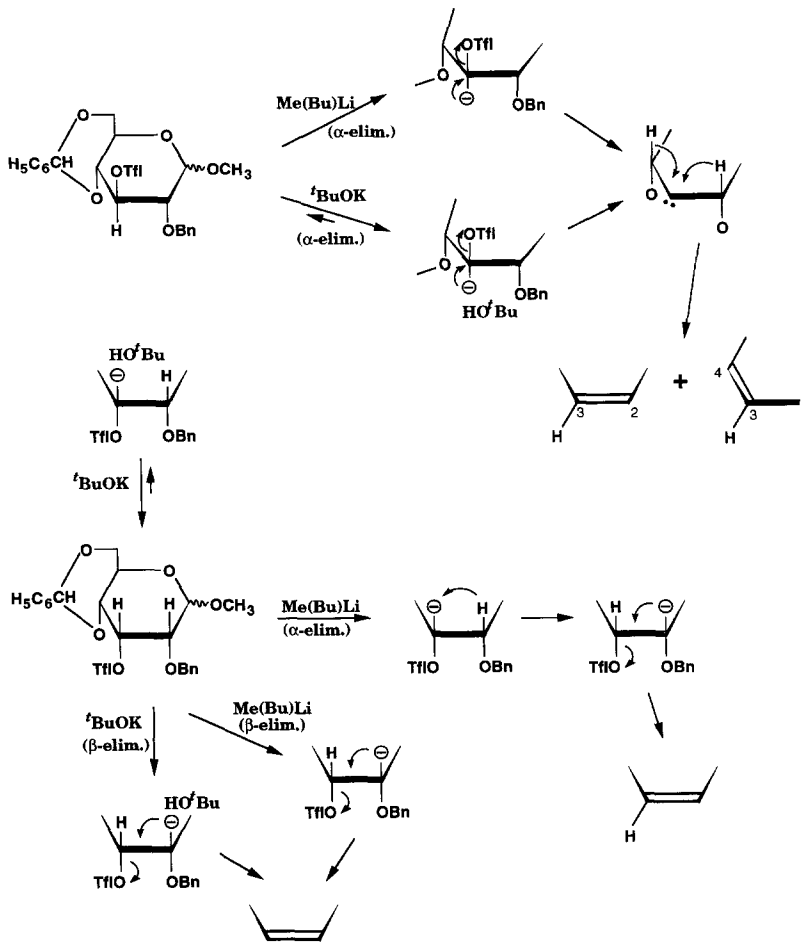
To compare the reactions with ^{t}BuOK and MeLi further, **17′** was treated with MeLi (this reaction was not reported yet in refs [11,12]), when unlabeled **12** (formed by α-elimination) and 3-labeled **12′** were produced simultaneously (total yield 86%) in a 1:2.7 ratio without giving the 3-ol **18**, as had been seen in the same reaction of the α-D isomer **15′** and MeLi [12]. This indicates again that considerable difference exists between the two reagents.

Finally the 3-deuterated **17′** was heated in pyridine, when no unsaturated compound was produced, and an SN2 product **23** was obtained in 22% yield, together with the 3-ol **18** (34%) and unknown products. This result shows that there is considerable difference between **17′** (β anomer) and **15′** (α anomer) in production of 3-pyridinium (much less in **17′**) and 3-ol compounds (much more in **17′**); this tendency is attributed in part to the relative difficulty of the pyridine-nitrogen in approaching C-3 in **17′**, compared to **15′**, because of electrostatic repulsion between the MeO-1(β) and lone-pair electrons of the nitrogen.

Throughout the studies described so far, specificity in the reactions of the 3-triflates examined with Me(Bu)Li, ^{t}BuOK, and pyridine was clarified to some extent. In the case of Me(Bu)Li, most of the 3-*O*-triflyl-α-D-glycosides were converted into the corresponding 2,3- and 3,4-unsaturated compounds through H-3-hydrogen elimination (α-elimination); only **15′** showed, in addition to the α-elimination, H-2-hydrogen elimination (β-elimination) (Tables 1 and 2). This result clearly indicates that Me(Bu)Li has a strong affinity to the most acidic CH-hydrogen in a molecule (this is the position bearing a CF_3SO_3 group) abstracting the hydrogen directly as a proton, giving the C-3 carbanion [10,11]; in other words, the hydrogen is kinetically the most readily accessible position for Me(Bu)Li. However, if viewed from another point, the reaction is irreversible, as evidenced by the formation of CH_3D [11].

In the case of ^{t}BuOK, the 3-triflates gave unsaturated compounds through α- or β-elimination or a mixture of both, depending on the structures, but the reactions are highly inclined to β-elimination. This difference between ^{t}BuOK and Me(Bu)Li suggests that the transition states (TS) differ each other. We propose that the reaction at C-3 with ^{t}BuOK is in an equilibrium such as TflOCH + $^{\ominus}$O^{t}Bu ⇄ TflOC$^{\ominus}$ + HO^{t}Bu. This equilibrium, which in principle is not expected for Me(Bu)Li, is based on the prediction that the TflOC$^{\ominus}$ carbanion produced may have strong affinity to the hydrogen of *H*O^{t}Bu just formed rebound. However, instead, a slightly different explanation is that of HO^{t}Bu, positioned near the C-3 carbanion, gives a different TS from that (isolated TS), generated by Me(Bu)Li, that is, TflOCH + $^{\ominus}$O^{t}Bu ⇄ TflOC$^{\ominus}$ · HO^{t}Bu (**A***). These assumptions on the equilibrium for the ^{t}BuOK reaction leads necessarily to another prediction: that the 2,3-unsaturation can occur through either the TS (**A***) at C-3 or the TS (**B***) at C-2 or C-4 such as TflOCH-C$^{\ominus}$ · HO^{t}Bu. In the compounds with the allo-type structure, **B*** is expected to possess an energy lower than that for **A*** because the C-2-anion-electron-pair and TflO-3 are located in antiperiplanar positions (Scheme 6). The difference in ratio (*r*) of 3,4-/2,3-unsaturation in the reactions of the D-gluco compounds (**7′** or **7″**) with Me(Bu)Li ($r < 1$) and ^{t}BuOK ($r > 1$) (both, α-elimination) would also be a reflection of the difference in TS-structure (Scheme 6).

Another characteristic point to be noted in the reactions of ^{t}BuOK is that all the α- and β-D-gluco-



Scheme 6.

pyranosides examined gave the 2,3- and 3,4-unsaturated products, whereas the α- and β-D-allopyranosides gave mainly (except for **15″**) the 2,3-unsaturated products. This tendency was also observed in the reactions with Me(Bu)Li, and can be explained [12], for the former compounds, by the fact that the initial α-elimination was followed by formation of the C-3 carbene, which induces the hydrogen-migration characteristic of carbenes [16–18] from both the C-2 and C-4 sides, and for the latter compounds reactions occur through either α-elimination followed by proton-shift (H-2 → C-3), or β-elimination (of H-2), each pathway having an ionic character (Scheme 6). The foregoing mechanism can also be applied to ^{t}BuOK, although, for the latter compounds, only β-elimination is observed. Summarizing this, the reactions through the C-3 carbene gave two compounds, and those through proton-shift or β-elimination gave a single compound, irrespective of the reagent [Me(Bu)Li or ^{t}BuOK]. However, previously, we reported [11] that compound **11** gave, on treatment with MeLi, only **12** in low yield (30%) without formation of **13**, even though the reaction is supposed to proceed through the C-3 carbene. Therefore, the reaction was reexamined and it was found that, although **11** gave a similar result at room temperature as before, it gave a ~ 1:4 mixture of **12** and **13** in high yield (82%) when performed at −50 °C, supporting the foregoing assumption. (The reason for the low yield at room temperature is not clear, but presumably **13** produced may be unstable under the reaction conditions, and decomposes rapidly).

The salient difference between ^{t}BuOK and pyridine is that the latter molecule reacts mainly as a nucleophile in most cases to give the 3-pyridinium derivatives under inversion, regardless of the C-3 configuration of the starting triflates.

3. 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 (^{1}H 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} (E. Merck 5715 and 5717), and detected by charring with aq 50% H_2SO_4. Column chromatography was performed on Wakogel C-200.

Preparation of triflates.—Triflates **1′**, **1″**, **4′**, **7**, **11**, **15**, and **7′**, **7″**, **15′**, and **15″** were prepared according to the procedure reported in refs [11] and [12], respectively, and triflates **11′** and **17′** were newly prepared as described later.

General procedure for reaction of triflates with ^{t}BuOK.—To a soln of a triflate (1 M equiv) in dry Et_2O (~ 30 v/w) was added ^{t}BuOK (3 M equiv, in Et_2O), and the mixture was stirred for 1–3 h at room temperature. Water was added, and the organic layer was separated. The aq layer remained was extracted with $CHCl_3$, and the organic solns combined were washed with water, dried (Na_2SO_4), and concd. The residue was chromatographed on silica gel to give the products.

General procedure for reaction of triflates with pyridine.—A soln of a triflate in pyridine (~ 15 v/w) was heated for 5–10 h at 70–80 °C. After excess pyridine was evaporated in vacuo, the residue was chromatographed on silica gel to give the products.

Procedure for reaction of **7** *or* **15** *with 2,6-di-t-butyl-4-methylpyridine.*—A mixture of the triflate (100 mg, 0.20 mmol) and 2,6-di-*t*-butyl-4-methylpyridine (326 mg, 1.6 mmol) in ether (4 mL) was refluxed for 7 h. After concn, the residue was treated in a conventional manner to give the starting material almost quantitatively.

Reaction of triflate **1′** *with ^{t}BuOK to give 3-deoxy-1,2;5,6-di-O-isopropylidene-α-D-erythro-hex-3-enofuranoside* (**2**) *and the corresponding (3-^{2}H)furanoside* (**2′**).—Treatment of **1′** (50 mg, 0.13 mmol; which contained ≤ 0.05% 3-H isomer as determined by the H-3 signal at δ 5.27) with ^{t}BuOK (0.39 mmol) according to the general procedure (chromatography, 4:1 hexane–EtOAc) gave a ~ 1:9 mixture of **2** and **2′** as a solid (23 mg, 74%): mp 49–50 °C (unlabeled **2**, lit. 49–50 °C [11]); $[\alpha]_D^{22}$ +27° (*c* 1, $CHCl_3$) {unlabeled **2**, lit. $[\alpha]_D^{21}$ +28° ($CHCl_3$) [11]}; ^{1}H NMR ($CDCl_3$): δ 1.39, 1.45, and 1.47 [s of 3, 3, and 6 H, respectively, 2 $C(CH_3)_2$], 3.98 (dd, 1 H, H-6), 4.15 (dd, 1 H, H-6′), 4.59 (dt, 1 H, H-5), 5.25 (dd, 0.094 H, H-3), 5.30 (dd, 1 H, H-2), 6.08 (d, 0.988 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. The second synthetic run, δ 5.25 (dd, 0.112 H, H-3), 6.08 (d, 1.000 H, H-1).

Reaction of triflate **1′** *with pyridine to give a mixture of* **2** *and* **2′**.—Treatment of **1′** (50 mg, 0.13 mmol) with pyridine as described in the general procedure (chromatography, 4:1 hexane–EtOAc) gave a ~ 1:4 mixture of **2** and **2′** as a solid (21 mg, 68%): mp 49–50 °C (unlabeled **2**, lit. 49–50 °C [11]); $[\alpha]_D^{22}$ +27° (*c* 1, $CHCl_3$) {unlabeled **2**, lit. $[\alpha]_D^{21}$ +28° ($CHCl_3$) [11]}; ^{1}H NMR ($CDCl_3$): δ 5.25 [dd, 0.198 and 0.210 H (the second synthetic run), H-3], 6.08 (d, 1.000 H, H-1).

Reaction of triflate **1′** *with NaOMe in MeOH to give* **2′** *and 1,2;5,6-di-O-isopropylidene-α-D-(3-^{2}H)glucofuranoside* (**3**).—A soln of **1′** (50 mg) and NaOMe (0.4 mL of 28% MeOH soln) in MeOH (1 mL) was kept overnight at room temperature. After addition of excess CO_2 (Dry Ice), the solvent was evaporated. Chromatography (4:1 hexane–EtOAc) of the residue gave, from the faster-moving fractions, compound **2′** as a solid (4 mg, 13%): mp 48–50 °C (lit. 48–50 °C [11]); $[\alpha]_D^{22}$ +27° (*c* 0.2, $CHCl_3$) {lit. $[\alpha]_D^{21}$ +27° ($CHCl_3$) [11]}. From the slower-moving fractions, compound **3** was obtained as a solid (28 mg, 84%): mp 108–110 °C (lit. 109–110 °C [19]); $[\alpha]_D^{22}$ −12° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D^{21}$ −12° ($CHCl_3$) [19]}; ^{1}H NMR ($CDCl_3$): δ 1.32, 1.37, 1.44, and 1.50 [each s of 3 H, 2 $C(CH_3)_2$], 2.72 (s, 1 H, OH), 4.00 (dd, 1 H, $J_{5,6}$ 5.1, $J_{6,6'}$ 8.5 Hz, H-6), 4.06 (d, 1 H, $J_{4,5}$ 8 Hz, H-4), 4.16 (dd, 1 H, $J_{5,6'}$ 6.2 Hz, H-6′), 4.33 (ddd, 1 H, H-5), 4.53 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 5.94 (d, 1 H, H-1).

Reaction of triflate **1″** *with ^{t}BuOK to give a mixture of* **2** *and* **2′**.—Treatment of **1″** (20 mg) with ^{t}BuOK (0.15 mmol) according to the general procedure (chromatography, 4:1 hexane–EtOAc) gave a ~ 9:1 mixture of **2** and **2′** as a solid (8.4 mg, 68%); ^{1}H NMR ($CDCl_3$): δ 5.25 (dd, 0.894 H, H-3), 6.08 (d, 1.000 H, H-1).

Reaction of triflate **1″** *with pyridine to give* **2**.—Treatment of **1″** (20 mg) with pyridine as described for the general procedure (chromatography, 4:1 hexane–EtOAc) gave **2** as a solid (7.8 mg, 63%); ^{1}H NMR ($CDCl_3$): δ 5.25 (dd, 1.000 H, H-3), 6.08 (d, 1.000 H, H-1).

Reaction of triflate **4′** *with ^{t}BuOK to give* **2′** *and 1,2;5,6-di-O-isopropylidene-α-D-(3-^{2}H)allofuranoside* (**5**).—Treatment of **4′** (100 mg, 0.26 mmol) with ^{t}BuOK (0.78 mmol) according to the general proce-

dure (chromatography, 3:1 hexane–EtOAc) gave, from the faster-moving fractions, compound **2′** as a solid (32 mg, 52%): mp 49–50 °C (lit. 48–50 °C [11]); $[\alpha]_D^{22}$ +27° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D^{21}$ +27° ($CHCl_3$) [11]}; ^1H NMR ($CDCl_3$): δ 1.39, 1.45, and 1.47 [s of 3, 3, and 6 H, respectively, 2 $C(CH_3)_2$], 3.98 (dd, 1 H, H-6), 4.15 (dd, 1 H, H-6′), 4.59 (dt, 1 H, H-5), 5.25 (dd, 0.039 H, H-3), 5.30 (dd, 1 H, H-2), 6.08 (d, 1.000 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. The second synthetic run, δ 5.25 (dd, 0.020 H, H-3), 6.08 (d, 1.000 H, H-1). From the slower-moving fractions, compound **5** was obtained as a solid (12 mg, 18%): mp 75–77 °C (lit. 76–78 °C [20]); $[\alpha]_D^{22}$ +36° (*c* 1.5, $CHCl_3$) {lit. $[\alpha]_D^{22}$ +34° (H_2O) [20]}.

Reaction of triflate **4′** *with pyridine to give 3-deoxy-1,2;5,6-di-*O*-isopropylidene-3-(pyridinium-1-yl)-α-*D*-(3-^2H)glucofuranoside triflate* (**6**).—Treatment of **4′** (60 mg) with pyridine as described for the general procedure (chromatography, 5:1 $CHCl_3$–MeOH) gave **6** as a syrup (65 mg, 90%): $[\alpha]_D^{22}$ −11° (*c* 0.5, $CHCl_3$) (unlabeled compound, lit. no data reported [21]); *m/z* 323.34 (M^+); Calcd for $C_{17}H_{23}DNO_5$: *m/z* 323.17 for M^+; ^1H NMR ($CDCl_3$): δ 1.29, 1.37, 1.44, and 1.59 [each s of 3 H, 2 $C(CH_3)_2$], 3.15 (ddd, 1 H, H-5), 3.97 (dd, 1 H, H-6), 3.99 (dd, 1 H, H-6′), 4.45 (d, 1 H, H-4), 5.32 (d, 1 H, H-1), 6.45 (d, 1 H, H-2), 8.18, 8.63, and 8.71 (each m of 2, 1, and 2 H, C_6H_5N): $J_{1,2}$ 3.6, $J_{4,5} \approx J_{6,6'}$ 9.5, $J_{5,6}$ 4.5, $J_{5,6'}$ 5.5 Hz. ^{19}F NMR ($CDCl_3$): δ −78.78 (s, CF_3SO_3).

Reaction of triflate **7** *with* ^{t}*BuOK to give methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-*D*-*erythro*-hex-2-enopyranoside* (**8**), *methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-*D*-*erythro*-hex-3-enopyranoside* (**9**), *and methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside* (**10**).—Treatment of **7** (0.40 g, 0.79 mmol) with ^{t}BuOK (2.38 mmol) as described for the general procedure (chromatography, 3:1 hexane–EtOAc) gave, from the faster-moving fractions, compound **8** as needles (62 mg, 22%): mp 133–134 °C (lit. 133–134 °C [11]); $[\alpha]_D^{22}$ +21° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D^{22}$ +21° ($CHCl_3$) [11]}. From the second-moving fractions, an unknown compound was obtained as a syrup (11 mg) and, from the third-moving fractions, compound **9** was obtained as needles (119 mg, 42%): mp 108–109 °C (lit. 108–109 °C [11]); $[\alpha]_D^{22}$ +51° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D^{22}$ +51° ($CHCl_3$) [11]}. From the last-moving fractions, compound **10** [13,14] was obtained as a solid (85 mg, 29%).

Reaction of triflate **7** *with pyridine to give methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-3-(pyridinium-1-yl)-α-*D*-allopyranoside triflate* (**19**) *and (1*S*,3*S*,4*R*,5*R*,6*R*)-4-benzyloxy-6-hydroxy-3-methoxy-2,7-dioxabicyclo[3.3.0]octane* (**20**).—Treatment of **7** (500 mg) with pyridine as described for the general procedure (chromatography, 1:1 hexane–EtOAc) gave, after a faster-moving unknown compound (25 mg), compound **20** as a syrup (29 mg, 11%): $[\alpha]_D^{22}$ +85° (*c* 1.2, $CHCl_3$) {lit. $[\alpha]_D$ +37.5° ($CHCl_3$) [8]} (the structure reported in ref. [8] may be incorrect); *m/z* 265.27 ($M^+ - 1$); Calcd for $C_{14}H_{18}O_5$: *m/z* 266.28 for M^+; ^1H NMR ($CDCl_3$): δ 2.90 (t, 1 H, H-5), 2.98 (d, 1 H, OH), 3.39 (s, 3 H, OCH_3), 3.70 (dd, 1 H, H-4), 3.90 (d, 1 H, H-8), 4.03 (dd, 1 H, H-8′), 4.61 (ABq, 2 H, CH_2Ph), 4.80 (d, 1 H, H-3), 4.81 (dd, 1 H, H-1), 5.32 (d, 1 H, H-6); $J_{1,5}$ 7, $J_{1,8}$ ~ 0, $J_{1,8'}$ 4, $J_{3,4}$ 4, $J_{4,5}$ 7, $J_{5,6}$ ~ 0, $J_{6,OH}$ 2.5, $J_{8,8'}$ 10.2 Hz. In NOESY, cross peaks were observed between H-1–H-5 (MeO-1, and H-8), H-3–H-4, and H-4–H-6. Subsequent elution with 5:1 $CHCl_3$–MeOH as the developer gave **19** as needles (482 mg, 83%): mp 83–85 °C; $[\alpha]_D^{22}$ +24° (*c* 1, $CHCl_3$); *m/z* 434.40 (M^+); Calcd for $C_{26}H_{28}NO_5$: *m/z* 434.20 for M^+; ^1H NMR ($CDCl_3$): δ 3.54 (s, 3 H, OCH_3), 3.64 (dt, 1 H, H-5), 3.72 (t, 1 H, H-6), 4.26 (dd, 1 H, H-6′), 4.31 (dd, 1 H, H-4), 4.52 (dd, 1 H, H-2), 4.68 (ABq, 2 H, CH_2Ph), 4.75 (d, 1 H, H-1), 6.26 (t, 1 H, H-3), 7.83, 8.38, 9.32 (each m of 2, 1, and 2 H, respectively, C_5H_5N); $J_{1,2}$ 4.5, $J_{2,3} \approx J_{3,4}$ 6.3, $J_{4,5}$ 10, $J_{5,6} \approx J_{6,6'}$ 10, $J_{5,6'}$ 4.5 Hz. ^{19}F NMR ($CDCl_3$): δ −78.59 (s, CF_3SO_3).

Reaction of triflate **7** *with NaOMe to give (1*S*,3*S*,4*R*,5*R*,6*S*)-4-benzyloxy-3,6-dimethoxy-2,7-dioxabicyclo[3.3.0]octane* (**21**) *and (1*S*,3*S*,4*R*,5*R*,6*R*)-4-benzyloxy-3,6-dimethoxy-2,7-dioxabicyclo[3.3.0]octane* (**21′**).—To a soln of **7** (2.00 g) in MeOH (20 mL) was added 28% NaOMe in MeOH (3 mL) and the soln was heated for 3 h at 70 °C. After addition of excess CO_2 (Dry Ice), the solvent was evaporated in vacuo and the residue was chromatographed (2:1 hexane–ether) to give, from the faster-moving fractions, compound **21** as a syrup (351 mg, 32%): $[\alpha]_D^{22}$ −110° (*c* 1, $CHCl_3$); *m/z* 279.27 ($M^+ - 1$); Calcd for $C_{15}H_{20}O_5$: *m/z* 280.30 for M^+; ^1H NMR ($CDCl_3$): δ 2.81 (d, 1 H, H-5), 3.31 and 3.32 (each s, 3H, OCH_3), 3.91 (dd, 1 H, H-8), 4.00 (d, 2 H, H-4, H-8′), 4.58 (s, 2 H, CH_2Ph), 4.98 (m, 3 H, H-1,3,6); $J_{1,5}$ 6.5, $J_{1,8}$ 3.8, $J_{4,5} \approx J_{5,6}$ ≈ 0, $J_{8,8'}$ 10.5 Hz. From the slower-moving fractions, compound **21′** was obtained as a syrup (572 mg, 51%): $[\alpha]_D^{22}$ +50° (*c* 1, $CHCl_3$); *m/z* 279.27 ($M^+ - 1$); Calcd for $C_{15}H_{20}O_5$: *m/z* 280.30 for M^+; ^1H NMR ($CDCl_3$): δ 2.85 (t, 1 H, H-5), 3.25 and 3.38 (each s, 3 H, OCH_3), 3.70 (dd, 1 H, H-4), 3.82

(dd, 1 H, H-8), 3.85 (dd, 1 H, H-8′), 4.61 (ABq, 2 H, CH_2Ph), 4.74 (s, 1 H, H-6), 4.77 (ddd, 1 H, H-1), 4.80 (d, 1 H, H-3); $J_{1,5}$ 7, $J_{1,8}$ 3.5, $J_{1,8'}$ 1.2, $J_{3,4}$ 4, $J_{4,5}$ 7, $J_{5,6}$ 0, $J_{8,8'}$ 10.5 Hz.

Reaction of triflate **7′** *with* ^{t}*BuOK to give* **8**, *methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-*D-erythro-*hex-2-eno-(3-*^{2}*H)pyranoside* (**8′**), **9**, *and methyl 2-O-benzyl-4,6-O-benzylidene-α-*D-*(3-*^{2}*H)glucopyranoside* (**10′**).—Treatment of **7′** (120 mg, 0.24 mmol) with ^{t}BuOK (0.72 mmol) as described for the general procedure (chromatography, 15:1 toluene–EtOAc) gave, from the faster-moving fractions, a 94:6 mixture of **8** and **8′** as needles (18 mg, 21%): mp 132–134 °C (unlabeled **8**, lit. 133–134 °C [11]); $[\alpha]_D^{22}$ +20° (*c* 1, $CHCl_3$) {unlabeled **8**, lit. $[\alpha]_D^{22}$ +21° ($CHCl_3$) [11]}; ^{1}H NMR ($CDCl_3$): δ 5.07 (d, 0.938 H, H-3), 5.57 (s, 1.000H, C*H*Ph); the second synthetic run, δ 5.07 (d, 0.941 H, H-3), 5.57 (s, 1.000 H, C*H*Ph). From the second-moving fractions, compound **9** was obtained as needles (32 mg, 38%); ^{1}H NMR ($CDCl_3$): δ 5.34 (small-range m, 1.001 H, H-3), 5.54 (s, 1.000H, C*H*Ph). The second synthetic run, δ 5.34 (small-range m, 0.980 H, H-3), 5.54 (s, 1.000 H, C*H*Ph). From the slowest-moving fractions, compound **10′** [12] was obtained as a solid (31 mg, 35%).

Reaction of triflate **7″** *with* ^{t}*BuOK to give* **8′**, *methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-*D-erythro-*hex-3-eno-(2-*^{2}*H)pyranoside* (**9′**), *and methyl 2-O-benzyl-4,6-O-benzylidene-α-*D-*(2-*^{2}*H)glucopyranoside* (**10″**).—Treatment of **7″** (120 mg, 0.24 mmol) with ^{t}BuOK (0.72 mmol) as described for the general procedure (chromatography, 15:1 toluene–EtOAc) gave, from the faster-moving fractions, compound **8′** as needles (11 mg, 13%): mp 132–133 °C (lit. 132–133 °C [12]); $[\alpha]_D^{23}$ +20° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D^{22}$ +20° ($CHCl_3$) [12]}; ^{1}H NMR ($CDCl_3$): δ 5.07 (d, 0.026 H, H-3), 5.57 (s, 1.000H, C*H*Ph); the second synthetic run, δ 5.07 (d, 0.066 H, H-3), 5.57 (s, 1.000 H, C*H*Ph). From the second-moving fractions, compound **9′** was obtained as needles (41 mg, 49%): mp 107–109 °C (lit. 107–109 °C [12]); $[\alpha]_D^{22}$ +50° (*c*, 0.5, $CHCl_3$) {lit. $[\alpha]_D^{23}$ +49° ($CDCl_3$) [12]}. From the slowest-moving fractions, compound **10″** was obtained as a solid (27 mg, 30%): mp 131–132 °C (lit. 130–132 °C [12]); $[\alpha]_D^{22}$ +34° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D^{22}$ +32° ($CHCl_3$) [12]}.

Reaction of triflate **11** *with* ^{t}*BuOK to give methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-β-*D-erythro-*hex-2-enopyranoside* (**12**), *methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-β-*D-erythro-*hex-3-enopyranoside* (**13**), *and methyl 2-O-benzyl-4,6-O-benzylidene-β-*D-*glucopyranoside* (**14**).—Treatment of **11** (200 mg, 0.40 mmol) with ^{t}BuOK (1.2 mmol) as described for the general procedure (chromatography, 2:1 hexane–EtOAc) gave, from the faster-moving fractions, a mixture of **12** and **13** having the same mobility as a semi-crystalline solid (86 mg, 61%), the ratio being 1:0.71 as determined by the ^{1}H NMR spectrum; ^{1}H NMR ($CDCl_3$): all signals for **12** were identical with those reported in ref. [11]; δ (for **13**) 3.53 (s, 3 H, OCH_3), 3.76 (t, 1 H, H-6), 4.10 (ddd, 1 H, H-2), 4.35 (dd, 1 H, H-6′), 4.42 (ddt, 1 H, H-5), 4.61 (d, 1 H, H-1), 4.68 (ABq, 2 H, CH_2Ph), 5.38 (dd, 1 H, H-3), and 5.56 (s, 1 H, C*H*Ph); $J_{1,2}$ 5.2, $J_{2,3}$ 3.2, $J_{2,5} \approx J_{3,5}$ 2, $J_{5,6} \approx J_{6,6'}$ 10, $J_{5,6'}$ 6.5 Hz. From the slower-moving fractions, compound **14** was obtained as needles (32 mg, 22%): mp 123–125 °C (lit. 124–125 °C [13]); $[\alpha]_D^{22}$ −27° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D$ −27° ($CHCl_3$) [13]}.

Reaction of triflate **11** *with MeLi in* Et_2O *to give* **12**, **13**, *and* **14**.—*(a).* To a cold (−50 °C) soln of **11** (210 mg, 0.42 mmol) in Et_2O (6 mL) was added MeLi (1.67 mmol) in Et_2O, and the mixture was kept for 2 h at that temperature. Water (5 mL) was added, and the mixture was extracted with $CHCl_3$. The organic layer was washed with water, dried (Na_2SO_4), and concd to give a residue, which was chromatographed (5:1 hexane–EtOAc) to give a ~1:4 mixture of **12** and **13** as a semi-crystalline solid (121 mg, 82%); ^{1}H NMR ($CDCl_3$): δ (only prominent peaks are shown) 3.47 (s, 0.66 H, OCH_3 for **12**) and 3.53 (s, 2.34 H, OCH_3 for **13**); 3.76 (t, 0.80 H, H-6 for **13**) and 3.88 (t, 0.20 H, H-6 for **12**); 4.61 (d, 0.80 H, $J_{1,2}$ 5.2 Hz, H-1 for **13**) and 5.29 (d, 0.2 H, $J_{1,4}$ 1.8 Hz, H-1 for **12**); 5.56 (s, 0.80 H, C*H*Ph for **13**) and 5.60 (s, 0.20 H, C*H*Ph for **12**). Further elution gave **14** as needles (12 mg, 8%).

(b). A soln of **11** (90 mg, 0.18 mmol) and MeLi (0.72 mmol) in Et_2O (3 mL) was kept for 30 min at room temperature and processed as described in *a* to give **12** as a syrup (21 mg, 33%; lit. 36% [11]).

*Methyl 2-O-benzyl-4,6-O-benzylidene-3-O-triflyl-β-*D-*(3-*^{2}*H)glucopyranoside* (**11′**).—To a cold (−20 °C) soln of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-β-D-(3-^{2}H)glucopyranoside (**14′**) [12] (500 mg, 1.34 mmol) in 2:1 CH_2Cl_2–pyridine (7 mL) was added $(CF_3SO_2)_2O$ (490 mg, 1.74 mmol), and the soln was kept for 2 h in the cold. After addition of water (1 mL), the mixture was concd, and the residue was chromatographed (3:1 hexane–EtOAc) to give **11′** as a solid (596 mg, 88%): mp 84–86 °C (decomp) [unlabeled, lit. 85–86 °C (decomp) [11]]; $[\alpha]_D^{20}$ −30° (*c* 1, $CHCl_3$) [unlabeled, lit. $[\alpha]_D^{25}$ −33° ($CHCl_3$)

[11]]; *m/z* 504.25 ($M^+ - 1$), 506.25 ($M^+ + 1$); Calcd for $C_{22}H_{22}DF_3O_8S$: *m/z* 505.11 for M^+; ^1H NMR ($CDCl_3$): δ 3.44 (dt, 1 H, H-5), 3.57 (d, 1 H, H-2), 3.59 (s, 3 H, OCH_3), 3.78 (d, 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, trace, H-3), 5.56 (s, 1 H, C*H*Ph); $J_{1,2}$ 7.5, $J_{4,5}$ 9.2, $J_{5,6} \approx J_{6,6'}$ 10, $J_{5,6'}$ 5.0 Hz.

Reaction of triflate **11′** *with* ^{t}*BuOK to give* **12**, **13**, *and* **14′**.—Treatment of **11′** (210 mg, 0.42 mmol) with ^{t}BuOK (12.5 mmol) as described for the general procedure (chromatography, 3:1 hexane–EtOAc) gave, from the faster-moving fractions, a mixture of **12** and **13** as a semi-crystalline solid (84 mg, 57%), the ratio being 1:0.9 as determined by the ^1H NMR spectrum; ^1H NMR ($CDCl_3$): whole signal patterns were identical with those for the same mixture from **11**. From the slower-moving fractions, compound **14′** [12] was obtained as needles (39 mg, 26%).

Reaction of triflate **15** *with* ^{t}*BuOK to give* **8** *and methyl 2-O-benzyl-4,6-O-benzylidene-α-D-allopyranoside* (**16**).—Treatment of **15** (270 mg, 0.53 mmol) with ^{t}BuOK (1.61 mmol) as described for the general procedure (chromatography, 4:1 hexane–EtOAc) gave, from the faster-moving fractions, compound **8** as needles (178 mg, 94%), and, from the slower-moving fractions, compound **16** [11] as a solid (8 mg, 4%).

Reaction of triflate **15** *with pyridine to give* **8**, **16**, *and methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-3-(pyridinium-1-yl)-α-D-glucopyranoside triflate* (**22**).—Treatment of **15** (400 mg) with pyridine as described for the general procedure (chromatography, 4:1 hexane–EtOAc) gave, from the faster-moving fractions, compound **8** as needles (65 mg, 23%), and, from the slower-moving fractions, compound **16** [11] as a solid (21 mg, 7%). Further development with 7:1 $CHCl_3$–MeOH gave **22** as a yellowish solid (315 mg, 68%): mp 76–78 °C; $[\alpha]_D^{22}$ +14° (*c* 1, $CHCl_3$); *m/z* 434.05 (M^+); Calcd for $C_{26}H_{28}NO_5$: *m/z* 434.20 for M^+; ^1H NMR ($CDCl_3$): δ 3.46 (s, 3 H, OCH_3), 3.99 (m, 2 H, H-5,6), 4.32 (dd, 1 H, H-6′), 4.44 (ABq, *J* 12 Hz, 2 H, CH_2Ph), 4.49 (dd, 1 H, H-2), 4.70 (t, 1 H, H-4), 4.76 (t, 1 H, H-3), 4.91 (d, 1 H, H-1), 5.66 (s, 1 H, C*H*Ph), 7.93, 8.37 and 8.99 (each m of 2, 1, and 2 H, C_5H_5N); $J_{1,2}$ 3.4, $J_{2,3} \approx J_{3,4} \approx J_{5,6}$ 10.2, $J_{4,5}$ 8.4, $J_{5,6'}$ 3.4 Hz. ^{19}F NMR ($CDCl_3$): δ −78.58 (s, CF_3SO_3).

Reaction of triflate **15** *with* $C_6H_5CO_2Na$ *to give* **8**.—A mixture of **15** (150 mg, 0.30 mmol) and $C_6H_5CO_2Na$ (130 mg, 0.90 mmol) in *N*,*N*-dimethylformamide (5 mL) was heated for 6 h at 70 °C. Water (20 mL) was added and the mixture was extracted with $CHCl_3$ (30 mL × 3). The extracts combined were washed with water, dried (Na_2SO_4), and concd to give a residue, which was chromatographed (4:1 hexane–EtOAc) to give **8** as needles (69 mg, 65%).

Reaction of triflate **15′** *with* ^{t}*BuOK to give* **8′** *and methyl 2-O-benzyl-4,6-O-benzylidene-α-D-(3-*^{2}*H)allopyranoside* (**16′**).—Treatment of **15′** (200 mg, 0.40 mmol) with ^{t}BuOK (1.2 mmol) as described for the general procedure (chromatography, 10:1 toluene–EtOAc) gave, from the faster-moving fractions, compound **8′** as needles (122 mg, 87%), ^1H NMR ($CDCl_3$): δ 5.07 (d, 0.035 H, H-3), 5.57 (s, 1.000H, C*H*Ph), and, from the slower-moving fractions, compound **16′** as a solid (9 mg, 6%): mp 72–74 °C (lit. 73–74 °C [12]); $[\alpha]_D^{20}$ +6° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D^{22}$ +6° ($CHCl_3$) [12]}.

Reaction of triflate **15′** *with pyridine to give* **8′**, **16′**, *and methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-3-(pyridinium-1-yl)-α-D-(3-*^{2}*H)glucopyranoside triflate* (**22′**).—Treatment of **15′** (200 mg) with pyridine as described for the general procedure (chromatography, 15:1 toluene–EtOAc) gave, from the faster-moving fractions, compound **8′** as needles (31 mg, 22%); ^1H NMR ($CDCl_3$): 5.07 (d, 0.066 H, H-3), 5.57 (s, 1.000H, C*H*Ph); and, from the slower-moving fractions, compound **16′** as a solid (12 mg, 8%). Further development with 7:1 $CHCl_3$–MeOH gave **22′** as a yellowish solid (139 mg, 60%): mp 75–77 °C; $[\alpha]_D^{22}$ +13° (*c* 1, $CHCl_3$) {unlabeled **22**, $[\alpha]_D^{22}$ +14° ($CHCl_3$)}; *m/z* 435.05 (M^+); Calcd for $C_{26}H_{27}DNO_5$: *m/z* 435.20 for M^+; ^1H NMR ($CDCl_3$): δ 3.45 (s, 3 H, OCH_3), 3.99 (m, 2 H, H-5,6), 4.31 (m, 1 H, H-6′), 4.43 (ABq, *J* 12 Hz, 2 H, CH_2Ph), 4.43 (d, 1H, H-2), 4.67 (d, 1 H, H-4), 4.92 (d, 1 H, H-1), 5.66 (s, 1 H, C*H*Ph), 7.92, 8.38, and 8.95 (each m of 2, 1, and 2 H, respectively, C_5H_5N); $J_{1,2}$ 3.4, $J_{4,5}$ 8.4 Hz. ^{19}F NMR ($CDCl_3$): δ −78.52 (s, CF_3SO_3).

Reaction of triflate **15″** *with* ^{t}*BuOK to give* **8**, **9′**, *and methyl 2-O-benzyl-4,6-O-benzylidene-α-D-(2-*^{2}*H)allopyranoside* (**16″**).—Treatment of **15″** (200 mg, 0.40 mmol) with ^{t}BuOK (1.2 mmol) as described for the general procedure (chromatography, 10:1 toluene–EtOAc) gave, from the faster-moving fractions, compound **8** as needles (115 mg, 82%), ^1H NMR ($CDCl_3$): δ 5.07 (d, 1.000 H, H-3), 5.57 (s, 1.038H, C*H*Ph), from the second-moving fractions, compound **9′** as needles (6 mg, 4%), and, from the slowest-moving fractions, compound **16″** as a solid

(13 mg, 9%): mp 72–73 °C (lit. 72–73 °C [12]); $[\alpha]_D^{20}$ +4° (*c* 1, $CHCl_3$) {lit. $[\alpha]_D^{23}$ +4° ($CHCl_3$) [12]}.

Reaction of triflate **15″** *with pyridine to give* **8**, **16″**, *and methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-3-(pyridinium-1-yl)-α-D-(2-²H)glucopyranoside triflate* (**22″**).—Treatment of **15″** (200 mg) with pyridine as described for the general procedure (chromatography, 15:1 toluene–EtOAc) gave, from the faster-moving fractions, compound **8** as needles (22 mg, 16%), ^{1}H NMR ($CDCl_3$): δ 5.07 (d, 1.009 H, H-3), 5.57 (s, 1.000H, C*H*Ph), and, from the slower-moving fractions, compound **16″** as a solid (18 mg, 12%). Further development with 7:1 ($CHCl_3$–MeOH) gave **22″** as a yellowish solid (148 mg, 64%): mp 74–76 °C; $[\alpha]_D^{22}$ +13.5° (*c* 1.1, $CHCl_3$) {unlabeled **22**, $[\alpha]_D^{22}$ +14° ($CHCl_3$)}; *m/z* 435.06 (M^+); Calcd for $C_{26}H_{27}DNO_5$: *m/z* 435.20 for M^+; ^{1}H NMR ($CDCl_3$): δ 3.46 (s, 3 H, OCH_3), 3.99 (m, 2 H, H-5,6), 4.31 (m, 1 H, H-6′), 4.43 (ABq, *J* 12 Hz, 2 H, CH_2Ph), 4.68 (dd, 1 H, H-4), 4.77 (d, 1 H, H-3), 4.92 (s, 1 H, H-1), 5.66 (s, 1 H, C*H*Ph), 7.94, 8.38 and 8.98 (each m of 2, 1, and 2 H, respectively, C_5H_5N); $J_{3,4}$ 10.2, $J_{4,5}$ 8.4 Hz. ^{19}F NMR ($CDCl_3$): δ −78.59 (s, CF_3SO_3).

Methyl 2-O-benzyl-4,6-O-benzylidene-β-D-ribo-hexopyranoside-3-ulose (**24**).—To a cold (−78 °C) soln of oxalyl chloride (820 mg, 6.46 mmol) in CH_2Cl_2 (10 mL) was added Me_2SO (1.01 mg, 12.93 mmol), and after 15 min, methyl 2-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside [13] (1.2 g, 3.22 mmol) in CH_2Cl_2 (10 mL) was added dropwise and the mixture was stirred for 30 min. After addition of Et_3N (3 g), the mixture was warmed to room temperature and kept for 1 h. Water (20 mL) was added, and the organic layer separated was washed with water, dried (Na_2SO_4), and concd. The residue was recrystallized from MeOH to give **24** as needles (1.12 g, 94%): mp 176–177 °C; $[\alpha]_D^{22}$ −96° (*c* 1, $CHCl_3$); *m/z* 371.32 (M^++1); Calcd for $C_{21}H_{22}O_6$: *m/z* 370.14 for M^+; ^{1}H NMR ($CDCl_3$): δ 3.59 (dt, 1 H, H-5), 3.61 (s, 3 H, OCH_3), 3.87 (t, 1 H, H-6), 3.97 (dd, 1 H, H-2), 4.23 (dd, 1 H, H-4), 4.48 (dd, 1 H, H-6′), 4.60 (d, 1 H, H-1), 4.83 (ABq, 2 H, CH_2Ph), 5.53 (s, 1 H, C*H*Ph); $J_{1,2}$ 7, $J_{2,4}$ 1.6, $J_{4,5}$ 9.8, $J_{5,6'}$ 5, $J_{5,6} \approx J_{6,6'}$ 10.2 Hz. ^{13}C NMR ($CDCl_3$): δ (benzene-ring carbons are not described) 57.81 (OCH_3), 66.47 (C-5), 69.22 (C-6), 73.60 (*C*H_2Ph), 81.84 (C-4), 82.83 (C-2), 101.76 (*C*HPh), 105.99 (C-1), 196.43 (C-3).

Methyl 2-O-benzyl-4,6-O-benzylidene-β-D-(3-²H)glucopyranoside (**14′**) *and methyl 2-O-benzyl-4,6-O-benzylidene-β-D-(3-²H)allopyranoside* (**18**).—To a soln of **24** (1.0 g, 2.70 mmol) in MeOH (30 mL) was added $NaBD_4$ (3.51 mmol) and the soln was kept for 30 min at room temperature. Excess CO_2 (Dry Ice) was added, and the soln was concd. The resulting residue was chromatographed (2:1 hexane–EtOAc) to give, from the faster-moving fractions, compound **14′** as a solid (61 mg, 6%): mp 122–124 °C (unlabeled compound, lit. 124–125 °C [13]); $[\alpha]_D^{22}$ −26° (*c* 1, $CHCl_3$) {unlabeled, lit. $[\alpha]_D$ −27° ($CHCl_3$) [13]}; *m/z* 374.35 (M^++1); Calcd for $C_{21}H_{23}DO_6$: *m/z* 373.16 for M^+; ^{1}H NMR ($CDCl_3$): δ 2.54 (s, 1 H, OH), 3.32 (d, 1 H, H-2), 3.41 (dt, 1 H, H-5), 3.52 (d, 1 H, H-4), 3.57 (s, 3 H, OCH_3), 3.76 (t, 1 H, H-6), 4.34 (dd, 1 H, H-6′), 4.41 (d, 1 H, H-1), 4.82 (ABq, *J* 12 Hz, 2 H, CH_2Ph), 5.51 (s, 1 H, C*H*Ph); $J_{1,2}$ 7.5, $J_{4,5}$ 9.4, $J_{5,6'}$ 5, $J_{5,6} \approx J_{6,6'}$ 10.2 Hz. From the slower-moving fractions, compound **18** was obtained as needles (915 mg, 91%): mp 125–126 °C; $[\alpha]_D^{22}$ −60° (*c* 1, $CHCl_3$); *m/z* 374.35 (M^++1); Calcd for $C_{21}DH_{23}O_6$: *m/z* 373.16 for M^+; ^{1}H NMR ($CDCl_3$): δ 2.50 (s, 1 H, OH), 3.30 (d, 1 H, H-2), 3.48 (d, 1 H, H-4), 3.58 (s, 3 H, OCH_3), 3.71 (t, 1 H, H-6), 4.02 (dt, 1 H, H-5), 4.38 (dd, 1 H, H-6′), 4.77 (d, 1 H, H-1), 4.78 (ABq, 2 H, CH_2Ph), 5.50 (s, 1 H, C*H*Ph); $J_{1,2}$ 7.5, $J_{4,5}$ 9.4, $J_{5,6'}$ 5.0, $J_{5,6} \approx J_{6,6'}$ 10 Hz.

Methyl 2-O-benzyl-4,6-O-benzylidene-3-O-triflyl-β-D-(3-²H)allopyranoside (**17′**).—Treatment of **18** (350 mg, 0.94 mmol) with $(CF_3SO_2)_2O$ (344 mg, 1.22 mmol) in a conventional manner [11] (chromatography, 3:1 hexane–EtOAc) gave **17′** as needles (364 mg, 77%): mp 84–85 °C; $[\alpha]_D^{22}$ −52° (*c* 1, $CHCl_3$); *m/z* 506.41 (M^++1); Calcd for $C_{22}H_{22}DF_3O_8S$: *m/z* 505.45 for M^+; ^{1}H NMR ($CDCl_3$): δ 3.42 (d, 1 H, H-2), 3.58 (s, 3 H, OCH_3), 3.61 (d, 1 H, H-4), 3.71 (t, 1 H, H-6), 3.89 (ddd, 1 H, H-5), 4.39 (dd, 1 H, H-6′), 4.72 (d, 1 H, H-1), 4.80 (ABq, 2 H, CH_2Ph), 5.50 (s, 1 H, C*H*Ph); $J_{1,2}$ 8, $J_{4,5}$ 9.5, $J_{5,6'}$ 5.0, $J_{5,6} \approx J_{6,6'}$ 10.3 Hz.

Reaction of triflate **17′** *with* ^{t}*BuOK to give methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-β-D-erythro-hex-2-eno-(3-²H)pyranoside* (**12′**) *and* **18**.—Treatment **17′** (120 mg, 0.24 mmol) with ^{t}BuOK (72 mmol) as described for the general procedure (chromatography, 4:1 hexane–EtOAc) gave, from the faster-moving fractions, compound **12′** as a syrup (26 mg, 31%): $[\alpha]_D^{22}$ −35° (*c* 0.5, $CHCl_3$) {unlabeled **12**, lit. $[\alpha]_D^{24}$ −38° ($CHCl_3$) [11]}; ^{1}H NMR ($CDCl_3$): δ 3.48 (s, 3 H, OCH_3), 3.67 (dt, 1 H, H-5), 3.89 (t, 1 H, H-6), 4.32 (dd, 1 H, H-6′), 4.39 (dd, 1 H, H-4), 4.84 (s, 2 H, CH_2Ph), 5.21 (sl, br s, 0.050H, H-3), 5.30 (d, 1 H, H-1), 5.61 (s, 1 H, C*H*Ph); $J_{1,4}$ ~1, $J_{4,5}$ 8.5,

$J_{5,6} \approx J_{6,6'}$ 10.3, $J_{5,6'}$ 5.0 Hz. From the slower-moving fractions, compound **18** was obtained as needles (38 mg, 43%).

Reaction of **17′** *with MeLi to give methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-β-*D*-erythro-hex-2-enopyranoside* (**12**) and **12′**.—Treatment of **17′** (25 mg, 0.05 mmol) with MeLi (0.2 mmol) in Et_2O (0.7 mL) for 2 h at room temperature gave, after chromatography (5:1 hexane–EtOAc), a 1:2.7 mixture of **12** and **12′** as a syrup (15 mg, 86%): $[\alpha]_D^{22}$ −36° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.48 (s, 3 H, OCH_3), 4.83 (s, 2 H, CH_2Ph), 5.21 (br s, 0.270 H, H-3), 5.30 (d, 0.985 H, H-1), 5.61 (s, 1.000 H, C*H*Ph).

Reaction of triflate **17′** *with pyridine to give* **18** *and methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-3-(pyridinium-1-yl)-β-*D*-(3-^{2}H)glucopyranoside triflate* (**23**).—Treatment of **17′** (60 mg) with pyridine as described for the general procedure (chromatography, 3:1 hexane–EtOAc) gave, after a faster-moving unknown compound (syrup, 6 mg), compound **18** as a solid (15 mg, 34%). Further development with 5:1 $CHCl_3$–MeOH gave **23** as a yellowish syrup (16 mg, 22%): $[\alpha]_D^{22}$ −20° (*c* 0.6, $CHCl_3$); *m/z* 435.33 (M^+); Calcd for $C_{26}H_{27}DNO_5$: *m/z* 435.20 for M^+; ^{1}H NMR ($CDCl_3$): δ 3.64 (s, 3 H, OCH_3), 3.72 (dt, 1 H, H-5), 3.87 (d, 1 H, H-2), 3.97 (t, 1 H, H-6), 4.41 (dd, 1 H, H-6′), 4.51 (d, 1 H, H-4), 4.56 (ABq, 2 H, CH_2Ph), 4.68 (d, 1 H, H-1), 5.66 (s, 1 H, C*H*Ph), 7.70, 8.13 and 8.72 (each m of 2, 1, and 2 H, respectively, C_5H_5N); $J_{1,2}$ 7.3, $J_{4,5}$ 8.8, $J_{5,6'}$ 5.0, $J_{5,6} \approx J_{6,6'}$ 10.4 Hz. ^{19}F NMR ($CDCl_3$): δ −78.54 (s, CF_3SO_3).

Acknowledgements

We express deep thanks to Dr. Hiroshi Naganawa of the Institute of Microbial Chemistry and Ms. Yoshiko Koyama of our institute for measurements of mass and NMR spectra, respectively.

References

[1] R.W. Binkley and M.G. Ambrose, *J. Carbohydr. Chem.*, 3 (1984) 1–49.
[2] P.J. Stang, M. Hanack, and L.R. Subramanian, *Synthesis*, (1982) 85–126.
[3] A. Streitwieser, Jr., C.L. Willinks, and E. Kiehlmann, *J. Am. Chem. Soc.*, 90 (1968) 1598–1601.
[4] A. Grouiller, H. Bazin, and C. Gagnieu, *Tetrahedron Lett.*, 23 (1982) 2559–2562.
[5] T. Tsuchiya, K. Ajito, S. Umezawa, and A. Ikeda, *Carbohydr. Res.*, 126 (1984) 45–60.
[6] H.H. Baer, F. Hernández Mateo, and L. Siemsen, *Carbohydr. Res.*, 187 (1989) 67–92.
[7] R.W. Binkley, *J. Org. Chem.*, 57 (1992) 2353–2356.
[8] M. Kassou and S. Castillón, *J. Org. Chem.*, 60 (1995) 4353–4358; related references are cited therein.
[9] R.W. Binkley, *J. Carbohydr. Chem.*, 10 (1991) 417–428.
[10] A. El Nemr and T. Tsuchiya, *Tetrahedron Lett.*, 36 (1995) 7665–7668.
[11] A. El Nemr, T. Tsuchiya, and Y. Kobayashi, *Carbohydr. Res.*, 293 (1996) 31–59.
[12] A. El Nemr and T. Tsuchiya, *Carbohydr. Res.*, 301 (1997) 77–87.
[13] P.J. Garegg, T. Iversen, and S. Oscarson, *Carbohydr. Res.*, 50 (1976) C12–C14; P.J. Garegg and H. Hultberg, *Carbohydr. Res.*, 93 (1981) C10–C11.
[14] J.M. Küstner and I. Dyong, *Justus Liebigs Ann. Chem.*, (1975) 2179–2189.
[15] P.W. Austin, J.G. Buchanan, and R.M. Saunders, *J. Chem. Soc., Chem. Commun.*, (1965) 146–147; *J. Chem. Soc. C*, (1967) 372–377.
[16] H.F. Schaefer III, *Acc. Chem. Res.*, 12 (1979) 288–296.
[17] G. Frenking and J. Schmidt, *Tetrahedron*, 40 (1984) 2123–2132.
[18] J.D. Evanseck and K.N. Houk, *J. Am. Chem. Soc.*, 112 (1990) 9148–9156.
[19] S.J. Gould, V.A. Palaniswamy, H. Bleich, and J. Wilde, *J. Chem. Soc., Chem. Commun.*, (1984) 1075–1077.
[20] H.J. Koch and A.S. Perlin, *Carbohydr. Res.*, 15 (1970) 403–410.
[21] L.D. Hall and D.C. Miller, *Carbohydr. Res.*, 47 (1976) 299–305.