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Carbohydrate Research 301 (1997) 77–87

CARBOHYDRATE RESEARCH

α-Hydrogen elimination in some 3- and 4-triflates of α-D-glycopyranosides

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Received 11 December 1996; accepted with revisions 19 February 1997

Abstract

In previous papers [A. El Nemr and T. Tsuchiya, *Tetrahedron Lett.*, 36 (1995) 7665–7668; A. El Nemr, T. Tsuchiya, and Y. Kobayashi, *Carbohydr. Res.*, 293 (1996) 31–59] we reported new reactions that occur when some carbohydrate triflates are treated with MeLi (or BuLi) in ether, giving *C*-methyl (or butyl) or unsaturated compounds. Both reactions may be explained by α-hydrogen elimination in the triflates. This paper is an extension of the previous work and describes the mechanism of unsaturation of some 3- or 4-triflylates of α-D-glycopyranosides. By using deuterated analogs, it was found that methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-D-glucopyranoside gives the 2,3- and 3,4-unsaturated compounds through α-hydrogen elimination, and the corresponding allopyranoside gives the 2,3-unsaturated compound through α- and β- (for **14**) and α-hydrogen eliminations (for **19**). Carbene formation is proposed as the key intermediate for the former eliminations, and a 1 → 2 proton-shift is proposed as the key reaction for the latter. © 1997 Elsevier Science Ltd.

Keywords: Triflate; Unsaturation; Methyllithium; Butyllithium; Deuterated compound; α-Elimination; Carbene; Proton 1,2-shift; Deuterium isotope effect

1. Introduction

Triflation of hydroxyl groups in carbohydrates is an effective method for substituting hydroxyl groups with nucleophiles with inversion [1], especially when mesylation or tosylation is ineffective, as exemplified [2] by the S_N2 reactions at C-2 of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-triflyl-α-D-glucopyranoside. This character of triflates is ascribed to the strongly electron-withdrawing trifluoromethyl group [3,4]. Other reactions sometimes encountered with triflates are elimination and ring-contraction [5–7], occurring by loss of CF_3SO_3H in each case. Deoxygenation through *O*-triflation and use of Na in liquid NH_3 has also been reported [8].

We have recently discovered [9,10], however, that when 1,2;5,6-di-*O*-isopropylidene-3-*O*-triflyl-α-D-allofuranoside (I) is treated with MeLi (or BuLi) in diethyl ether, a product formed by neither substitution, elimination, nor ring-contraction was obtained. Instead, loss of a CF_3SO_2H fragment gave a compound that proved to be the corresponding 3-*C*-methyl(or butyl)-α-D-allofuranoside (III). A mechanism was proposed in which MeLi (BuLi) initially abstracts H-3, the most acidic hydrogen in the molecule I, as a proton to give the C-3 carbanion; the

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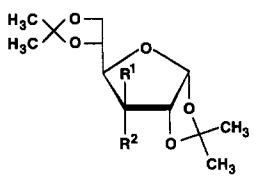
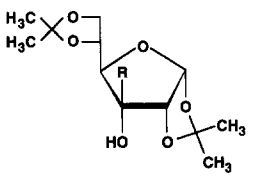
PII S0008-6215(97)00080-3

latter then donates its charge into the oxygen of the geminal CF_3SO_2O group, releasing a CF_3SO_2 group as an anion, and the resulting C-3 ketone reacts immediately with another MeLi (BuLi) molecule to give the final product III.



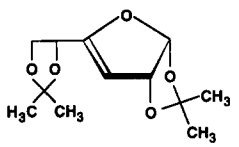
I $R^1 = H$, $R^2 = OSO_2CF_3$

II $R^1 = OSO_2CF_3$, $R^2 = H$



III $R = CH_3$ or C_4H_9

This interpretation, however, leads necessarily to the prediction that the structurally related 3-epimer (II) of I should also give the same C-3-alkyl derivatives, through the same C-3 carbanion, without giving a 3,4-unsaturated compound IV; however, this expectation was not borne out in fact. This contradiction was solved experimentally and theoretically by carrying out the same reactions for the 3- and 4-deuterated analogs of II, as described in a previous paper [10], and a C-4 → C-3 proton-migration was confirmed to occur in II immediately after the C-3 carbanion was formed; this interpretation was supported by MOPAC/PM3 calculations using a structurally related model for the transition state of the conversion of II → IV.

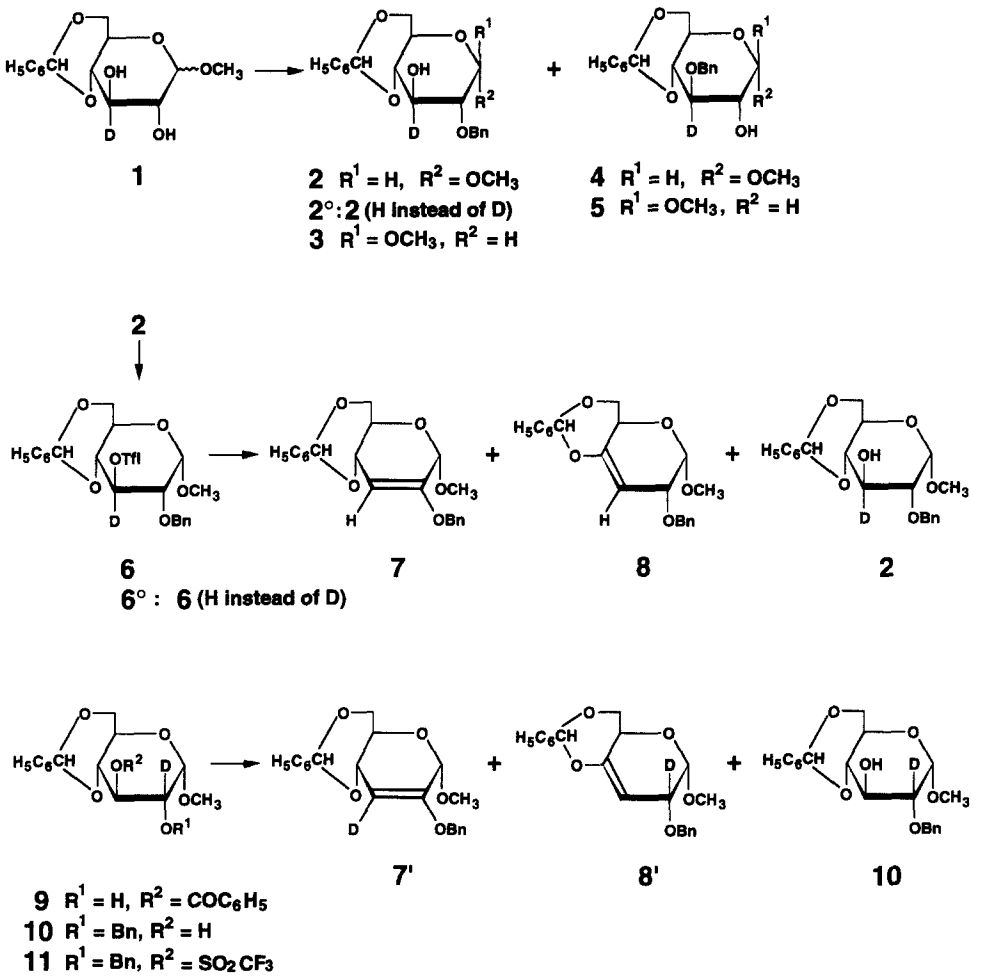


IV

In this study, the behavior of several 2-, 3-, and 4-triflates of glyco*pyrano*sides was also examined [9,10], and it was found that some 2-triflates gave the corresponding C-2-alkyl derivatives, whereas 3- and 4-triflates gave unsaturated compounds. These differences were explained on the basis the difference in stability between the C-2 (more stable) and C-3 (or C-4) carbanions just formed from the corresponding triflates [10]. However, for the latter reactions, a more precise study will be needed to clarify the correct mechanism, that is, will the C*H*-hydrogen bearing a CF_3SO_3 group first be eliminated (α-elimination) by MeLi (or BuLi) as is the case for II, or will a vicinal hydrogen first be eliminated as for conventional β-eliminations? In this paper we have investigated the problem utilizing some deuterated D-glycopyranosides triflated at HO-3 or 4.

2. Results and discussion

Synthesis of deuterated triflates.—The 3-deuterated analog **6** of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-D-glucopyranoside (**6**°: **35** in ref. [10]) was prepared from 1,2;5,6-di-*O*-isopropylidene-α-D-(3-^{2}H)glucofuranoside [11]; after conversion into the corresponding methyl glucopyranosides, the mixture was benzylidenated and the products **1** were benzylated to give a mixture of four benzyl derivatives (**2**, **3**, **4**, and **5**), which were separated by chromatography. The major isomer isolated, **2**, was triflated to give **6**. The corresponding 2-deuterated analog (**11**) of **6** was prepared from methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-(2-^{2}H)glucopyranoside **9** [12]; benzylation of **9** with benzyl trichloroacetimidate followed by debenzoylation gave **10**, which was triflated to give **11**. (See Schemes 1 and 2.) The 3-deuterio analog **14** of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-D-allopyranoside (**41** in ref. [10]) was prepared by Swern oxidation of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside [13] (to give **12**), followed by reduction with $NaBD_4$ (to give **13**) and triflation. The corresponding 2-deuterio analog **19** was prepared initially by a similar route, that is, by oxidation of the 2-deuterio derivative **10** followed by reduction with $NaBD_4$ and triflation, but the product (**19**) obtained was a mixture of compounds with 2D:2H ≈ 4:1 (proved by the ^{1}H NMR spectrum), indicating that the original deuterium at C-2 in the starting material had been partially replaced by hydrogen during the process, possibly by keto-enol tautomerization. A more successful route was developed as follows: A solution of the 3-oxo compound **12** in a mixture of 1,4-dioxane–THF–Et_3N–D_2O (4:4:2:3) was kept for 3 days, and the resulting 2-deuterated analog (**15**) of **12**, which was not contaminated with the 4-D analog and was scarcely soluble in 1,4-dioxane-D_2O (3:1), was separated from the soluble 2-deuterated 3-oxo-D-*arabino*-hexopyranoside **16**, formed simultaneously during the reaction. Compound **15** was then reduced with $NaBH_4$ to give the 3-ol **18**, which was triflated to give **19** isotopically pure. Treatment of a mixture of **15** and **16** with $NaBH_4$ followed by chromatography gave the 2-deuterated D-*altro* isomer **17**. Next,

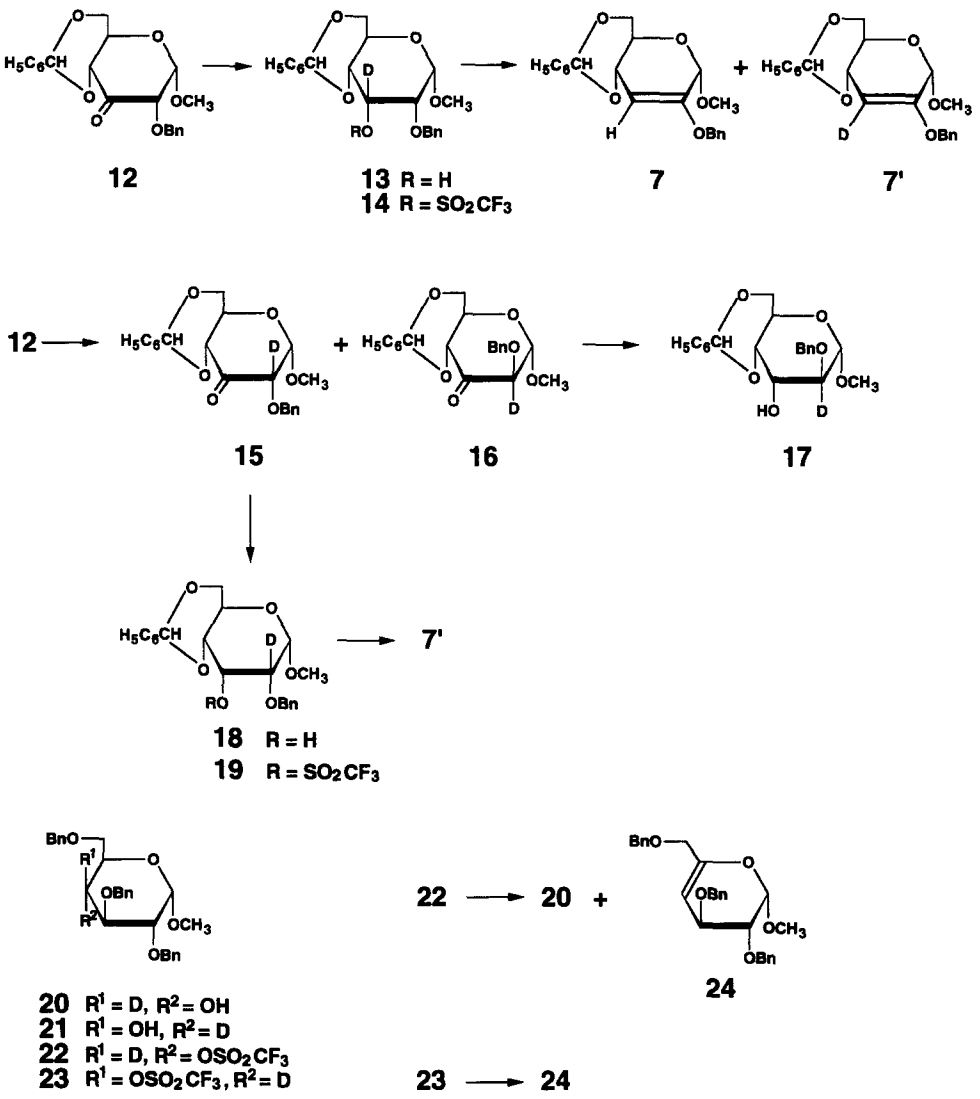


Scheme 1.

the 4-deuterated analogs (**22** and **23**) of methyl 2,3,6-tri-*O*-benzyl-4-*O*-triflyl-α-D-gluco- (**42** in ref. [10]) and galacto-pyranosides (**44** in ref. [10]) were prepared by triflation of a ~1:6 mixture of methyl 2,3,6-tri-*O*-benzyl-α-D-(4-^{2}H)gluco- and -(4-^{2}H)galacto-pyranosides [10], followed by chromatographic separation.

Reactions of deuterated triflates with MeLi and BuLi.—When the 3-deuterio-3-triflate **6** of α-D-*gluco* structure was treated with MeLi in diethyl ether, 3-deoxy-α-D-*erythro*-hex-2-enopyranoside **7** [10] and 3-deoxy-α-D-*erythro*-hex-3-enopyranoside **8** [10], both unlabeled, were obtained in ~50 and ~36% isolated yields, respectively. Similar treatment of the 2-deuterio analog (**11**) of **6** with MeLi gave the 3-deuterio analog (**7′**, ~41%) of **7** and 2-deuterio analog (**8′**, ~33%) of **8** (Table 1). By checking the ^{1}H NMR spectra, each of **7**, **8**, **7′**, and **8′** was proved to be pure isotopically, within experimental error. This result clearly indicates that **6** and **11**, and therefore non-labeled **6°**, are converted into the corresponding C-3 carbanions initially by α-hydrogen(deuterium) elimination [10] without accompanying of β-elimination, and formation of the 2-eno and 3-eno compounds followed, with vicinal hydrogen(deuterium) migration (from C-2 or 4). This means that H-2- or H-4-hydrogen(deuterium) abstraction by the reagents does not occur, and the present mechanism of elimination is different from the generally accepted β-elimination for this kind of reactions [1].

Compound **6** and **11** were next treated with BuLi in diethyl ether, whereupon α-elimination also occurred to give **7** and **8** (from **6**), and **7′** and **8′** (from **11**), as expected from the result with MeLi, but in addition, detriflyl products (**2** from **6**, and **10** from **11**) were produced in non-negligible yields (15–22%). This result indicates that MeLi and BuLi do not necessarily act in the same way, and this may be ascribed to the difference in bulkiness of the two reagents. Approach of a Bu^- ion to H-3 of **6** or **11** from the lower face may be hindered more than that of a Me^- ion owing to steric repulsions caused by



Scheme 2.

MeO-1, BnO-2, and O-4. In this case, the small difference in electronic charges between C-1's of H_3CLi (−0.483) and $Me(CH_2)_2CH_2Li$ (−0.478), calculated by MOPAC93/PM3 (see [10]), indicates that the difference between Me^- and Bu^- ions for electrostatic repulsion caused by the three oxygens is only small. This steric situation may cause a Bu^- ion to approach the sulfur of the TfO-3 group more readily than a Me^- ion, to cleave the triflyl group with release of an alcohol in competition with the attack on C*H*-3.

Next, the 3-deuterio-3-triflate (**14**) of α-D-*allo* structure was treated with MeLi or BuLi (Table 2). As this substance has a TfO-3 group in antiperiplanar position with respect to H-2, formation of C-3-labeled **7'** is expected to occur through β-hydrogen elimination. However, **14** gave actually mixtures of **7** (α-elimination) and **7'** (β-elimination) in high yields for both reactions, in the ratio of 2:3 (α:β) for MeLi, and 3:1 for BuLi, without accompaniment by the 3,4-unsaturated product (as shown in **41** in [10]); these ratios were confirmed by the ^1H and ^{13}C NMR spectra of the products. These results show that both abstraction of D-3 (α-elimination) and H-2 (β-elimination) occurred competitively, and the large difference in the two ratios (that is, $\alpha < \beta$ for MeLi, and $\alpha > \beta$ for BuLi) may be attributed to the differences in reactivity at, and approach to, D-3 and H-2 by the two reagents. As regards the approach of a Me^- or Bu^- ion to H-2ax, this may be somewhat hindered by the presence of axial lone-pair electrons at the ring-oxygen, the effect being more marked for Bu^- than Me^-, but to equatorial D-3, the two ions may be able to approach with similar ease. Finally, the 2-deuterio-3-triflate **19** was treated similarly with MeLi or BuLi, whereupon the same **7'** was obtained

from both reagents, although with the latter reagent the yield was slightly less than with the former. Lack of observation of β-elimination in these reactions indicates that abstraction of deuterium from C-2 is more difficult than hydrogen, which accords with the deuterium-isotope effect in conventional eliminations [14].

Treatment of the 4-deuterio-4-triflate **23** with the α-D-*galacto* structure with MeLi produced the unlabeled 4-enopyranoside **24** in 36% yield, indicating that only α-hydrogen elimination occurred; the poor yield was of a similar level as in the same reaction [10] of the unlabeled compound (**44** in ref. [10]) of **23**. Similar treatment of the 4-deuterio-4-triflate **22** with the α-D-*gluco* structure gave the corresponding 4-ol **20** by splitting off the triflyl group [10], although a small amount of **24** was also formed. The reason for the sluggishness of elimination in 4-triflates is not clear.

Here we compare the results obtained from the D-*gluco* (Table 1) and D-*allo* series of compounds (Table 2). For that purpose, compound **6°** (which is equal to **11°**), the most fundamental non-labeled compound, was treated with MeLi and BuLi. As shown in Table 1, **6°** gave, in treatment with BuLi, the corresponding 3-ol **2°**, in addition to **7** and **8** as reported [10], but in much lower yield (8%) than that from **6** or **11**. This suggests that a reactivity difference exists between labeled and non-labeled compounds. On the ratio of **8**/**7** or **8′**/**7′** for the D-*gluco* compounds (**6**, **6°**, and **11**), however, no regularity was observed; for example, the highest proportion (~0.8) of 3,4-unsaturation in **11** by MeLi (**11** > **6°**, **6**) is reversed (~0.43) in the reaction with BuLi (**6** > **6°** > **11**). This suggests that the deuterium-isotope effect [14] in this reaction operates complicated manner (see later description). On the other hand, in the D-*allo* series (**14** and **19**), the reactions [abstraction and migration of hydrogen (deuterium)] seem to proceed by an ion-like fashion, faster for hydrogen. Such a difference between the D-*gluco* and D-*allo* series of compounds may originate from the difference in reaction-mode (Scheme 3). The C-3 carbanion just formed from **6** (**6°** or **11**) will not be able to withdraw H(D)-2 or 4 as a proton(deuteron) across the C-2–C-3 bond, and therefore the atom is obliged to migrate to C-3 after formation of the C-3 carbene is mostly complete with removal of a triflyloxy group, according to the 1,2-shift rule for carbenes. [1] In contrast, in **14** or **19** the C-3 carbanion formed can degenerate directly by abstracting the H(or D)-2 atom as a proton(deuteron) to give the 2,3-unsaturated compounds; in this case, formation of the corresponding 3,4-unsaturated compound by migration of H-4 to C-3 may be suppressed by less acidic character of H-4 as compared to H(or D)-2 [10]. In our opinion, in the D-*gluco* series of compounds (**6**, **6°**, and **11**), the whole process toward unsaturation proceeds concertedly with removal of the H(D)-2 or 4 in a radical-like fashion for many the carbene, unlike in the D-*allo*

Table 1
The reaction yields (isolated, %) for **6°** (= **11°**) → **7** (α-elimination) + **8** (α-elim.) + **2°**, **6** → **7** (α-elim.) + **8** (α-elim.) + **2**, and **11** → **7′** (α-elim.) + **8′** (α-elim.) + **10** [a]

Reagent	**6°**		**6**			**11**		
MeLi	**7**	48	**7**	50,	49	**7′**	43,	39
	8	35	**8**	37,	35	**8′**	35,	30
	2°	0	**2**	t,	t	**10**	t,	t
	8/**7**	0.73	**8**/**7**	0.74,	0.71	**8′**/**7′**	0.82,	0.77
BuLi	**7**	46	**7**	43,	41	**7′**	42,	40
	8	25	**8**	27,	25	**8′**	19,	16
	2°	8	**2**	15,	19	**10**	18,	22
	8/**7**	0.54	**8**/**7**	0.63,	0.61	**8′**/**7′**	0.45,	0.40

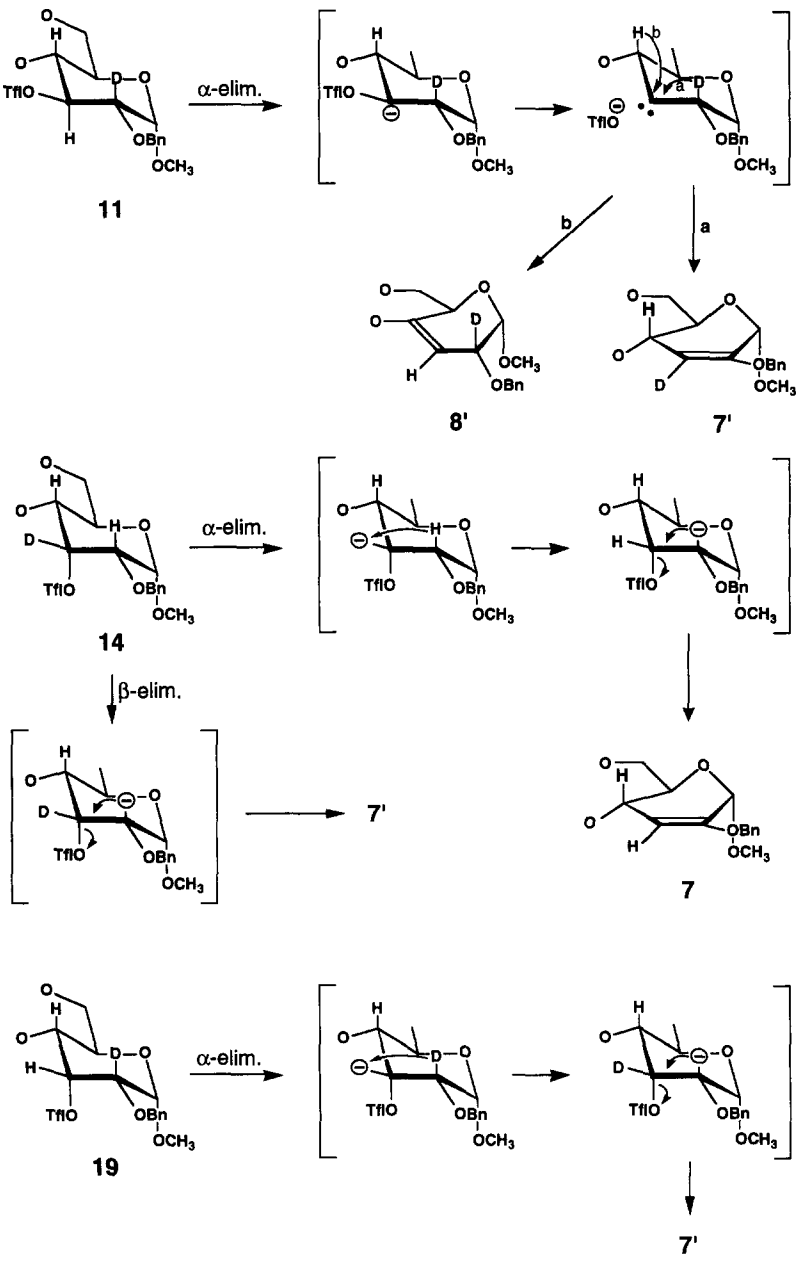
[a] Numerals in the same column are for respective synthetic runs; the second run as well as that for **6°** were performed in a similar scale and similar conditions as described in Section 3 (Experimental), respectively; as non-deuterated compound **6°** (= **11°**) gave comparative yields of products as shown for **6** or **11** for both MeLi and BuLi (see also [10]), influence by contamination (~5%) of **6°** (in **6**) and **11°** (in **11**) upon the present data will be only slight; thus no correction based on the experimental values was made; t: trace.

Table 2
Total yields [a] (isolated, %) of **7** (from **14** or **19** through α- and β-elimination, respectively) and **7′** (from **14** or **19** through β- and α-elimination, respectively), and the calculated β/α ratios [b] for the reaction of isotopically pure **14** (or **19**) to **7** + **7′**

Reagent		**14**		**19**	
MeLi	**7** + **7′**	80,	84	82,	80
	β/α	1.50 (1.32) [c],	1.50	0,	0
BuLi	**7** + **7′**	75,	72	72,	74
	β/α	0.33 (0.34) [c],	0.39	0,	0

[a] Numerals in the same column are for respective runs.
[b] Corrections were made based on the deuterium (and hydrogen) contents (determined by the NMR data; see Section 3, Experimental) of the starting compounds (**14** and **19**) and the products (**7** and **7′**).
[c] Based on the H*C*-3 (in **7**) and D*C*-3 (in **7′**) signals.

[1] See the description (p. 41) in [10] together with related references on carbene.



Scheme 3.

series (**14** and **19**), and this would be the reason why the former compounds insensitively discriminate C–H-2 and -4, or C–H and C–D giving the 2,3- and 3,4-unsaturated products simultaneously. The fact is shown straightforwardly by the difference in migratory ratios (4-H → 3)/(2-D → 3) (≡ **8′**/**7′**) for **11** → **7′** + **8′** (the ratio being 0.8 and 0.43) and **19** → **7′** + **8′** (the ratio being zero) (see Tables 1 and 2).

Throughout the experiments on 3- and 4-triflates, it was concluded that unsaturation occurs mainly through α-hydrogen elimination, and this feature may be attributed to the strongly electron-withdrawing character of trifluoromethyl group.

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 and ^{13}C at 62.9 MHz) were recorded with Bruker AC-250P and AMX-500 spectrometers, using Me_4Si as the internal references. 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.

Methyl 4,6-O-benzylidene-D-(3-^{2}H)glucopyranosides (**1**).—A solution of 1,2;5,6-di-*O*-isopropylidene-α-D-(3-^{2}H)glucofuranoside [11] (4.0 g, 15.3 mmol) in a mixture of 1,4-dioxane (50 mL) and aq 10 M HCl (4 mL) was kept overnight at room temperature. Evaporation of the solvent gave a crystalline residue, which was dissolved in HCl–MeOH (70 mL, saturated with gaseous HCl) and the solution was refluxed for 3 h. After concentration in vacuo, the resulting crystalline residue was dissolved in DMF (20 mL) containing $PhCH(OMe)_2$ (7.0 g, 46 mmol) and TsOH (400 mg), and the solution was kept overnight at room temperature. Addition of powdered NaOH (140 mg) followed by stirring for 30 min, and concentration of the organic solution in vacuo gave a residue, which was chromatographed (10:1 $CHCl_3$–MeOH) to give an anomeric mixture **1** as a solid (2.92 g, 67%). Recrystallization from hexane–EtOAc gave the pure α-anomer as a crystalline solid, mp 162–163 °C (unlabeled compound [15], 163–164 °C), $[\alpha]_D^{22}$ +108° (*c* 1, $CHCl_3$) [unlabeled [15], $[\alpha]_D^{20}$ +110° ($CHCl_3$)]; mass spectrum: *m/z* 284.20 (M^+ + 1); Calcd for $C_{14}H_{17}DO_6$: *m/z* 283.12 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.87 (d, 1 H, $J_{OH,2}$ 8 Hz, OH-2), 3.40 (s, 3 H, OCH_3), 3.43 (d, 1 H, $J_{4,5}$ 9 Hz, H-4), 3.47 (br s, 1 H, OH-3), 3.56 (br s, H-2), 3.70 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 11 Hz, H-6), 3.77 (ddd, 1 H, *J* 4, 9, and 11 Hz, H-5), 4.25 (dd, 1 H, $J_{5,6'}$ 4, $J_{6,6'}$ 11 Hz, H-6′), 4.42 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.52 (s, 1 H, C*H*Ph).

Methyl 2-O-benzyl-4,6-O-benzylidene-α- and -β-D-(3-^{2}H)glucopyranosides (**2** *and* **3**, *respectively) and methyl 3-O-benzyl-4,6-O-benzylidene-α- and -β-D-(3-^{2}H)glucopyranosides* (**4** *and* **5**, *respectively).*—To a solution of **1** (1.90 g, 6.71 mmol) in CH_2Cl_2 (100 mL) were added $Bu_4N^+HSO_4^-$ (456 mg), $C_6H_5CH_2Br$ (0.95 mL, 8.0 mmol), and aq 5% NaOH (20 mL), and the mixture was refluxed for 48 h. After cooling, the organic layer separated was washed with water, dried (Na_2SO_4), and concentrated. The residue was chromatographed (2:1 hexane–EtOAc) to give, from the faster-moving fractions, **3** as needles (352 mg, 14%), mp 122–124 °C (unlabeled compound [13], mp 124–125 °C), $[\alpha]_D^{22}$ −27° (*c* 1, $CHCl_3$) [unlabeled [13], $[\alpha]_D$ −27° ($CHCl_3$)]; mass spectrum: *m/z* 374.35 (M^+ + 1); Calcd for $C_{21}H_{23}DO_6$: *m/z* 373.16 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.54 (s, 1 H, OH), 3.32 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-2), 3.42 (ddd, 1 H, $J_{4,5}$ 10, $J_{5,6}$ 10.5, $J_{5,6'}$ 5 Hz, H-5), 3.52 (d, 1 H, $J_{4,5}$ 10 Hz, H-4), 3.57 (s, 3 H, OCH_3), 3.76 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10.5 Hz, H-6), 4.34 (dd, 1 H, H-6′), 4.41 (d, 1 H, H-1), 4.82 (ABq, 2 H, CH_2Ph), 5.51 (s, 1 H, C*H*Ph).

From the second-moving fractions, **2** was obtained as a crystalline solid (1.25 g, 50%), mp 129–130 °C (unlabeled compound [13], mp 131–132 °C), $[\alpha]_D^{22}$ +36° (*c* 1.6, $CHCl_3$) [unlabeled [13], $[\alpha]_D$ +35° ($CHCl_3$)]; mass spectrum: *m/z* 374.24 (M^+ + 1); Calcd for $C_{21}H_{23}DO_6$: *m/z* 373.16 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.61 (s, 1 H, OH), 3.37 (s, 3 H, OCH_3), 3.46 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-2), 3.48 (d, 1 H, $J_{4,5}$ 9 Hz, H-4), 3.70 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 3.80 (dt, 1 H, $J_{4,5} \approx J_{5,6} \sim 10$, $J_{5,6'}$ 4.5 Hz, H-5), 4.25 (dd, 1 H, H-6′), 4.61 (d, 1 H, H-1), 4.74 (ABq, 2 H, CH_2Ph), 5.51 (s, 1 H, C*H*Ph).

From the third-moving fractions a mixture of **4** and **5** was obtained as a solid (675 mg, 27%), which was chromatographed (20:1 $CHCl_3$–acetone) to give, from the faster-moving fractions, **4** as needles (485 mg, 19%), mp 186–188 °C (unlabeled compound [13], mp 187–188 °C), $[\alpha]_D^{22}$ +76° (c 1, $CHCl_3$) [unlabeled [13], $[\alpha]_D$ +78° ($CHCl_3$)]; mass spectrum: *m/z* 374.35 (M^+ + 1); Calcd for $C_{21}H_{23}DO_6$: 373.16 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.30 (slightly br d, 1 H, $J_{OH,2}$ 7 Hz, HO-2), 3.45 (s, 3 H, OCH_3), 3.63 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.72 (unresolved m, 1 H, H-2), 3.75 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 3.82 (dt, 1 H, $J_{4,5} \approx J_{5,6} \sim 10$, $J_{5,6'}$ 4.5 Hz, H-5), 4.29 (dd, 1 H, H-6′), 4.80 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.79 and 4.95 (each d of 1 H, *J* 11.5 Hz, CH_2Ph), 5.56 (s, 1 H, C*H*Ph).

From the slower-moving fractions **5** was obtained as needles (178 mg, 7%), mp 182–184 °C (unlabeled compound [13], mp 184–185 °C), $[\alpha]_D^{22}$ −49° (*c* 1, $CHCl_3$) [unlabeled [13], $[\alpha]_D$ −48° ($CHCl_3$)]; mass spectrum: *m/z* 374.27 (M^+ + 1); Calcd for $C_{21}H_{23}DO_6$: *m/z* 373.16 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.44 (slightly br d, 1 H, $J_{OH,2} \sim 2$ Hz, HO-2), 3.46 (dt, 1 H, $J_{4,5} \approx J_{5,6} \sim 10$, $J_{5,6'} \sim 5$ Hz, H-5), 3.55 (br dd, *J* ~ 2 and ~ 8 Hz, H-2), 3.58 (s, 3 H, OCH_3), 3.71 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.81 (t, 1 H, *J* 10 Hz × 2, H-6), 4.33 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.37 (dd, 1 H, H-6′), 4.80 and 4.98 (each d of 1 H, *J* 11.5 Hz, CH_2Ph), 5.58 (s, 1 H, C*H*Ph).

Methyl 2-O-benzyl-4,6-O-benzylidene-3-O-triflyl-α-D-(3-^{2}H)glucopyranoside (**6**).—To an ice-cold solution of **2** (630 mg, 1.70 mmol) in 1:2 pyridine–CH_2Cl_2 (12 mL) was added $(CF_3SO_2)_2O$ (624 mg, 2.2 mmol) and the solution was kept for 1 h in the cold. After addition of water (1 mL), the mixture was concentrated, and the residue was chromatographed (3:1 hexane–EtOAc) to give **6** as a solid (825 mg, 97%), mp 94–96 °C (decomp) [unlabeled compound [10], mp 96–97 °C (decomp)], $[\alpha]_D^{22}$ +0.5° (*c* 1, $CHCl_3$) [unlabeled [10], $[\alpha]_D^{24}$ −0.5° ($CHCl_3$)]; mass

spectrum: m/z 506.28 ($M^+ + 1$); Calcd for $C_{22}H_{22}DF_3O_8S$: m/z 505.11 (M^+); ^1H NMR ($CDCl_3$): δ 3.35 (s, 3 H, OCH_3), 3.64 (d, 1 H, $J_{1,2}$ 4 Hz, H-2), 3.70 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.73 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 3.83 (dt, 1 H, $J_{4,5} \approx J_{5,6} \sim 10$, $J_{5,6'}$ 4.5 Hz, H-5), 4.29 (dd, 1 H, H-6'), 4.55 (d, 1 H, H-1), 4.58 and 4.83 (each d of 1 H, J 12 Hz, CH_2Ph), 5.21 (t, $J_{2,3} \approx J_{3,4}$ 9.5 Hz, ~ 0.07 H, H-3), 5.54 (s, 1 H, CHPh).

Reaction of **6** *with MeLi–Et_2O giving methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-*D-erythro-*hex-2-enopyranoside* (**7**) *and methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-*D-erythro-*hex-3-enopyranoside* (**8**).—To a cold (−50 °C) solution of **6** (170 mg, 0.34 mmol) in dry Et_2O (6 mL) was added MeLi (1.36 mmol; commercial 1.4 M MeLi in Et_2O was used), and the solution was kept for 1 h at room temperature. Aqueous 2 M NH_4Cl and $CHCl_3$ (50 mL) were stirred in and the organic layer separated was washed with water, dried (Na_2SO_4), and concentrated. Chromatography (4:1 hexane–EtOAc) of the residue gave **7** as needles (59 mg, 50%), mp 132–133 °C (ref. [10], mp 133–134 °C), $[\alpha]_D^{22}$ +21° (c 0.5, $CHCl_3$) [ref. [10], $[\alpha]_D^{22}$ +21° ($CHCl_3$)], and **8** as needles (44 mg, 37%), mp 108–109 °C (ref. [10], mp 108–109 °C), $[\alpha]_D^{22}$ +50° (c 1, $CHCl_3$) [ref. [10], $[\alpha]_D^{22}$ +51° ($CHCl_3$)]. ^1H NMR ($CDCl_3$) compound **7**: δ 3.50 (s, 3 H, OCH_3), 3.83 (t, 1 H, H-6), 4.00 (ddd, 1 H, H-5), 4.29 (d, 1 H, H-4), 4.30 (dd, 1 H, H-6'), 4.82 (s, 1 H, H-1), 4.83 (ABq, 2 H, CH_2Ph), 5.07 [d, $J_{3,4} \sim 1$ Hz, 1.003 H (another synthetic run: 0.984 H), H-3], 5.58 (s, 1.000 H, CHPh). Compound **8**: δ 3.51 (s, 3 H, OCH_3), 3.70 (t, 1 H, H-6), 4.26–4.41 (m, 3 H, H-2,5,6'), 4.64 (ABq, 2 H, CH_2Ph), 4.79 (dd, 1 H, H-1), 5.34 (s with small splitting, 0.978 H, H-3), 5.54 (s, 1.000 H, CHPh).

Reaction of **6** *with BuLi–Et_2O giving* **7**, **8**, *and* **2**. —Compound **6** (110 mg, 22 mmol) was treated with BuLi (0.66 mmol; 2.5 M in hexane solution was used) as described for **6** to **7** to give **7** as needles (33 mg, 43%), **8** as needles (21 mg, 27%), and **2** as a solid (12 mg, 15%). ^1H NMR ($CDCl_3$) compound **7**: δ 5.07 (d, 0.973 H, H-3), 5.58 (s, 1.000 H, CHPh). Compound **8**: δ 5.34 (s, 0.982 H, H-3), 5.54 (s, 1.000 H, CHPh); compare compound **8** prepared from **6**° with BuLi: δ 4.79 (dd, 0.97 H, H-1), 5.34 (s, 0.95 H, H-3), 5.54 (s, 1.00 H, CHPh).

*Methyl 3-O-benzoyl-4,6-O-benzylidene-α-*D-*(2-*^{2}H*)glucopyranoside* (**9**).—To a cold solution (−78 °C) of oxalyl chloride (7.86 g, 61.9 mmol) in CH_2Cl_2 (100 mL) was added $(CH_3)_2SO$ (8.8 mL, 124 mmol), and after 15 min, methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside [16] (6.0 g, 15.5 mmol) in CH_2Cl_2 (60 mL) was added gradually, and the mixture was stirred for 30 min at −78 °C. Et_3N (20 mL, 143 mmol) was added, and the solution was kept for 1 h at 0 °C. After the solution was washed with water, the organic layer was dried (Na_2SO_4) and concentrated. To a cold (0 °C) solution of the residue in MeOH (30 mL) was added $NaBD_4$ (1.0 g, 24 mmol), and after 15 min, water (30 mL) was added and the precipitate was dried to give **9** as a solid (5.61 g, 94%); recrystallization (3:1 hexane–EtOAc) gave needles, mp 218–219 °C [ref. [12], no data reported; unlabeled compound [16], mp 217–218 °C (from EtOH)], $[\alpha]_D^{22}$ +33° (c 1.2, $CHCl_3$) [ref. [12], no data reported; unlabeled [16], $[\alpha]_D^{23}$ +32° ($CHCl_3$)]; mass spectrum: m/z 356.19 ($M^+ -$ OMe), 388.18 ($M^+ + 1$); Calcd for $C_{21}H_{21}DO_7$: m/z 387.14 (M^+); ^1H NMR ($CDCl_3$): δ 2.49 (s, 1 H, OH), 3.50 (s, 3 H, OCH_3), 3.76 (t, 1 H, $J_{3,4} \approx J_{4,5}$ 10 Hz H-4), 3.80 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 3.94 (dt, 1 H, J 4, 5, 10, and 10 Hz, H-5), 4.34 (dd, 1 H, $J_{5,6'}$ 4.5, $J_{6,6'}$ 10 Hz, H-6'), 4.86 (s, 1 H, H-1), 5.53 (s, 1 H, CHPh), 5.59 (d, 1 H, $J_{3,4}$ 10 Hz, H-3).

*Methyl 2-O-benzyl-4,6-O-benzylidene-α-*D-*(2-*^{2}H*)glucopyranoside* (**10**).—To a solution of **9** (4.3 g, 11.1 mmol) in 1:1 cyclohexane–CH_2Cl_2 (250 mL) were added benzyl trichloroacetimidate (4.12 mL, 22.2 mmol) and CF_3SO_3H (100 μL), and the solution was kept overnight at room temperature. CH_2Cl_2 (150 mL) and aq M $NaHCO_3$ (80 mL) were added, and after shaking, the organic layer separated was dried (Na_2SO_4) and concentrated. The residue was dissolved in MeOH, slight amount of NaOMe was added (Zemplén deacylation), and after 1 h, the solution was concentrated to give a residue, which was chromatographed (2:1 hexane–EtOAc) to give **10** as a crystalline solid (2.86 g, 69%), mp 130–132 °C (unlabeled compound [13], mp 131–132 °C), $[\alpha]_D^{22}$ +32° (c 3, $CHCl_3$) [unlabeled [13], $[\alpha]_D^{22}$ +35° ($CHCl_3$)]; mass spectrum: m/z 342.19 ($M^+ -$ OMe), 372.19 ($M^+ - 1$), 374.19 ($M^+ + 1$); Calcd for $C_{21}H_{23}DO_6$: m/z 373.16 (M^+); ^1H NMR ($CDCl_3$): δ 2.61 (d, 1 H, $J_{OH,3}$ 2 Hz, OH), 3.37 (s, 3 H, OCH_3), 3.49 (t, 1 H, $J_{3,4} \approx J_{4,5}$ 9.5 Hz, H-4), 3.70 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 3.80 (ddd, 1 H, J 4.5, 9.5, and 10 Hz, H-5), 4.14 (slightly broadened dd, 1 H, H-3), 4.25 (dd, 1 H, H-6'), 4.61 (s, 1 H, H-1), 4.74 (ABq, 2 H, CH_2Ph), 5.51 (s, 1 H, CHPh).

*Methyl 2-O-benzyl-4,6-O-benzylidene-3-O-triflyl-α-*D-*(2-*^{2}H*)glucopyranoside* (**11**).—Compound **10**

(2.0 g) was triflated as described for **6** to give **11** as a solid (2.26 g, 86%), mp 97–98 °C (decomp) [unlabeled compound [10], mp 96–97 °C (decomp)], $[\alpha]_D^{23}$ −1.5° (*c* 3, $CHCl_3$) [unlabeled [10], $[\alpha]_D^{24}$ −0.5° ($CHCl_3$)]; mass spectrum: *m/z* 504.20 (M^+ − 1), 506.19 (M^+ + 1); Calcd for $C_{22}H_{22}DF_3O_8S$: *m/z* 505.11 (M^+); ^1H NMR ($CDCl_3$): δ 3.35 (s, 3 H, OCH_3), 3.64 (dd, ~0.05 H, H-2), 3.71 (t, 1 H, $J_{3,4} \approx J_{4,5} \sim 10$ Hz, H-4), 3.72 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 3.83 (dt, 1 H, *J* 4.5, 10, and 10 Hz, H-5), 4.29 (dd, 1 H, H-6′), 4.55 (s, 1 H, H-1), 4.58 and 4.83 (each d of 1 H, *J* 12 Hz, CH_2Ph), 5.20 (d, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 5.54 (s, 1 H, C*H*Ph).

Reaction of **11** *with MeLi–Et_2O giving methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-D-(3-^{2}H)erythro-hex-2-enopyranoside* (**7′**), *methyl 2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-D-(2-^{2}H)erythro-hex-3-enopyranoside* (**8′**).—Compound **11** (150 mg, 0.3 mmol) was treated with MeLi (1.2 mmol) as described for **6** to **7** to give **7′** as needles (45 mg, 43%) and **8′** as needles (37 mg, 35%). Compound **7′**, mp 132–133 °C (unlabeled compound [10], mp 133–134 °C), $[\alpha]_D^{22}$ +20° (*c* 1, $CHCl_3$) [unlabeled [10], $[\alpha]_D^{22}$ +21° ($CHCl_3$)]; mass spectrum: *m/z* 324.18 (M^+ − OMe), 354.19 (M^+ − 1); Calcd for $C_{21}H_{21}DO_5$: *m/z* 355.15 (M^+); ^1H NMR ($CDCl_3$): δ 3.51 (s, 3 H, OCH_3), 3.83 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 4.00 (ddd, 1 H, $J_{4,5}$ 9, $J_{5,6}$ 10, $J_{5,6'}$ 4.5 Hz, H-5), 4.29 (d, 1 H, $J_{4,5}$ 9 Hz, H-4), 4.30 (dd, 1 H, H-6′), 4.82 (s, 1 H, H-1), 4.83 (ABq, 2 H, CH_2Ph), 5.07 (d, 0.037 H, H-3), 5.58 (s, 1.000 H, C*H*Ph). Compound **8′**, mp 107–109 °C (unlabeled compound [10], 108–109 °C), $[\alpha]_D^{23}$ +49° (*c* 1, $CHCl_3$) (unlabeled compound [10], $[\alpha]_D^{22}$ +51°); mass spectrum: *m/z* 356.24 (M^+ + 1), 354.24 (M^+ − 1); Calcd for $C_{21}H_{21}DO_5$: *m/z* 355.15 (M^+); ^1H NMR ($CDCl_3$): δ 3.51 (s, 3 H, OCH_3), 3.70 (t, 1 H, H-6), 4.26–4.41 (m, 2 H, H-5,6′), 4.65 (ABq, 2 H, CH_2Ph), 4.79 (s, 1.010 H, H-1), 5.34 (apparently short-range t, 0.971 H, H-3), 5.55 (s, 1.000 H, C*H*Ph).

Reaction of **11** *with BuLi–Et_2O giving* **7′**, **8′**, *and methyl 2-O-benzyl-4,6-O-benzylidene-α-D-(2-^{2}H)glucopyranoside* (**10**).—Compound **11** (200 mg, 0.39 mmol) was treated with BuLi (1.48 mmol) as described for **6** to **7** to give **7′** as needles (59 mg, 42%), **8′** as needles (27 mg, 19%), and **10** as a crystalline solid (26 mg, 18%). ^1H NMR ($CDCl_3$) compound **7′**: δ 5.07 (d, 0.036 H, H-3), 5.58 (s, 1.000 H, C*H*Ph). Compound **8′**: δ 4.97 (s, 0.994 H, H-1), 5.34 (apparently short-range t, 0.980 H, H-3), 5.55 (s, 1.000 H, C*H*Ph).

Methyl 2-O-benzyl-4,6-O-benzylidene-α-D-ribo-hexopyranosid-3-ulose (**12**).—To a cold solution (−78 °C) of oxalyl chloride (6.12 g, 48.2 mmol) in CH_2Cl_2 (150 mL) was added Me_2SO (7.56 mL, 96.7 mmol), and after 15 min, methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside [13] (6.00 g, 16.2 mmol) in CH_2Cl_2 (60 mL) was added gradually, and the mixture was stirred for 30 min at −78 °C. Et_3N (22 mL, 160 mmol) was added, and the solution was kept for 1 h at room temperature. After the solution had been washed with water, the organic layer separated was dried ($NaSO_4$) and concentrated to give a crystalline residue (6.35 g), which was recrystallized from MeOH to give **12** as a crystalline solid (5.16 g, 86%), mp 181–182 °C, $[\alpha]_D^{22}$ −35° (*c* 2, $CHCl_3$); mass spectrum: *m/z* 371.32 (M^+ + 1); Calcd for $C_{21}H_{22}O_6$: *m/z* 370.14 (M^+); ^1H NMR ($CDCl_3$): δ 3.44 (s, 3 H, OCH_3), 3.87 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 4.08 (ddd, 1 H, $J_{4,5}$ 9.5, $J_{5,6}$ 10, $J_{5,6'}$ 4.5 Hz, H-5), 4.14 (dd, 1 H, $J_{1,2}$ 4.8, $J_{2,4}$ 1.5 Hz, H-2), 4.19 (dd, 1 H, $J_{2,4}$ 1.5, $J_{4,5}$ 9.5 Hz, H-4), 4.38 (dd, 1 H, H-6′), 4.60 and 4.96 (each d of 1 H, *J* 12 Hz, CH_2Ph), 5.06 (d, 1 H, H-1), 5.52 (s, 1 H, C*H*Ph). ^{13}C NMR ($CDCl_3$): d 55.64 (OCH_3), 65.44 (C-5), 69.46 (C-6), 72.63 (CH_2Ph), 79.60 (C-2), 82.16 (C-4), 101.95 (*C*HPh), 102.58 (C-1), 196.29 (C-3).

Methyl 2-O-benzyl-4,6-O-benzylidene-α-D-(3-^{2}H)allopyranoside (**13**).—To a solution of **12** (3.70 g, 10.0 mmol) in MeOH (90 mL) was added $NaBD_4$ (0.59 g, 14.1 mmol) and the solution was kept for 2 h at room temperature. After excess CO_2 (dry ice) had been added, the solution was concentrated and the residue was chromatographed (2:1 hexane–EtOAc) to give **13** as a crystalline solid (3.65 g, 98%), mp 73–74 °C (unlabeled compound [10], mp 73 °C), $[\alpha]_D^{22}$ +6° (*c* 1, $CHCl_3$) [unlabeled [10], $[\alpha]_D^{25}$ +5° ($CHCl_3$)]; mass spectrum: *m/z* 374.24 (M^+ + 1); Calcd for $C_{21}H_{23}DO_6$: *m/z* 373.16 (M^+); ^1H NMR ($CDCl_3$): δ 3.17 (s, 1 H, OH), 3.41 (d, 1 H, $J_{4,5}$ 10 Hz, H-4), 3.45 (s, 3 H, OCH_3), 3.51 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 3.71 (t, 1 H, H-6), 4.15 (dt, 1 H, $J_{4,5} \approx J_{5,6}$ 10, $J_{5,6'}$ 5 Hz, H-5), 4.35 (dd, 1 H, H-6′), 4.70 (ABq, 2 H, CH_2Ph), 4.76 (d, 1 H, H-1), 5.53 (s, 1 H, C*H*Ph).

Methyl 2-O-benzyl-4,6-O-benzylidene-3-O-triflyl-α-D-(3-^{2}H)allopyranoside (**14**).—To a cold (−20 °C) solution of **13** (1.6 g, 5.88 mmol) in 1:5 pyridine–CH_2Cl_2 (20 mL) was added $(CF_3SO_2)_2O$ (2.16 g, 7.64 mmol), and the solution was kept for 6 h in the cold. Water (1 mL) and CH_2Cl_2 (200 mL) were added, and the solution was poured into aq M HCl

(50 mL) under stirring. The organic layer separated was washed with water and aq $NHCO_3$ (saturated), dried (Na_2SO_4), and concentrated to give a residue, which was chromatographed (2:1 hexane–EtOAc) to give **14** as a solid (1.76 g, 81%), mp 87–89 °C (decomp)], $[\alpha]_D^{22}$ −5° (*c* 1, $CHCl_3$) [unlabeled [10], $[\alpha]_D^{23}$ −3° ($CHCl_3$)]; mass spectrum: *m/z* 506.38 ($M^+ + 1$); Calcd for $C_{22}H_{22}DF_3O_8S$: *m/z* 505.11 (M^+); ^1H NMR ($CDCl_3$): δ 3.45 (s, 3 H, OCH_3), 3.58 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 3.61 (d, 1 H, $J_{4,5}$ 10 Hz, 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, C*H*$_2$Ph), 5.43 [t, *J* ~ 3 Hz × 2, 0.051 H (another synthetic run: 0.054 H), H-3], 5.52 (*c*, 1 H, C*H*Ph).

Reaction of **14** *with MeLi–Et$_2$O to give a mixture of* **7** *and* **7′**.—Treatment of **14** (110 mg, 0.22 mmol) with MeLi (0.88 mmol) as described for **6** to **7** gave a solid (61 mg, 80%); ^1H NMR ($CDCl_3$): δ 3.51 (s, 3 H, OCH_3), 3.83 (t, 1 H, H-6), 4.00 (ddd, 1 H, H-5), 4.29 (apparently d, 1 H, $J_{4,5}$ 9 Hz, H-4), 4.30 (dd, 1 H, $J_{5,6'}$ 4.5, $J_{6,6'}$ 10 Hz, H-6′), 4.82 (s, 1 H, H-1), 4.83 (ABq, 2 H, C*H*$_2$Ph), 5.07 [br d, 0.430 H (the second synthetic run: 0.430 H), $J_{3,4}$ 1.5 Hz, H-3], 5.58 (s, 1.000 H, C*H*Ph). ^{13}C NMR ($CDCl_3$): all signals except for C-3 were the same with those for **7** reported [10]; δ 98.37 (s, the strength was taken as 1 C, H*C*-3), 98.10 (t of equal strength *J* 25 Hz, 1.17 C, D*C*-3).

Reaction of **14** *with BuLi–Et$_2$O to give a mixture of* **7** *and* **7′**.—Treatment of **14** (120 mg, 0.24 mmol) with BuLi (0.72 mmol) as described for **6** to **7** gave needles (63 mg, 75%); ^1H NMR ($CDCl_3$): δ 3.51 (s, 3 H, OCH_3), 3.83 (t, 1 H, H-6), 4.00 (ddd, 1 H, H-5), 4.29 (apparently d, 1 H, $J_{4,5}$ 9 Hz, H-4), 4.30 (dd, 1 H, H-6′), 4.82 (s, 1 H, H-1), 4.83 (ABq, 2 H, C*H*$_2$Ph), 5.07 [br d, 0.763 H (the second synthetic run: 0.733 H), $J_{3,4}$ 1.5 Hz, H-3), 5.58 (s, 1 H, C*H*Ph). ^{13}C NMR ($CDCl_3$): all signals except for C-3 were the same with those for **7** reported [10]; δ 98.37 (s, the strength was taken as 1 C, H*C*-3), 98.10 (t of equal strength, *J* 25 Hz, 0.32 C, D*C*-3).

*Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-(2-^{2}H)ribo-hexopyranosid-3-ulose* (**15**), *methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-(2-^{2}H)altropyranoside* (**17**), *and methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-(2-^{2}H)allopyranoside* (**18**).—A solution of **12** (2.5 g, 6.75 mmol) in a 4:4:2:3 mixture of 1,4-dioxane–THF–Et_3N–D_2O (13 mL) was kept for 3 days at room temperature. After concentration in vacuo, 1,4-dioxane (3 mL) and D_2O (1 mL) were added and, after shaking awhile, the mixture was filtered and dried to give **15** as a solid (1.5 g, 60%), mp 180–182 °C (unlabeled **12**, 181–182 °C), $[\alpha]_D^{24}$ −37° (*c* 1, $CHCl_3$) [unlabeled **12**, $[\alpha]_D^{22}$ −35° (*c* 2, $CHCl_3$)]; ^1H NMR ($CDCl_3$): 3.44 (s, 3 H, OCH_3), 3.86 (t, 1 H, H-6), 4.08 (ddd, 1 H, H-5), 4.14 (dd, < 0.05 H, H-2), 4.19 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.38 (dd, 1 H, H-6′), 4.60 and 4.96 (each d of 1 H, C*H*$_2$Ph), 5.05 (s, 1 H, H-1), 5.52 (s, 1 H, C*H*Ph).

The filtrate just described containing **15** and **16** was concentrated in vacuo, $NaBH_4$ (200 mg, 5.26 mmol) in MeOH (10 mL) was added, and the solution was kept for 1 h at room temperature. Concentration gave a residue, which was chromatographed (3:1 toluene–EtOAc) to give **17** as crystals (0.75 g, 30%), mp 94–96 °C, $[\alpha]_D^{23}$ +50° (*c* 2, $CHCl_3$); mass spectrum: *m/z* 374.05 ($M^+ + 1$); Calcd for $C_{21}H_{23}DO_6$: *m/z* 373.16 (M^+); ^1H NMR ($CDCl_3$): δ 2.89 (d, 1 H, $J_{OH,3}$ 7 Hz, OH), 3.42 (s, 3 H, OCH_3), 3.85 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ 10 Hz, H-6), 3.98 (dd, 1 H, $J_{3,4}$ 3.0, $J_{4,5}$ 10 Hz, H-4), 4.13–4.24 (m, 2 H, H-3,5), 4.34 (dd, $J_{5,6'}$ 5, $J_{6,6'}$ 10 Hz, H-6′), 4.64 (ABq, 2 H, C*H*$_2$Ph), 4.73 (slightly br s, H-1), 5.64 (s, 1 H, C*H*Ph); no peak was observed at d 3.71 (dd, 1 H, $J_{1,2}$ ~ 1, $J_{2,3}$ 3.2 Hz, H-2), which appeared in the non-labeled analog of **17** prepared from **12** with $NaBH_4$ in the manner already described.

Compound **15** (1.4 g, 3.77 mmol) was reduced with $NaBH_4$ (0.22 g, 5.79 mmol) as before to give **18** as needles (1.36 g, 97%), mp 72–73 °C (unlabeled compound [10], mp 73 °C), $[\alpha]_D^{23}$ +4° (*c* 3, $CHCl_3$) [unlabeled [10], $[\alpha]_D^{25}$ +5°($CHCl_3$)]; mass spectrum: *m/z* 374.21 ($M^+ + 1$); Calcd for $C_{21}H_{23}DO_6$: *m/z* 373.16 (M^+); ^1H NMR ($CDCl_3$): δ 3.19 (d, 1 H, $J_{OH,3}$ 7 Hz, OH), 3.42 (dd, 1 H, $J_{3,4}$ 3, $J_{4,5}$ 10 Hz, H-4), 3.45 (s, 3 H, OCH_3), 3.51 (t, *J* 3.5 Hz × 2, 0.045 H, H-2), 3.71 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ ~ 10 Hz, H-6), 4.16 (dt, 1 H, *J* 5, 10, and 10 Hz, H-5), 4.35 (dd, 1 H, H-6′), 4.44 (slightly br dd, 1 H, $J_{3,4}$ 3, $J_{OH,3}$ 7 Hz, H-3), 4.70 (ABq, 2 H, C*H*$_2$Ph), 4.76 (s, 1 H, H-1), 5.53 (s, 1 H, C*H*Ph).

*Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-triflyl-α-*D*-(2-^{2}H)allopyranoside* (**19**).—Triflation of **18** (1.2 g, 3.21 mmol) as described for **14** gave **19** as a solid (1.38 g, 85%), mp 88–90 °C (decomp) [unlabeled compound [10], mp 87–89 °C (decomp)], $[\alpha]_D^{24}$ −7° (*c* 3, $CHCl_3$) [unlabeled [10], $[\alpha]_D^{23}$ −3° ($CHCl_3$)]; mass spectrum: *m/z* 474.16 (M^+ − OMe), 504.20 ($M^+ - 1$), 506.19 ($M^+ + 1$); Calcd for $C_{22}H_{22}DF_3O_8S$: 505.11 (M^+); ^1H NMR ($CDCl_3$): δ 3.44 (s, 3 H, OCH_3), ~ 3.58 (~ 0.05 H, partly overlapped with H-4 signals, H-2), 3.60 (dd, 1 H, $J_{3,4}$ 2.5, $J_{4,5}$ 10 Hz, H-4), 3.67 (t, 1 H, $J_{5,6} \approx J_{6,6'}$ ~ 10 Hz, H-6), 4.17 (dt, 1 H, *J* 5, 10, and 10 Hz, H-5),

4.32 (dd, 1 H, H-6′), 4.70 (s, 1 H, H-1), 4.71 (ABq, 2 H, CH_2Ph), 5.42 (d, 1 H, $J_{3,4}$ 2.5 Hz, H-3). 5.52 (s, 1 H, C*H*Ph).

Reaction of **19** *with MeLi–Et_2O to give* **7′**.—Treatment of **19** (130 mg, 0.26 mmol) with MeLi (1.04 mmol) as described for **6** to **7** gave **7′** as needles (75 mg, 82%); ^{1}H NMR ($CDCl_3$): δ (all signals were identical with those for **7′** prepared from **11**) 5.07 [d, 0.075 H (the second synthetic run: 0.052 H), H-3].

Reaction of **19** *with BuLi–Et_2O to give* **7′**.—Treatment of **19** (140 mg, 0.28 mmol) with BuLi (0.84 mmol) as described for **6** to **7** gave **7′** as needles (71 mg, 72%); ^{1}H NMR ($CDCl_3$): δ (all signals were identical with those for **7′** prepared from **11**) 5.07 [d, 0.067 H (the second synthetic run: 0.055 H), H-3].

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-triflyl-α-*D*-(4-^{2}H)glucopyranoside* (**22**) *and methyl 2,3,6-tri-*O*-benzyl-4-*O*-triflyl-α-*D*-(4-^{2}H)galactopyranoside* (**23**).—A cold (−30 °C) pyridine solution (20 mL) of a ~1:6 mixture of **20** and **21** (1.50 g, 3.21 mmol), which was prepared [10] by oxidation of methyl 2,3,6-tri-O-benzyl-α-D-glucopyranoside followed by reduction with $NaBD_4$, was treated with $(CF_3SO_2)_2O$ (1.20 g, 4.20 mmol) as described for **14**. The resulting mixture of triflates was chromatographed (15:1 toluene–EtOAc) to give, from the faster-moving fractions, **22** as a solid (249 mg, 13%), mp 78–79 °C (unlabeled compound [17], mp 80 °C), $[\alpha]_D^{24}$ +26° (*c* 1.1, $CHCl_3$) (unlabeled [17], no data reported); mass spectrum: *m/z* 506.18 ($M^+ - CH_2Ph$), 596.18 ($M^+ - 1$); Calcd for $C_{29}H_{30}DF_3O_8S$: *m/z* 597.18 (M^+); ^{1}H NMR ($CDCl_3$): d 3.38 (s, 3 H, OCH_3), 3.59 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 9.5 Hz, H-2), 3.65 (dd, 1 H, $J_{5,6}$ 3.5, $J_{6,6'}$ 11 Hz, H-6), 3.68 (dd, 1 H, $J_{5,6'}$ 2, $J_{6,6'}$ 11 Hz, H-6′), 3.91 (t, 1 H, J ~ 3 Hz × 2, H-5), 4.05 (d, 1 H, $J_{2,3}$ 9.5 Hz, H-3), 4.54 (ABq, 2 H, CH_2Ph), 4.55 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.56 and 4.74 (each d, 1 H, J 12 Hz, CH_2Ph), 4.89 (ABq, 2 H, CH_2Ph), 5.01 (t, J ~ 10 Hz × 2, < 0.03 H, H-4).

From the slower-moving fractions **23** was obtained as a syrup (1.45 g, 75%), $[\alpha]_D^{24}$ +30° (*c* 2, $CHCl_3$) [ref. [10], $[\alpha]_D^{22}$ +30° ($CHCl_3$)]. Its Mass and ^{1}H NMR spectra were identical with those for the same compound reported [10] [substantially no peak was observed at δ 5.40 (H-4)].

Reaction of **22** *with MeLi–Et_2O to give* **20** *and* **24**.—Treatment of **22** (50 mg, 0.08 mmol) with MeLi (0.32 mmol) as described for **7** gave **20** [10] (31 mg, 79%) together with **24** (6.0 mg, 16%), the latter being identical with the specimen prepared from the non-deuterated analog of **23** [10] in every ^{1}H NMR signal.

Reaction of **23** *with MeLi–Et_2O to give methyl 2,3,6-tri-*O*-benzyl-4-deoxy-β-*L*-threo-hex-4-enopyranoside* (**24**).—Treatment of **23** (120 mg, 0.20 mmol) with MeLi (0.8 mmol) as described for **7** gave, after chromatography (3:1 hexane–EtOAc), **24** [10] as a syrup (32 mg, 36%) together with unknown compounds, **24** being identical with the specimen prepared from the non-deuterated analog of **23** in every ^{1}H NMR signal.

Acknowledgements

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

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