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α-Hydrogen Elimination in Some Carbohydrate Triflates

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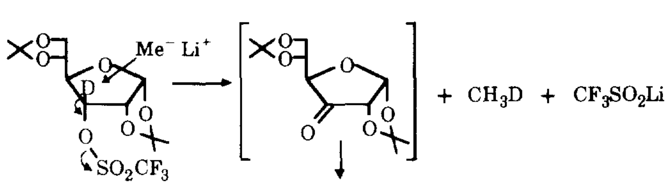
Abstract: In some carbohydrate triflates, treatment with MeLi (or BuLi) in ether caused α-hydrogen elimination initially, then the resulting carbanion is stabilized to give either *C*-methyl(or butyl)-hydroxy derivatives or unsaturated products.

Substitution reactions using triflates are one of the most fundamental procedures widely used[1] in carbohydrate chemistry. The relative reactivities of mesylate, tosylate, and triflate are reported[2] to be 1.00, 0.70, and 56,000, respectively. Other reactions frequently observed[1] in triflates are elimination (by loss of elements of CF_3SO_3H) and several rearrangements (all initiated by loss of $CF_3SO_2^-$). However, we have found that, on treatment with BuLi in ether, some carbohydrate triflates showed a new-type reaction. In this communication, we describe such examples as well as the elimination reactions, which are considered to be closely correlated with the above new reactions.

When 1,2:5,6-di-*O*-isopropylidene-3-*O*-triflyl-D-allofuranose[3] (**3**) was treated with BuLi in ether (3 molar excess for **3**, 2 h, at room temperature), a compound which was neither a 3-butyl-D-gluco derivative [derived from S_N2 process; compound **3** is known[1,4] to give a number of substitution products (NH_2, NHC_6H_5, F, Cl, Br, I, SCN, etc.) readily] nor a 3,4 (or 2,3) unsaturated compound, was produced in high yield. By chemical analysis (^1H and ^{13}C NMR, and other usual tools) the compound was identified as 1,2:5,6-di-*O*-isopropylidene-3-*C*-butyl-D-allofuranose[5] (**5**), the structure being confirmed by comparison with the compound prepared from **6** and BuLi. Treatment of **3** with MeLi gave an analogous result (Table 1).

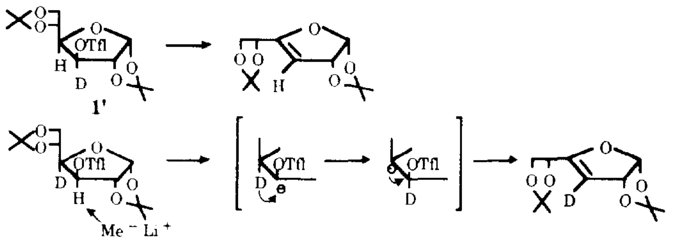
To clarify the mechanism, 3-deuterio compound **3'** was prepared by triflation of the [3-^2H] derivative[6] of 1,2:5,6-di-*O*-isopropylidene-D-allofuranose[7] and treated with MeLi, whereupon **4** having no deuterium was produced under evolution of CH_3D[8] together with CF_3SO_2Li (^{19}F NMR in D_2O: δ −88.3 from external $CFCl_3$; the reference compound was prepared[9] by reduction of CF_3SO_2Cl). This result indicates that no β-elimination relating to H-2 (or H-4) and subsequent deuteron shift occurred, and suggests that H-3 (i.e., α-hydrogen bearing the CF_3SO_2O group) was first eliminated to give the C-3 carbanion, which then stabilized to form a carbonyl group by releasing the triflyl group (Scheme 1). The 3-oxo intermediate[10] will then react with MeLi to give **4**[11]. This initial abstraction of H-3 by a base (MeLi) will be rather reasonable from the viewpoint of the least electron-density of H-3 among the hydrogens in the molecule.



3' **4** **Scheme 1**

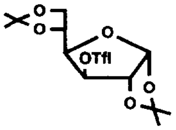
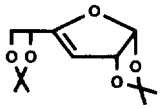
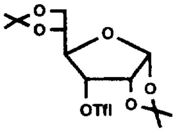
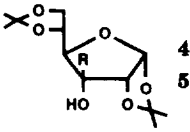
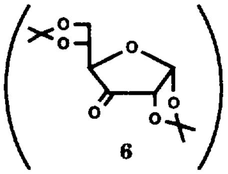
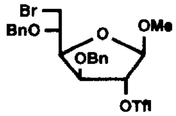
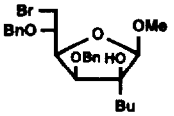
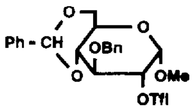
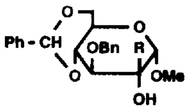
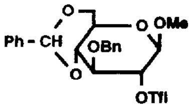
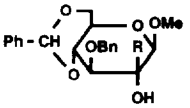
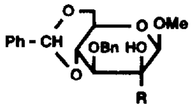
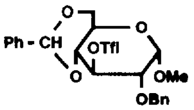
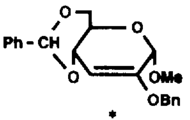
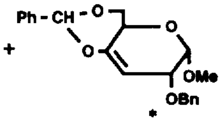
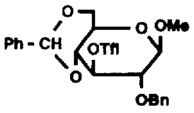
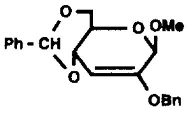
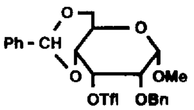
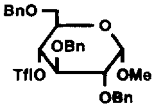
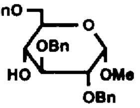
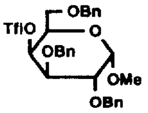
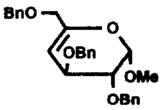
To trace the occurrence of this reaction in other compounds, several triflates were prepared. As shown in Table 1, 2-*O*-triflyl derivatives **7**, **9**, and **12** gave the corresponding *C*-butyl derivatives readily, but the other triflates (except **23**) gave unsaturated products. The specific position of 2-triflates in this reaction is not clear, but enhancement of acidity of H-2 by a vicinal electron-withdrawing acetal group will be one of the reasons. Changing the reagent from BuLi to MeLi also gave analogous results (Table 1).

At this stage we felt the necessity to reinvestigate the elimination reaction of the triflates. Compound **1**, taken as an example, was reported[12] to give 3,4-unsaturated compound **2** in the presence of F⁻ or base (DBU or KOCMe$_3$). In our reaction also **1** gave **2**. This kind of unsaturation has been explained[1] to start from β-elimination, that is, H-4 is initially removed by a base (typical E2 reaction[13]). However, judging from the poor electron-density at H-3, this hydrogen should be eliminated first (α-elimination). To clarify this, 3-[14] (**1'**) and 4-deuterio analogs[15] (**1"**) of **1** were prepared. Compound **1'**, on treatment with MeLi in ether, gave **2** without deuterium and **1"** gave the corresponding 3-deuterio isomer. This result indicates that α-hydrogen (H-3) is abstracted initially to give the C-3 carbanion, which then induces the H-4 shift (as a proton), and finally the resulting C-4 carbanion stabilized by forming a 3,4-double bond by releasing the CF$_3$SO$_3^-$ (Scheme 2). As a whole, the reaction proceeds as if by β-elimination, but in reality it should be regarded as α-elimination[16]. One requirement of this reaction will be *cis* relationship for removing and migrating hydrogens. Thus, **17** and **20** might give products by true β-elimination. In **23**, MeLi may attack the sulfur of the triflyl group.



1" **Scheme 2**

Table 1 Reactions of Triflates with MeLi(A) or BuLi(B) in Ether

Starting material		Reagent	Product[a]			
	1	A, B		2[12] (~70%)		
	3[3]	A B		4[11] (R= Me, 47%[b]) 5[5] (R= Bu, 62%)		6
	7*	B		8* (64%)		
	9[17]	A B		10* (R= Me, 91%) 11* (R=Bu, 77%)		
	12[18]			+		
		A B	13* (R= Me, 39%) 15* (R= Bu, 18%)		14* (R= Me, 52%) 16* (R= Bu, 59%)	
	17*	B	 18* (51%)	+	 19* (23%)	
	20*	A		21* (36%) + UK		
	22*	A	18* (91%)			
	23[19]	A		24[20] (80%)		
	25[21]	A		26* (45%) + UK		

[a] New compounds prepared are marked by * and characterized.[22] ; UK: unknown compound.

[b] Corresponding allose derivative (R= H) was obtained in 25% yield.

In summary, we have been able to show, in some carbohydrate triflates, α-hydrogen elimination occurred on treatment with MeLi or BuLi in ether, and the resulting α-carbanion is either transformed into ketone or induces unsaturation depending on the structures.

References and Notes

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8) Trapped in cold $CDCl_3$. ^1H NMR: δ – 0.015 (1 : 1 : 1 t, *J* 2.0 Hz) from CH_4; see Jimenez, L.; Diederich, F. *Tetrahedron Lett.* **1989**, *30*, 2755 - 2758.
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10) Attempts to isolate **6** by use of a limited amount of MeLi failed, due to the high reaction rate of **6** with MeLi. Treatment of **3** with *t*-BuLi, *sec*-BuLi, or LDA recovered the starting material mainly without forming trace amount of **6**. Details will be described in a full paper.
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14) Compound **1'** was prepared by triflation of [3-^2H] 1,2 : 5,6-di-*O*-isopropylidene-D-glucofuranose (Koch, H. J.; Perlin, A. S. *Carbohydr. Res.* **1970**, *15*, 403 – 410).
15) Compound **1"** was prepared as follows: [4-^2H] methyl α-D-glucopyranoside was prepared according to O. Gabriel basically (*Carbohydr. Res.* **1968**, *6*, 319 – 327), and after hydrolysis, the free sugar was converted into the diacetonide, and triflated.
16) Further research is necessary to draw a general conclusion (experiments utilizing the deuterio isomers of **17**, **22**, and **25** are now under study).
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21) Doboszewski, B.; Hay, G. W.; Szarek, W. A. *Can. J. Chem.* **1987**, *65*, 412 – 419.
22) NOE enhancements were observed between CH_3-2 (or CH_2-2) and H-4 in **10**, **11**, **13**, and **15**, respectively, but not in **14** and **16**. In **8**, irradiation at H-1, H-3, and H-4 enhanced the signals for β-, α- and β-, and α-CH_2 of -$CH_2(\alpha)$-$CH_2(\beta)$-CH_2CH_3, respectively; ^1H NMR (only important signals; all in $CDCl_3$) **8**: 0.90 (t, 3H, Me), 1.25 – 1.6 (m, 6H), 3.32 (s, 1H, OH), 3.41 (s, 3H, OMe), 3.74 (d, *J* 5.5Hz, H-3), ABq centered at 3.82 (2H, H-6, 6'), 3.99 (dt, H-5), 4.24 (dd, H-4), 4.46 (s, 1H, H-1). **10**: 1.37 (s, 3H, Me), 2.55 (s, 1H, OH), 3.65 (t, *J* 9.5 Hz, H-4), 3.81 (d, H-3), 4.43 (s, 1H, H-1), 5.56 (s, C*H*Ph). **13**: 1.32 (s, 3H, Me), 2.12 (s, 1H, OH), 3.48 (m, H-5), 3.56 (s, 3H, OMe), 3.6 – 3.7 (m, H-3, 4), 4.27 (s, 1H, H-1), 5.57 (s, C*H*Ph); (py-d_5): 1.73 (s, CH_3), 3.97 (t, H-4), 4.04 (d, H-3). **14**: 1.25 (s, 3H, Me), 2.31 (s, 1H, OH), 3.38 (d, *J* 9.5 Hz, H-3), 3.39 (dt, H-5), 3.55 (s, 3H, OMe), 4.14 (t, H-4), 5.62 (s, C*H*Ph). **18**: 3.50 (s, 3H, OMe), 3.82 (t, 1H, H-6), 4.00 (ddd, 1H, H-5). 4.28 (dd, 1H, H-4), 4.30 (dd, 1H, H-6'), 4.81 (s, 1H, H-1), 4.83 (q, 2H, CH_2Ph), 5.07 (d, 1H, H-3), 5.57 (s, 1H, C*H*Ph); $J_{3,4}$ ~1, $J_{4,5}$ 9 Hz. **19**: 3.51 (s, 3H, OMe), 3.70 (t, 1H, H-6), 4.30 (dd, 1H, H-6'), 4.33 (ddd, 1H, H-2), 4.37 (dddd, 1H, H-5), ABq centered at 4.64 (CH_2Ph), 4.80 (dd, 1H, H-1), 5.34 (small range m, 1H, H-3), 5.54 (s, C*H*Ph); $J_{1,2}$ 4, $J_{2,3}$ 1.5, $J_{1,3}$ <1, $J_{2,5}$ <1, $J_{3,5}$ <1. **26**: 3.49 (s, 3H, OMe), 3.78 (dd, 1H, H-2), 3.92 (sl. br s, 2H, H-6, 6'), 4.23 (ddt, 1H, H-3), 4.85 (d, 1H, H-1), 5.03 (d, 1H, H-4); $J_{1,2}$ 2.5, $J_{2,3}$ 7, $J_{3,4}$ 3, $J_{3,6} = J_{3,6'}$ ~1 Hz.

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