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Mechanism of anomerization of permethylated methyl D-glycopyranosides by trimethylsilyl trifluoromethanesulfonate

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Abstract

Anomerization of permethylated methyl D-glycopyranosides catalyzed by trimethylsilyl trifluoromethanesulfonate was examined by NMR spectroscopy and gas–liquid chromatography. The initial-rate analysis showed that the rates of anomerization of β to α were faster than those of the opposite at various concentrations of the catalyst. The overall rates of disappearance of the substrates were faster than the rates of appearance of the opposite anomers because of the formation of a pyrylium-type of compound. The structure of the latter was proposed based on ^{1}H and ^{13}C NMR spectra, although it was not isolable. Both cyclic and acyclic oxonium ions appear to be intermediates in the anomerization. The former seems to be the key intermediate for the formation of the pyrylium-type of compound as well as the anomerization of α-glycosidic linkages. β-Glycosidic linkages, on the other hand, appear to undergo anomerization mostly via acyclic oxonium ions.

Keywords: Anomerization; Transglycosylation; Cyclic oxonium ion

1. Introduction

The anomerization of methyl glycopyranosides has been the subject of extensive investigation. The mechanism of the reaction is important because any intermediate involved is relevant to understanding the reactions taking place at the glycoside linkage, i.e. hydrolysis, transglycosylation, reductive cleavage, etc.

Capon [1,2] suggested a cyclic oxonium ion such as I as the intermediate in the anomerization of methyl β-D-glucopyranoside in methanol at 70 °C catalyzed by methanesulfonic acid. Based on an NMR study, an acyclic oxonium intermediate such as II was ruled out in the report. Lemieux and Shyluk [3] investigated the anomerization of acetylated alkyl glycopyranosides in chloroform saturated with boron trifluoride at room temperature or at 61 °C in the presence of titanium tetrachloride, and suggested an intermediate ion-pair such as III. The intermediate III may be considered to be a modification of I in the sense that both contain a cyclic oxonium ion, but the outcome is quite different in that collapse of III to the α anomer will result in no incorporation of externally

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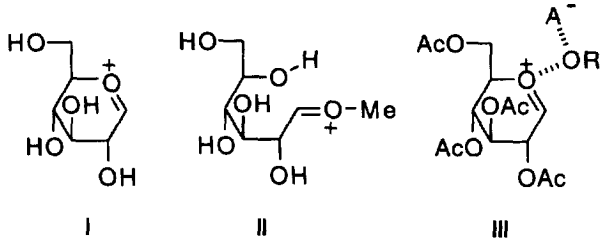
added CD_3OD. In fact, the process involving III was called "intramolecular", and the outcome is thus similar to the process in which II is involved.



I II III

Jansson and Lindberg [4] carried out the anomerization of isopropyl tetra-*O*-methyl-β-D-glucopyranoside in 10:3 acetic anhydride–acetic acid catalyzed by H_2SO_4 and suggested that both cyclic and acyclic oxonium ions may be possible as intermediates and one or the other may predominate depending on the substrates and conditions of reaction.

In the course of our study on the reductive-cleavage reaction of permethylated methyl D-glycopyranosides we observed anomerization of the glycosidic linkage in the presence of trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf), boron trifluoride etherate ($BF_3.OEt_2$), and trimethylsilyl methanesulfonate (Me_3SiOMs)–$BF_3{\cdot}OEt_2$ (5:1 mol/mol) in dichloromethane [5]. Based on the analysis of the product compositions of the reaction mixtures of anomerization and transglycosylation in the presence of ethanol we proposed reaction pathways for β-glycosides in which both cyclic and acyclic intermediates compete and for α-glycosides in which a cyclic oxonium ion is the sole intermediate. Here we report the results of our extensive investigation on the mechanism of anomerization by NMR spectroscopy.

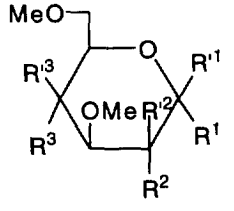
We understand that H^+ and $(CH_3)_3Si^+$ probably do not exist as free ions in these solutions, but donors of these species do exist, and it is frequently unclear which donor is at work. In this paper we have often followed the practice of writing the free ions into equations and schemes, because any alternative was unreasonably complicated, but it should be understood that these ions are always bound to something.

2. Results and discussion

At first we were interested in the fate of Me_3SiOTf in the course of anomerization. The term such as "catalyst" is somewhat misleading because none of it was recovered after the reaction. Furthermore, the molar ratio employed in the reaction was 5 or 10 equivalents. Therefore, one can conclude that attachment of cationic species to merely one or both of the oxygen atoms which form the acetal functionality may not be enough to cause anomerization or transglycosylation. Therefore, we examined the effect of the Lewis acids by examining the ^{13}C NMR chemical shift of permethylated methyl D-glycosides.

Complete assignments of the ^{13}C NMR spectra of methyl 2,3,4,6-tetra-*O*-methyl-α- and β-D-glucopyranosides (**1α** and **1β**) in acetonitrile have been reported [6]. The ^{13}C NMR spectrum of methyl 2,3,4,6-tetra-*O*-methyl-β-D-galactopyranoside (**3β**) in D_2O has also been reported [7]. The chemical-shift values of the ^{13}C signals of C-1–C-6 of **1α** in dichloromethane were shifted slightly to higher field (0.5–0.7 ppm) than the reported values, which were obtained in acetonitrile. The signals corresponding to methyl carbons were also shifted to higher field (0.1–0.2 ppm) except that of C-2–OCH_3 which showed a downfield shift by 0.2 ppm. Considering the difference in polarity of acetonitrile ($\varepsilon = 35.94$) and dichloromethane ($\varepsilon = 8.93$) the upfield shift is understandable [8].

In a comprehensive review it has been reported that solvent-induced shifts are usually less than 1 ppm and the choice of solvent does not have a large effect on proton-decoupled ^{13}C NMR spectra, except in the case of basic or acidic carbohydrates [9]. However, our observation with the β-glucopyranoside (**1β**) is quite contrary to the general statement. As shown in Table 1 the chemical shift values of C-1–C-6 were significantly changed (0.7–5.4 ppm) to the upfield region while those of methyl carbons varied to a lesser extent (ca. 0.6 ppm). Other notable phenomena were the slight upfield shifts ($\Delta\delta < 1$ ppm) of ^{13}C signals in the presence of Me_3SiOTf.



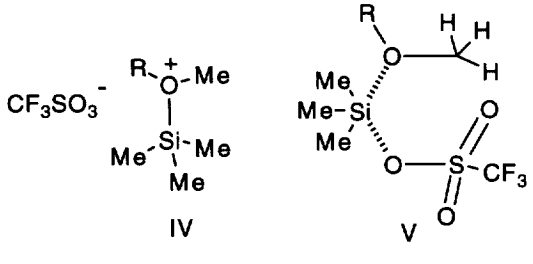
	R^1	R'^1	R^2	R'^2	R^3	R'^3
α-Glc (**1α**)	OMe	H	OMe	H	OMe	H
β-Glc (**1β**)	H	OMe	OMe	H	OMe	H
α-Man (**2α**)	OMe	H	H	OMe	OMe	H
α-Gal (**3α**)	OMe	H	OMe	H	H	OMe
β-Gal (**3β**)	H	OMe	OMe	H	H	H

Table 1
^{13}C Chemical-shift values of methyl 2,3,4,6-tetra-*O*-methyl-D-glycopyranosides

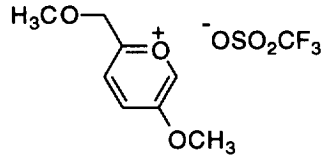
		C–1	C–2	C–3	C–4	C–5	C–6	1-Me	2-Me	3-Me	4-Me	6-Me
1α	A	97.7	82.0	83.7	79.9	70.3	71.7	55.1	58.6	60.7	60.4	59.1
	B	97.5	81.8	83.6	79.6	70.3	71.8	55.0	58.5	61.0	58.9	57.7
	C	98.2	82.6	84.3	80.6	71.0	72.4	55.3	58.4	60.7	60.5	59.2
1β	A	104.7	80.8	84.2	75.1	73.2	71.1	56.7	59.1	61.2	60.6	58.1
	B	104.3	80.6	83.7	74.9	72.8	70.9	56.5	59.0	60.9	60.4	57.9
	C	105.0	84.6	87.2	80.5	75.4	72.4	57.0	60.5	60.8	60.6	59.3
2α	A	98.6	77.4	76.5	71.9	81.7	71.5	54.9	60.6	59.2	59.1	57.6
	B	98.5	77.4	76.4	71.0	81.7	72.0	55.2	60.7	59.5	59.2	57.9
3α	A	98.2	76.5	80.5	78.2	69.2	71.6	55.3	61.3	59.2	58.7	58.1
	B	97.6	76.0	80.0	78.0	68.7	71.3	55.0	61.0	59.0	58.6	57.7
3β	A	104.8	80.9	84.3	75.2	71.2	73.3	56.8	61.2	60.7	59.3	58.2
	B	104.7	81.0	84.1	75.3	71.3	73.2	56.8	60.7	60.0	59.0	58.3
	D	103.4	79.8	85.2	73.1	74.9	71.0	57.1	60.9	60.2	58.5	57.1

A: In dichloromethane-d_2.
B: In dichloromethane-d_2 with 5 equiv of Me_3SiOTf added.
C: In acetonitrile-d_3 and from ref. [6].
D: In D_2O and from ref. [7].

The upfield shift does not seem to be the result of the change in polarity of the solvent by the presence of Me_3SiOTf. Polarity would be increased by Me_3SiOTf and, if that were the case, the shift should be in the downfield direction. Complexation of the lone-pair electrons on the oxygen atom of the alcohol with a proton derived from trifluoroacetic acid was known to cause an upfield shift of the signals of all carbon atoms in 1-butanol except the α carbon [10]. Complexation of a methyl ether with Me_3SiOTf may be visualized either as IV or as V. Once trimethylsilyl cation is attached to an oxygen atom forming an oxonium ion of type IV, C–O bond cleavage may take place. The cleavage would be facilitated if lone-pair electrons in a neighboring oxygen atom could assist the departure of methoxytrimethylsilane. On the other hand, the complexation of type V may not cause any bond cleavage but it would be enough to cause a change in chemical shift of attached carbon atoms. The observed shift may be the result of such association.



When a solution of **1α** and Me_3SiOTf (1:5 by mole) in CD_2Cl_2 was monitored by NMR spectroscopy, anomerization of **1α** to **1β** was observed. However, another component was noticable after 3 h. The yield of the component reached about 20–25% (by NMR) after 48 h. Although we were not able to isolate the component by employing various work-up procedures, the NMR spectrum of the reaction mixture leads us to propose a structure of the component as **4**. The ^1H NMR spectrum of the mixture showed, besides the peaks corresponding to **1α** and **1β**, peaks at δ 3.65 (s, 3H), 4.17 (s, 3H), 4.94 (s, 2H), 8.30 (d, 1H, $J=9.0$ Hz), 8.68 (dd, 1H, $J=3.0$ and 9.0 Hz), and 9.27 (d, 1H, $J=9.0$ Hz) while the ^{13}C NMR spectrum showed peaks at 52.5, 58.8, 70.3, 120.5, 124.7, 145.9, 153.3, and 175.8 ppm. The ^1H chemical-shift values of pyrylium perchlorate were reported to be δ 9.70, 9.36, and 8.53 for α-, γ-, and β-protons, respectively, in trifluoroacetic acid [11]. The ^{13}C chemical shift values were also reported as 169.3, 127.7, and 161.2 ppm for α-, γ-, and β-carbons, respectively [12]. Therefore, the values observed in the present investigation seem to be consistent with the proposed structure **4**. Formation of **4** was observed from all the glycosides (**1–3**) although their relative abundance and rate of formation were different. When a mixture of Me_3SiOMs–$BF_3{\cdot}OEt_2$ (5:1 mol/mol) was used the anomerization reaction took place but the formation of pyrylium ion **4** was not observed even after 48 h. Similary, $BF_3.OEt_2$ alone did not give **4** even after 4 days. Apparently, the presence of Me_3Si^+ ion seems to be essential to cause breaking the C–O bond which may lead to formation of **4**.



4

The disappearance of permethylated methyl D-glycosides was monitored by proton NMR spectroscopy. The ratio of the anomeric proton of the reactant to the protons of CH_2Cl_2, which was present in the solvent, was measured, and designated A_t. A_t reached a constant value, designated A_∞, in about 1 h. Plots of ln $(A_t - A_\infty)$ against time were linear, and their slopes gave k_{obs}, which is the sum of k_1 and k_{-1}. After reaction had proceeded for about 1 h and a constant value of A_t had been reached the ratio of the product to the reactant anomeric proton was measured, and taken as the anomerization equilibrium constant, K. K is the ratio, k_1/k_{-1}. From these ratios and sums the individual rate constants could be calculated, and they are tabulated in Table 3. The formation of **4** could not be detected during the first hour of reaction, but began to appear after longer times. The rate constants for the formation of **4** were determined from the build-up of its peak at δ 4.94, which obeyed the first-order rate law through at least 24 h. This rate constant is k'. All of these rate constants depend on the initial solution composition, and are pseudo first-order rate constants.

We measured the rate of anomerization at different concentrations of the catalyst for the first five minutes by gas–liquid chromatography (GLC), in which the rates of the reverse reaction and formation of **4** were almost negligible. The results are listed in Table 4.

The rate constants in the Table 4 are larger than those in the Table 3, but the same isomer is favored in each case. The difference is due to the fact that the equilibrium constants in the case of Table 4 are pretty much independent of the catalyst concentration, even though the individual rate constants are not.

Although it is difficult to derive a rate equation which is consistent with the results in Table 4, it seems apparent that the rate does not increase linearly as the concentration of Me_3SiOTf increases. This and the observed downfield shift of the methoxy proton peaks (Table 2) may be consistent with the complexation of undissociated Me_3SiOTf with the oxygen atoms in the substrate.

The anomerization of **1**β and **3**β appeared to reach equilibrium within 30 min and the ratios of the α and β anomers were about 4:1 and 5:1, respectively, based upon integration of the anomeric protons. However, the total amounts of α and β anomers gradually decreased with time because of the formation of **4**.

As illustrated in Scheme 1, a cyclic oxonium intermediate VI would be formed as a sole intermediate in the formation of **4**. Sequential elimination of methoxy groups from VI would then give rise to **4**. The formation of **4** may be explained as shown in Scheme 2. Three methoxy groups have to be eliminated from a substrate in order to form **4**.

Table 2
^{1}H Chemical-shift values of methyl 2,3,4,6-tetra-*O*-methyl-D-glycopyranosides

		H-1 (J, Hz)	OCH_3				
1α	A	4.74 d (3.6)	3.34,	3.35,	3.43,	3.48,	3.55
	B	4.85 d (3.5)	3.38,	3.42,	3.50,	3.52,	3.53
1β	A	4.09 d (6.3)	3.36,	3.46,	3.46,	3.47,	3.50
	B	4.15 d (6.5)	3.39,	3.43,	3.44,	3.51,	3.59
2α	A	4.69 d (1.7)	3.32,	3.36,	3.43,	3.43,	3.45
	B	4.75 d (1.7)	3.35,	3.46,	3.49,	3.51,	3.75
3α	A	4.79 d (3.3)	3.34,	3.35,	3.42,	3.45,	3.49
	B	4.87 d (3.9)	3.39,	3.44,	3.52,	3.53,	3.55
3β	A	4.09 d (7.4)	3.36,	3.46,	3.47,	3.50,	3.50
	B	4.14 d (7.0)	3.42,	3.50,	3.52,	3.53,	3.56

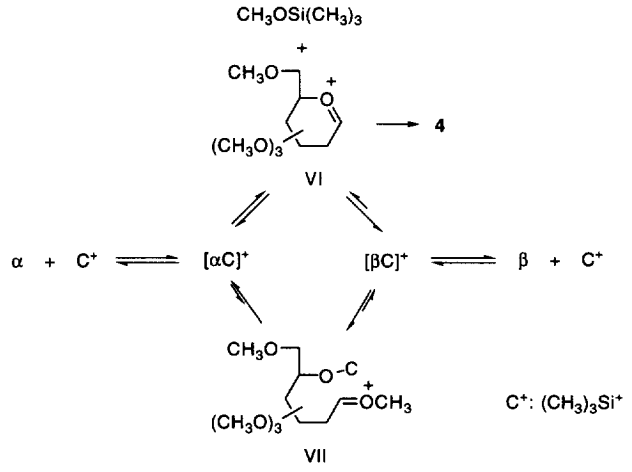
A: In dichloromethane-d_2.
B: In dichloromethane-d_2 with 5 equiv of Me_3SiOTf added.

Table 3
Rate constants for the anomerization (k_1) of methyl 2,3,4,6-tetra-*O*-methyl-D-glycopyranosides and the formation (k') of **4** in the presence of Me_3SiOTf at 25 °C in CH_2Cl_2

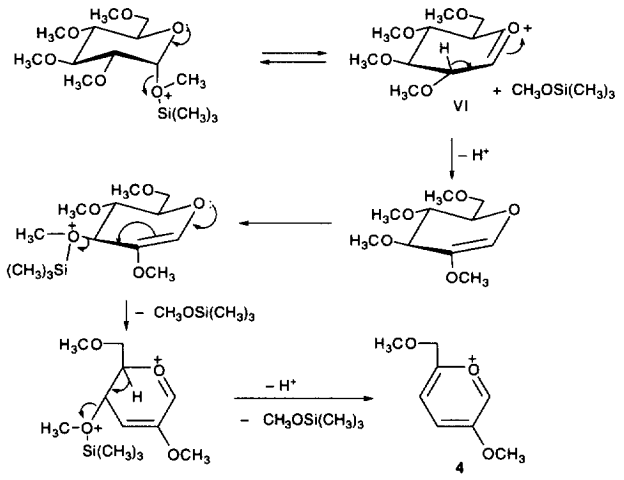
Glycoside	k_1, min^{-1}	k', min^{-1}	k_1/k'
1α	$1.0(\pm0.5)\times10^{-2}$	$1.3(\pm0.5)\times10^{-4}$	76.9
1β	$4.3(\pm0.5)\times10^{-2}$	$1.0(\pm0.5)\times10^{-4}$	430.0
2α	$1.1(\pm0.5)\times10^{-4}$	$1.0(\pm0.5)\times10^{-4}$	1.1
3α	$3.8(\pm0.5)\times10^{-2}$	$1.2(\pm0.5)\times10^{-3}$	31.6
3β	$1.4(\pm0.5)\times10^{-1}$	$3.5(\pm0.5)\times10^{-4}$	400.0

Table 4
Rates of anomerization of methyl 2,3,4,6-tetra-*O*-methyl-D-glycopyranosides in the presence of various molar equivalents of Me_3SiOTf and docosane at 25 °C

Glycoside	k_1, min^{-1} ($\times10^2$)				
	0.1	0.5	1.0	2.0	5.0
1α	0.9	1.6	2.3	2.6	2.8
1β	8.1	10.3	11.6	17.4	26.7
3α	2.9	5.0	7.5	9.0	9.9
3β	11.8	15.3	27.5	49.5	59.3



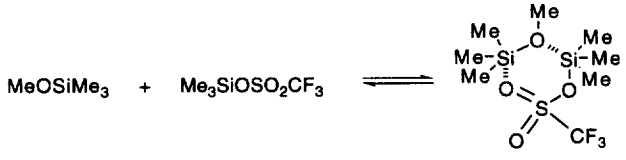
Scheme 1.



Scheme 2.

They seem to form methoxytrimethylsilane, and in fact, the formation of **4** was not observed at all in the presence of externally added methoxytrimethylsilane (5 equiv).

Formation of $MeOSiMe_3$ could be detected by NMR spectroscopy. The NMR spectra of the reaction mixtures clearly showed a peak at δ 3.43 which was proved to correspond to the methoxy group of $MeOSiMe_3$ in the presence of Me_3SiOTf. The chemical shift values of CH_3O and $Si(CH_3)_3$ of methoxytrimethylsilane in CD_2Cl_2 are δ 3.38 and δ 0.09, respectively, but they are shifted to δ 3.43 and δ 0.32, respectively, in the presence of Me_3SiOTf. The shift may be the result of formation of a complex in fast equilibrium as follows:



Such complexation may decrease the possibility of formation of the substrate–Me_3SiOTf complex that leads to anomerization by reducing the effective concentration of the catalyst. Added methoxytrimethylsilane may also inhibit the formation of **4** by forcing the reversible step in Scheme 2 toward the reverse direction.

A mixture of **1**β, $CD_3OSi(CH_3)_3$, and Me_3SiOTf (1:5:5 mol/mol/mol) in CD_2Cl_2 was examined by NMR, and it was found that the anomerization took place much more slowly; about 25% of the β anomer was converted to the α anomer in 24 h. Without the presence of the silane the anomerization reached equilibrium in 30 min in which about 80% of the α anomer was present. Although the formation of both $CH_3OSi(CH_3)_3$ and the methyl-d_3 glucopyranosides were confirmed by the experiment it was not possible to make a quantitative assessment because of the difficulty in integrating the individual CH_3O resonances. Furthermore, the GLC retention times of the permethylated methyl glycosides and the corresponding deuterated compounds were identical on a DB-5 column, and several variations in GLC conditions failed to separate the components.

Table 5
Composition (mol %) of the mixture of permethylated methyl D-glucopyranosides, ethoxytrimethylsilane, and Me_3SiOTf (1:5:5 by molar equiv) at 25 °C[a]

Glycoside	1α					1β				
	1 h	12 h	24 h[b]	48 h	72 h	1 h	12 h	24 h[b]	48 h	72 h
α-OMe	100	92.0	72.1 (11.9)	68.9	48.0	0	16.2	12.5 (13.4)	4.3	7.3
β-OMe	0	0	0.8 (2.4)	0.9	1.8	100	80.0	65.4 (2.7)	26.0	7.5
α-OEt	0	5.6	17.9 (67.4)	20.1	35.8	0	2.0	12.1 (65.7)	44.3	61.0
β-OEt	0	2.4	9.2 (18.3)	10.0	14.4	0	1.8	10.0 (18.1)	25.4	24.2

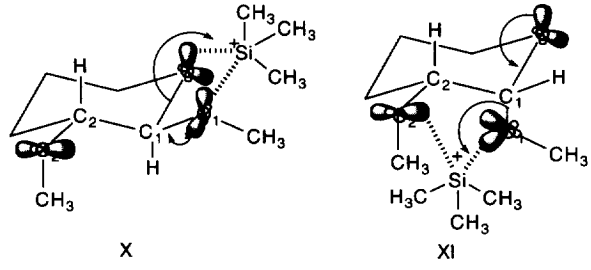
[a] The analysis was carried out by GLC.
[b] Values in parentheses are the results of transglycosylation with ethanol (10 equiv) and Me_3SiOTf (10 equiv) from ref. [5].

The transglycosylation of **1**α and **1**β were investigated further with ethoxytrimethylsilane and the results are summarized in Table 5. Although it was not surprising that the anomerization and transglycosylation of both substrates were retarded significantly, a few important observations were made. First, the ratio of α-OEt and β-OEt in the reaction of **1**β was about 1.2:1 after 24 h. Considering that the ratio of α and β isomers of a solution of **1**β and Me_3SiOTf in CH_2Cl_2 after the same period is 4.26:1 [5], the observed ratio is difficult to be explained by a pathway in which a cyclic oxonium ion is involved. If the ethoxysilane attacks the cyclic oxonium ion, the α anomer should be preferably formed. This may be evidence for the presence of an acyclic oxonium ion intermediate. We propose an alternative pathway for the transglycosylation of **1**β in the presence of ethoxytrimethylsilane as shown in Scheme 3. The key step may be the formation of an acetal VIII which can be transformed to IX. Ring closure of VIII and IX may not have any significant preference and both the α-OEt and β-OEt compounds could be formed in equal amounts at this stage. The ethyl β-Glc may then undergo anomerization so that the ethyl α-Glc exists as the major product when equilibrium is reached.

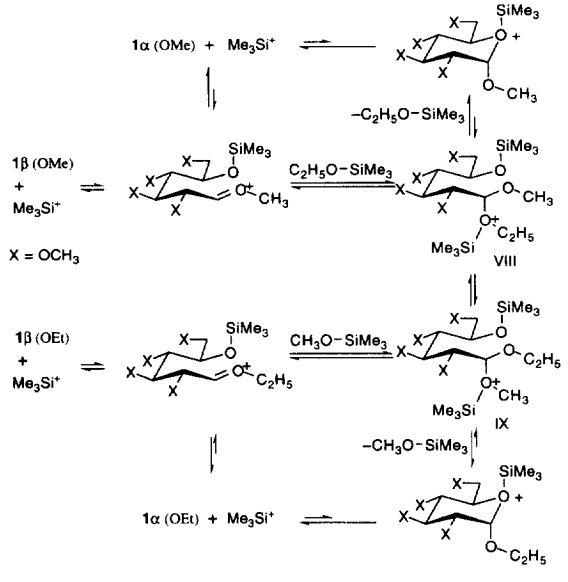
In the case of **1**α, transglycosylation via the cyclic oxonium ion intermediate should favor the formation of the Et α-Glc and, in fact, the α : β ratio was about 2:1 after 24 and 48 h and 2.5:1 after 72 h.

A molecular model study using PCMODEL gave results consistent with the formation of cyclic and acyclic oxonium ions. As illustrated in structure X, the most stable conformation of the β-glycoside appears to be the arrangement in which C-2 and the CH_3 at O-1 are *anti*. One of the lone-pair orbitals of the O-1 atom therefore becomes *syn* with a lone-pair orbital of the ring oxygen atom. The two syn orbitals may thus form a complex with Me_3Si^+, such as X, and in this complex, the other lone-pair orbital of O-1, which is *anti* to the O–C-1 bond, would facilitate O–C-1 bond breaking to form acyclic oxonium intermediate VII.

The *anti* arrangement (XI) of C-2 and the CH_3 at O-1 along C-1–O-1 bond in the α-glycoside prohibits a *syn* arrangement of either of the lone-pair orbitals of O-1 and those of the ring oxygen atom as shown in XI. Therefore, complexation of Me_3Si^+ between O-1 and O-5 should be unlikely. On the other hand, complexation of Me_3Si^+ between O-2 and O-1 becomes favorable because the lone-pair orbitals of the two oxygen atoms are arranged so that a five-membered ring is readily formed. In this complex (XI), the lone-pair orbital of the ring oxygen atom, which is *anti* to the C-1–O bond, will assist the C-1–O-1 bond breaking to give the cyclic oxonium ion VI.



X XI



Scheme 3.

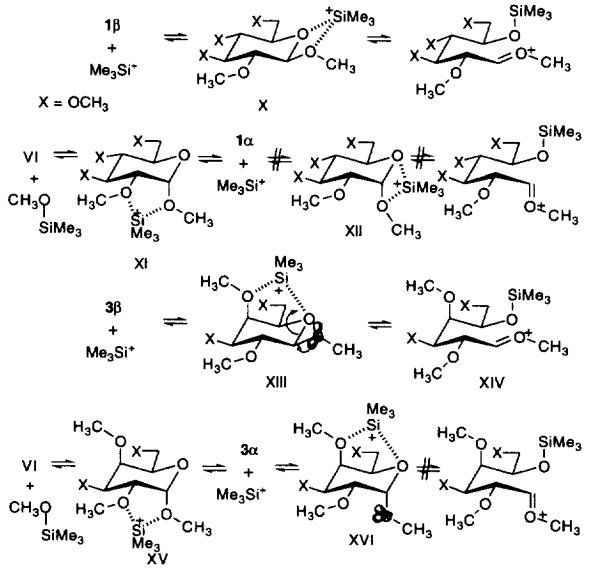
The observed rate of anomerization of the galacto isomer (**3**β) was the fastest while the formation of **4** from it was not. We propose (Scheme 4) that a complex (XIII) is formed with Me_3Si^+ in which the oxygen atom at C-4 and the ring oxygen atom form a 5-membered ring.

Formation of XIII will facilitate the ring opening and will result an acyclic intermediate XIV. The rate of disappearance of **3**β is about 4 times faster than that of **3**α. On the other hand, the rate of formation of **4** from **3**β is about 0.3 times faster than from **3**α. The reverse in the ratios of rate may be explained by different fates of XIII and XVI formed from **3**β and **3**α, respectively. As shown in Scheme 4, one of the lone-pair orbitals on the oxygen atom of the anomeric equatorial methoxy group in XIII may undergo effective overlapping

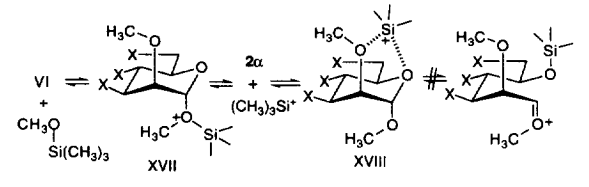
with an sp^3 orbital of C-1, resulting in cleavage of the ring. On the other hand, similar overlapping is not effectively taking place with the axial methoxy group in XVI. Therefore, recomplexing of Me_3Si^+ with **3**α will take place to form XV, which can subsequently undergo elimination of the α-OCH_3 group, resulting in a cyclic oxonium ion. Once the latter forms, anomerization and formation of **4** will compete. For all α-glycosides, complexation of Me_3Si^+ involving oxygen atoms in the ring and the axial methoxy group (XII) appears to be unfavorable.

Permethylated methyl α-D-mannopyranoside (**2**α) did not undergo anomerization in the presence of Me_3SiOTf as previously reported [5], but it also gave **4**. The rate of disappearance of **2**α was essentially identical to the rate of formation of **4**. As in the case of **3**α, formation of a 5-membered ring complex (XVIII) in **2**α involving the oxygen atoms in the ring and the axial methoxy group at C-2 is expected, as illustrated in Scheme 5.

However, the axial methoxy group at C-1 cannot transform the complex to either a cyclic or an acyclic intermediate because of unfavorable overlapping. Instead, a cyclic oxonium ion may be derived from an intermediate such as XVII. The observed rate of disappearance of **2**α was the slowest among all the substrates examined. It seems probable that catalysis of anomerization by Me_3Si^+ may arise via formation of a cyclic complex (such as XV; Scheme 4) involving two vicinal oxygen atoms. Such kind of complexation is not feasible in **2**α.



Scheme 4.



Scheme 5.

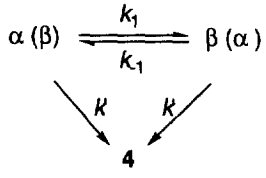
3. Experimental

Starting materials.—Methyl α- and β-D-glucopyranosides, methyl α-D-mannopyranoside, methyl α- and β-galactopyranosides, and ethoxytrimethylsilane were all commercial products. Permethylated methyl D-glycopyranosides (**1**α, **1**β, **2**α, **3**α, **3**β) were prepared as described previously [5]. Trideuteriomethoxytrimethylsilane was prepared by refluxing chlorotrimethylsilane (8.9 mL, 0.07 mol) and CD_3ONa–CD_3OD (prepared from 5 mL of CD_3OD and 1.61 g of freshly cut Na) for 3 h and subsequent distillation. The purity of the product was confirmed to be >99% by ^1H and ^{13}C NMR spectroscopy as well as by GLC. Commercial trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf), trimethylsilyl methanesulfonate (Me_3SiOMs), and boron trifluoride etherate ($BF_3{\cdot}OEt_2$) were distilled under mild vacuum prior to use. Dichloromethane was dried over CaH_2 and distilled prior to use.

Analytical methods.—^1H NMR spectra were recorded on a Varian 500 VXR-FT NMR spectrometer in CD_2Cl_2 containing tetramethylsilane (Me_4Si) as an internal standard. A Hewlett–Packard 5890 Plus gas–liquid chromatograph equipped with a capillary column (HP-5, 25 m, 0.53 m×1.0 μm) and a flame-ionization detector was used for analysis. The column was held at 120 °C for 2 min after injection then programmed to 250 °C at 6 °C/min. Nitrogen was used as the carrier gas at a flow rate of 1 mL/min.

Determination of rate constants.—Stock solutions of each glycoside were prepared in a 1 mL volumetric flask by dissolving 36.5 mg of the substrate in CD_2Cl_2 so that the concentration was 0.146 M. A solution of Me_3SiOTf was prepared by dissolving 0.200 mL in CD_2Cl_2 in a 2 mL volumetric flask so that the concentration was 0.517 M. The solution of glycoside (0.2 mL) was taken with a gas-tight syringe (0.25 mL) and placed in an NMR tube (5 mm diameter) and the solution of

Me_3SiOTf (0.29 mL) was introduced by a gas-tight syringe (0.50 mL). The final concentration of glycoside was 0.06 M and the final concentration of Me_3SiOTf was 0.30 M. ^1H NMR spectra of the solution were obtained at predetermined intervals using a kinetics program. The spectra were retrieved and the peaks corresponding to H-1 at around δ 4.1 and 4.8 for β and α anomers, respectively, and CH_2Cl_2 at around δ 5.2 were integrated. The pseudo-first order rate constants (k_{obs}) were calculated from the slope of a plot of time versus $\ln[(A_o - A_\infty)/(A_t - A_\infty)]$ [13] for the period of 1 h after which equilibrium of α and β anomers is reached. The rate constant k_1 for the forward reaction was calculated by the following equations:



$$k_{obs} = k_1 + k_{-1} = k_1(1 + 1/K)$$

where

$$K = k_1/k_{-1} = [\alpha(\text{or } \beta)]_\infty/[\beta(\text{or } \alpha)]_\infty$$

"A_t" values were calculated from the ratio of the integrations of the anomeric proton and CH_2Cl_2 which was present in the solvent. The value of A_o was the one obtained from the first spectra of each run and the value of A_∞ was the one at which the concentration of the opposite anomer reached a maximum. The first spectrum was obtained usually within 2 min and the progress of the reaction during the period was less than 1% for α and 3% for β anomers.

Determination of initial rate by GLC. An illustrative procedure.—A stock solution of **1**α was prepared in a 10-mL volumetric flask by dissolving 454.7 mg of the substrate (0.182 M) and 0.2920 g of docosane. Trimethylsilyl trifluoromethanesulfonate (35.1 mL, 0.0182 M) was added and the solution was stirred with a magnetic stirrer. A portion (0.5 mL) of the solution was transferred every 30 s, using a gas-tight syringe, into saturated $NaHCO_3$ solution and, after thorough mixing the organic layer was separated and analyzed by GLC. The rate of the reaction was calculated from the plot of $(R_o - R_t)$ versus time, where R_o is the ratio of the substrate to docosane immediately after the mixing and R_t was that at time t.

Transglycosylation in the presence of alkoxytrimethylsilane. An illustrative procedure

A solution (5 mL) of **1**α (4×10^{-5} M), EtO-$Si(CH_3)_3$ (2×10^{-4} M), and Me_3SiOTf (2×10^{-4} M) in CH_2Cl_2 was prepared. The solution was divided into five Wheaten v-vials and stirred at 25 °C. After the pre-determined period the solution was treated with satd $NaHCO_3$ solution and the organic layer was examined with GLC.

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