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HIGHLY STEREOSELECTIVE C-ALLYLATION OF GLYCOPYRANOSIDES WITH ALLYLSILANES CATALYZED BY SILYL TRIFLATE OR IODOSILANE[1]

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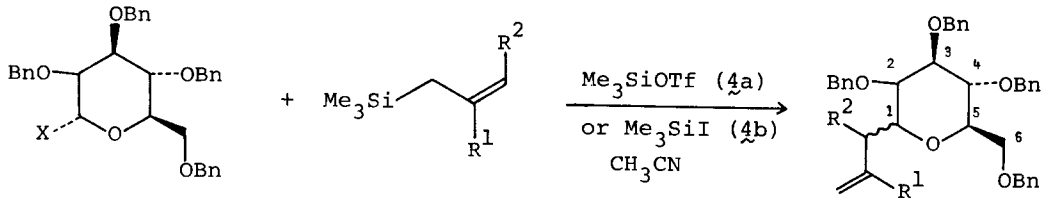
Summary: Methyl α-D-glucopyranoside, methyl α-D-mannopyranoside and, in particular, the corresponding α-D-glycopyranosyl chlorides readily undergo allylation with allylsilanes catalyzed by trimethylsilyl triflate or iodotrimethylsilane in a highly stereoselective mode.

Much attention has been focused on the stereocontrolled synthesis of functionalized C-glycosides,[2] in relation to synthesis of natural products as chiral building blocks and to potential C-nucleoside precursors. For this purpose, it becomes very important to select both the leaving group at the anomeric position and the activator in the alkylation, and, therefore, many reports have appeared recently.[3]

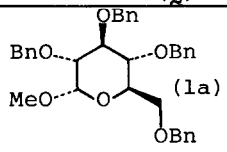
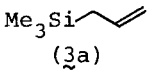
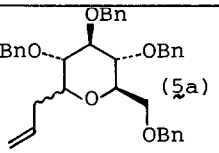
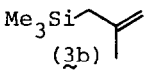
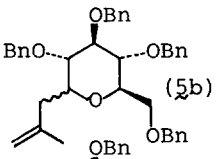
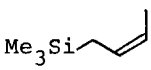
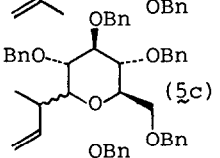
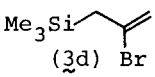
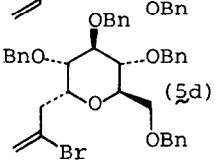
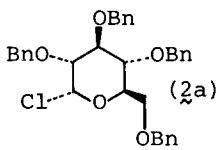
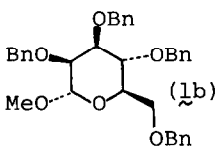
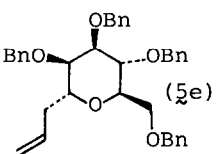
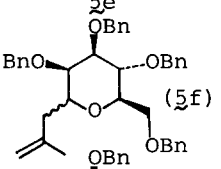
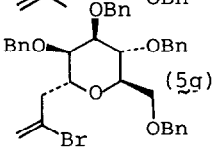
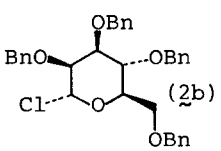
We have previously reported that the activation of a carbon-heteroatom bond of α-heteroatom substituted ethers such as α-chloroalkyl ethers can be readily achieved by trimethylsilyl trifluoromethanesulfonate (4a) and iodotrimethylsilane (4b).[4,5] In an extention of the study, we now demonstrate that the reaction of methyl α-D-gluco- and mannopyranosides (1)[6] and α-D-glycopyranosyl chlorides (2)[7] with allylsilanes (3) can be effectively catalyzed by these reagents (4)[8] to give the corresponding C-allylated glycopyranosides (5) stereoselectively where the α anomer overwhelmingly dominates over the β anomer in excellent yields. The results are listed in Table 1.



1a (2α), X = OMe
b (2β), X = OMe
2a (2α), X = Cl
b (2β), X = Cl

3a, $R^1 = R^2 = H$
b, R^1 = Me, $R^2 = H$
c, $R^1 = H$, R^2 = Me
d, R^1 = Br, $R^2 = H$

Table 1. Stereoselective Synthesis of C-Allylated Glycopyranosides (5)

Run	Pyranoside (1) or Pyranosyl Chloride (2)	Allylsilane (3)	Conditions[a]	Product	% Yield[b]	(α/β)[c]
1	 (1a)	 (3a)	Me_3SiOTf (4a) 16 h	 (5a)	86 54 (23)[d]	(10/ 1) (10/ 1)
2	1a	3a	Me_3SiI (4b) 27 h	5a	60 (22)	(10/ 1)
3	1a	 (3b)	4a, 10 h	 (5b)	87	(6/ 1)
4	1a	 (3c)	4a, 24 h	 (5c)	68	e
5	1a	 (3d) Br	4a, 16 h	 (5d)	71	(1/ 0)
6	 (2a)	3a	4a, 6.5 h	5a	81	(10/ 1)
7	2a	3a	4b, 16 h	5a	75	(10/ 1)
8	 (1b)	3a	4a, 25 h	 (5e)	87	(1/ 0)
9	1b	3a	4b, 23 h	5e	68 (20)	(1/ 0)
10	1b	3b	4a, 8 h	 (5f)	81	(8/ 1)
11	1b	3c	4b, 12 h	 (5g)	45 (35)	(1/ 0)
12	 (2b)	3a	4a, 4 h	5e	80	(1/ 0)
13	2b	3c	4b, 20 h	5g	65	(1/ 0)

[a]At rt in CH_3CN. 4 was used 50 mol% for 1 and 20 mol% for 2. [b]Isolated by TLC. Recovered 1 was shown in parenthesis. [c]Determined by HPLC. [d]In the presence of 4a (20 mol%) for 35 h. [e]Possibly 5c is a mixture of four stereoisomers (two diastereomers of α and β anomers).

Methyl 2,3,4,6-tetra-O-benzyl-α-D-glucopyranoside (1a) reacts with allyltrimethylsilane (3a) very smoothly in the presence of a catalytic amount of silyl triflate (4a) in acetonitrile at room temperature to afford a ca. 10:1 (α:β) stereoisomeric mixture of C-allylated glucopyranosides (5) in high yield.[9] Iodotrimethylsilane (4b) also promotes the reaction, although less effectively. The yield of the reaction depends on the solvent and the amount of the catalyst employed. Acetonitrile is the most suitable solvent for the present allylation of carbohydrates among examined. Dichloromethane, the most commonly used solvent for the allylation with allylsilanes,[10] does not bring satisfactory results. Although the reaction of 1 proceeds very slowly when promoted by less than 5 mol% of 4, the starting 1 being recovered along with a small amount of 5, the use of 50 mol% of 4 is enough to complete the reaction, giving a allylated glycopyranoside (5) stereoselectively.

Similarly, α- and β-methallyl groups can be introduced with 2-butenyltrimethylsilane (3c) and 2-methyl-2-propenyltrimethylsilane (3b), respectively. The allylation with 2-bromo-2-propenyltrimethylsilane (3d) proceeds very stereoselectively to afford the corresponding α anomer only. Both electronic and steric effects may account for the results, since the nucleophilicity of the double bond of 3d decreased in some extent owing to electron withdrawal of the bromine group. However, the latter effect seems to be important, since the reaction with 3b gave slightly lower selectivity than with 3a, presumably due to the sterically more hindered and more reactive β-methallyl group in 3b. Moreover, the reaction of methyl 2,3,4,6-tetra-O-benzyl-α-D-mannopyranoside (1b) whose benzyloxy group at 2 position orients to β with 3a takes place more selectively to give the corresponding α-C-allylated 5e exclusively. The β isomer could not be detected at all in this case.

Perhaps more interestingly to note, glycopyranosyl chlorides (2), instead of 1, can be allylated more readily and mildly by the catalysis with 4, the similar stereochemical outcome being obtained. In these cases the use of 20 mol% of 4 is enough to promote the allylation. Furthermore 4b can activate the carbon-chlorine bond of 2 sufficiently in a similar way to the reaction of a variety of α-chloroalkyl ethers.[4] Thus the catalytic activity of 4 toward carbohydrates has been best exerted to the pyranosyl chloride.

The allyl group is useful as a masked functional group such as formyl, acetonyl and formylmethyl.[11] In addition, the stereospecific introduction of β-bromoallyl group[12] that involved two functionalities could be useful for further transformation of 5d and 5g as a chiral building block. The synthetic utility of the present reaction was best displayed by the stereoselectivity of the allylation, ready accessibility of starting materials, and simple and mild manipulation of the conversion.[13]

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References and Notes

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8. When our work was in progress, 4a was used for the activation of O-acetyl-α-L-lyxose and O-acetyl-β-D-ribofuranose. However the yield was not always good[3a] and the excess of 4a was necessary for the conversion.[2d]
9. The stereochemical assignment was conducted by the following sequence. Each stereoisomer, isolated by HPLC (an α isomer elutes later than a β isomer in general), was debenzylated and hydrogenated by H_2/Pd-C in MeOH-AcOH and the resulting alcohol was acylated with Ac_2O-pyridine. By 200 MHz NMR, the coupling constant of the α isomer (J_{12} = ∿6 Hz) showed smaller than that of the corresponding β isomer (J_{12} = ∿10Hz)[2a].
10. Recent works in this field can be traced by the following references. See a) H. Sakurai, Pure & Appl. Chem., 54, 1 (1982); b) A. Hosomi, H. Iguchi, and H. Sakurai, Chem. Lett., 1982, 223; c) A. Hosomi, M. Saito, and H. Sakurai, Tetrahedron Lett., 21, 3783 (1980); d) A. Hosomi and H. Sakurai, ibid., 1978, 2589; e) Idem, J. Am. Chem. Soc., 99, 1973 (1977); f) H. Sakurai, A. Hosomi, M. Saito, K. Sasaki, H. Iguchi, J. Sasaki, and Y. Araki, Tetrahedron, 39, 883 (1983) and references cited therein.
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13. As a general procedure, a glycopyranosyl chloride (1 mmol), an allylsilane (2 mmol) and acetonitrile (2 ml) as a solvent were placed in a flask under argon. From a syringe, a catalyst (4) (0.2 mmol) was added and the resulting mixture was pyridine was added at 0 °C, the mixture was hydrolyzed with aqueous saturated sodium hydrogencarbonate. After work-up, a pure allylated glycopyranoside (5) was isolated by TLC. Each isomer was separated by HPLC. All compounds obtained in this work gave satisfactory spectral and elemental analysis.

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