C-Glucopyranosyl Derivatives from Readily Available 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl Chloride

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Readily available 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride smoothly reacts with various silyl enol ethers and silver(I) trifluoromethanesulphonate (triflate) to afford D-*C*-glucopyranosyl derivatives of α-configuration in high yields, whereas reaction with an electron-rich aromatic nucleophile yields the corresponding β-anomer.

Although there is currently intense interest in a new synthetic approach to *C*-glycosyl derivatives[1] owing to their biological[2] and chemical[3] relevance, glycopyranosyl chlorides have received relatively little attention in spite of the fact that 2,3,4,6-tetra-*O*-benzyl-α-D-glycopyranosyl chloride (**1**) is stable and readily available.[4]

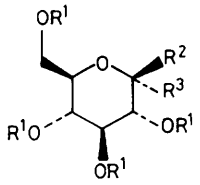
The successful *C*-allylation of α-D-glycopyranosyl chlorides with allylsilane under trimethylsilyl trifluoromethylsulphonate (triflate) or iodotrimethylsilane catalysis was recently reported.[5] However, no successful *C*-glucosidation has been reported using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (**1**) and silyl enol ethers even though the products would carry a functionalized side chain useful for complex targets.[1c]

We now report a mild method for *C*-glucosidation of a glucopyranosyl chloride using silver(I) activation. 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl chloride (**1**) (1 equiv.) was allowed to react with the nucleophile (3 equiv.) and silver(I) triflate (1.2 equiv.) in dry dichloromethane at room temperature in the dark for 10 min to yield the corresponding *C*-glucopyranosyl ester or ketone. Table 1 shows some examples.

Table 1. Synthesis of *C*-glycosyl derivatives from (**1**).

Reagent	Product	Yields[a] /%	Stereochemistry	M.p./°C	$[\alpha]_D$/° ($CHCl_3$, *c* 1)	Ref.
$EtOCOCH{=}C(OSiMe_3)OEt$	(**2**)	75	α	64—65	62.8	6
$CH_2{=}C(OSiMe_3)Ph$	(**3**)	88	α	76—77	45	9
$CH_2{=}C(OSiMe_3)C_6H_4Cl$-*p*	(**4**)	80	α	120—121	47.5	
$CH_2{=}C(OSiMe_3)Bu^t$	(**5**)	83	α	92—93	48.5	9
$CH_2{=}C(OSiMe_3)Me$	(**6**)	85	α	93—94	31	9
m-$(MeO)_2C_6H_4$	(**9**)	40	β	86	16	7

[a] Yields refer to pure isolated (flash column chromatography-silica and crystallized) products.



(**1**); R^1 = Benzyl (Bn), R^2 = H, R^3 = Cl
(**2**); R^1 = Bn, R^2 = H, R^3 = $CH(CO_2Et)_2$
(**3**); R^1 = Bn, R^2 = H, R^3 = CH_2COPh
(**4**); R^1 = Bn, R^2 = H, R^3 = $CH_2COC_6H_4Cl$-*p*
(**5**); R^1 = Bn, R^2 = H, R^3 = CH_2COBu^t
(**6**); R^1 = Bn, R^2 = H, R^3 = CH_2COMe
(**7**); R^1 = Ac, R^2 = H, R^3 = $CH(CO_2Et)_2$
(**8**); R^1 = Ac, R^2 = H, R^3 = CH_2CO_2Me
(**9**); R^1 = Bn, R^2 = *o*,*p*-$(MeO)_2C_6H_3$, R^3 = H

Assignment of the α-configuration for compound (**2**) was based on debenzylation (H_2, Pd–C, EtOH, room temp.) and then acetylation [Ac_2O, 4-*N*,*N*-dimethylaminopyridine (DMAP), pyridine, room temp.] to afford the tetra-acetate (**7**) identical (^{1}H n.m.r., optical rotation, m.p.) with that obtained by Hanessian.[6] Compounds (**3**), (**5**), and (**6**) were identical (^{1}H n.m.r., optical rotation, m.p.) with those obtained by literature methods.[1b] Assignment of the α-configuration for compound (**4**) was arrived at by conversion into its methyl ester (**8**) {m.p. 54—55 °C, $[\alpha]_D$ 46°, ^{1}H n.m.r.: δ 4.40—5.50 (m, 9H, H-1, 4 benzyl-CH_2) and 3.50—3.87 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6′)}, *via* Baeyer–Villiger oxidation [$(CF_3CO)_2O$, 30% aqueous H_2O_2–CH_2Cl_2], saponification (KOH, MeOH), and esterification (CH_2N_2). The methyl ester (**8**) was obtained with the same sequence from the α-C-glucosyl derivatives (**3**), (**5**), and (**6**), thus confirming the stereochemistry assigned to (**4**).

The reaction of (**1**) with *m*-dimethoxybenzene yielded the β-*C*-glucosyl derivative (**9**) identical with that prepared by Schmidt and Hoffmann.[7] This result is in accordance with the hypothetical initial formation of a pyranoxonium triflate[8] by action of silver(I) on α-D-glucopyranosyl chloride.

The preferential α-configuration of the *C*-glucosyl derivatives obtained from silyl enol ethers and (**1**) can be rationalized by considering the possibility that the hypothetical pyranoxonium triflate would preferentially accept these nucleophiles from the α (axial) side of the molecule owing to the anomeric effect of the ring oxygen.[1a]

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