

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 derivatives¹ owing to their biological² and chemical³ relevance, glucopyranosyl chlorides have received relatively little attention in spite of the fact that 2,3,4,6-tetra-*O*-benzyl- α -D-glucopyranosyl chloride (**1**) is stable and readily available.⁴

The successful C-allylation of α -D-glucopyranosyl 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

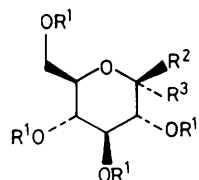
chloride (**1**) and silyl enol ethers even though the products would carry a functionalized side chain useful for complex targets.^{1c}

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	$[\alpha]_D^{20}$ (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 ₆ H ₄ Cl- <i>p</i>	(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
<i>m</i> -(MeO) ₂ C ₆ H ₄	(9)	40	β	86	16	7

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



- (1); R¹ = Benzyl (Bn), R² = H, R³ = Cl
 (2); R¹ = Bn, R² = H, R³ = CH(CO₂Et)₂
 (3); R¹ = Bn, R² = H, R³ = CH₂COPh
 (4); R¹ = Bn, R² = H, R³ = CH₂COC₆H₄Cl-*p*
 (5); R¹ = Bn, R² = H, R³ = CH₂COBu^t
 (6); R¹ = Bn, R² = H, R³ = CH₂COMe
 (7); R¹ = Ac, R² = H, R³ = CH(CO₂Et)₂
 (8); R¹ = Ac, R² = H, R³ = CH₂CO₂Me
 (9); R¹ = Bn, R² = *o,p*-(MeO)₂C₆H₃, R³ = H

Assignment of the α -configuration for compound (2) was based on debenzoylation (H₂, Pd-C, EtOH, room temp.) and then acetylation [Ac₂O, 4-*N,N*-dimethylaminopyridine (DMAP), pyridine, room temp.] to afford the tetra-acetate (7) identical (¹H n.m.r., optical rotation, m.p.) with that obtained by Hanessian.⁶ Compounds (3), (5), and (6) were identical (¹H 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, [α]_D 46°, ¹H n.m.r.: δ 4.40–5.50 (m, 9H, H-1, 4 benzyl-CH₂) and 3.50–3.87 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6')}, via Baeyer–Villiger oxidation [(CF₃CO)₂O, 30% aqueous H₂O₂–CH₂Cl₂], saponification (KOH, MeOH), and esterification (CH₂N₂). 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 triflate⁸ 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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