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RESEARCH

Note

One-step glycosylation and selective deprotection of peracetylated monosaccharides for facile syntheses of allyl glycosides with a free C-2 hydroxyl group

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Many naturally occurring oligosaccharides and glycoconjugates contain (1 → 2)-linked disaccharide units [1]. Thus, the preparation of monosaccharide derivatives bearing only a free C-2 hydroxyl group has become an interesting subject, because these are important intermediates for the synthesis of the above natural products. Several methods [2] have been developed for the preparation of various monosaccharides having a free C-2 hydroxyl group, but all of them are multi-step procedures involving several steps of regioselective protections and deprotections of the monosaccharides, which makes the syntheses of these intermediates very tedious and low yielding. Here, we wish to report a one-step procedure for the preparation of allyl glycosides with free C-2 hydroxyl groups by reaction of peracetylated monosaccharides with an excess of allyl alcohol in the presence of an optimum amount of boron trifluoride–diethyl ether complex in good yield. Using one of these intermediates as a glycosyl acceptor, we have conveniently synthesized the protected derivative of a naturally occurring (1 → 2)-linked disaccharide [1,3], allyl 2,3,4-tri-*O*-acetyl-*α*-L-rhamnopyranosyl-(1 → 2)-3,4-di-*O*-acetyl-D-xylopyranoside (**8**).

Reaction of peracetylated monosaccharides (e.g., **1**) with one equivalent of an alcohol catalyzed by Lewis acids normally gives the corresponding glycosylation products **2** [4].

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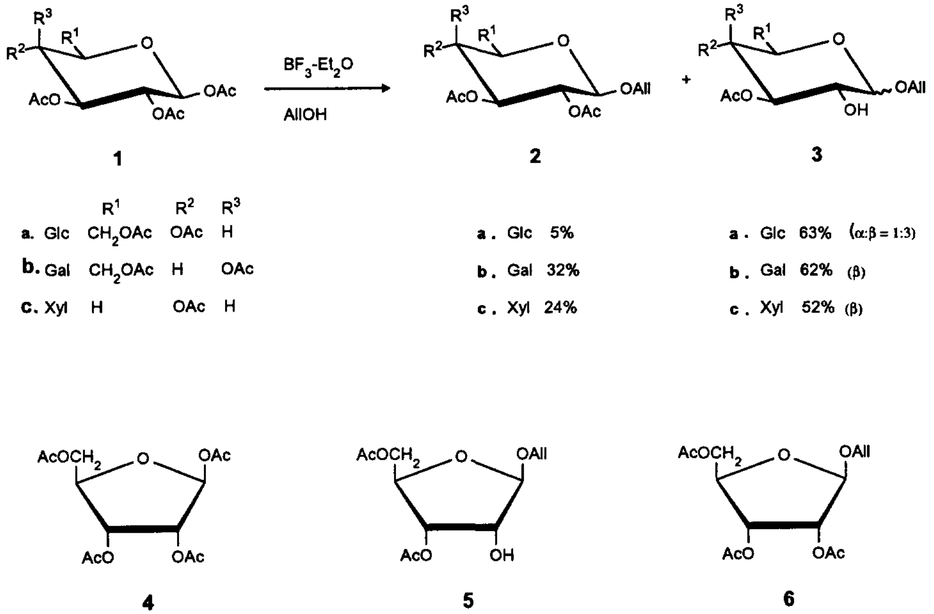
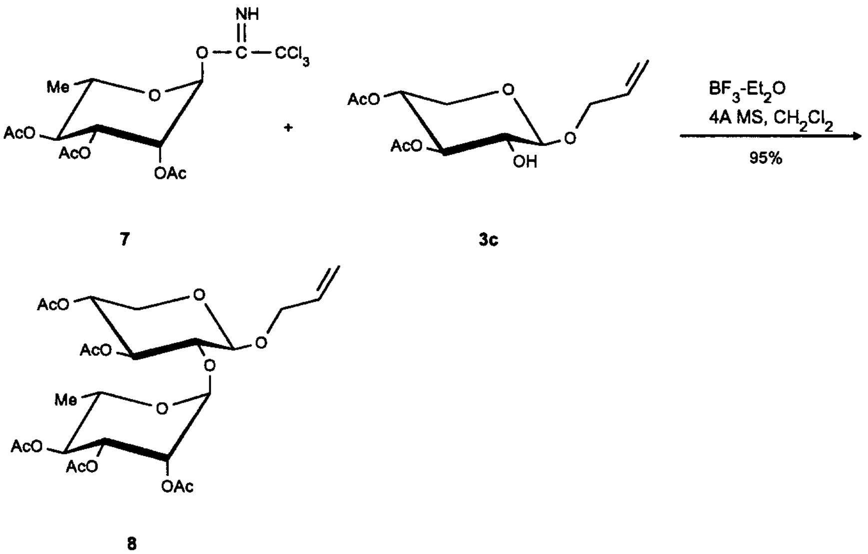


Scheme 1.

However, we recently found that the reaction of peracetylated β-D-glucopyranose (**1a**) with an excess of an alcohol in the presence of a Lewis acid produced substantial amounts of the glycosylation products with deacetylation of C-2 (e.g., **3a**, Scheme 1) [5], and optimized yields of these products were obtained with molecular ratios of **1a**:alcohol:$BF_3 \cdot Et_2O$ = 1.0:4.0:1.5. Similarly, we have also conveniently prepared allyl 3,4,6-tri-*O*-acetyl-β-D-galactopyranoside (**3b**) and allyl 3,4-di-*O*-acetyl-β-D-xylopyranoside (**3c**) from 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose (**1b**) and 1,2,3,4-tetra-*O*-acetyl-β-D-xylopyranose (**1c**) by this one-step procedure in good yields (52–62%, Scheme 1). For all these reactions, the β anomers of **3** were obtained as the major products; however, the reaction of 1,2,3,4-tetra-*O*-acetyl-β-D-ribofuranose (**4**) under the same conditions only gave a moderate yield (35%) of the ribofuranoside **5** with a free C-2 hydroxyl group, with **6** as the predominant product (60%). Furthermore, reactions of peracetylated D-mannopyranose and peracetylated L-rhamnopyranose only produced the corresponding glycosides. These results suggest that C-2 stereochemistry and the ring structures of the starting materials are important in determining the pathways and results of these reactions. The structures of all products were confirmed by elemental analysis, IR, ^1H NMR spectroscopy, and MS. A reaction mechanism involving the first attack of allyl alcohol on orthoester cations, which were formed by interaction of the neighbouring C-2 OAc group with anomeric carbocations, followed by attack of another allyl alcohol molecule on the anomeric center, was proposed to explain the formation of **3** [5].

Using the intermediate **3c** as the glycosyl acceptor and 2,3,4-tri-*O*-acetyl-β-L-rhamnopyranosyl trichloroacetimidate (**7**) as the glycosyl donor, we have conveniently realized the first chemical synthesis of the derivative of a naturally occurring disaccha-



Scheme 2.

ride, allyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1 → 2)-3,4-di-*O*-acetyl-β-D-xylopyranoside (**8**), in excellent yield (Scheme 2).

1. Experimental

General methods.—Optical rotations were determined with a Perkin–Elmer Model 241 MC polarimeter at ambient temperature (25 °C). TLCs were performed on precoated plates of Silica Gel HF_{254} (0.5 mm, Qingdao, China). Flash column chromatography was performed on Silica Gel H (200–400 mesh). ^1H NMR spectra were recorded at 300 MHz on a Bruker AM-300 spectrometer with tetramethylsilane as the internal standard and $CDCl_3$ as the solvent. IR spectra were recorded with a Shimadzu IR-440 spectrophotometer. Mass spectra were obtained on a VG QUATTRO MS instrument. Allyl alcohol was treated with sodium followed by distillation before application.

General procedure for the preparation from various monosaccharides of allyl glycosides with a free C-2 hydroxyl group.—To a mixture of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose (**1b**, 0.195 g, 0.5 mmol), which was prepared from D-galactose in acetic anhydride–NaOAc, and dry allyl alcohol (0.14 mL, 2.0 mmol) in anhydrous CH_2Cl_2 (4.00 mL), was added freshly distilled $BF_3 \cdot Et_2O$ (0.10 mL, 0.75 mmol) under a nitrogen atmosphere at 0 °C. The reaction solution was stirred at 0 °C for 1 h, then at room temperature overnight, and then poured into ice–water and extracted with EtOAc. The combined extracts were concentrated under diminished pressure and chromatographed on a silica gel column to afford products **2b** (0.062 g, 32%) and **3b** (0.107 g, 62%).

Allyl 3,4,6-tri-*O*-acetyl-α-D-glucopyranoside (**3a**-α, 0.027 g, 16%); colourless syrup; $[\alpha]_D$ +75.7° (*c* 0.9, $CHCl_3$); IR (film): ν 3455, 1750, 1365, 1245, 1050 cm^{-1}; ^1H NMR: δ 5.95 (m, 1 H, C*H*=CH_2), 5.34 and 5.26 (2 m, 1 H each, CH=CH_2), 5.21 (dd, 1 H, $J_{3,4}$ 10.0, $J_{4,5}$ 9.7 Hz, H-4), 4.99 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-3), 4.95 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.27 (m, 1 H, OCH_2CH=), 4.23 (dd, 1 H, $J_{5,6}$ 4.6, $J_{6,6'}$ 12.3 Hz, H-6), 4.08 (m, 1 H, OCH_2CH=), 4.05 (dd, 1 H, $J_{5,6'}$ 2.3 Hz, H-6′), 3.96 (ddd, 1 H, H-5), 3.66 (dd, 1 H, H-2), 2.08, 2.07, and 2.03 (3 s, 3 H each, 3 OAc); EIMS (*m/z*): 346 (M^+- 1), 289 (M^+- OAll); Anal. Calcd for $C_{15}H_{22}O_9$: C, 52.02; H, 6.36. Found: C, 52.13; H, 6.75.

Allyl 3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (**3a**-β, 0.082 g, 48%); colourless syrup; IR (film): ν 3450, 1750, 1370, 1240, 1050 cm^{-1}; ^1H NMR: δ 5.92 (m, 1 H, C*H*=CH_2), 5.33 and 5.23 (2 m, 1 H each, CH=CH_2), 5.11 (dd, 1 H, $J_{3,2} = J_{3,4} = 9.4$ Hz, H-3), 4.99 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 4.43 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.37 (m, 1 H, OCH_2CH=), 4.34 (dd, 1 H, $J_{5,6}$ 4.9, $J_{6,6'}$ 12.1 Hz, H-6), 4.18 (m, 1 H, OCH_2CH=), 4.11 (dd, 1 H, $J_{5,6'}$ 2.3 Hz, H-6′), 3.71 (ddd, 1 H, H-5), 3.59 (dd, 1 H, H-2), 2.09, 2.05, and 2.02 (3 s, 3 H each, 3 OAc); EIMS (*m/z*): 346 (M^+- 1), 289 (M^+- OAll); Anal. Calcd for $C_{15}H_{22}O_9$: C, 52.02; H, 6.36. Found: C, 52.13; H, 6.75.

Allyl 3,4,6-tri-*O*-acetyl-β-D-galactopyranoside (**3b**, 0.107 g, 62%); colourless syrup; $[\alpha]_D$ +59.4° (*c* 0.9, $CHCl_3$); ^1H NMR: δ 5.95 (m, 1 H, C*H*=CH_2), 5.40 (wd, 1 H, $J_{4,3}$ 3.3 Hz, H-4), 5.34 and 5.25 (2 m, 1 H each, CH=CH_2), 4.90 (dd, 1 H, $J_{3,2}$ 10.2 Hz, H-3), 4.42 (m, 1 H, OCH_2CH=), 4.40 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.20–4.08 (m, 3 H, OCH_2CH=, H-6 and H-6′), 3.89 (m, 1 H, H-5), 3.82 (dd, 1 H, 2-H), 2.14, 2.05, and 2.05 (3 s, 3 H each, 3 OAc); EIMS (*m/z*): 347 (M^++ 1), 289 (M^+- OAll); Anal. Calcd for $C_{15}H_{22}O_9$: C, 52.02; H, 6.36. Found: C, 52.24; H, 6.53.

Allyl 3,4-di-*O*-acetyl-β-D-xylopyranoside (**3c**, 52%); colourless syrup; $[\alpha]_D$ +27.7° (*c* 0.9, $CHCl_3$). IR (film): ν 3450, 1745, 1370, 1240, 1045 cm^{-1}; ^1H NMR: δ 5.91 (m, 1 H, C*H*=CH_2), 5.32 and 5.24 (2 m, 1 H each, CH=CH_2), 5.09 (dd, 1 H, $J_{3,4} = J_{3,2} = 8.8$ Hz, H-3), 4.92 (ddd, 1 H, $J_{4,5a}$ 9.2, $J_{4,5e}$ 5.1 Hz, H-4), 4.40 (d, 1 H, $J_{1,2}$ 7.0 Hz, H-1), 4.34 and 4.12 (2 m, 1 H each, OCH_2CH=), 4.08 (dd, 1 H, $J_{5e,5a}$ 11.7 Hz, H-5e), 3.57 (dd, 1 H, H-2), 3.33 (dd, 1 H, H-5a), 2.04 and 2.03 (2 s, 3 H each, 2 OAc); EIMS (*m/z*): 273 (M^+- 1), 217 (M^+- OAll); Anal. Calcd for $C_{12}H_{18}O_7$: C, 52.55, H, 6.57. Found: C, 52.80; H, 6.62.

Allyl 3,5-di-*O*-acetyl-β-D-ribofuranoside (**3d**, 35%); colourless syrup; $[\alpha]$ −36.8° (*c* 0.9, $CHCl_3$); ^1H NMR: δ 5.88 (m, 1 H, C*H*=CH_2), 5.30 and 5.25 (2 m, 1 H each, CH=CH_2), 5.21 (m, 2 H, H-3 and H-4), 4.87 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1), 4.22 and 4.03 (2 m, 1 H each, OCH_2CH=), 3.98 (wd, 1 H, $J_{5,5'}$ 12.3 Hz, H-5), 3.78 (ws, 1 H, H-2), 3.74 (dd, 1 H, $J_{4,5'}$ 2.0 Hz, H-5), 2.16 and 2.10 (2 s, 1 H each, 2 OAc); EIMS (*m/z*): 275 (M^++ 1), 217 (M^+- OAll); Anal. Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.57. Found: C, 52.74; H, 6.70.

Preparation of allyl 2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl-(1 → 2)-3,4-di-O-acetyl-β-D-xylopyranoside (**8**).—The mixture of **3c** (0.274 g, 1.0 mmol), **7** (0.520 g, 1.2 mmol, freshly prepared from 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranose), 4A molecular sieve (0.200 g) in dry CH_2Cl_2 (10.0 mL) was stirred at room temperature for 1 h and then was cooled down to −20 °C and $BF_3 \cdot Et_2O$ (0.66 mL, 0.5 mmol) was added dropwise. After stirring at −20 °C for 2 h, the reaction was quenched with aq $NaHCO_3$ solution. Workup as above and purification of the product gave **8** (0.518 g, 95%) as a colourless solid: mp 42–43 °C; $[\alpha]_D$ +75.7° (c 0.9, $CHCl_3$); IR (KBr): ν 1750, 1365, 1220, 1030 cm^{-1}; ^1H NMR: δ 5.93 (m, 1 H, $C\mathit{H}{=}CH_2$), 5.32 and 5.23 (2 m, 1 H each, $CH{=}C\mathit{H}_2$), 5.26 (dd, 1 H, $J_{2',3'} = J_{3',4'} = 10.3$ Hz, H-3′), 5.20 (dd, 1 H, $J_{2,3} = J_{3,4} = 8.8$ Hz, H-3), 5.05 (dd, 1 H, $J_{4',5'}$ 10.0 Hz, H-4′), 5.02 (dd, 1 H, $J_{2',1'}$ 1.60 Hz, H-2′), 4.93 (d, 1 H, H-1′), 4.91 (ddd, 1 H, $J_{4,5e}$ 5.2, $J_{4,5a} = J_{4,3} = 8.9$ Hz, H-4), 4.51 (d, 1 H, $J_{1,2}$ 6.9 Hz, H-1), 4.33 and 4.10 (2 m, 1 H each, $OC\mathit{H}_2CH{=}$), 4.06 (dd, 1 H, $J_{5e,5a}$ 11.7 Hz, H-5e), 3.98 (dq, 1 H, H-5′), 3.67 (dd, 1 H, H-2), 3.37 (dd, 1 H, H-5a), 2.13, 2.09, 2.06, 2.05, 1.98 (5 s, 3 H each, 5 OAc), 1.16 (d, 1 H, $J_{6',5'}$ 6.27 Hz, $C\mathit{H}_3$-6′); EIMS (m/z): 489 ($M^+ -$ OAll); Anal. Calcd for $C_{24}H_{34}O_{14}$: C, 52.75; H, 6.23. Found: C, 52.76; H, 6.15.

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