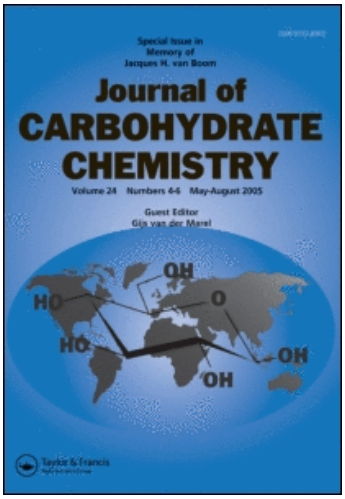

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STUDIES OF C-GLYCOSIDES XIX. SELECTIVE ACETOLYSIS OF PRIMARY BENZYL ETHERS OF C-GLUCOSIDES

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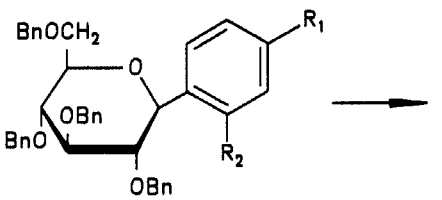
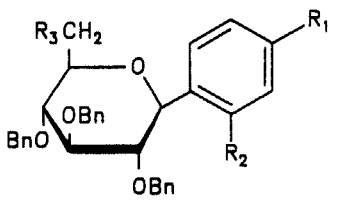
ABSTRACT

Selective acetolysis of primary benzyl ethers of O-benzyl C-glucosides has been investigated. β-anomers were shown to give fully acetylated compounds, while the α-anomers remained unchanged under the same conditions. The products were assigned by IR, ^{1}H NMR, ^{13}C NMR, and EI-MS.

INTRODUCTION

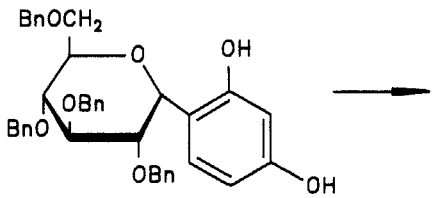
Selective protection and deprotection of hydroxy groups are very important reactions in carbohydrate chemistry.[1-3] The conventional method of etherifying secondary hydroxy groups, while maintaining the free primary hydroxy group, is as follows: (1) tritylation, (2) etherification, and (3) detritylation.[4] However, it would be more convenient if the hydroxy groups were completely benzylated first, and then the benzyl ether of the primary hydroxy group were selectively cleaved by acetolysis.[5] This method, using acetic anhydride-sulfuric acid, has been successfully applied to D-glucose, D-galactose, and D-mannose in the form of hemiacetals, glycosides, and orthoesters.[6] The present report deals with the selective acetolysis of primary benzyl ether of C-glucosides.





1. $R_1 = R_2 = OH$
2. $R_1 = R_2 = OMe$
3. $R_1 = OMe$, $R_2 = H$
4. $R_1 = R_2 = H$

5. $R_1 = R_2 = OAc$, $R_3 = OBn$
6. $R_1 = R_2 = R_3 = OAc$
7. $R_1 = R_2 = OMe$, $R_3 = OAc$
8. $R_1 = OMe$, $R_2 = H$, $R_3 = OAc$
9. $R_1 = R_2 = H$, $R_3 = OAc$



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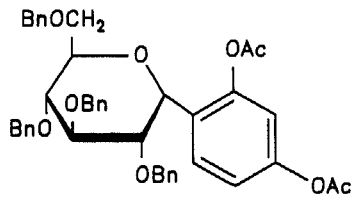
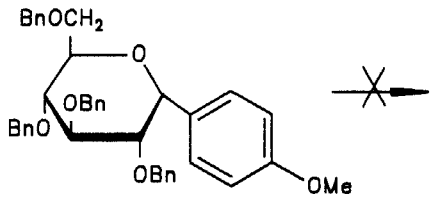


11

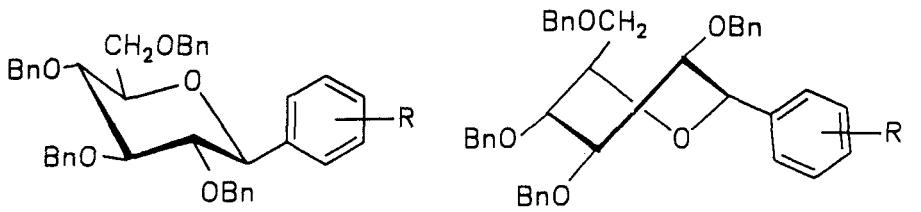


12

SCHEME 1

RESULTS AND DISCUSSION

In the synthesis of naturally occurring C-glycosylflavonoids, C-acylation of the aglycone of 1-(2',3',4',6'-tetra-O-benzyl-β-D-glucopyranosyl)-2,4-dihydroxy-benzene (1) was studied by treating 1 with acetic anhydride - boron trifluoride etherate.[7] Surprisingly, only O-acylated 5 and O-debenzylated 6 were obtained. The ^1H NMR spectrum of 6



β-anomer α-anomer

SCHEME 2

showed that there were three singlets at ca. δ2 ppm. In the ^{13}C NMR spectrum of this compound, the resonance of C-6' shifted to higher field (from δ69.9 to 63.8 ppm) in comparison with both **1** and **5**. An APT experiment also showed that only four CH_2 peaks appeared, one of them appearing at δ63.8 ppm. Thus selective acetolysis was shown to occur at the C-6' position. Our method has been extended to three other O-benzyl-β-C-glucosides, whereby the 6-O-debenzylated products were also formed. In the case of compound **4**, a twofold reaction time was necessary to effect complete reaction. However, acetolysis was shown not to occur with α-anomers. Compound **10** gave an O-acetylated product **11**, while **12** remained unchanged.

It is speculated that the α-anomers of O-benzyl C-glucosides may exist in the twist-boat conformation instead of the normal chair conformation due to the larger axial group at the C-1' position. Thus selective acetolysis might not occur with α-anomers due to steric hindrance at the C-6' position (see Scheme 2).

EXPERIMENTAL

General Procedures. Infrared (IR) spectra were recorded with a Perkin-Elmer 983 spectrometer. ^1H NMR spectra were determined with a Jeol-90 spectrometer (solutions in chloroform-d), with TMS as the

internal standard. ^{13}C NMR spectra were measured on a JEOL-100 spectrometer (solutions in DMSO-d_6). Chemical shifts are given on the δ scale. EI-MS were recorded with VG-ZAB-HS instrument. Preparative TLC was performed on precoated silica gel plates with 7:3 cyclohexane - ethyl acetate as eluent.

1-(2',3',4',6'-Tetra-O-benzyl-β-D-glucopyranosyl)-2,4-diacetyloxybenzene (5) and 1-(2',3',4'-tri-O-benzyl-6'-O-acetyl-β-D-glucopyranosyl)-2,4-diacetyloxybenzene (6). A mixture of 1 (20 mg, 0.031 mmol) and acetic anhydride (0.1 g, an excess) in anhydrous ether was stirred at 0 °C, and 2 drops of $BF_3 \cdot Et_2O$ were added. Stirring was continued for 2 h at 0 °C, followed by stirring for 12 h at 15 °C. TLC revealed that a new compound which had a larger R_f value than that for 1 was formed after stirring for 2 h at 15 °C. Most of this compound was subsequently converted into another new product which had a smaller R_f value than 1 when stirring was continued under the same conditions. Separation by preparative TLC gave two new compounds:

5, syrup; $[\alpha]_D^{25}$ +10.0° (c 1.4, $CHCl_3$); IR (KBr): 1750 ($OCOCH_3$); ^{13}C NMR: δ69.9 (C-6'), 73.8 (C-1'), 79.0 (C-4'), 79.2 (C-2'), 82.2 (C-5'), 86.6 (C-3'), 168.4 (OC^*OCH_3), 20.7 ($OCOC^*H_3$); MS (EI^+): calcd. for M^+-$PhCH_2$, 625.2332; found, 625.2384.

6, syrup; $[\alpha]_D^{25}$ +6.0° (c 1.9, $CHCl_3$); IR (KBr), 1736, 1765 ($OCOCH_3$); ^1H NMR: δ2.04, 2.28, 2.30 (3s, 9H, $OCOCH_3$); ^{13}C NMR: δ63.8 (C-6'), 76.6 (C-1'), 77.3 (C-4'), 78.7 (C-2'), 82.0 (C-5'), 86.6 (C-3'), 170.2, 168.8, 168.5 (OC^*OCH_3), 26.8, 20.9, 20.7 ($OCOC^*H_3$); MS (EI^+): calcd. for M^+-$PhCH_2$, 577.2048; found, 577.2061.

1-(2',3',4'-Tri-O-benzyl-6'-O-acetyl-β-D-glucopyranosyl)-2,4-dimethoxybenzene (7). Compound **2**[8] (20 mg, 0.032 mmol) was reacted with acetic anhydride and $BF_3 \cdot Et_2O$ under the same conditions. Preparative TLC separation gave 10 mg (54%) of **7**: syrup; $[\alpha]_D^{25}$ +4.1° (c 0.97, $CHCl_3$); IR (KBr), 1740 ($OCOCH_3$); ^1H NMR: δ2.01 (s, 3H, $OCOCH_3$), 3.74, 3.80 (2S, 6H, OCH_3); MS (EI^+): calcd. for M^+-$PhCH_2$, 521.2175; found, 521.2174.

1-(2',3',4'-Tri-O-benzyl-6'-O-acetyl-β-D-glucopyranosyl)-4-methoxybenzene (8). Compound 3[10] (20 mg, 0.032 mmol) reacted with large excess of acetic anhydride and $BF_3 \cdot Et_2O$ to give 10 mg (54%) of **8** after preparative TLC separation: syrup; $[\alpha]_D^{25}$ -48.0° (c 1.25, $CHCl_3$); IR (KBr), 1740 ($OCOCH_3$); ^1H NMR: δ 2.02 (s, 3H, $OCOCH_3$), 3.80 (S, 3H, OCH_3); MS (EI^+): calcd. for M^+, 582.2617; found, 582.2614.

1-(2',3',4'-Tri-O-acetyl-β-D-glucopyranosyl)benzene (9). A mixture of 4[10] (20 mg, 0.033 mmol) and acetic anhydride (0.1 g) and 2 drops of $BF_3 \cdot Et_2O$ in anhydrous ether was stirred at 0 °C for 2 h, then at 15 °C for 12 h. TLC showed that no new compound had appeared. Stirring was continued overnight, at the end of which time TLC indicated that a new compound was formed. Isolation of the product as before gave 8 mg (42%) of **9**: syrup; $[\alpha]_D^{25}$ +7.3° (c 1.09, $CHCl_3$); ^1H NMR: δ 2.10 (s, 3H, $OCOCH_3$); MS (EI^+): calcd. for M^+-$PhCH_2$, 461.1963; found, 461.1970.

1-(2',3',4',6'-Tetra-O-benzyl-α-D-glucopyranosyl)-2,4-diacetyloxybenzene (11). Compound 10[9] (25 mg, 0.04 mmol) was reacted with a large excess of acetic anhydride and $BF_3 \cdot Et_2O$ to give 20 mg (71%) of 11 after stirring for 2 h at 0 °C, then for 24 h at 15 °C. Syrup; $[\alpha]_D^{25}$ -28.6° (c 0.63, $CHCl_3$); ^1H NMR: δ 2.21, 2.24 (2s, 6H, 2 $OCOCH_3$); EI-MS: 656 (M^+), 625 (M^+-$PhCH_2$).

Compound 12[10] was treated with acetic anhydride and $BF_3 \cdot Et_2O$ under the same conditions as compound **4**, but no new compound formed as revealed by TLC analysis.

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