Carbohydrate Research, 148 (1986) 349–352
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Stereoselective synthesis of 1-*O*-trimethylsilyl-α- and -β-D-glucopyranuronate

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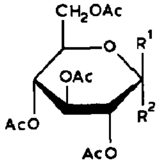
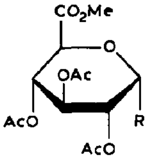
(Received July 30th, 1985; accepted for publication, November 8th, 1985)

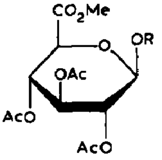
1-*O*-Trimethylsilyl derivatives of aldoses are of interest for the synthesis of glycosides of aldehydes, phenols, and alkanols[1,2]. Thus, the reaction of 2,3,4,6-tetra-*O*-acetyl-1-*O*-trimethylsilyl-α- and β-D-glucopyranose (**1** and **2**) with formaldehyde dimethyl acetal in the presence of catalytic amounts of trimethylsilyl trifluoromethanesulfonate gave, stereoselectively, the glycosides **3** and **4**.



1 $R^1 = H, R^2 = OSiMe_3$
2 $R^1 = OSiMe_3, R^2 = H$
3 $R^1 = H, R^2 = OCH_2OMe$
4 $R^1 = OCH_2OMe, R^2 = H$



5 R = Br
6 R = OH
10 R = $OSiMe_3$



7 R = H
8 R = Bzl
9 R = $SiMe_3$

Application of this reaction for the synthesis of β-D-glucuronides was not possible hitherto because the necessary pure 1-*O*-trimethylsilyl derivative **9** was not available. Thus, hydrolysis of the glycosyl bromide **5** with silver carbonate yielded[3,4] a 4:1 α,β-mixture from which the α anomer **6** could be crystallised. However, it was not possible to isolate the β anomer **7**.

We now describe a convenient procedure for the synthesis of methyl 2,3,4-tri-*O*-acetyl-1-*O*-trimethylsilyl-α- and -β-D-glucopyranuronate (**10** and **9**).

The reaction of the easily obtainable[5] glycosyl bromide **5** with benzyl alcohol at 100° for 1 h in the presence of 1 equiv. of mercury cyanide gave 75% of the benzyl β-glycoside **8**. Although **8** could be hydrogenated in the presence of Pd/C at

0008-6215/86/$ 03.50

0° without anomerisation, the isolation of the product **7** was difficult because of rapid isomerisation. Therefore, **7** was treated immediately with equivalent amounts of hexamethyldisilazane and chlorotrimethylsilane in pyridine to give crystalline **9**, which could be stored at −20° for several months without decomposition. However, **9** was susceptible to hydrolysis and attempted chromatography on silica gel resulted in complete decomposition.

The crystalline α anomer **10** could be obtained simply by anomerisation of **9** in dichloromethane at −50° in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate. The β anomer **9** could not be detected, by ^{1}H- and ^{13}C-n.m.r. spectroscopy, in the crude product after anomerisation. This procedure for the synthesis of **10** is superior to that involving the trimethylsilylation of **6**. Trimethylsilylation of the mixture of **6** and **7**, obtained by treatment[3] of **5** with silver carbonate, gave a mixture of **9** and **10** which could not be resolved because of decomposition on the adsorbent.

The structures of **9** and **10** were confirmed by ^{1}H- and ^{13}C-n.m.r. spectroscopy. Thus, the doublets for H-1 of **9** and **10** had $J_{1,2}$ values of 7.5 and 3.5 Hz, respectively. The decoupled ^{13}C-n.m.r. spectra of **9** and **10** contained singlets at δ 95.6 and 90.3, respectively, for C-1.

EXPERIMENTAL

Methyl (benzyl 2,3,4-tri-O-acetyl-β-D-glucopyranosid)uronate (**8**). — To a solution of methyl (2,3,4-tri-*O*-acetyl-α-D-glucopyranosyl bromide)uronate[5] (**5**; 1.30 g, 3.27 mmol) in benzyl alcohol (20 mL) was added $Hg(CN)_2$ (1.02 g, 4.04 mmol). The mixture was stirred at 100° for 30 min and then at room temperature for 2 h. After removal of the benzyl alcohol at 60°/0.1 Torr, CH_2Cl_2 (30 mL) was added, the mixture was filtered and concentrated, and the residue was crystallised from ether to afford **8** (1.07 g, 75%), m.p. 135°, $[\alpha]_D^{20}$ −66° (*c* 1, chloroform); lit.[6] m.p. 135–136° (yield, 46.5%), $[\alpha]_D^{20}$ −66.2° (chloroform).

Methyl 2,3,4-tri-O-acetyl-1-O-trimethylsilyl-β-D-glucopyranuronate (**9**). — To a solution of **8** (2.0 g, 4.72 mmol) in ethyl acetate–ethanol (1:1, 50 mL) were added 10% Pd/C (1.5 g) and 10% $Pd/CaCO_3$ (0.5 g). The hydrogenation was carried out at 0° and was complete after 6 h. After removal of the catalyst, the filtrate was concentrated *in vacuo*. A solution of the residue in dry pyridine (50 mL) was stirred at 0° whilst hexamethyldisilazane (0.76 g, 4.72 mmol) and chlorotrimethylsilane (0.61 g, 4.72 mmol) were added dropwise. After removal of the pyridine salt, the filtrate was concentrated by azeotropic distillation with toluene at 50° (bath)/5 Torr. Recrystallisation of the product from ether–light petroleum gave **9** (1.61 g, 84%), m.p. 76–77°, $[\alpha]_D^{20}$ −18° (*c* 1, chloroform), R_F 0.46 (silica gel; hexane–ethyl acetate, 1:1); ν_{max}^{KBr} 1760 (C=O), 1255 (SiMe), 1230 (C-O), 860 cm^{-1} (SiMe). N.m.r. data ($CDCl_3$): ^{1}H, δ 5.32–5.18 (m, 2 H, H-3,4), 5.01–4.87 (m, 1 H, H-2), 4.78 (d, 1 H, *J* 7.5 Hz, H-1), 4.13–4.00 (m, 1 H, H-5), 3.76 (s, 3 H, CO_2Me), 2.05, 2.04, 2.03 (3 s, 9 H, 3 Ac), 0.18 (s, 9 H, $SiMe_3$); ^{13}C, δ 170.22, 169.41, 169.26, 167.24 (CO-CH_3), 95.58 (C-1), 73.14, 72.66, 72.09, 69.49 (C-2 to C-5), 52.85 (CO_2CH_3), 20.69, 20.66, 20.54 ($CO\text{-}CH_3$), −0.24 ($SiMe_3$). Mass spectrum: *m/z* 391 (M^+ − Me), 347 (M^+ − OAc), 317 (M^+ − $OSiMe_3$), 286 (M^+ − 2 OAc), 229 (M^+ − 3 OAc), 73 ($SiMe_3$).

Anal. Calc. for $C_{16}H_{26}O_{10}Si$: C, 47.28; H, 6.45. Found: C, 47.28; H, 6.45.

Methyl 2,3,4-tri-O-acetyl-α-D-glucopyranuronate (**6**). — To a solution of **5** (8.90 g, 22.4 mmol) in dry acetone (50 mL) at 0° were added water (0.25 mL) and Ag_2CO_3 (4.90 g, 18.0 mmol). The mixture was stirred for 2 h, filtered, and concentrated *in vacuo*, and the residual oil was eluted from a column of neutral aluminium oxide with hexane–ethyl acetate (1:1) to give a 4:1 α,β-mixture (**6** and **7**). Crystallisation of the mixture from propanol gave **6** (3.1 g, 41%), m.p. 116°, $[\alpha]_D^{20}$ +81° (*c* 1, chloroform). N.m.r. data ($CDCl_3$): ^1H, δ 5.68–5.46 (m, 2 H, H-1,4), 5.17 (t, 1 H, *J* 10 Hz, H-3), 4.87 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 10 Hz, H-2), 4.58 (d, 1 H, *J* 10 Hz, H-5), 4.17–3.92 (m, 1 H, OH), 3.78 (s, 3 H, CO_2Me), 2.08, 2.04, 2.03 (3 s, 9 H, 3 OAc).

Anal. Calc. for $C_{13}H_{18}O_{10}$: C, 46.71; H, 5.43. Found: C, 46.62; H, 5.54.

Methyl 2,3,4-tri-O-acetyl-1-O-trimethylsilyl-α-D-glucopyranuronate (**10**). — (*a*) Using the procedure described above for the preparation of **9**, **6** (3.10 g, 9.28 mmol) was converted into **10** (2.76 g, 73%), m.p. 85° (from ether–light petroleum).

(*b*) 0.10M Trimethylsilyl trifluoromethanesulfonate in dichloromethane (0.60 mL) was added to a solution of **9** (812 mg, 2.00 mmol) in anhydrous dichloromethane (5 mL) under N_2 at −50° and the mixture was stirred at this temperature for 10 h. After the addition of triethylamine (0.20 mL), the mixture was eluted from a column of silica gel with hexane–ethyl acetate (1:1). The eluate was concentrated and the residue was crystallised from ether–light petroleum to give **10** (763 mg, 94%), m.p. 85°, $[\alpha]_D^{20}$ +119° (*c* 1, chloroform), R_F 0.49 (silica gel; hexane–ethyl acetate, 1:1); lit.[3] m.p. 86°, $[\alpha]_D^{25}$ +108.9° (chloroform). N.m.r. data ($CDCl_3$): ^1H, δ 5.56 (t, 1 H, *J* 10 Hz, H-4), 5.47 (d, 1 H, *J* 3.5 Hz, H-1), 5.15 (t, 1 H, *J* 10 Hz, H-3), 4.83 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 10 Hz, H-2), 4.45 (d, 1 H, *J* 10 Hz, H-5), 3.75 (s, 3 H, CO_2Me), 2.04, 2.02, 2.01 (3 s, 9 H, 3 OAc), 0.18 (s, 9 H, $SiMe_3$); ^{13}C, δ 169.76, 169.64, 169.27, 168.03 ($CO\text{-}CH_3$), 90.30 (C-1), 71.22, 69.51, 69.09, 67.88 (C-2 to C-5), 52.51 (CO_2CH_3), 20.40, 20.36, 20.22 ($CO\text{-}CH_3$), −0.55 ($SiMe_3$).

Anal. Calc. for $C_{16}H_{26}O_{10}Si$: C, 47.28; H, 6.45. Found: C, 47.44; H, 6.46.

ACKNOWLEDGMENT

This work was supported by the Fonds der Chemischen Industrie.

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