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Preliminary communication

Regioselective enhancement of the nucleophilicity of hydroxyl groups through trialkylstannylation: a route to partial alkylation of polyhydroxy compounds

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As part of a project on efficient transformation of carbohydrates through trialkylstannylation[1], we report here the preparation of partially benzylated and partially allylated methyl hexosides[2] that may be useful intermediates[3] for the synthesis of branched-chain oligosaccharides of biological interest[4].

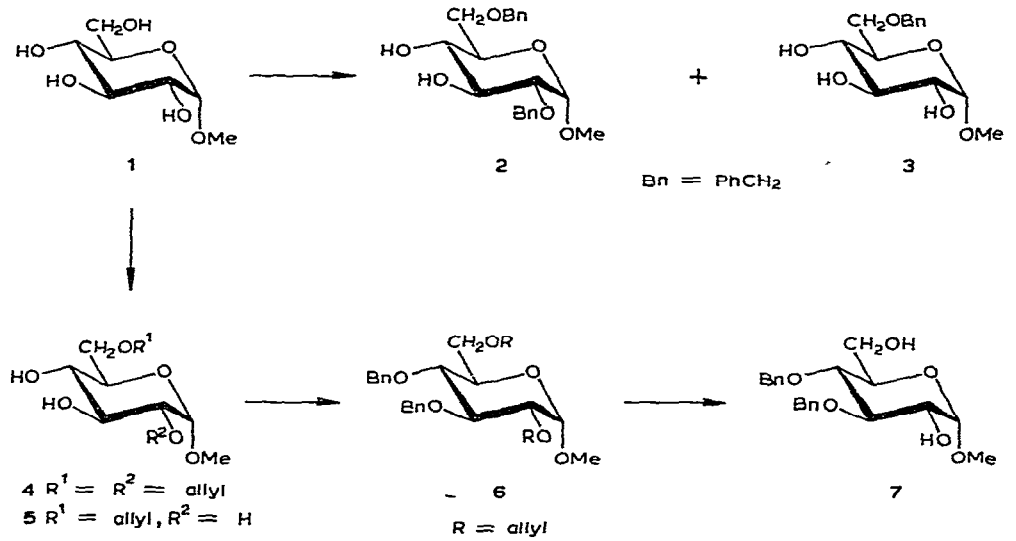
Finely powdered methyl α-D-glucopyranoside (**1**) was treated with 1.5 molar proportions (3 equivalents) of bis(tributylstannyl) oxide in toluene for 4 h at 140° with continuous removal of water, to give, after evaporation of the toluene, partially stannylated product as an oil which was heated in a large excess of α-bromotoluene (benzyl bromide) under nitrogen during 2 days at 85–90°. Subsequent chromatography of the reaction product on a column of silica gel (CH_2Cl_2–acetone) gave methyl 2,6-di-*O*-benzyl-α-D-glucopyranoside[5] (**2**), m.p. 80–82°, $[\alpha]_D$ +58.7° (*c* 0.73)* and methyl 6-*O*-benzyl-α-D-glucopyranoside (**3**). m.p, 58–61°, $[\alpha]_D$ +104.7° (*c* 0.43) in 31 and 49% yield, respectively. As minor products, methyl 3,6-di-*O*-benzyl-α-D-glucopyranoside[5] $[\alpha]_D$ +79.2° (*c* 3.50) and methyl 4,6-di-*O*-benzyl-α-D-glucopyranoside[5], m.p. 70–73°, $[\alpha]_D$ +109.0° (*c* 0.47) were also isolated, in 4.5 and 6.0% yield, respectively.

The same sequence of reactions of **1** with allyl bromide, instead of benzyl bromide, gave methyl 2,6-di-*O*-allyl-α-D-glucopyranoside (**4**), $[\alpha]_D$ +106.5° (*c* 0.76) and methyl 6-*O*-allyl-α-D-glucopyranoside (**5**), $[\alpha]_D$ +133.0° (*c* 0.87) in 42 and 23% yield, respectively, with concomitant formation of methyl 3,6-di-*O*-allyl-α-D-glucopyranoside, $[\alpha]_D$ +103.1° (*c* 0.39), in 8% yield.

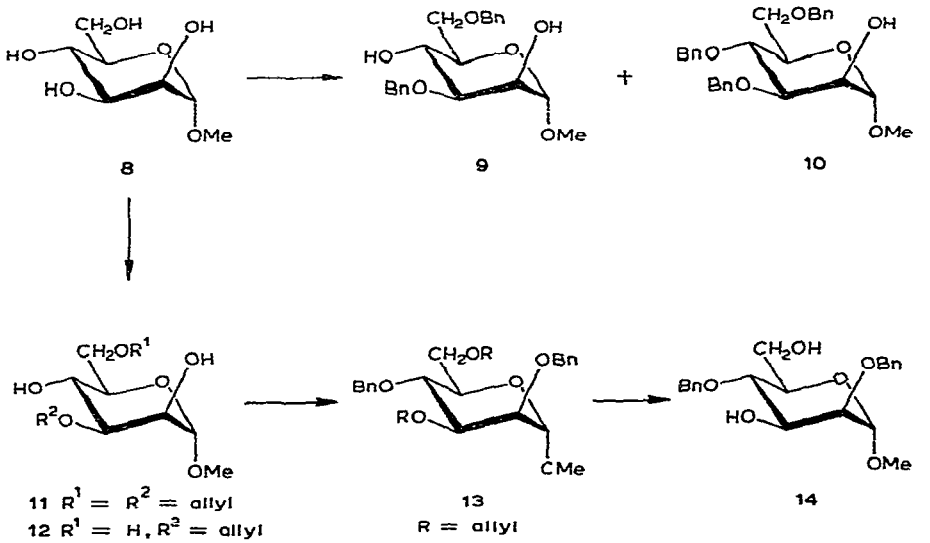
Benzylation of **4** with sodium hydride and benzyl bromide in *N,N*-dimethylformamide[6] during 2 h at −10° gave a quantitative yield of methyl 2,6-di-*O*-allyl-3,4-di-*O*-benzyl-α-D-glucopyranoside (**6**), $[\alpha]_D$ +40.3° (*c* 0.34). Removal of the allyl groups could be effected by reaction of **6** with a catalytic amount of[7] 10% Pd–C in 2:1:1 ethanol–acetic acid–water at 75° to give methyl 3,4-di-*O*-benzyl-α-D-glucopyranoside[5]

*The value of $[\alpha]_D$ was measured for a solution in chloroform, unless otherwise noted. All compounds for which $[\alpha]_D$ is recorded gave an acceptable elemental analysis, and reasonable ^{1}H- and ^{13}C-n. m. r. data.

(7), $[\alpha]_D$ +101.3° (*c* 0.55), m.p. 105–106° in 63% yield. The overall yield** of 7 from 1 was 26%.



Essentially the same approach was applicable to both methyl α-D-mannopyranoside (8) and methyl β-D-galactopyranoside (15), to achieve a regioselective protection of hydroxyl groups. Thus, stannylation of 8 with 1.5 molar proportions of bis(tributylstannyl) oxide, and subsequent benzylation with benzyl bromide for 20 h at 90° under nitrogen, gave an 81% yield of methyl 3,6-di-*O*-benzyl-α-D-mannopyranoside

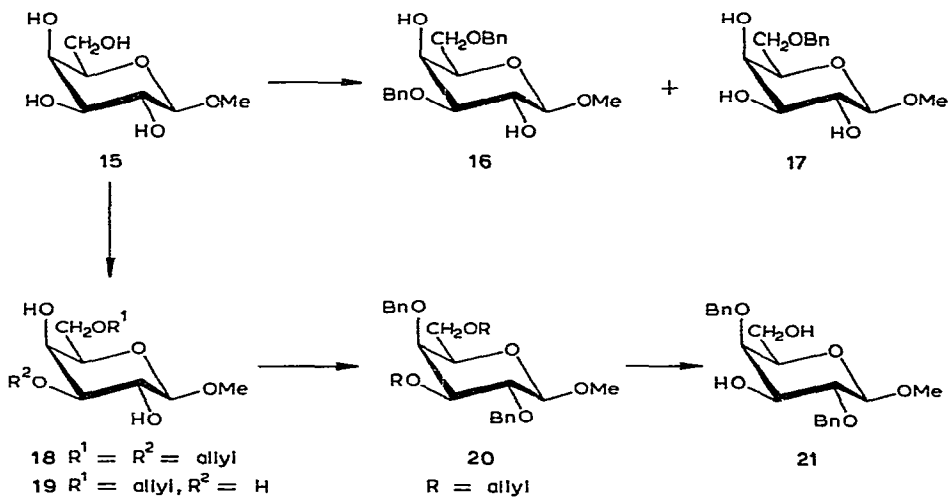


**Yields were not optimized.

(9), $[\alpha]_D$ +20.3° (*c* 0.63), and an 11% yield of methyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**10**), $[\alpha]_D$ +50.4° (*c* 0.84). The reaction of stannylated **8** with allyl bromide for 7 days at 80° afforded methyl 3,6-di-*O*-allyl-α-D-mannopyranoside (**11**), $[\alpha]_D$ +29.6° (*c* 1.6), and methyl 3-*O*-allyl-α-D-mannopyranoside (**12**), $[\alpha]_D$ +51.4° (*c* 0.93), in 71 and 13% yield, respectively. Benzylation of **11** afforded methyl 3,6-di-*O*-allyl-2,4-di-*O*-benzyl-α-D-mannopyranoside (**13**), $[\alpha]_D$ +33.5° (*c* 0.55), and subsequent removal of the allyl groups as already described gave methyl 2,4-di-*O*-benzyl-α-D-mannopyranoside (**14**), $[\alpha]_D$ +23.5° (*c* 0.77), in 53% overall yield from **8**.

Stannylation of **15** with 1.5 molar proportions of bis(tributylstannyl) oxide and subsequent benzylation with benzyl bromide under nitrogen during 3 days at 80–85° afforded methyl 3,6-di-*O*-benzyl-β-D-galactopyranoside (**16**), $[\alpha]_D$ −1.9° (*c* 1.60) and methyl 6-*O*-benzyl-β-D-galactopyranoside (**17**), $[\alpha]_D$ −26.1° (*c* 0.46), in 49 and 24% yield, respectively.

Similarly, stannylated **15** was heated in allyl bromide during 8 days at 80–85°, to afford methyl 3,6-di-*O*-allyl-β-D-galactopyranoside (**18**), $[\alpha]_D$ +1.3° (*c* 0.60) and methyl 6-*O*-allyl-β-D-galactopyranoside (**19**), $[\alpha]_D$ −23.0° (*c* 0.90), in 51 and 11% yield, respectively. Benzylation of **18** afforded methyl 3,6-di-*O*-allyl-2,4-di-*O*-benzyl-β-D-galactopyranoside (**20**), $[\alpha]_D$ −9.9° (*c* 0.90). Subsequent removal of the allyl groups from **20** afforded methyl 2,4-di-*O*-benzyl-β-D-galactopyranoside (**21**), $[\alpha]_D$ −10.6° (*c* 0.41), m.p. 144–146°, in 31% overall yield from **15**.



In conclusion, simple and efficient preparation of partially benzylated monosaccharides could be achieved in a regiocontrolled way, starting from methyl hexosides having the proper anomeric stereochemistry[8].

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