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## Note

# The Koenigs–Knorr reaction of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide

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The reaction[1] between methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**1**) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**2**) in the presence of silver carbonate yielded derivatives of disaccharide methyl glycosides containing (1→2)-α, (1→2)-β, (1→3)-β, and (1→6)-β linkages, and trisaccharide methyl glycosides containing (1→2)-β,(1→3)-β and (1→2)-β,(1→6)-β linkages.

We now report on the condensation, under the Koenigs–Knorr[2,3] conditions, between **1** and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**3**), using silver carbonate, Drierite, and 1,2-dichloroethane. From the product mixture, 24% of crystalline methyl 4,6-*O*-benzylidene-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranoside (**4**) was isolated. The remaining products were debenzylidenated and deacetylated, and then fractionated on Dowex 1-X8 ($HO^-$) resin. Nine fractions were obtained, and each was subjected to $^{13}C$-n.m.r. spectroscopy (Table I) and methylation analysis by the modified Hakomori method[4]. The resulting, partly methylated alditol acetates were analysed by g.l.c.–m.s. Thus, the position and configuration of each linkage were established.

The condensation of **1** and **3** gave two disaccharide derivatives (**5** and **8**) containing (1→2)-α and (1→3)-α linkages, respectively, and trisaccharide derivatives (**10**, **12**, and **6**) containing (1→2)-β,(1→3)-β, (1→3)-β,(1→6)-β, and (1→2)-α,(1→3)-β linkages, respectively. A trisaccharide derivative analogous to **10** was isolated after condensation[1] of **1** and **2**. Takeo[6] condensed methyl 4,6-*O*-benzylidene-β-D-glucopyranoside with **2** and obtained a trisaccharide derivative analogous to **12**. The trisaccharide derivative **6** has not been isolated hitherto.

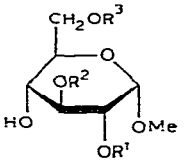
Comparison of the results obtained for the condensations of **1** and **3**, and **1** and **2**, shows that the configuration at C-4 in the glycosyl bromide affects the proportions of the major disaccharide products. Thus, the condensation of **1** and **3** gave mainly (63.4% combined yield) **1** [(1→2)-β] and **11** [(1→3)-β] in the ratio 5:4, whereas the condensation of **1** and **2** gave mainly (73.6% combined yield) products with (1→2)-β and (1→3)-β linkages in the ratio 5:2.

TABLE I

$^{13}$C-N.M.R. CHEMICAL SHIFTS (p.p.m.) FOR SOME METHYL OLIGOSACCHARIDES IN $(CD_3)_2SO$

| *Compound* | *C-1* | *C-2* | *C-3* | *C-4* | *C-5* | *C-6* | *C-1′* *C-1″* | *C-2′* *C-2″* | *C-3′* *C-3″* | *C-4′* *C-4″* | *C-5′* *C-5″* | *C-6′* *C-6″* | *OMe* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **7** | 98.8 | 81.7 | 72.8 | 69.6 | 71.7 | 60.5 | 105.6 | 70.7 | 72.2 | 68.0 | 75.0 | 60.4 | 54.2 |
| **11** | 98.9 | 70.3 | 84.9 | 68.3[a] | 72.2[b] | 60.4 | 104.4 | 70.8 | 72.3[b] | 68.2[a] | 75.2 | 60.4 | 54.1 |
| **10** | 98.7 | 78.4 | 82.7 | 68.6 | 72.1 | 60.4 | 104.4 | 70.8 | 73.3 | 68.2 | 75.1 | 60.4 | 54.1 |
| | | | | | | | 103.6 | 71.0 | 73.3 | 68.2 | 75.3 | 60.4 | |
| **12** | 98.9 | 70.5 | 84.8 | 68.0 | 70.5 | 68.0 | 104.5 | 70.9 | 73.2 | 68.0 | 74.9 | 60.2 | 54.3 |
| | | | | | | | 103.8 | 70.9 | 73.2 | 68.0 | 75.4 | 60.2 | |
| **9** | | | | | | | 99.0 | 70.3 | 73.3 | 67.9 | 75.2 | 60.2 | |
| **5** | 96.5 | 76.2 | 72.4 | 69.9 | 71.5[a] | 60.3 | 96.5 | 68.7 | 69.2 | 68.3 | 70.9[a] | 60.7 | 54.3 |
| **8** | 99.8[a] | 70.1 | 82.5 | 68.7[b] | 72.1 | 60.4 | 99.4[a] | 69.4[c] | 69.5[c] | 68.9[b] | 71.1 | 60.4 | 54.4 |
| **6** | 95.7 | 72.9 | 80.6 | 68.4 | 72.1 | 60.3 | 95.7 | 68.8 | 68.8 | 68.4 | 70.9 | 60.2 | 54.3 |
| | | | | | | | 103.3 | 70.7 | 72.9 | 68.4 | 75.4 | 60.2 | |

[a–c]Assignments which may be reversed.




5 $R^1$ = α-D-Galp, $R^2$ = $R^3$ = H
6 $R^1$ = α-D-Galp, $R^2$ = β-D-Galp, $R^3$ = H
7 $R^1$ = β-D-Galp, $R^2$ = $R^3$ = H
8 $R^1$ = $R^3$ = H, $R^2$ = α-D-Galp
10 $R^1$ = $R^2$ = β-D-Galp, $R^3$ = H
11 $R^1$ = $R^3$ = H, $R^2$ = β-D-Galp
12 $R^1$ = H, $R^2$ = $R^3$ = β-D-Galp

## EXPERIMENTAL

The general methods used are described elsewhere[1].

*Condensation of methyl 4,6-O-benzylidene-α-D-glucopyranoside* (**1**) *with 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide* (**3**). — The reaction was carried out as described previously[1]. Compound **1** (6.7 g) was dissolved in anhydrous dichloroethane (200 mL). Dry silver carbonate (21 g) and Drierite (36 g) were added, and the mixture was stirred for 2 h at room temperature in the dark with exclusion of moisture. Iodine (2.8 g) and **3** (32.6 g, 3.3 mol. equiv.) were added, and stirring was continued for 48 h at room temperature. The reaction mixture was filtered through Celite, and the inorganic solids were washed with chloroform. The combined filtrate and washings were evaporated to give a syrup, which was extracted with boiling water (3 × 300

mL). The resulting residue was dissolved in ethanol. Methyl 4,6-*O*-benzylidene-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranoside (**4**, 24%) crystallised from the mixture; m.p. 197–198°, $[\alpha]_D^{25}$ +46° (*c* 1, chloroform)[3]. The filtrate was concentrated and the syrupy residue was treated with 60% acetic acid in water at 100° for 1 h. The solvent was removed and the residue was deacetylated conventionally with methanolic sodium methoxide. The sodium ions were removed using Dowex 50 ($H^+$) resin, the solvent was removed, and the residue (5.5 g) was fractionated on a column (2.5 × 60 cm) of Dowex 1-X8 ($HO^-$) resin (250 g). The column was eluted with aqueous 10% 1,4-dioxane (12-mL fractions), and the fractions were analysed by t.l.c. (1-propanol–ethyl acetate–water 3:2:1).

Fractions 31–45 contained traces of methyl D-glucopyranoside.

Fractions 50–74 contained methyl 2-*O*-α-D-galactopyranosyl-α-D-glucopyranoside (**5**; 180 mg, 2.1%), m.p. 198–200°, $[\alpha]_D^{25}$ +189° (*c* 0.59, water). Acetylation gave the hepta-acetate, m.p. 104–105°, $[\alpha]_D^{25}$ +180° (*c* 0.5, chloroform).

*Anal.* Calc. for $C_{27}H_{38}O_{18}$: C, 49.84; G, 5.90. Found: C, 50.0; H, 5.91.

Acid hydrolysis of **5** gave D-glucose and D-galactose in the ratio 1:1.

Fractions 106–135 contained methyl 2-*O*-α-D-galactopyranosyl-3-*O*-β-D-galactopyranosyl-α-D-glucopyranoside (**6**; 170 mg, 1.4%), $[\alpha]_D^{25}$ +107° (*c* 0.85, water). Acetylation gave the deca-acetate, $[\alpha]_D^{25}$ +95° (*c* 0.6, chloroform).

*Anal.* Calc. for $C_{39}H_{54}O_{26}$: C, 49.89; H, 5.81. Found: C, 49.87; H, 5.72.

Acid hydrolysis of **6** gave D-glucose and D-galactose in the ratio 1:2.

Fractions 147–160 contained methyl 2-*O*-β-D-galactopyranosyl-α-D-glucopyranoside (**7**; 860 mg, 10.2%), m.p. 252°, $[\alpha]_D^{25}$ +77° (*c* 2.1, water)[5].

Fractions 165–210 contained methyl 3-*O*-α-D-galactopyranosyl-α-D-glucopyranoside (**8**; 85 mg, 0.7%), $[\alpha]_D^{25}$ +152° (*c* 0.4, water). Acetylation gave the hepta-acetate, $[\alpha]_D^{25}$ +130° (*c* 1.25, chloroform).

*Anal.* Calc. for $C_{27}H_{38}O_{18}$: C, 49.84; H, 5.90. Found: C, 49.74; H, 5.85.

Acid hydrolysis of **8** gave D-glucose and D-galactose in the ratio 1:1.

Fractions 211–250 contained β-D-galactopyranosyl β-D-galactopyranoside (**9**; 900 mg, 3.8% relative to **3**), m.p. 147–150°, $[\alpha]_D^{25}$ +23° (*c* 2.3, water); lit.[7] m.p. 108°, $[\alpha]_D$ +20° (water). Acetylation gave the octa-acetate, $[\alpha]_D^{25}$ +40° (*c* 2.6, chloroform).

*Anal.* Calc. for $C_{28}H_{38}O_{19}$: C, 49.55; H, 5.66. Found: C, 49.51; H, 5.55.

Acid hydrolysis of **9** gave D-galactose only.

Fractions 255–310 contained methyl 2,3-di-*O*-β-D-galactopyranosyl-α-D-glucopyranoside (**10**; 460 mg, 3.7%), m.p. 247°, $[\alpha]_D^{25}$ +60° (*c* 0.85, water). Acetylation gave the deca-acetate, $[\alpha]_D^{25}$ +22° (*c* 1.36, chloroform).

*Anal.* Calc. for $C_{39}H_{54}O_{26}$: C, 49.89; H, 5.81. Found: C, 50.10; H, 5.73.

Acid hydrolysis of **10** yielded D-glucose and D-galactose in the ratio 1:2.

Fractions 320–490 contained methyl 3-*O*-β-D-galactopyranosyl-α-D-glucopyranoside (**11**; 2.47 g, 29.2%), m.p. 229–230°, $[\alpha]_D^{25}$ +95° (*c* 4.1, water). Acetylation gave the hepta-acetate, m.p. 120–122°, $[\alpha]_D^{25}$ +46° (*c* 1.5, chloroform).

*Anal.* Calc. for $C_{27}H_{38}O_{18}$: C, 49.84; H, 5.90. Found: C, 49.82; H, 6.01.

Acetolysis[5] of **11** gave 1,2,4,6-tetra-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-D-glucopyranose (**13**), $[\alpha]_D^{25}$ +29° (*c* 0.7, chloroform).

*Anal.* Calc. for $C_{28}H_{38}O_{19}$: C, 49.55; H, 5.66. Found: C, 49.60; H, 5.82.

Deacetylation of **13** with methanolic sodium methoxide gave 3-*O*-β-D-galactopyranosyl-D-glucose (**14**), m.p. 204–205°, $[\alpha]_D^{25}$ +85→+48° (*c* 1, water); lit.[8] m.p. 205–206°, $[\alpha]_D$ +76.7→+41.2° (water).

Fractions 492–570 contained methyl 3,6-di-*O*-β-D-galactopyranosyl-α-D-glucopyranoside (**12**; 510 mg, 4.1%), m.p. 244–246°, $[\alpha]_D^{25}$ +60° (*c* 2, water). Acetylation gave the deca-acetate, $[\alpha]_D^{25}$ +34° (*c* 1.35, chloroform).

*Anal.* Calc. for $C_{39}H_{54}O_{26}$: C, 49.89; H, 5.81. Found: C, 49.75; H, 5.67.

Acid hydrolysis of **12** yielded D-glucose and D-galactose in the ratio 1:2.

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