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Preliminary communication

Stereoselective synthesis of a 4-*O*-methyl-α-D-glucopyranosyluronic acid linkage[*]

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During the last decade, considerable effort has been directed towards the stereoselective synthesis of glycosides and oligosaccharides having the glycosidic bond *cis* to the substituent on C-2. Glycosyl halides bearing a non-participating group at C-2 have been widely used in these syntheses. Because the synthesis of this class of substance derived from uronic acids is difficult, a systematic approach towards stereoregulated synthesis of aldobiouronic acids has not been carried out.

There is only one example of a glycoside synthesis involving a glycosyl halide derived from 4-*O*-methyl-D-glucuronic acid: the acetylated α-bromide was used in a synthesis of a (1→6)-β-D-linked aldobiouronic acid derivative by the orthoester method[2]. We now report on the reaction of glycosyl halides **6** and **7** with methyl 3,4-di-*O*-acetyl-β-D-xylopyranoside[3].

The syrupy bromide **6** {$[\alpha]_D^{22}$ +129° (*c* 1)}[**] was prepared by treatment with hydrogen bromide in dichloromethane of the acetates **4** {syrup, $[\alpha]_D^{22}$ +72° (*c* 1)} or **5** {m.p. 75–76°, $[\alpha]_D^{22}$ +19° (*c* 1)}[†], obtained by acetolysis of methyl (benzyl 2,3-di-*O*-benzyl-4-*O*-methyl-β-D-glucopyranosid)uronate[4] or by acetylation of **3**, in combined yields of 56 and ~100%, respectively. The ester **3** {m.p. 107.5–108.5°, $[\alpha]_D^{22}$ +26° (*c* 1)} was synthesised (70% overall yield) from benzyl 2,3-di-*O*-benzyl-4-*O*-methyl-β-D-glucopyranoside[4] (**1**) by oxidation[5] with potassium dichromate to give benzyl 2,3-di-*O*-benzyl-4-*O*-methyl-β-D-glucopyranosiduronic acid {**2**, 90%, m.p. 148–149°, $[\alpha]_D^{22}$ −20° (*c* 1)}, followed by hydrolysis, and treatment of the crude product with ethereal diazomethane.

The syrupy chloride **7** {$[\alpha]_D^{22}$ +45° (*c* 1), α:β ratio, ~1:3.5} was obtained by treatment of **3** with thionyl chloride.

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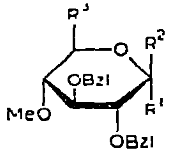
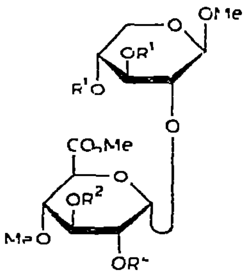
[*] Synthesis and reactions of uronic acid derivatives. Part XVI[1].

[**] $[\alpha]_D$ values determined on chloroform solutions unless stated otherwise.

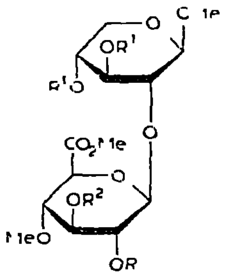
[†] Crystalline compounds gave correct microanalyses. All monosaccharide derivatives exhibited 80-MHz p.m.r.-spectral characteristics consistent with their structures.



	R^1	R^2	R^3
1	H	OBzl	CH_2OH
2	H	OBzl	CO_2H
3	OH	H	CO_2Me
4	OAc	H	CO_2Me
5	H	OAc	CO_2Me
6	Br	H	CO_2Me
7	H	Cl	CO_2Me



	R^1	R^2
8	Ac	Bzl
10	H	H
12	Ac	Ac



	R^1	R^2
9	Ac	Bzl
11	H	H
13	Ac	Ac

Reaction[6] of **6** with methyl 3,4-di-*O*-acetyl-β-D-xylopyranoside in nitromethane–benzene in the presence of mercuric cyanide at 20° was complete within 1 h. Column chromatography of the product afforded the aldobiouronic acid derivatives **8** {m.p. 110.5–111.5°, $[\alpha]_D^{22}$ +57° (*c* 1)} and **9** {m.p. 84–86°, $[\alpha]_D^{22}$ +1.5° (*c* 2.7)} in the ratio 1.4:1 (combined yield, 69%). Catalytic hydrogenolysis of **8** and **9** followed by deacetylation (Zemplen) gave **10** {m.p. 167–168°, $[\alpha]_D^{22}$ +75° (*c* 1, methanol)} and **11** {m.p. 209.5–212.5°, $[\alpha]_D^{22}$ –37.5° (*c* 1, methanol)}, respectively, which were further characterized as the acetates **12** {m.p. 201–203°, $[\alpha]_D^{22}$ +89° (*c* 1)} and **13** {m.p. 107–108°, $[\alpha]_D^{22}$ –48° (*c* 1)}. The 70-eV mass spectra of **12** and **13** were qualitatively identical, and consistent[7] with their structures.

The p.m.r. spectrum [D_2O, internal sodium 3-(trimethylsilyl)propionate-d_4] of **10** showed, *inter alia*, doublets for H-1 at δ 4.42 ($J_{1,2}$ 7.3 Hz) and H-1′ at δ 5.25 ($J_{1',2'}$ 3.2 Hz), and that of **11** showed corresponding doublets at δ 4.41 ($J_{1,2}$ 7.2 Hz) and 4.71 ($J_{1',2'}$ 7.4 Hz), indicative of α and β interglycosidic linkages, respectively.

In contrast to the poor stereoselectivity of the above reaction, the condensation[8] of **7** in the presence of silver perchlorate was highly stereoselective. Thus, a solution[8] of silver perchlorate (1.66 g, 8 mmol) was stirred at 0° for 1 h with a solution of **7** [prepared from 3.2 g (8 mmol) of **3**], *sym*-collidine (1.06 ml, 8 mmol), and methyl 3,4-di-*O*-acetyl-β-D-xylopyranoside (1 g, 4 mmol). T.l.c. (benzene–acetone, 15:1) then showed that the reaction was complete, and disaccharides **8** and **9** were subsequently isolated by column chromatography in the ratio 18:1 (combined yield, 90.5%).

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