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## Facile Synthesis of Aryl $\beta$ -D-Mannopyranosides

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The preparation of  $\beta$ -D-mannopyranosides is a long-standing problem in carbohydrate chemistry.<sup>1-4</sup> It is important that efficient routes to these glycosides are found:  $\beta$ -D-mannopyranose units are widespread in oligo- and polysaccharide sequences of natural origin and their synthesis may be required in various biological contexts. 4-Nitrophenyl  $\beta$ -D-mannopyranoside

is useful for linking  $\beta$ -D-mannopyranose units to proteins; after the reduction of the nitro to an amino group, this can be joined to proteins in several ways.<sup>7</sup> Various aryl  $\beta$ -D-mannopyranosides are useful in the assay of  $\beta$ -D-mannopyranosidases.

We have briefly described new methods for the synthesis of alkyl and aryl  $\beta$ -D-mannopyranosides as well as of a disaccharide containing  $\beta$ -D-mannopyranose units.<sup>8,9</sup> The key compound, 2,3:4,6-di-O-cyclohexylidene- $\alpha$ -D-mannopyranose is obtained in a 55 % crystalline yield from D-mannose without resorting to the use of chromatography, by means of cyclohexylideneation of D-mannose under kinetic control.<sup>8,9</sup> We have now explored the scope of this methodology for the preparation of aryl  $\beta$ -D-mannopyranosides.

2,3:4,6-Di-O-cyclohexylidene- $\alpha$ -D-mannopyranose, diethyl azodicarboxylate, triphenylphosphine and a phenol were allowed to react in toluene at room temperature. The reaction product was purified by means of silica gel column chromatography. Results are shown in Table 1. The results in Table 2 indicate that the  $\alpha/\beta$  ratio of anomers obtained in the reaction increases with solvent polarity. The cyclohexylidene groups were removed with acid under mild conditions.

*Experimental.* General methods were the same as those described before.<sup>10</sup>

*Glycosylation procedure.* Diethyl azodicarboxylate (0.40 g, 2.3 mmol) in dry toluene (2.5 ml) was added to a stirred solution of 2,3:4,6-di-O-cyclohexylidene- $\alpha$ -D-mannopyranose (0.50 g, 1.5 mmol), triphenylphosphine (0.55 g, 2.1 mmol) and the phenol (2.1 mmol) in dry toluene (10 ml) at room temperature. The reaction was monitored by TLC (solvent, Table 1). When the reaction was complete, the solution was concentrated and the  $\beta$ -D-mannopyranoside derivative was obtained in a pure state by means of silica gel column chromatography.

*3-Nitrophenyl  $\beta$ -D-mannopyranoside (11).* A solution of **1** (510 mg, 1.1 mmol) in 80 % aqueous acetic acid (15 ml) was heated for 1 h at 100 °C. Concentration and crystallization from acetone yielded **11** (200 mg, 60 %) m.p. 73–75 °C [ $\alpha$ ]<sub>D</sub><sup>20</sup> – 69° (c 0.7, H<sub>2</sub>O).

*4-Nitrophenyl  $\beta$ -D-mannopyranoside (12).* A solution of **3** (480 mg, 1.0 mmol) in 80 % aqueous acetic acid (15 ml) was heated for 1 h at 100 °C. Concentration and crystallization from water yielded **12** (180 mg, 58 %) m.p. 205–207 °C, [ $\alpha$ ]<sub>D</sub><sup>20</sup> – 108° (c 1, H<sub>2</sub>O).<sup>2,3,9,11</sup>

*Phenyl 2,3:4,6-tetra-O-acetyl- $\beta$ -D-mannopyranoside (13).* A solution of **5** (450 mg, 1.1 mmol) in 90 % aqueous trifluoroacetic acid (5 ml) was kept for 30 min at 0 °C. The solution was concentrated and the residue treated with acetic anhydride (2 ml) in pyridine (3 ml) for 15 min at 100 °C. Concentration and crystallization from ethanol yielded **13** (232 mg, 49 %) m.p. 163–165 °C, [ $\alpha$ ]<sub>D</sub><sup>20</sup> – 61° (c 0.8, CHCl<sub>3</sub>). Anal: C<sub>26</sub>H<sub>24</sub>O<sub>10</sub>: C, H.

Table 1. Yields and physical properties of aryl 2,3,4,6-di-O-cyclohexylidene-D-mannopyranosides.

Aglycone	Anomeric configuration	Yield (%)	M.p. (°C)	$[\alpha]_D^{20}$ (CHCl <sub>3</sub> ) (°)	Reaction time (h)	Solvent for crystallization	Chromatographic solvent
3-Nitrophenyl (1)	$\beta^a$	81	147–149	-129	1/2	ethanol	toluene/ethyl acetate 4:1
3-Nitrophenyl (2)	$\alpha$	8	131–133	+65			
4-Nitrophenyl (3)	$\beta$	72	158–160	-153	1/2	ethanol	toluene/ethyl acetate 4:1
4-Nitrophenyl (4)	$\alpha$	22	161–163	+83	1	ethanol	toluene/ethyl acetate 4:1
Phenyl (5)	$\beta$	82	syrup	-95			
Phenyl (6)	$\alpha$	4	syrup	+53			
2,4-Dinitrophenyl (7)	$\beta^b$	53	133–135	-159	5	diethyl ether/light petroleum 40–60 °C	toluene/ethyl acetate 4:1
2,4-Dinitrophenyl (8)	$\alpha$	37	101–105	+79		diethyl ether/light petroleum 40–60 °C	toluene/ethyl acetate 4:1
$\beta$ -Methyl umbifelleronyl (9)	$\beta^c$	79	75–77	-157	1/2	diethyl ether/light petroleum 40–60 °C	toluene/ethyl acetate 3:2
$\beta$ -Methyl umbifelleronyl (10)	$\alpha$	11	syrup	+84		diethyl ether/light petroleum 40–60 °C	toluene/ethyl acetate 3:2

<sup>a</sup> Anal. C<sub>24</sub>H<sub>31</sub>NO<sub>8</sub>; C, H. <sup>b</sup> Anal. C<sub>24</sub>H<sub>30</sub>N<sub>2</sub>O<sub>10</sub>; C, H. <sup>c</sup> Anal. C<sub>28</sub>H<sub>34</sub>O<sub>8</sub>; C, H.

Table 2. Dependence of anomeric composition upon solvent used in glycosidation of 4-nitrophenol.

Solvent	$\alpha$	$\beta$	Total yield (%)
Toluene	23	77	94
Tetrahydrofuran	36	64	91
Acetonitrile	54	46	70

2,4-Dinitrophenyl 2,3,4,6-tetra-O-acetyl- $\beta$ -D-mannopyranoside (14). A solution of 7 (510 mg, 1.0 mmol) in 90 % aqueous trifluoroacetic acid (5 ml) was kept for 20 min at 0 °C. The solution was concentrated and the residue treated with acetic anhydride (2 ml) in pyridine (3 ml) for 1 h at room temperature. Concentration and crystallization from ethanol–2-propanol yielded 14 (335 mg 65 %), m.p. 167–168 °C,  $[\alpha]_D^{20}$  -102° (c 1.6, CHCl<sub>3</sub>).

$\beta$ -Methylumbifelleronyl  $\beta$ -D-mannopyranoside (15). A solution of 9 (550 mg, 1.1 mmol) in 80 % aqueous acetic acid (15 ml) was heated for 1 h at 100 °C. The solution was concentrated and the residue crystallized from water–acetone to yield 15 (217 mg 58 %) m.p. 242–243 °C,  $[\alpha]_D^{20}$  -70° (c 0.5, CH<sub>3</sub>OH).

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