

Silver Imidazolate-assisted Glycosidations. Part 7.*

Synthesis of 1,2-*trans*-Linked Aryl Glycosides

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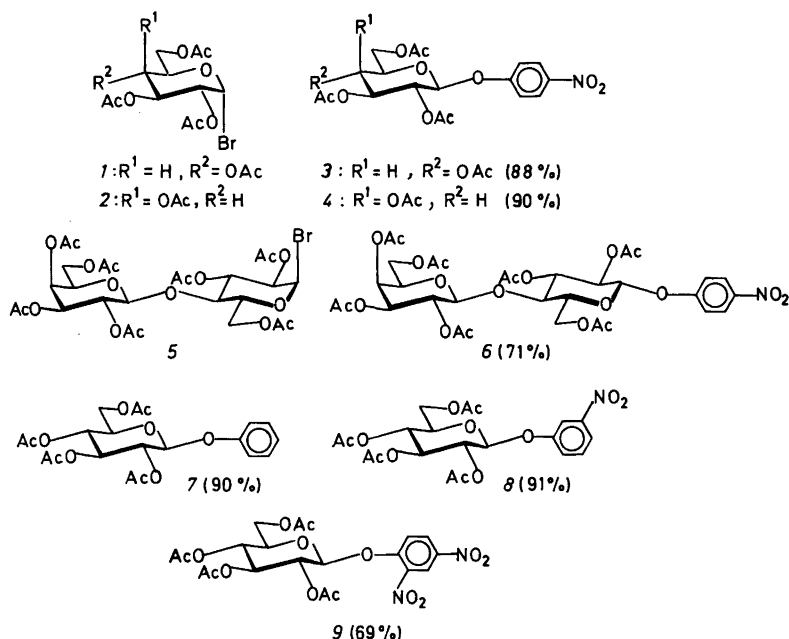
Efficient preparations of 1,2-*trans*-linked aryl glycosides starting from fully acetylated glycopyranosyl bromides are described. The promoting system is silver imidazolate and zinc chloride.

p-Nitrophenyl glycosides are useful intermediates for linking carbohydrates to proteins in the preparation of artificial antigens.^{1,2} An efficient way of achieving this is to first reduce the nitro group to an amino group and then transform the latter into

an isothiocyanato group by reaction with thiophosgene. On reaction of the resulting *p*-isothiocyanatophenyl glycoside with a free amino group in a protein, the carbohydrate moiety becomes linked to the protein *via* a phenyl thiourea residue.³

We now present an efficient synthesis of 1,2-*trans*-linked *p*-nitrophenyl glycosides, starting from fully acetylated glycopyranosyl bromides using silver imidazolates and zinc chloride as promoters.⁴ The molar proportions of glycosyl bromide, *p*-nitrophenol, zinc chloride, and silver imidazolate

*Part 6, Ref. 4.



were 1:1.5: ~6:0.75 and the yields of 1,2-*trans*-linked *p*-nitrophenyl glycosides varied from 71 to 90%. Other 1,2-*trans*-linked aryl glycosides (7–9) were similarly obtained in yields ranging from 69 to 91%. The yields obtained are, with one exception only (compound 4⁵), higher than those previously reported^{5–13} for the synthesis of 1,2-*trans*-linked aryl glycosides from fully acetylated glycopyranosyl bromides.

EXPERIMENTAL

General methods were the same as those reported elsewhere.^{4,14}

***p*-Nitrophenyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranoside (3).** A mixture of 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl bromide (1) (400 mg, 1 mmol), *p*-nitrophenol (180 mg, 1.5 mmol), silver imidazolate^{15,16} (131 mg, 0.75 mmol) and zinc chloride (dry weight 0.8–1 g, ~6 mmol⁴) in dichloromethane (10 ml) containing 3 Å molecular sieves was stirred in the dark at 40 °C for 48 h, when TLC indicated complete reaction. The reaction mixture was diluted with dichloromethane and filtered. The solids were washed with dichloromethane. The combined filtrates were partitioned between toluene (200 ml) and aqueous sodium carbonate (200 ml). The organic phase was washed with water. The solution was dried (MgSO₄), filtered and concentrated. Crystallization of the product from ethanol gave 3 (383 mg, 88%), m.p. 175–176 °C, $[\alpha]_D^{22}$ –41° (c 1, CHCl₃) [lit.^{5–7,13} m.p. 174–175 °C, $[\alpha]_D$ –37°, –41° (CHCl₃)].

***p*-Nitrophenyl 2,3,4,6-tetra-O-acetyl- β -D-galactopyranoside (4)** was obtained from 2 as described above for 3, in a yield of 90%, m.p. 148–149 °C, $[\alpha]_D^{22}$ –11° (c 1, CHCl₃) [lit.^{5,8} m.p. 145–146 °C, 144–145 °C, $[\alpha]_D$ –11°, –8°, –10° (CHCl₃)].

***p*-Nitrophenyl 4-O-(2,3,4,6-tetra-O-acetyl- β -D-galactopyranosyl)-2,3,6-tri-O-acetyl- β -D-glucopyranoside (6)** was obtained from 5 as described above for 3, in a yield of 71%, m.p. 131–133 °C, $[\alpha]_D^{22}$ –37° (c 1, CHCl₃) [lit.⁹ 132–133 °C, $[\alpha]_D$ –35° (CHCl₃)].

Phenyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranoside (7) was obtained from the reaction of 1 with phenol as described above for 3. The reaction mixture was diluted with dichloromethane and filtered. The combined filtrates were washed with aqueous ammonia, 2 M sodium hydroxide, and water, dried (MgSO₄), filtered and concentrated. Crystallization from ethanol gave 7, 90%, m.p. 124–125 °C, $[\alpha]_D^{22}$ –22° (c 1, CHCl₃) [lit.¹⁰ m.p. 124–125 °C, $[\alpha]_D$ –22° (CHCl₃)].

***m*-Nitrophenyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranoside (8)** was obtained from the reaction of 1 with *m*-nitrophenol as described above for 7, in a yield of 91%, m.p. 136–137 °C, $[\alpha]_D^{22}$ –37° (c 1,

CHCl₃) [lit.^{5,6} m.p. 136–137 °C, $[\alpha]_D$ –42°, –37° (CHCl₃)].

***o,p*-Dinitrophenyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranoside (9)** was obtained from the reaction of 1 with *o,p*-dinitrophenol as described above for 7, in a yield of 69%, m.p. 176–177 °C, $[\alpha]_D^{22}$ +35° (CHCl₃) [lit.^{11,12} m.p. 177–179 °C and 173–177 °C, $[\alpha]_D$ +34.5°, +33°].

Acknowledgements. This paper is submitted in acknowledgement of Professor Holger Erdtman's contribution to natural products chemistry. We are indebted to Professor Bengt Lindberg for his interest, to the Swedish Board for Technical Development and the Swedish Natural Science Research Council for financial support, and to Ekström's och Rietz' Fond and CONACYT, Mexico for maintenance grants to H.H. and C.O., respectively.

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Received February 9, 1982.