

0040-4039(94)E0300-M

An Easy Route to Methyl 6-O-Alkyl Glycosides

Corinne Bayle, Andrée Gadelle*

CEA, Département de Recherche Fondamentale sur la Matière Condensée, SESAM / MV - 38054 Grenoble Cedex 9 (France).

Abstract: Methyl 6-O-alkyl-glycopyranosides were obtained in excellent yield from methyl 6-deoxy-6-iodo-glycopyranoside and the appropriate alcohol in the presence of chlorine.

The selective functionalization of carbohydrates and their derivatives by alkyl groups is a subject of continuing interest. The conventional approach to such ethers is based on the protection of the more reactive groups, followed by alkylation with an excess of a reagent, and subsequent deprotection. This approach is more and more replaced by direct regioselective mono, di-, or trialkylation¹. The methylation techniques are variants of the Williamson reaction and are generally used in oligo and polysaccharide structure analysis, as well as a method of ring size² assignment. Usual methylation reagents are either dimethyl sulfate³ or methyl iodide⁴; the former is used in conjunction with a strong alkali, which serves to promote ionization of the pertinent hydroxyl function, and the latter with an agent such as silver oxide, which has a catalytic role as well.

Introduction of fatty alkyl chains on carbohydrates leads to the formation of nonionic surfactants. A new approach to the synthesis of methyl 6-O-alkyl-glycopyranosides is proposed⁵. The starting materials are the methyl 6-deoxy-6-iodo-glycopyranosides which were prepared in almost quantitative yields using a Vilsmeier-Haack's type reagent⁶. These compounds are very sensitive to alkaline medium in which they are prone to dehydrohalogenation leading to the formation of double bond and/or anhydro derivative depending on the configuration of the starting sugar^{6,7}. In alcohol and in the presence of chlorine these compounds give exclusively the corresponding methyl 6-O-alkyl-glycopyranosides (Figure 1).

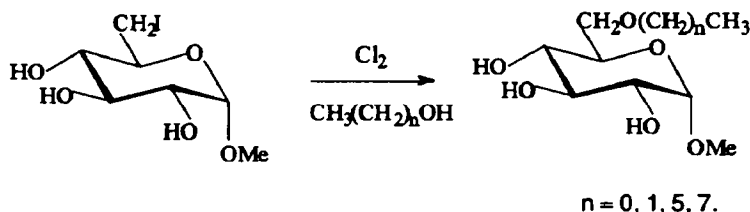
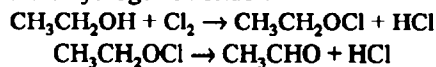
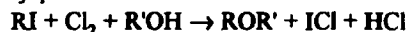


Figure 1

Reaction of chlorine on ethyl alcohol produces ethyl hypochlorite and hydrogen chloride, the former is responsible for the yellow colour of the solution. In the presence of unchanged alcohol, the hypochlorite very quickly breaks down into acetaldehyde and hydrogen chloride⁸:



Due to the presence of hydrogen chloride, the aldehyde polymerized to paracetaldehyde. The alkyl hypochlorites have been little studied, owing to their explosive properties⁹, but when generated *in situ* they quickly react with iodides present in the alcoholic solution (2 min). Addition of mixed resin to remove hydrogen chloride inhibit formation of by-products. Thus:



The problem of the solubility of the starting iodide can be solved by acetylation of the remaining hydroxyl groups. Addition of carbon tetrachloride allows to minimize the volume of alcohol used. In some case, carbon tetrachloride is necessary to solubilized the appropriate alcohol.

In a typical experiment, chlorine is generated by oxydation of concentrated hydrochloric acid (2 mL) with potassium permanganate (0.35 g). It paddles through the appropriate alcoholic solution (50 mL) containing the corresponding iodide (0.5 g). After demineralization (Amberlite[®] MB1113) and evaporation to dryness *in vacuo*, the oily residue is distilled under reduced pressure. Products were characterized by their ¹³C NMR spectra and their microanalysis.

Compounds	Yield (%)	Boiling point under 4 Pa (°)	[α] _D
methyl 6-O-methyl-α-D-glucopyranoside ¹⁰	85	135	+143 (c 1.8, MeOH)
methyl 6-O-ethyl-α-D-glucopyranoside	74	140	+156 (c 0.7, EtOH)
methyl 6-O-hexyl-α-D-glucopyranoside	85	165	+91 (c 0.6, CHCl ₃)
methyl 6-O-octyl-α-D-glucopyranoside	83	175	+57 (c 1.3, CHCl ₃)

REFERENCES

1. Stanek Jr, J. *Topics in Current Chemistry* 1990, 154, 209-255.
2. a) Rolf, D. ; Gray, G.R. *J. Am. Chem. Soc.* 1982, 104, 3539-3541. b) Rolf, D. ; Bennek, J.A. ; Gray, G.R. *Carbohydr. Res.* 1985, 137, 183-196. c) Jun, J.G. ; Gray, G.R. ; *Carbohydr. Res.* 1987, 163, 247-261
3. Kuhn, R. ; Trischman, H. *Chem. Ber.* 1963, 96, 284-287.
4. a) Purdie, T. ; Irvine, J.C. *J. Chem. Soc.* 1903, 83, 1021-1037. b) Kuhn, R. ; Trishman, H. ; Löw, I. *Angew. Chem. Int. Ed.* 1955, 67, 32-. c) Hakomori, S. ; *J. Biochem. (Tokio)*, 1964, 55, 205-208.
5. Bayle, C. ; Gadelle, A. *XVIIth Int. Carbohydr. Symp. (Paris)* July 5-10, 1992, abstract p 87.
6. a) Garegg, P.I. ; Samuelson, B. *J. Chem. Soc., Chem. Commun.* 1979, 978-980. b) *ibid. J. Chem. Soc., Perkin Trans. I* 1980, 2866-2869. c) Garegg, P.J. ; Johansson, R. ; Ortega, C. ; Samuelsson, B. *J. Chem. Soc., Perkin Trans. I* 1982, 681-683. d) Classon, B. ; Garegg, P.J. ; Samuelsson, B. *Can. J. Chem.* 1991, 59, 339-344. e) Garegg, P.J. ; Regberg, T. ; Stawinski, J. ; Strömberg, R. *J. Chem. Soc., Perkin Trans. II* 1987, 271-274. f) Classon, B. ; Liu, Z. ; Samuelsson, B. *J. Org. Chem.* 1988, 53, 6126-6130. g) Léon-Rnaud, P. ; Plusquellec, D. *Tetrahedron* 1991, 47, 5185-5192. h) Benazza, M. ; Uzan, R. ; Beaupère, D. ; Demailly, G. *Tetrahedron Letters* 1992, 33, 3129-3132 and 4901-4904.
7. Defaye, J. *Angew. Chem. Int. Ed. Eng.* 1991, 30, 78-80.
8. Chattaway, F.D. ; Backeberg, O.G. *J. Chem. Soc.* 1924, 125, 1097-1101.
9. Chattaway, F.D. ; Backeberg, O.G. *J. Chem. Soc.* 1923, 123, 2999-3303.
10. a) Helferich, B. ; Klein, W. ; Schäfer, W. *Ber.* 1926, 59, 79-85. b) Timell, T.E. ; Enterman, W. ; Spencer, F. ; Soltes, E.J. *Can. J. Chem.* 1965, 43, 2296-2305.

(Received in France 13 October 1993; accepted 5 February 1994)