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AN EFFICIENT METHOD FOR GLUCOSYLATION OF HYDROXY COMPOUNDS USING GLUCOPYRANOSYL FLUORIDE

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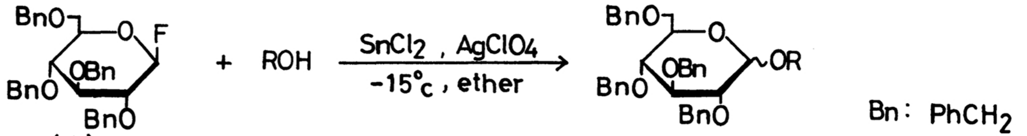
Glucosides and disaccharides are prepared in good yields from 2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl fluoride and hydroxy compounds in the presence of stannous chloride and silver perchlorate. In most cases, α-glucosides are predominantly ($\alpha/\beta = 80/20 \sim 92/8$) obtained.

Stereoselective synthesis of glycosides is one of the most important problems in the synthetic field of carbohydrate chemistry. To achieve high stereoselectivity, many devices have been employed by the combination of various sugar derivatives and activating reagents.$^{1)}$

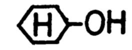
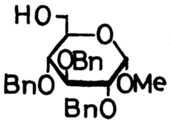
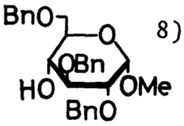
In the previous paper, we have shown that α-glucosides are obtained predominantly from 2-benzothiazolyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-glucopyranoside and hydroxy compounds in the presence of cupric triflate.$^{2)}$ However, good stereoselectivity could not be realized in several cases, especially sterically hindered hydroxy compounds probably owing to the high leaving ability of benzothiazolylthio group. We therefore postulated that the use of a poorer leaving group should give better stereoselectivity. Based on this hypothesis, we chose β-glucosyl fluoride$^{3)}$ as starting material. After screening various activating reagents, for example Lewis acids as $AlCl_3$, $FeCl_3$ and $SnCl_4$, we finally found that the combined use of stannous chloride and silver perchlorate effectively promotes the stereoselective reaction of glucosyl fluoride and hydroxy compounds. Namely, α-glucosides are predominantly prepared by the reaction of 2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl fluoride$^{6)}$ with various hydroxy compounds including sterically hindered ones.



(1)

A typical procedure is described for the reaction of 1 with 3β-cholestanol. To the mixture of stannous chloride (0.2 mmol), silver perchlorate (0.2 mmol), and 4A molecular sieves, was added an ether solution (4 ml) of 3β-cholestanol (0.17 mmol) and 1 (0.2 mmol) at -15°C, and the reaction mixture was stirred at the same temperature for 24 h. After filtration, the filtrate was washed with aqueous sodium

Table

Alcohol	Yield(%)	α / β[c)]
MeOH[a)]	82[b)]	86 / 14
	88	83 / 17
t-BuOH	87	81[9)]/ 19[10)]
Cholesterol	76	89 / 11
3β-Cholestanol	96	92 / 8
 8)	84	84 / 16[11)]
 8)	91	80 / 20[11)]

a) 2eq. of methanol was used.
b) Yield based on 1
c) These compounds were purified by TLC and were identified by ^{1}H-NMR spectra.

bicarbonate and dried over sodium sulfate. After removal of the solvent, the residue was purified by TLC (silica gel) to give 3β-cholestanyl 2,3,4,6-tetra-O-benzyl-α-D-glucopyranoside[2)] (88%) and the corresponding β-anomer[2)] (8%).

In a similar manner, several glucosides were prepared in good yields. (See Table).

It is noted that α-glucosides are obtained predominantly from glucopyranosyl fluoride 1 and various hydroxy compounds including sterically hindered ones such as methyl 2,3,6-tri-O-benzyl-α-D-glucopyranoside or tertiary butanol under mild conditions.

References and Notes

1) G. Wulff and G. Röhle, Angew. Chem. Int. Ed. Engl., 13, 157 (1974); R. U. Lemieux, K. B. Hendricks, R. U. Stick, and K. James, J. Am. Chem. Soc., 97, 4056 (1975); J. R. Pougny, J. C. Jaquinet, M. Nassr, D. Duchet, M. L. Milat, and P. Sinäy, J. Am. Chem. Soc., 99, 6762 (1977); K. Igarashi, J. Irisawa, and T. Honma, Carbohydr. Res., 39, 341 (1975). 2) T. Mukaiyama, T. Nakatsuka, and S. Shoda, Chem. Lett., 1979, 487. 3) Concerning the use of glycosyl fluoride, there have been reported only two reactions with methanol in the presence of HCl[4)] or NaOMe.[5)] 4) K. P. Wood, P. W. Kent, and D. Fisher, J. Chem. Soc. (C), 1966, 912. 5) F. Micheel and A. Flemer, Advances in Carbohydrate Chemistry, 16, 85 (1961). 6) This compound was prepared from 2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl chloride and silver fluoride by the method of L. D. Hall et al[7)]. mp 42-44°C, $[\alpha]_D^{24}$+31°(c 1.03, CHCl$_3$). The configuration of anomeric carbon was determined by ^{1}H-NMR [(CDCl$_3$) 5.45 ppm (J=5.0 Hz)] and ^{19}F-NMR [(CDCl$_3$, C$_6$F$_6$) 136 ppm (J$_{1,F}$ 47Hz, J$_{2,F}$ 8Hz)]. 7) L. D. Hall, J. F. Manville, and N. S. Bhacca, Can. J. Chem., 47, 1 (1969). 8) J. M. Kuster and I. Dyong, Justus Liebigs Ann. Chem., 1975, 2179. 9) $[\alpha]_D^{22}$+39° (c 1.15, CHCl$_3$) 10) mp 95-96.5°C, $[\alpha]_D^{22.5}$+18°(c 0.65, CHCl$_3$) 11) These compounds were identified by physical constants reported by P. Sinäy et al[1)].

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