Acta Chemica Scandinavica B 33 (1979) 116—118

Observations on Silver Trifluoromethane Sulfonate-promoted Syntheses of 1,2-*trans*-Glycosides from Acylated Glycosyl Bromides

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Efficient silver trifluoromethane–sulfonate-promoted syntheses of β-D-galactopyranosides, β-D-glucopyranosides and β-D-xylopyranosides starting from benzoylated α-D-glycopyranosyl bromides are described.

The use of trifluoromethanesulfonyl as leaving group in the 1-position, and the use of silver triflate-promoted glycosylation starting from glycosyl halides have received considerable attention.[1–5] In 1,2-*trans*-glycoside synthesis, high stereoselectivity has resulted from the reaction of acylated glycosyl halides with alcohols (*e.g.* suitably protected monosaccharide derivatives) or other nucleophiles in the presence of silver triflate and 2,6-lutidine,[3] 2,4,6-collidine,[3] 1,1,3,3-tetramethylurea [4] or a pyrimidine base.[5]

We now report that in this type of 1,2-*trans*-glycoside synthesis, improved yields are obtained starting from benzoylated rather than from acetylated glycosyl halides. The presence of base may often be unnecessary and even lead to a deterioration of the yield of desired product.

In a recent synthesis of *O*-β-D-galactopyranosyl-(1→4)-*O*-β-D-xylopyranosyl-L-serine, we required high-yield, stereospecific 1,2-*trans*-glycoside formation of the two glycosidic bonds.[6] Silver triflate-promoted glycosidation appeared most promising and we thus reacted 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide with the alcohol *7a* under the conditions described by Hanessian and Banoub.[4] A multicomponent mixture was obtained. Substituting 1,1,3,3-tetramethylurea with 2,4,6-collidine [3] gave as product mainly the orthoester *13*. However, when benzobromogalactose (*1*) was allowed to react with the alcohol *7a* in the presence of silver triflate and 2,4,6-collidine in nitromethane, the required disaccharide *7b* was obtained in an 80 % yield. This result led us to explore the same conditions for the formation of the required β-D-xylosyl linkage. Indeed, in the glycosylation of *N*-benzyloxycarbonyl-L-serine benzyl ester with 4-*O*-(β-D-galactopyranosyl)-α-D-xylopyranosyl bromide hexabenzoate, the required β-D-xylosyl linkage was formed in a 72 % yield; the presence of 2,4,6-collidine was, however, found to be unnecessary. These facts have led us to investigate the use of silver triflate-promoted 1,2-*trans*-glycoside formation in both the absence and presence of collidine as base, using various benzoylated glycosyl bromides. The results are summarized in Table 1. Starting materials and products are shown in Fig. 1.

The yields obtained vary from 67 to 93 %. In four of the examples 2,4,6-collidine was absent. In the condensation of 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (*3*) with methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside (*11a*), the amount of 2,4,6-collidine present was critical for the outcome of the reaction in that the presence of 1 mol equivalent or more of the base promoted the formation of orthoester in addition to the formation of glycoside. This may indicate the presence of orthoesters as intermediates in these glycosylations and that,

0302-4369/79/020116-03$02.50

Table 1. Disaccharide syntheses.

Bromo sugar	Alcohol	Mol ratio bromo sugar/ alcohol	Solvent	Temperature (°C)	Mol ratio 2,4,6-collidine/alcohol	Reaction time (min)	Product	Yield %
1	*7a*	1.1	CH_3NO_2	−20 to −25	1.1	15	*7b*	80
2	*7a*	1.1	CH_3NO_2/C_7H_8 1:1	−20 to −30	1.3	10	*7c*	92
2	*8a*	1.1	CH_3NO_2/C_7H_8 1:1	−25 to −30	0	3	*8b*	93
1	*9a*	1.1	C_7H_8	−5 to −10	0	5	*9b*	77
1	*9a*	1.1	CH_3NO_2	−20 to −30	1.1	15	*9b*	87
3	*9a*	1.1	C_7H_8	−5 to −10	0	5	*9c*	75
3	*10a*	1.1	$CHCl_3/C_7H_8$ 1:1	−5 to −10	0	10	*10b*	90
3	*11a*	1.0	CH_3NO_2/C_7H_8 1:1	−20 to −30	0.9	10	*11b*	90
1	*12a*	1.1	CH_3NO_2/C_7H_8 1:1	−20 to −30	0.85	10	*12b*	67

at least in some reactions, weakly acidic conditions are required to obtain high yields of disaccharides.

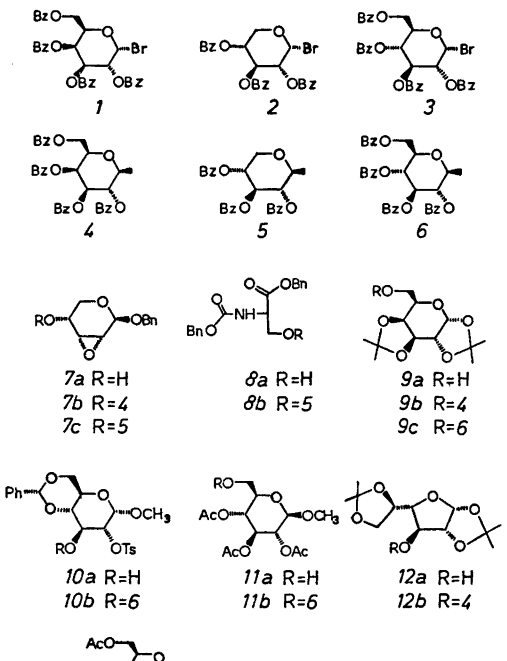

Fig. 1. Starting materials and products.

EXPERIMENTAL

General methods were the same as those reported before.[7,8] Preparative separations were performed on 175 g silica gel columns (Merck Kieselgel 60, 0.040 − 0.063 mm) using toluene − ethyl acetate (4:1 or 9:1) as eluent. Reagents: Spectrograde nitromethane and chloroform were distilled from phosphorus pentaoxide immediately before use. Sodium-dried toluene was used. All new substances gave ^1H and ^{13}C NMR spectra in agreement with the postulated structures.

General glycosylation procedure. A solution of the appropriate benzoylated halide (2.0 mmol) and the alcohol (1.8 − 2.0 mmol) in solvent (10 ml, see Table 1) was cooled in an ethanol − dry ice bath. Silver triflate (2.3 mmol) and, where indicated in Table 1, 2,4,6-collidine (1.5 − 2.3 mmol) dissolved in solvent (10 ml) was added through a dropping funnel with cooling and magnetic stirring. After the appropriate reaction time (3 − 15 min), pyridine (1 ml) was added to neutralize any liberated acid in those reactions in which excess 2,4,6-collidine was not used. The solution was diluted with diethyl ether, filtered, washed successively with aqueous sodium thiosulfate, water, 2 M aqueous sulfuric acid, and saturated aqueous sodium bicarbonate, dried ($MgSO_4$), filtered and concentrated to a syrup from which the main sugar component was obtained by chromatography. In syrups that were hard to dry, traces of residual solvents were estimated from ^1H NMR integrals, and the yields determined by weighing were corrected accordingly.

Characterization of disaccharides. Benzyl 2,3-anhydro-4-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-β-D-ribopyranoside (7b). The physical constants were in agreement with those previously reported.[6]

Benzyl 2,3-anhydro-4-O-(2,3,4-tri-O-benzoyl-β-D-xylopyranosyl)-β-D-ribopyranoside (7c). Syrup, $[\alpha]_D$ −40° ($CHCl_3$). Debenzoylation (sodium methoxide−methanol) and acetylation (acetic anhydride−pyridine) afforded benzyl 2,3-anhydro-4-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-ribopyranoside, m.p. 134 °C, $[\alpha]_D$ −55° ($CHCl_3$) [lit.[9], m.p. 131−132 °C, $[\alpha]_D$ −48° ($CHCl_3$)].

N-*Benzyloxycarbonyl-3-O-(2,3,4-tri-O-benzoyl-β-D-xylopyranosyl)-L-serine benzyl ester* (8b). M.p. 106−108 °C, $[\alpha]_D$ −36° ($CHCl_3$). NMR ($CDCl_3$, δ in ppm downfield from internal TMS): ^1H: δ 4.84, $J \sim 6$ Hz (1H, H-1, xylose residue), ^{13}C: δ 99.85, $J_{C,H}$ 166.0 Hz (C-1, xylose residue). Anal. $C_{44}H_{39}NO_{12}$: C, H, N.

1,2:3,4-Di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-α-D-galactopyranose (9b). Syrup, $[\alpha]_D$ +45° ($CHCl_3$). Debenzoylation and acetylation as for *7c* afforded 1,2:3,4-di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-galactopyranose, $[\alpha]_D$ −42° ($CHCl_3$) [lit.[10,11], $[\alpha]_D$ −47° ($CHCl_3$)].

1,2:3,4-Di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-α-D-galactopyranose (9c). Syrup, $[\alpha]_D$ −18° ($CHCl_3$). Debenzoylation and acetylation as for *7c* afforded 1,2:3,4-di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-galactopyranose, m.p. 140−141 °C, $[\alpha]_D$ −56° ($CHCl_3$) [lit.[11], m.p. 141 °C, $[\alpha]_D$ −55° ($CHCl_3$)].

Methyl 4,6-O-benzylidene-2-O-(p-tolylsulfonyl)-3-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (10b). Syrup, $[\alpha]_D$ +38° ($CHCl_3$). Debenzoylation and acetylation as for *7c* afforded methyl 4,6-*O*-benzylidene-2-*O*-(*p*-tolylsulfonyl)-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-glucopyranoside, $[\alpha]_D$ +5° ($CHCl_3$) [lit.[4], $[\alpha]_D$ +9° ($CHCl_3$)].

Methyl-6-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-O-acetyl-β-D-glucopyranoside (11b). Syrup, $[\alpha]_D$ +9° ($CHCl_3$), deacylated (sodium methoxide−methanol) to give methyl 6-*O*-β-D-glucopyranosyl-β-D-glucopyranoside, $[\alpha]_D$ −32° (H_2O) [lit.[12] −36° (H_2O)].

1,2:5,6-Di-O-isopropylidene-3-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-α-D-galactofuranose (12b). Syrup, $[\alpha]_D$ +64° ($CHCl_3$). Debenzoylation (sodium methoxide−methanol) and mild acid hydrolysis (80 % aqueous acetic acid, 70 °C, 4 h) afforded 3-*O*-β-D-galactopyranosyl-D-galactose, m.p. 161−164 °C, $[\alpha]_D$ +83° (5 min) → +61° (equilibrium value, H_2O) [lit.[13], m.p. 163−170 °C, $[\alpha]_D$ +60° (equilibrium value, H_2O)].

Acknowledgements. We are indebted to Professor Bengt Lindberg for his interest and to the Swedish Natural Science Research Council for financial support.

REFERENCES

1. Leroux, J. and Perlin, A. S. *Carbohydr. Res.* *47* (1976) C8.
2. Eby, R. and Schuerch, C. *Carbohydr. Res.* *60* (1978) 85.
3. Lemieux, R. U., Takeda, T. and Chung, B. Y. In El Khadem, S., Ed., *Synthetic Methods for Carbohydrates, ACS Symposium Ser. 39* (1974).
4. Hanessian, S. and Banoub, J. *Carbohydr. Res. 53* (1977) C13.
5. Shone, R. L. *Tetrahedron Lett.* (1977) 993.
6. Erbing, B., Lindberg, B. and Norberg, T. *Acta Chem. Scand. B 32* (1978) 308.
7. Ekborg, G., Garegg, P. J. and Josephson, S. *Carbohydr. Res. 65* (1978) 301.
8. Garegg, P. J. and Gotthammar, B. *Carbohydr. Res. 58* (1977) 345.
9. Aspinall, G. O. and Ross, K. M. *J. Chem. Soc.* (1961) 3674.
10. Wolf, A., Knopf, E. and Zaheer, S. H. *Ber. Dtsch. Chem. Ges. 61* (1928) 1743.
11. a. Kochetkov, N. K., Khorlin, A. Ya. and Bochkov, A. F. *Tetrahedron 23* (1967) 693; b. Kochetkov, N. K., Bochkov, A. F., Sokolovskaya, T. A. and Suyatkova, V. J. *Carbohydr. Res. 16* (1971) 17.
12. Hudson, C. S. and Johnson, J. M. *J. Am. Chem. Soc. 39* (1917) 1272.
13. Ball, D. H. and Jones, J. K. N. *J. Chem. Soc.* (1958) 905.

Received September 12, 1978.