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Note

Selective 3-*O*-allylation and 3-*O*-benzylation of methyl α-D-manno-, α-L-rhamno- and β-L-fuco-pyranoside*

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The selective 3-*O*-allylation or 3-*O*-benzylation of methyl glycosides is a very useful procedure in anhydro sugar synthesis[1] and oligosaccharide synthesis[2], because it can substantially simplify the reaction pathways. The "direct stannylation method"[3], by which unprotected glycopyranosides were treated with dibutyltin oxide and then alkylated, was effective for the 3-*O*-allylation of methyl α- (ref. 1) and β-D-galactopyranoside[4], but "gave a quantitative recovery of starting material" in the case of methyl α-D-mannopyranoside[3]. We report here a slightly modified procedure for direct stannylation that successfully accomplishes the 3-*O*-allylation and 3-*O*-benzylation of methyl α-D-manno-, α-L-rhamno- and β-L-fuco-pyranoside.

The direct stannylation method as described[3] involved the preparation of a glycoside–stannylene complex in boiling benzene solution, followed by reaction in boiling benzene with an alkyl bromide in the presence of tetrabutylammonium iodide. In the present study the procedure was modified so that the glycoside–stannylene complex was prepared in methanol, and then the residue obtained after stripping off the solvent was treated with alkyl bromide and tetrabutylammonium iodide in toluene. Because of the use of methanol the stannylation of the glycoside proceeded very rapidly and the tedious azeotropic removal of water was avoided. Subsequently the alkylation carried out in toluene at 60–70° gave 3-*O*-alkyl glycosides in good or acceptable yields. No 2-*O*-alkyl or di-*O*-alkyl derivatives were detected in the case of the manno- and rhamno-pyranoside, but a small amount of disubstituted fucopyranoside appeared when the conversion of the starting glycoside surpassed 70%. To prevent the formation of dialkylated derivatives, the conversion of fucopyranoside was controlled in the range of 50%, and the unchanged starting material was recovered for re-use.

The 3-*O*-allyl derivative (**2**) prepared from methyl α-D-mannopyranoside by the new method was identified by acetylation to give the crystalline triacetate (**4**), which

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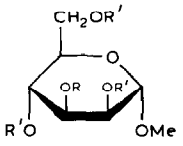
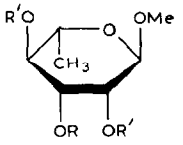
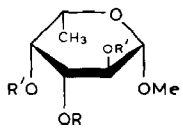


	R	R′
1	H	H
2	All	H
3	Bn	H
4	All	Ac



	R	R′
5	H	H
6	All	H
7	Bn	H
8	All	Ac
9	All	Bn



	R	R′
10	H	H
11	All	H
12	Bn	H
13	All	Ac
14	Bn	Ac

showed m.p. 64–65° and gave ^{1}H-n.m.r. data the same as those reported for the compound prepared by allylation in N,N-dimethylformamide[5]. The methyl 3-*O*-benzyl-α-D-mannopyranoside (**3**) prepared by the modified procedure gave ^{1}H-n.m.r. data identical with the reported values for the compound obtained by benzylation in 1,4-dioxane[6].

The 3-*O*-allyl derivatives of methyl α-L-rhamnopyranoside and β-L-fucopyranoside were characterized by elemental analysis, and by the ^{1}H-n.m.r. spectra of their diacetates. Single frequency decoupling was used for full assignments of the chemical shifts of the diacetates. It was found from the spectra that both the rhamno- and the fuco-pyranoside allyl ethers gave signals for H-3 upfield and H-2 and H-4 downfield, clearly indicating the 3-*O*-allyl substitution. The structure of methyl 3-*O*-benzyl-β-L-fucopyranoside was confirmed by the same technique. Methyl 3-*O*-benzyl-α-L-rhamnopyranoside (**7**) was characterized by comparison of its ^{1}H-n.m.r. data with the reported values[7]. Benzylation of methyl 3-*O*-allyl-α-L-rhamnopyranoside by the conventional method afforded the corresponding dibenzyl ether, which was an important intermediate in the synthesis of 1,3-anhydro-2,4-di-*O*-benzyl-β-L-rhamnopyranoside[8] and also useful for the synthesis of (1→3)-linked oligosaccharides.

The results of elemental analysis and the optical rotatory data for compounds **6**,

TABLE I

Selective alkylation of methyl α-D-manno-(**1**), α-L-rhamno-(**5**), and β-L-fuco-pyranoside(**10**)

Parent glycoside	*Product*	*Yield*[a] *(%)*	*Starting material recovered (%)*
1	3-*O*-allyl- (**2**)	60.5	~30
	3-*O*-benzyl- (**3**)	64	~25
5	3-*O*-allyl- (**6**)	70	~20
	3-*O*-benzyl- (**7**)	71	~20
10	3-*O*-allyl- (**11**)	40	~50
	3-*O*-benzyl- (**12**)	56	~40

[a] Of product isolated, uncorrected for recovered starting material.

9, **11**, and **12** are indicated in Table II and the ^{1}H-n.m.r. data for **9** and the acetates **4**, **8**, **13**, and **14** are shown in Table III.

TABLE II

Characterization of compounds **6**, **9**, **11**, and **12**

Compound	*Formula*	*Elemental analysis*				*M.p.* (°)	$[\alpha]_D^{20}$ *in* $CHCl_3$, *degrees* (*conc.*,%)
		Calc.		*Found*			
		C	*H*	*C*	*H*		
6	$C_{10}H_{18}O_5$	55.05	8.26	54.78	8.13	syrup	−335 (*c* 2.0)
9	$C_{24}H_{30}O_5$	72.36	7.54	72.48	7.56	syrup	−320 (*c* 5.0)
11	$C_{10}H_{18}O_5$	55.05	8.26	54.87	8.28	74–75[a]	−54 (*c* 1.0)
12	$C_{14}H_{20}O_5$	62.65	7.46	61.97	7.69	91–92[a]	−53 (*c* 1.0)

[a] Crystallized from diethyl ether.

TABLE III

^{1}H-N.m.r. chemical shifts and coupling constants for compounds **4**, **8**, **9**, **13**, and **14**

H atom (s)	*δ Values (multiplicities); J values in Hz*				
	4	**8**	**9**	**13**	**14**
H-1	4.72(d)	4.61(d)	4.63(d)	4.30(d)	4.27(d)
	$J_{1,2}$ 1.4	$J_{1,2}$ 0.7	$J_{1,2}$ 0.7	$J_{1,2}$ 8.0	$J_{1,2}$ 7.8
H-2	5.27(dd)	5.20(m)	3.71(m)	5.06(t)	5.10(dd)
	$J_{1,2}$ 1.2			$J_{1,2}$ &	$J_{1,2}$ 7.8
	$J_{2,3}$ 2.6			$J_{2,3}$ 8.4	$J_{2,3}$ 8.4
H-3	4.27–3.95(m)	3.75(m)	3.75(m)	3.50(dd)	3.56(dd)
				$J_{2,3}$ 8.2	$J_{2,3}$ 8.3
				$J_{3,4}$ 3.3	$J_{3,4}$ 3.5
H-4	5.24(m)	4.98(t)	3.59(t)	5.27(m)	5.35(d)
		$J_{3,4}$ &	$J_{3,4}$ &		$J_{3,4}$ 3.4
		$J_{4,5}$ 10	$J_{4,5}$ 9.8		
H-5	3.80(m)	3.75(m)	3.65(m)	3.69(dd)	3.68(dd)
				$J_{5,6}$ 6.3	$J_{5,6}$ 6.3
H-6	4.27–3.95(m)	1.22(d)	1.35(d)	1.23(d)	1.28(d)
		$J_{5,6}$ 6.3	$J_{5,6}$ 6.4	$J_{5,6}$ 6.2	$J_{5,6}$ 6.2
CH_2=C*H*	5.80(m)	5.78(m)	5.93(m)	5.78(m)	
CH_2=CH	5.21(m)	5.28–5.13(m)	5.33(m)	5.24(m)	
			5.20(m)	5.15(m)	
CH_2=CHCH_2	4.10(m)	4.40–3.85(m)	4.10(m)	4.12(dd)	
				3.92(dd)	
CH_3CO	2.15(s)	2.13(s)		2.16(s)	2.19(s)
	2.11(s)	2.08(s)		2.08(s)	2.05(s)
	2.08(s)				
PhCH_2			4.95(d)		4.21(d)
			4.13(d)		3.92(d)
			4.75(q_{AB})		
Ar-H			7.42–7.24(m)		7.33–7.25(m)

EXPERIMENTAL

General methods. — These were as given in ref. 1.

General procedure for monoalkylation of methyl glycosides. — To a solution of methyl glycoside (1 mmol) in methanol (5 mL) was added dibutyltin oxide (250 mg, 1 mmol), and the mixture was boiled under reflux. After the mixture became clear, heating was continued for 1 h, and the stannylene complex was obtained as a white foamy residue by evaporation of the methanol under diminished pressure. To the residue was added toluene (6 mL), tetrabutylammonium iodide (370 mg, 1 mmol), and allyl bromide (0.88 mL, 10 mmol) or benzyl bromide (0.12 mL, 1.1 mmol), and the mixture was stirred for 18 to 24 h at 60–70°. The use of excess allyl bromide was necessary to compensate for some loss of the reagent, due to its low boiling point. The reaction was monitored by t.l.c., with 1:4 methanol–dichloromethane as the developing solvent. After completion of the alkylation, the solvent was evaporated under diminished pressure, and the residue was subjected to column chromatography on silica gel with ethyl acetate as the eluent. The acetylation of the 3-*O*-substituted glycosides was carried out quantitatively with acetic anhydride in pyridine. The benzylation of methyl 3-*O*-allyl-α-L-rhamnopyranoside (110 mg, 0.5 mmol), was conducted quantitatively with benzyl bromide (0.12 mL, 1.1 mmol) and sodium hydride (120 mg of 80% dispersion in oil, 4.0 mmol) in oxolane (10 mL) under reflux for 3 h. The reaction mixture was partitioned between water and dichloromethane, the organic phase was evaporated under reduced pressure, and the pure, syrupy product was obtained after separation on a silica gel column with 1:4 ethyl acetate–petroleum ether as eluent.

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