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Note

Synthesis of partially protected benzyl and methyl α-L-rhamnopyranosides by the phase-transfer technique

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For the synthesis of the repeating units of bacterial polysaccharides[1–4], L-rhamnose derivatives containing persistent and/or temporary blocking-groups and one free hydroxyl group are needed. Recent publications have described the preparation of some disubstituted benzyl α-L-rhamnopyranosides[5,6]. The synthesis of the corresponding methyl α-L-rhamnopyranosides has also been achieved[7]. An alternative approach to some of these and other compounds is now reported.

The regioselective substitution of several monosaccharides has been studied in detail[8]. Recently, it has been shown that the phase-transfer technique[9] is a simple and excellent tool for the regioselective monobenzylation[10] and monotosylation[11] of gluco- and manno-pyranosides having unsubstituted hydroxyl groups at C-2 and C-3. There is, however, little information available on the possibility of selective alkylation and acylation of the secondary hydroxyl groups of L-rhamnose[12].

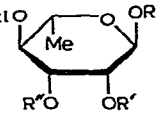
In the present study, it was found that the reaction of benzyl[6,13] (**1**) and methyl 4-*O*-benzyl-α-L-rhamnopyranoside[14] (**2**) with various reagents (benzyl and allyl bromide, methyl iodide, and tosyl chloride; see Table I), under catalysis by tetrabutylammonium ion, gave good yields of the 2,4-disubstituted derivatives; 8–15% of the 3,4-disubstituted and less than 5% of the corresponding 2,3,4-trisubstituted derivatives were also formed, and negligible amounts of the starting diols remained unreacted.

In a typical procedure, a mixture of either **1** or **2** (2 mmol), tetrabutylammonium bromide (0.5 mmol), the alkylating (tosylating) agent (2.1–2.5 mmol or more of methyl iodide), and aqueous sodium hydroxide (2 ml of a 5–20% solution) in dichloromethane (20 ml) was stirred with a high-speed magnetic stirrer at room temperature for between 4 h and 4 days. The organic layer was separated, washed with water (3 × 10 ml), dried (Na_2SO_4), and concentrated. The residual syrup was chromatographed on silica gel with (*A*) benzene–methanol (100:3) or (*B*) light petroleum (b.p. 60–80°)–ethyl acetate (4:1).

The structures of the products were proved by p.m.r. spectroscopy (100 MHz) and by a direct comparison with known compounds.

TABLE I

DERIVATIVES OF BENZYL (R = Bzl, R′ = R″ = H) AND METHYL 4-*O*-BENZYL-α-L-RHAMNOPYRANOSIDES (R = Me, R′ = R″ = H)



Reagent	*Product*				*Yield*[a] *(%, isolated)*	$[\alpha]_D$[b] *(degrees)*	R_F[c]	R_T[d] *(min)*	*Ref.*
	R	*R′*	*R″*						
Benzyl bromide	Me	Bzl	H	syrup	71	−15	0.46	4.98	7
	Me	H	Bzl	syrup	9	−44	0.34	4.33	7
	Bzl	Bzl	H	syrup	75	−38.5	0.56	10.75	5, 6
	Bzl	H	Bzl	syrup	8	−49	0.40	10.03	5, 6
Allyl bromide	Me	Allyl	H	syrup	75	−36	0.41	1.87	
	Me	H	Allyl	syrup	9	−71	0.28	1.65	
	Bzl	Allyl	H	syrup	73	−49	0.52	6.14	
	Bzl	H	Allyl	syrup	9	−67	0.41	5.59	
Methyl iodide	Me	Me	H	syrup	43	−56	0.35	1.43	
	Me	H	Me	syrup	8	−83	0.26	1.24	
	Bzl	Me	H	syrup	44	−62	0.50	5.23	
	Bzl	H	Me	syrup	15	−80	0.27	4.73	
Tosyl chloride	Me	Ts	H	m.p. 82–83°[e]	65	−19	0.46		
	Bzl	Ts	H	syrup	63	−42	0.51		

[a]Yields were not optimized. [b]In chloroform. [c]On pre-coated layers of Kieselgel on aluminium foil (Merck, Cat. No. 5562) with solvent *A*. [d]The compounds were acetylated before chromatography. G.l.c. was performed with a Hewlett–Packard 5830A gas chromatograph, on a column (4 ft × 2.16 mm) of 10% of UCW 982 on Gas Chrom Q (80–100 mesh). First isothermal period, 1 min, 225°; injection temperature, 275°; rate of heating, 5°/min; flame-ionization detector, 300°; nitrogen flow-rate, 20 ml/min. [e]Determined on a Kofler hot-stage, not corrected.

Our results on the selective substitution of **1** and **2** further support the simplified theory put forward by Garegg *et al.*[10], according to which the regioselectivity is determined by the relative acidities of the hydroxyl groups, and steric factors are relatively unimportant.

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