Carbohydrate Research, 56 (1977) 191–194

Note

New syntheses of mono- and di-*O*-methyl derivatives of methyl α-L-rhamnopyranoside

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(Received August 1st, 1976; accepted for publication, September 10th, 1976)

In our studies of pectinic polymers of the bark of the white willow (*Salix alba* L.), several degradation procedures afforded fragments containing high proportions of L-rhamnose residues[1]. On methylation analysis of these fragments, the resulting methyl ethers of methyl α-L-rhamnopyranoside were subjected to g.l.c.–m.s., but our mass spectra differed[2] from those published[3], and authentic reference compounds were therefore required.

Syntheses of some methyl ethers of methyl α-L-rhamnopyranoside require multistep procedures[4], but others are unknown. We now report on a convenient method for the preparation of some of these derivatives, which involves catalysed methylation by diazomethane[5]. The use of stannous chloride dihydrate, titanium tetrachloride, and cerium trichloride not only gave high yields but also very different isomer distributions. A detailed study of the reaction mechanism was not undertaken, the primary purpose being the synthesis of partially methylated derivatives of methyl α-L-rhamnopyranoside.

Methanolic methyl α-L-rhamnopyranoside containing catalyst (mM) was treated with diazomethane at room temperature. The resulting methyl 2- and 3-*O*-methyl-α-L-rhamnopyranosides were isolated by chromatography; the respective yields for each catalyst were as follows: $SnCl_2 \cdot 2H_2O$, 38 and 60%; $CeCl_3$, 65 and 32%; $TiCl_4$, 12 and 85%.

Likewise, methylation of methyl 4-*O*-methyl-α-L-rhamnopyranoside[6] gave a mixture of methyl 3,4- and 2,4-di-*O*-methyl-α-L-rhamnopyranosides, the respective yields of which for each catalyst were as follows: $SnCl_2 \cdot 2H_2O$, 65 and 34%; $CeCl_3$, 32 and 65%; $TiCl_4$, 81 and 18%. The location of the methoxyl groups in methylated derivatives of methyl α-L-rhamnopyranoside can be assigned on the basis of n.m.r. data (Table I), since there is an upfield shift of the signal for a proton attached to a carbon atom carrying a methoxyl group and, in the acetylated derivatives, a downfield shift of the signal for the proton in the HCOAc group.

The catalysts used for monomethylation of the *cis*-glycol system of methyl α-L-rhamnopyranoside and its 4-*O*-methyl derivative effect selectivity similar to that observed in methylations of nucleosides[5], but the yields were substantially higher.

TABLE I

N.M.R. DATA FOR METHYLATED DERIVATIVES OF METHYL α-L-RHAMNOPYRANOSIDE[a]

Location of methyl groups[c]	*Solvent*	*Chemical shifts*[b] (δ)									*Coupling constants (Hz)*				
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*Me*	*OMe*	*OAc*	*OH*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	J_{5,CH_3}
—	$(CD_3)_2CO$	4.58d	3.81q	3.30———		———3.75m	1.24m[d]	3.31	—	4.13[e]	1.5	3.0	[f]	[f]	5.6
2	$CDCl_3$	4.71d	3.43q	3.30———		———3.80m	1.31d	3.34 3.45	—	3.60[g]	1.8	~3.0	[f]	[f]	6.5
2*	$CDCl_3$	4.71d	3.61q	5.21q	5.06t	3.78o	1.20d	3.39 3.46	2.04; 2.08	—	1.8	2.9	9.0	9.1	6.5
3	C_5D_5N[h]	5.03d	4.42q	3.73q	4.17t	3.98o	1.55d	3.38; 3.46	—	2.96[g]	1.7	3.2	9.3	9.3	6.5
3*	$CDCl_3$	4.64d	5.31q	3.58q	4.98t	3.69o	1.21d	3.33; 3.48	2.08; 2.14	—	1.9	3.1	9.5	9.5	6.5
4	$CDCl_3$	4.63d	3.93q	3.80q	3.10t	3.72o	1.33d	3.34; 3.56	—	3.89[g]	1.6	3.4	9.0	9.0	6.3
4*	$CDCl_3$	4.55bd[d]	4.95———	5.30m	3.18bt[d]	3.69o	1.33d	3.34; 3.46	2.04; 2.13	—	~1.6	[f]	[f]	[f]	6.2
3,4	$CDCl_3$	4.68d	4.00q	3.41q	3.08t	3.59o	1.29d	3.35; 3.49; 3.54	—	2.78	1.8	3.2	9.1	9.1	6.5
3,4*	$CDCl_3$	4.58d	5.23q	3.54q	3.03t	3.59o	1.34d	3.34; 3.39; 3.54	2.11	—	1.7	3.4	9.1	9.1	6.0
2,4	$CDCl_3$	4.71d	3.44q	3.80q	2.97t	3.55o	1.29d	3.35; 3.50; 3.58	—	2.83	1.8	3.8	9.2	9.2	6.5
2,4*	$CDCl_3$	4.68d	3.61q	5.09q	3.23t	3.66o	1.31d	3.37; 3.45; 3.48	2.14	—	1.8	3.3	9.5	9.5	6.5
2,3[7]	$CDCl_3$	4.76d	3.63bt[d]	3.30———		———3.75m	1.31m[d]	3.38; 3.45; 3.48	—	3.08	1.6	[f]	[f]	[f]	~5.9
2,3*	$CDCl_3$	4.73d	3.63q	3.50q	5.00t	3.68o	1.20d	3.36; 3.40; 3.51	2.06	—	1.7	3.3	9.5	9.5	6.5
2,3,4	$CDCl_3$	4.71d	3.55q	3.43q	3.09t	3.52o	1.29d	3.34; 3.47; 3.48; 3.53	—	—	1.6	3.2	9.1	9.1	6.2

[a]Sweep width, 100 Hz. [b]Key: d, doublet; t, triplet; q, quartet; o, octet; m, multiplet; b, broad. [c]An asterisk (*) denotes the acetylated derivative. [d]Further splitting due to the second-order effect. [e]3-Proton bs. [f]First-order coupling not observed. [g]2-Protons s. [h]In $CDCl_3$, the first-order spectrum was not observed.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage. Optical rotations were measured on solutions in chloroform with a Perkin–Elmer Model 141 polarimeter. N.m.r. spectra were measured at 80 MHz (internal Me_4Si) with a Tesla BS-487-B spectrometer. The proton-signal assignments were made by the INDOR technique. T.l.c. was performed on Silufol plates (Kavalier, Czechoslovakia) with *A*, chloroform–methanol (9:1); and *B*, light petroleum (b.p. 35–50°)–acetone (5:2), and detection by charring after spraying with 20% aqueous ammonium sulphate. Dry-column chromatography was carried out on Silikagel L (40–56 μm, Lachema n.p. Brno). Solutions were concentrated below 50° under reduced pressure.

Selective methylations. — (*a*) *Methyl* α-L-*rhamnopyranoside.* To a mixture of the title compound (4.6 g, 25.8 mmol), methanol (50 ml), and stannous chloride dihydrate (12 mg), stirred at room temperature, ~0.6M diazomethane in dichloromethane was added slowly until a yellow colour persisted. The two major products (R_F 0.5 and 0.4, t.l.c., solvent *A*) were isolated by chromatography on a column (4.8 × 60 cm) of silica gel with solvent *A*.

The faster-moving component was syrupy methyl 2-*O*-methyl-α-L-rhamnopyranoside (1.88 g), $[\alpha]_D^{22}$ −49° (*c* 1.1), which gave a 3,4-diacetate, m.p. 70–71° (from ethanol), $[\alpha]_D^{22}$ −79° (*c* 1.2) (Found: C, 52.08; H, 7.09; OMe, 22.69. $C_{12}H_{20}O_7$ calc.: C, 52.16; H, 7.29; OMe, 22.46%).

The slower-moving component was syrupy methyl 3-*O*-methyl-α-L-rhamnopyranoside (2.97 g), $[\alpha]_D^{22}$ −61° (*c* 1.3), which gave a 2,4-diacetate, m.p. 104–105° (from ethanol), $[\alpha]_D^{22}$ −26° (*c* 0.9) (Found: C, 52.20; H, 7.54; OMe, 22.50. $C_{12}H_{20}O_7$ calc.: C, 52.16; H, 7.29; OMe, 22.46%).

Similar treatment of methyl α-L-rhamnopyranoside in the presence of cerium trichloride and titanium tetrachloride gave the product yields noted in the Discussion.

(*b*) *Methyl 4-O-methyl-*α-L-*rhamnopyranoside.* The title compound[6] was methylated with diazomethane in the presence of catalyst following the procedure described in (*a*). The reaction mixture was concentrated, and the residue was eluted from a column of silica gel with solvent *B*. The faster-moving product (R_F 0.6, t.l.c., solvent *B*) was syrupy methyl 3,4-di-*O*-methyl-α-L-rhamnopyranoside, $[\alpha]_D^{22}$ −88.5° (*c* 2.0), hydrolysis of which gave 3,4-di-*O*-methyl-α-L-rhamnopyranose, m.p. 87.5–88° (from ether–hexane), $[\alpha]_D^{22}$ +17° (equil.; *c* 2, water); lit.[6] m.p. 91–92°, $[\alpha]_D^{20}$ +18° (water).

Eluted second was syrupy methyl 2,4-di-*O*-methyl-α-L-rhamnopyranoside, $[\alpha]_D^{22}$ −56° (*c* 1.5), R_F 0.5, hydrolysis of which gave 2,4-di-*O*-methyl-L-rhamnose, $[\alpha]_D^{22}$ +12° (*c* 1.2, water) {lit.[6] $[\alpha]_D^{22}$ +10.6° (water)}, characterised as the 2,4-dinitrophenylhydrazone, m.p. 161–162°; lit.[6] m.p. 164–165°.

The yields of the 3,4- and 2,4-di-*O*-methyl derivatives for the other catalysts used are given in the Discussion.

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