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Note

Carbon-13 n.m.r.-spectral study of L-rhamnose acetates

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Although ^{13}C-n.m.r. spectroscopy is used in carbohydrate chemistry as a routine, spectroscopic method[1], only a few, systematic, ^{13}C-n.m.r. studies have been published on carbohydrate compounds that are closely related structurally. A recent paper[2] reported ^{13}C-n.m.r. studies on D-glucopyranose acetates, and, very recently, the ^{13}C, shift parameters were described for di- and tri-*O*-(3-nitropropanoyl)-D-glucopyranoses[3] and for mono- and di-methylated derivatives of methyl 2-acetamido-2-deoxy-α- and -β-D-glucopyranosides[4]. However, no systematic study has yet appeared on the substituent-induced, ^{13}C chemical-shift parameters for carbohydrate structures other than those having the D-*gluco* configuration.

In this article, we report ^{13}C assignments for some partially and two fully acetylated L-rhamnose derivatives, and discuss the displacement of the ^{13}C-lines of the ring-carbon atoms that occurs upon acetylation.

EXPERIMENTAL

General. — For general methods, see ref. 5. The ^{13}C-n.m.r. spectra were recorded with a Varian XL-100-FT spectrometer at 25.16 MHz, for solutions in chloroform-*d*, using tetramethylsilane as the internal reference standard, with proton-noise decoupling. The $^{1}J_{C\text{-}1,H\text{-}1}$ values were measured by using the gated decoupling technique. The $[\alpha]_D$ values were measured for solutions in chloroform, at concentrations of 0.5–2.0; those for compounds having HO-1 free refer to the equilibrium values. Acetic anhydride–pyridine was used for acetylation, acetolysis was performed at 0° in a mixture of acetic anhydride and sulfuric acid, and hydrogenolysis was conducted at atmospheric pressure and room temperature in ethanol in the presence of 10% Pd–C.

1,2,3,4-Tetra-*O*-acetyl-α-L-rhamnopyranose (**1**) was prepared by acetylation

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of 1,2,3-tri-*O*-acetyl-α-L-rhamnopyranose (**2**), which was obtained from methyl 4-*O*-benzyl-α-L-rhamnopyranoside[6] by acetolysis followed by chromatography to yield 1,2,3-tri-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranose (**3**), and hydrogenolysis of **3**. 1,2,3,4-Tetra-*O*-acetyl-β-L-rhamnopyranose[7,8] (**4**) was obtained by acetylation of 1,3,4-tri-*O*-acetyl-β-L-rhamnopyranose* (**5**), which was prepared either by hydrolysis of 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (**6**) in aqueous acetone in the presence of silver carbonate, or by hydrolysis of **6** in acetate buffer solution[10].

Treatment of **5** in aqueous ethanol with pyridine caused migration of the acetyl group from O-1 to O-2, yielding 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranose (**7**) together with a small proportion of the β anomer. The 2,3-diacetate (**8**), as an ~5:1 mixture of the α and β anomers, was prepared by hydrogenolysis of benzyl 2,3-di-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranoside (**9**). The 2,4-diacetate (**10**) was obtained in controlled, acid methanolysis of 3,4-di-*O*-acetyl-1,2-*O*-(1-methoxyethylidene)-β-L-rhamnopyranose[13,14,16] (**11**), which was synthesized in 73% yield from **6** and methanol in the presence of ethyldiisopropylamine in *N,N*-dimethylformamide–dichloromethane. Acetic acid hydrolysis of 3,4-di-*O*-benzyl-1,2-*O*-(1-methoxyethylidene)-β-L-rhamnopyranose[14,16] (**12**) gave mainly 2-*O*-acetyl-3,4-di-*O*-benzyl-L-rhamnopyranose (**13**), acetylation of which yielded a mixture of 1,2-di-*O*-acetyl-3,4-di-*O*-benzyl-α- (**14**) and -β-L-rhamnopyranose (**15**), from which **14** could be isolated in pure form by crystallization. Catalytic hydrogenation of **14** gave 1,2-di-*O*-acetyl-α-L-rhamnopyranose (**16**). 1,2-Di-*O*-acetyl-β-L-rhamnopyranose (**17**) was obtained, in admixture with **16**, from the mixture of **14** and **15**.

The 3,4-diacetate **18** was prepared from benzyl 3,4-di-*O*-acetyl-2-*O*-benzyl-α-L-rhamnopyranoside[16] (**19**) by hydrogenolysis. The fifth diacetate, 1,4-di-*O*-acetyl-α-L-rhamnopyranose (**20**) was obtained from benzyl 4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**21**) by successive catalytic hydrogenation, acetylation, and hydrolysis with trifluoroacetic acid. Benzyl 4-*O*-acetyl-α-L-rhamnopyranoside (**22**) was obtained by acetic acid hydrolysis of benzyl 4-*O*-acetyl-*exo*- and -*endo*-2,3-*O*-benzylidene-α-L-rhamnopyranoside[11]. Finally, the 4-acetate **23** was prepared by hydrogenolysis of this benzylidene mixture. The physical data for, and ^{1}H-n.m.r. spectra of, these compounds are summarized in Table I.

RESULTS AND DISCUSSION

The ^{13}C-n.m.r., chemical-shift assignments for the acetylated L-rhamnopyranosides are shown in Table II, which also includes, for reference purposes, derivatives containing both acetyl and benzyl groups. The lines corresponding to C-1 and C-6 were readily recognized by their characteristic, chemical shifts. In the partially benzylated derivatives (**3**, **9**, **13**, **14**, **15**, **19**, and **22**), the carbon atoms linked to benzyloxy groups could be easily selected, because of a large, downfield shift

*Compound **5** was previously reported[9] as a minor side-product in a glycosidation reaction. Neither the m.p. nor the $[\alpha]_D$ value was given.

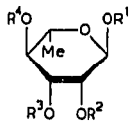
TABLE I

PHYSICAL DATA FOR SOME COMPOUNDS REPORTED HEREIN

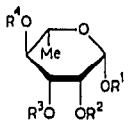
Compound	*^{1}H-n.m.r. data (p.p.m.)*						*M.p. (degrees)*	*Lit. m.p. (degrees)*	*$[\alpha]_D$ (degrees)*	*Lit. $[\alpha]_D$ (degrees)*	*Reference*
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6[a]*					
1[b]							syrup	syrup	−63	−62	12a
										−63	12b
2	5.98 $J_{1,2}$ 1.7 Hz	5.05 ⟷	5.25	3.56	3.98	1.35	syrup		−46		
3	5.98	5.2 ⟷	5.4	3.56	3.92	1.34	syrup		−52		
4	5.85 $J_{1,2}$ 1.5 Hz	5.47	5.05 ⟷	5.15	3.70	1.28	99–101 (aqueous methanol)	98–99	+13	+13	8
5	5.78 $J_{1,2}$ 1 Hz	4.18 $J_{2,3}$ 2.7 Hz	4.98 $J_{3,4}$ 9 Hz	5.18	3.65	1.28	119–121		+7.5		
8	4.96 ⟷		5.35	3.54 $J_{3,4} = J_{4,5} = 9.6$ Hz	3.98	1.26	syrup		+3.5		
9	4.6	5.25 ⟷	5.45	3.50 $J_{3,4} = J_{4,5} = 9$ Hz	3.88	1.33	syrup		−57		
10[c]	5.6 ⟷	5.8	4.76 $J_{2,3}$ 3 Hz	5.58 $J_{3,4} = J_{4,5} = 9.5$ Hz	4.50	1.36	120–130 (ethyl acetate)		−1.7		
11[d]							84–86 (aqueous methanol)	83	+35	+35	13,14,16
12[d]							106 (ether–hexane)	110–111	+1.7	+0.6	14,16
14	6.0 $J_{1,2}$ 2 Hz	5.35	3.92 $J_{2,3}$ 3 Hz	3.46 $J_{3,4} = J_{4,5} = 9$ Hz	3.82	1.32	106–107 (methanol)		−20		
16	5.98 $J_{1,2}$ 1.6 Hz	5.14	3.98 $J_{2,3}$ 3.5 Hz	3.50 $J_{3,4} = J_{4,5} = 9$ Hz	3.75	1.32	122–124		−40		
18[c]	5.6–5.9	4.35–4.65	5.6 ⟷	5.9	4.35–4.65	1.28	syrup		−40		
19							syrup		−50		

20[c]	5.97 $J_{1,2}$ 1.5 Hz	3.65 ⟷ 4.1	4.94 $J_{3,4} = J_{4,5} = 9.4$ Hz	3.65-4.1	1.07	120–122	−82
21	5.08	4.16 ⟷ 4.24	4.88	3.80 $J_{4,5}$ 9.5 Hz	1.16	112–113 (hexane)	−34
22	4.90	3.75 ⟷ 4.0	4.90 $J_{3,4} = J_{4,5} = 9$ Hz	3.75-4.0	1.18	118–120	−85
23						syrup	−2.6 (methanol)

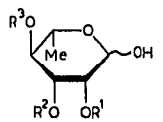
[a]The value of $J_{5,6}$ for all compounds reported here is 6 Hz. [b] ^{1}H-N.m.r. spectrum is identical with that published in refs. 9 and 12. [c] ^{1}H-N.m.r. spectrum is recorded for a solution in pyridine-d_5. [d]^{1}H-N.m.r. spectrum is identical with that published in ref. 14.



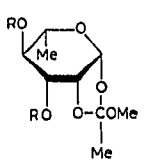
	R^1	R^2	R^3	R^4
1	Ac	Ac	Ac	Ac
2	Ac	Ac	Ac	H
3	Ac	Ac	Ac	Bn
7	H	Ac	Ac	Ac
9	Bn	Ac	Ac	Bn
14	Ac	Ac	Bn	Bn
16	Ac	Ac	H	H
19	Bn	Bn	Ac	Ac
20	Ac	H	H	Ac
21	Bn			Ac
22	Bn	H	H	Ac



	R^1	R^2	R^3	R^4
4	Ac	Ac	Ac	Ac
5	Ac	H	Ac	Ac
15	Ac	Ac	Bn	Bn
17	Ac	Ac	H	H



	R^1	R^2	R^3
8	Ac	Ac	H
10	Ac	H	Ac
13	Ac	Bn	Bn
18	H	Ac	Ac
23	H	H	Ac



11 R = Ac
12 R = Bn

Ac = acetyl, Bn = benzyl

TABLE II

^{13}C-N.M.R. CHEMICAL-SHIFTS AND $^{1}J_{C-1,H-1}$ COUPLING-CONSTANTS[a] OF ACETYLATED L-RHAMNOSE DERIVATIVES

	Atom					
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
Compound[b]						
1	90.9 (177)	68.9	69.0	70.7	68.9	17.5
2	91.2 (176.9)	69.1	71.9	70.7	71.0	17.6
3	91.0	69.4	71.5	78.6	70.2	18.0
7	92.1 (172.4)	70.9	69.3	71.6	66.3	17.5
8	92.1 (171.2)	71.2	72.0	71.2	68.6	17.7
9	96.8	70.6	71.8	79.1	68.0	18.0
10	92.0 (170.8)	73.5	68.2	75.0	66.2	17.5
13	92.3	69.9	77.6	80.3	67.7	18.0
14	91.3	68.1	77.7	79.6	70.1	18.0
16	91.4 (176.1)	71.4	70.2	72.9	70.6	17.6
18	94.2	70.0	71.8	71.0	66.3	17.5
19	97.3	76.1	71.9	71.7	66.8	17.5
20	93.7	70.1	69.9	74.5	68.5	17.5
22	99.4 (172)	71.2	70.1	75.0	66.4	17.4
23	94.2	71.8	69.6	74.5	66.1	17.4
Compound[c]						
4	90.6 (163)	68.8	70.9	70.6	71.5	17.5
5	92.0 (163.5)	68.7	73.2	70.6	71.4	17.4
8	92.6 (160)	70.5	71.2	74.1	72.6	17.7
13	93.0	69.9	77.6	79.6	71.7	18.0
15	91.3	67.8	79.4	79.9	71.7	17.9
17	91.6 (166)	71.3	72.1	73.5	72.7	17.6
18	93.9	70.0	73.7	70.3	71.8	17.5

[a]In Hz, in parentheses. [b]α at C-1. [c]β at C-1.

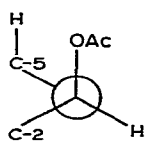
(5–7 p.p.m.) induced by the benzyl groups. The assignments for the other carbon atoms were made possible mainly by the regularities to be described.

The acetylation of HO-1 induces an upfield shift for C-1 of ~0.5 p.p.m. in the α series, and ~1.5 p.p.m. in the β series. The direction and the relative magnitudes of these shifts are in agreement with those observed for D-glucose acetates[2] and *O*-

(3-nitropropanoyl)-D-glucopyranoses[3]. This phenomenon seems to be a general one for pyranoses having an acyloxyl group at C-1. It has been presumed[3] that the shielding of C-1 relative to the derivatives having HO-1 free is caused by the carbonyl group at O-1, which is forced into a shielding orientation by the ring-oxygen atom with respect to C-1. A similar, but less well-defined, mechanism has been suggested for this phenomenon in connection with the D-glucose acetates[2]. We consider that the upfield shift of the C-1 signal that is caused by acylation of HO-1 may be occasioned by more than one factor, and, although steric interactions cannot be neglected, through-bond interactions between the *p*-orbitals of the ring-oxygen atom and the acyloxyl group should also be considered as providing a possible contribution to the increased shielding at C-1. These interactions are obviously more favorable in the β anomer, as reflected by the greater chemical shift-difference induced by the β- than by the α-acyloxyl group.

The introduction of an acetyl group onto any of the secondary hydroxyl groups of L-rhamnopyranose causes a 1.7–3-p.p.m., negative (upfield) shift for the β-carbon atoms. However, the shifts for the α-carbon atom showed a rather inconsistent variation, ranging from 0 p.p.m. ($\Delta\delta$ at C-4, in **2** compared to **1**) to +2.2 p.p.m. ($\Delta\delta$ at C-3, in **23** compared to **18**). A probable explanation for the seeming discrepancy of these data is the following: if the new acetyl group interacts with the neighboring substituent(s), forcing it into a shielding orientation with respect to the α-carbon atom, the usual, positive (downfield) shift, found[15] on acetylation of cyclohexanol, is cancelled out. On the other hand, the typical α, downfield shifts of $\sim +2$ p.p.m. are observed when such interactions are negligible (*e.g.*, **16** compared to **2**, **23** to **18**, and **23** to **10**). This explanation might account for the observation of only positive (downfield) α-shifts of acylation for *O*-acyl-D-glucopyranoses[3] having only a relatively small number of acyl substituents located relatively far from each other, and therefore lacking appreciable interactions between the substituents, and also for the negative (upfield) shifts* for the α-carbon atoms in acetylated D-glucopyranoses when the introduction of a new acetyl group results in fully substituted derivatives[2].

The configuration and type of substituent at C-1 have a characteristic effect upon the chemical shift of C-5. A significant, downfield shift (+2.5 p.p.m.) is observed for C-5 when an α-OH is acetylated, whereas acetylation of a β-OH group has practically no effect upon the chemical shift for C-5; this is readily understandable on the basis of the partial structure **A**, the effect of the α-acetoxyl group presumably



A

*Actually, the "deacetylation shifts" were reported[2] as being downfield. Conversely, the acetylation shifts are considered to be upfield.

being transferred sterically, and not through chemical bonds (1,3-diaxial interaction). If an α-acetoxyl group is linked to C-1, the C-5 signal appears in the range of 68.5 to 71 p.p.m., whereas, when C-1 bears a free α-OH group, or[9] α-OMe or α-OBn group, the C-5 signal always appears below 69 p.p.m. On the other hand, if C-1 bears a β-OH or β-acetoxyl group, the resonance line of C-5 is always found to appear above 71.4 p.p.m. Therefore, the position of the resonance line of C-5 can serve to distinguish between the anomers of an L-rhamnopyranoside.

The observed, characteristic effects induced by the acetyl group(s) in the ^{13}C-n.m.r. spectra of L-rhamnose acetates should contribute to making ^{13}C-n.m.r. assignments for more-complicated carbohydrate structures containing acetylated L-rhamnose units.

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