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^{13}C-N.M.R. SPECTROSCOPY OF α- AND β-ANOMERIC SERIES OF ALKYL L-ARABINOPYRANOSIDES

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ABSTRACT

Anomeric pairs of L-arabinopyranosides of a variety of aliphatic alcohols were prepared, and their n.m.r. spectroscopy, especially the glycosylation shift of their ^{13}C signals, was investigated in comparison with those of D-glucopyranosides, D-mannopyranosides, and L-rhamnopyranosides reported previously. It was found that the glycosylation shift of the L-arabinopyranosides in the present study is almost the same as that of D-glucopyranosides, and the conformational equilibrium of each of these L-arabinopyranosides is very similar to that of the corresponding anomer of methyl L-arabinopyranoside, namely, a preponderance of the $^4C_1$ form, regardless of the structure of the aglycon alcohol. The present results are also useful for structural study of naturally occurring arabinopyranosides.

INTRODUCTION

^{13}C-N.m.r. spectroscopy is now a most powerful tool for identification, structure determination, and stereochemical investigation in the field of carbohydrate chemistry. For the purpose of the development of its application, a variety of α- and β-anomeric pairs of D-glucopyranosides[1,2], D-mannopyranosides, and L-rhamnopyranosides[3] was synthesized, and their glycosylation shifts (carbon-resonance displacement, for both the sugar and the aglycon moiety, on glycoside formation) were reported. With regard to the glycosylation shift for glycosides of aldopentoses, D-xylopyranosides would be expected to exhibit values similar to those of D-glucopyranosides, because the favored conformation must be exclusively the $^4C_1$ conformer. In contrast, further investigation is necessary for the glycosylation shift of L-arabinopyranosides, as, in this case, the conformation equilibrium, $^4C_1 \rightleftarrows {}^1C_4$, might depend upon the structure of the aglycon. The present paper deals with the synthesis, and an n.m.r. study, of anomeric pairs of alkyl L-arabinopyranosides.

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RESULTS AND DISCUSSION

Synthesis of L-*arabinopyranosides.* — α-L-Arabinopyranosides were synthesized according to the Koenigs–Knorr procedure for the synthesis of β-D-glucopyranosides[4], namely, condensation of 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide with an excess of an aglycon alcohol in the presence of $Hg(CN)_2$ at room temperature, followed by deacetylation.

The preparation of β-L-arabinopyranosides, which are 1,2-*cis*-glycosides, is known to be difficult. Several attempts according to the procedures used for the synthesis of α-D-glucopyranosides resulted in failure. However, the desired result was obtained by application of the Jennings procedure[5] for the preparation of α-D-xylopyranosides, namely, condensation of α-L-arabinopyranosyl chloride 2,3,4-tri(chlorosulfate) with an aglycon alcohol in the presence of Ag_2CO_3.

By means of the foregoing procedures, α- and β-L-arabinopyranosides of the following alcohols were prepared: methyl, propyl, and isopropyl alcohol, *trans*-4-*tert*-butylcyclohexanol, *tert*-butanol, and *d*- and *l*-menthol, respectively designated **1α, 1β; 2α, 2β; 3α, 3β; 4α, 4β; 5α, 5β; 6α, 6β**; and **7α, 7β**. Their physical constants are listed in Table I.

N.m.r. spectroscopy of the sugar moiety. — In the following discussion, all of the glycosides are pyranosides. By referring to the assignments of methyl α- and β-L-arabinosides reported by Bock and Pederson[6], identification of the carbon signals of the sugar moiety was established, as shown in Table II. As already observed for D-glucosides[1,2], D-mannosides, and L-rhamnosides[3], the anomeric carbon atom of

TABLE I

PHYSICAL CONSTANTS OF L-ARABINOPYRANOSIDES

L-*Arabino-side*	*State*[a]	*M.p. (degrees)*	*Crystallization solvent*	$[\alpha]_D^{25}$ *(degrees)*[b]	*Concentration*
1α	needles	131.5–132.5	ethanol	+4.7	1.07
1β	needles	171.0–173.0	ethanol	+239.4	2.18
2α	needles	121.5–123.0	hexane–chloroform	+3.8	0.93
2β	needles	145.0–146.5	hexane–chloroform	+192.0	0.90
3α	needles	124.0–126.0	benzene–acetone	+8.9	0.45
3β	needles	168.0–169.5	hexane–chloroform	+204.4	0.16
4α	needles	164.0–166.0	benzene–acetone	−8.3	1.08
4β	needles	232.0–234.0	chloroform	+154.8	0.29
5α	syrup			+31.8	1.89
5β	syrup			+197.9	0.25
6α	syrup			+60.3	2.47
6β	syrup			+137.5	0.47
7α	needles	142.0–143.0	hexane–chloroform	−52.7	5.34
7β	syrup			+85.3	0.34

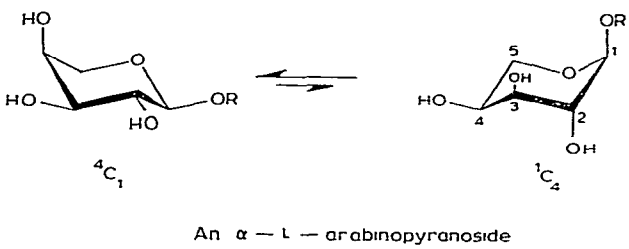
[a]All colorless [b]In pyridine.

TABLE II

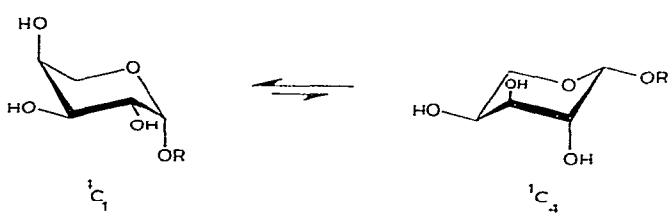
^{13}C CHEMICAL SHIFTS OF SUGAR MOIETIES

Compound	δ_{C-1}	$\Delta\delta_{C-1}$[a]	$^1J_{C-1,H-1}$ *(Hz)*	δ_{C-2}	δ_{C-3}	δ_{C-4}	δ_{C-5}
α-L-Arabinopyranose	99.2			73.9	74 7	69 3	66 3
1α	105.8	+6.6	158	72.1	74 2	69 0	66 5
2α	104.7	+5.5	156	72.1	74 1	69.1	66.5
3α	103.0	+3.8	157	72 1	74.1	69.3	66.6
4α	103.0	+3.8	158	72.1	74 2	69.1	66.4
5α	99.1	−0.1	157	72.1	74 2	69.2	66.3
β-L-Arabinopyranose	94.6			71 6[b]	71 3[b]	69.7	64 1
1β	102.1	+7.5	168	70 0[b]	70.5[b]	70.9[b]	63.9
2β	100.9	+6 3	166	70.1[b]	70.7[b]	71 0[b]	64.1
3β	99.0	+4.4	167	70 1[b]	70.6[b]	71.1[b]	64 1
4β	99.0	+4.4	168	70.1[b]	70 6[b]	71.0[b]	64.1
5β	95.1	+0 5	168	70 0[b]	70 7[b]	71 1[b]	63 8

[a] $\Delta\delta_{C-1}$ = δ_{C-1} of glycoside − δ_{C-1} of corresponding L-arabinose [b] These assignments may be reversed in each horizontal row.



An α — L — arabinopyranoside



A β — L — arabinopyranoside

L-arabinose is generally deshielded on glycosylation, in the decreasing order of methyl, other primary alcohols, and secondary alcohols. On glycosylation with a tertiary alcohol, as in **5**, the signal of C-1 remains almost unshifted. In contrast to that of C-1, the C-2 signal was found to be displaced slightly upfield on glycosylation.

Bock and Pedersen[6] reported that the $^4C_1$ conformer is preponderant for both methyl α- and β-L-arabinoside (**1α** and **1β**) in solution. For the L-arabinosides examined in the present study, sugar-carbon signals other than C-1 were found to be only slightly affected by change in structure of the aglycon, and the C-2, -3, -4, and -5

TABLE III

ANOMERIC PROTON, CHEMICAL SHIFTS AND COUPLING CONSTANTS

Aglycon alcohol of	*α-L-Arabinopyranoside*		*β-L-Arabinopyranoside*	
	δ_{H-1}	($^1J_{1,2}$, *Hz*)	δ_{H-1}	($^1J_{1,2}$, *Hz*)
1	4.58	(7)	5.00	(3)
2	4.62	(7)	5.23	(3)
3	4.64	(7)	5.24	(3)
4	4.70	(7)	5.50	(3)
5	4.72	(7)	5.46	(3)
6	4.70	(7)	5.40	(3)
7	4.71	(7)	5.29	(3)

signals appeared at almost the same positions as those of the corresponding methyl L-arabinosides; this indicates that these L-arabinosides have a similar conformational equilibrium for the glycosyl group, regardless of the structure of the aglycon. The direct-bonded, C–H coupling-constant of the C-1 signal ($^1J_{C\text{-}1,H\text{-}1}$) of hexo- and pento-pyranoses is known to be characteristic of the orientation of the anomeric proton[3]; $^1J_{C\text{-}1,H\text{-}1}$ of an equatorial, anomeric proton is observed to be nearly 165 Hz, whereas that of an axial one is[6] ~155 Hz. As shown in Tables II and VI, $^1J_{C\text{-}1\ H\text{-}1}$ values of the L-arabinosides in the present study were recorded in the range of 164–168 Hz (±2 Hz) for the β-anomeric series, and of 156–158 Hz (±2 Hz) for the α-anomeric series, respectively, demonstrating the preponderance of the $^4C_1$ conformer for each anomeric series, regardless of the structure of the aglycon. This finding was supported by the coupling constant between the anomeric proton and H-2; $J_{1,2}$ was consistently observed to be 3 Hz for the β-anomeric series, and 7 Hz for the α series. It is notable that the anomeric-proton signals of the β-anomeric series generally appear at lower field than those of their α-anomeric counterparts, namely, δ 5.0–5.5 for the β series and 4.6–4.7 for the α series, as shown in Table III.

Glycosylation shifts of the carbon signals of the aglycons. — As already observed for D-glucosylation, D-mannosylation, and L-rhamnosylation, a carbonyl carbon atom (designated a-C) is deshielded by ~7.0 p.p.m. on α-L-arabinosylation, except for the glycosides of the relatively hindered, secondary alcohols (*vide infra*). As regards β-L-arabinosylation, the magnitude of this downfield shift is a little smaller than that of the corresponding α-anomeric counterpart, as shown in Table IV, although this difference is less evident than for D-mannosylation and L-rhamnosylation[3].

It had already been found that signals due to the carbon atoms vicinal to a-C (designated b-C) are displaced upfield on glycosylation, and the magnitude of the shifts of two equivalent methyl or methylene groups of secondary-alcohol aglycons, such as those in **3** and **4** are significantly different from each other, depending upon the stereochemical relationship between the chirality of C-1 and that[1–3] of a-C. These novel, glycosylation shifts of b-C were also observed for L-arabinosylation,

TABLE IV

COMPARISON OF L-ARABINOSYLATION SHIFT[a] OF AGLYCON *a*-C, WITH CORRESPONDING D-GLUCOSYLATION SHIFT (IN PARENTHESES)

Aglycon alcohol of	*α-L-Arabinopyranoside (β-D-glucopyranoside)* $\Delta\delta_{a-C}$[b]	*β-L-Arabinopyranoside (α-D-glucopyranoside)* $\Delta\delta_{a-C}$[b]
1	+6.7 (+7.3)	+5.9 (+5.5)
2	+7.0 (+7.3)	+6.2 (+5.7)
3	+7.3 (+7.6)	+6.3 (+6.3)
4	+7.2 (+7.4)	+6.7 (+6.6)
5	+7.1 (+7.5)	+6.5 (+6.9)

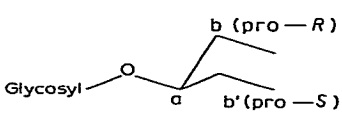
[a]In p.p.m. [b]δ_{a-C} of glycoside − δ_{a-C} of aglycon.

TABLE V

COMPARISON OF L-ARABINOSYLATION SHIFT[a] OF AGLYCON *b*-C AND *b'*-C, WITH CORRESPONDING D-GLUCOSYLATION SHIFT

Compound	*Moiety*	*Chir*[b]	$\Delta\delta_{b-C}$	$\Delta\delta_{b'-C}$	*Moiety*	*Chir*[b]	$\Delta\delta_{b-C}$	$\Delta\delta_{b-C}$
	α-D-Glc	*S*	−3.5		β-D-Glc	*R*	−3.3	
2	β-L-Ara	*S*	−3.4		α-L-Ara	*R*	−3.3	
	α-D-Glc	*S*	−3.9	−2.0	β-D-Glc	*R*	−1.8	−3.6
3	β-L-Ara	*S*	−3.9	−2.1	α-L-Ara	*R*	−1.8	−3.7
	α-D-Glc	*S*	−4.2	−2.4	β-D-Glc	*R*	−2.2	−3.9
4	β-L-Ara	*S*	−4.2	−2.3	α-L-Ara	*R*	−2.1	−3.9
	α-D-Glc	*S*	−2.8		β-D-Glc	*R*	−2.6	
5	β-L-Ara	*S*	−2.8		α-L-Ara	*R*	−2.6	

[a]In p.p.m. [b]Chirality of anomeric carbon atom as a free form [c]$\Delta\delta_{b-C\text{ or }b'-C} = \delta_{b-C\text{ or }b'-C}$ of glycoside − $\delta_{b-C\text{ or }b'-C}$ of aglycon.



being identified in analogy to D-glucosylation, as summarized in Table V. On α-L-arabinosylation [the chirality of C-1 is (*R*), as a free form], pro-(*S*)-b-C (b'-C) is always more shielded than pro-(*R*)-C (b-C), whereas, on β-L-arabinosylation [the chirality of C-1 is (*S*) as a free form], b-C is more shielded than b'-C.

Glycosylation shifts for relatively hindered secondary alcohols. — As already reported for D-glucosides[1,2], D-mannosides, and L-rhamnosides[3], the glycosylation shifts both of C-1 and of the aglycon signals of glycosides of relatively hindered, secondary alcohols, such as **6**, **7**, and a 3β-hydroxyl group of triterpenes, are charac-

TABLE VI

^{13}C CHEMICAL SHIFTS OF SUGAR MOIETIES OF L-ARABINOPYRANOSIDES (**6** AND **7**) OF *d*- AND *l*-MENTHOL

Compound	δ_{C-1}	$\Delta\delta_{C-1}$[a]	$^1J_{C-1\ H-1}$ (*Hz*)	δ_{C-2}	δ_{C-3}	δ_{C-4}	δ_{C-5}
6α	106.3	+7.1	156	72.6	74.3	69.1	66.4
7α	101.4	−2.2	158	72.2	74.4	69.2	66.6
6β	96.8	+2.2	166	70.0[b]	70.6[b]	71.2[b]	64.6
7β	102.8	+8.2	164	70.0[b]	71.0[b]	71.0[b]	64.4

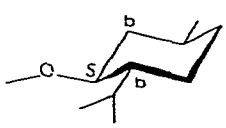
[a] $\Delta\delta_{C-1}$ = δ_{C-1} of glycoside − δ_{C-1} of corresponding L-arabinose [b] These assignments may be reversed in each horizontal row.

TABLE VII

COMPARISON OF L-ARABINOSYLATION SHIFT[a] OF a-C, b-C, AND b′-C OF GLYCOSIDES (**6** AND **7**) OF *d*- AND *l*-MENTHOL, WITH THE CORRESPONDING D-GLUCOSYLATION SHIFT (IN PARENTHESES)

Compound	α-L-*Arabinopyranoside* (β-D-*glucopyranoside*)			β-L-*Arabinopyranoside* (α-D-*glucopyranoside*)		
	$\Delta\delta_{a-C}$	$\Delta\delta_{b-C}$	$\Delta\delta_{b'-C}$	$\Delta\delta_{a-C}$	$\Delta\delta_{b-C}$	$\Delta\delta_{b'-C}$
	+7.2	−2.1	−3.9	+6.7	−4.2	−2.3
4	(+7.4)	(−2.2)	(−3.9)	(+6.6)	(−4.2)	(−2.4)
	+10.1	−1.8	−1.3	+5.0	−5.7	−2.1
6	(+10.5)	(−1.8)	(−1.1)	(+4.7)	(−5.9)	(−2.1)
	+5.9	−2.3	−5.3	+10.2	−1.2	−2.4
7	(+6.4)	(−2.1)	(−4.9)	(+10.4)	(−1.3)	(−2.6)

[a] In p.p.m. [b] $\Delta\delta_{a-C\ b-C\ or\ b'-C}$ = $\delta_{a-C\ b-C,\ or\ b'-C}$ of glycoside − $\delta_{a-\ b-,\ or\ b'-C}$ of aglycon



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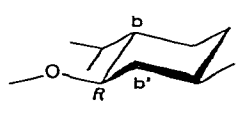

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teristically different from those of the aforementioned glycosides of less hindered, secondary alcohols, because of the change of the orientation of the glycosyl linkage[7]. The degree of this "anomalous" shift was found to depend upon the combination of the chiralities of C-1 and a-C. In the present study, the glycosylation shifts of L-arabinosides **6** and **7** were demonstrated to be quite similar to those for the D-glucosides. Combination of α-L-arabinose (C-1: (*R*)] with the aglycan [a-C: (*S*)] of **6** as well as that of β-L-arabinose (C-1: (*S*)] with that [a-C: (*R*)] of **7** resulted in a more remarkable, downfield displacement of signals of both C-1 and a-C than those of the corresponding L-arabinoside, such as **4**, of the less hindered secondary alcohols.

In contrast, on α-L-arabinosylation to give **7α**, and β-L-arabinosylation to give **6β**, both C-1 and a-C were found to be less deshielded than those for the corresponding L-arabinosylation of the less-hindered, secondary alcohols

With regard to the sugar-carbon resonances other than that of C-1, the spectra of **6α**, **6β**, **7α**, and **7β** exhibited the C-2, -3, -4, and -5 signals at almost the same positions as those of the corresponding L-arabinosides of the less-hindered alcohols, indicating the existence of a similar, conformational equilibrium for the glycosyl group; this conclusion was supported by the $^1J_{C\text{-}1,H\text{-}1}$ and $J_{1,2}$ values (see Table III).

EXPERIMENTAL

Synthesis of α-L-arabinopyranosides. — A mixture of 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide (340 mg), $Hg(CN)_2$ (300 mg), and an excess of the aglycon alcohol in anhydrous CH_3CN (10 mL) was stirred for 10 h at room temperature, diluted with $CHCl_3$, and the precipitate removed by filtration. The filtrate was evaporated to dryness, and the residue was deacetylated with 5% KOH in MeOH (30 mL) by standing for 30 min at room temperature. After de-ionizing with Amberlite MB-3, the solution was evaporated to dryness. The residue was chromatographed on silica gel by eluting with C_6H_6–acetone (gradient elution, from a ratio of 3:1 to 1:2), to give an α-L-arabinopyranoside. The elemental analysis of each glycoside was consistent with the molecular formula expected. The physical constants of each glycoside are summarized in Table I. The yields of α-L-arabinosides were ~90% (from the glycosyl bromide).

Synthesis of β-L-arabinopyranosides. — A mixture of α-L-arabinopyranosyl chloride 2,3,4-tri(chlorosulfate)[5] (450 mg), Ag_2CO_3 (1.39 g), and an excess of the aglycon alcohol in $CHCl_3$ (4 mL) was stirred for 10 h at room temperature. After dilution of the mixture with $CHCl_3$ (30 mL), followed by removal of the precipitate by filtration, the filtrate was evaporated to dryness. The residue was de(chlorosulfated) with NaI in acetone solution in the presence of $BaCO_3$, according to the procedure reported by Jennings and Jones[8]. The crude product, which consisted of the α and β anomers, was separated by chromatography on a column of silica gel by eluting with the following solvent systems: 60:10:1 $CHCl_3$–MeOH–H_2O for **1β**, and 70:10:1 for **2β** and **3β**, 10:1 $CHCl_3$–MeOH for **5**, and 15:1 for **4β** and **6β**. The separation of **7α** from **7β** was achieved as follows: the reaction product was chromatographed on silica gel by eluting with 15:1 $CHCl_3$–MeOH, to give a mixture of **7α** and **7β** which was acetylated with 1:1 Ac_2O–C_5H_5N for 10 h at room temperature. After processing in the usual way, the resulting mixture of acetates was subjected to preparative, thin-layer chromatography on silica gel (solvent, $CHCl_3$), which effectuated the separation of the peracetates of **7α** and **7β**. The acetate of **7β** was deacetylated with 5% methanolic KOH by standing for 30 min at room temperature, to give **7β**.

The elemental analysis of each glycoside was consistent with the molecular formula expected, and the physical constants are listed in Table I. The yields of the β-L-arabinosides from the glycosyl chloride were nearly 10%.

N.m.r.-spectral measurements. — Spectra were recorded with a JEOL JNM-PFT-100 spectrometer at 25° for 0.06–2.0M solutions in C_5D_5N, at 25.15 MHz for ^{13}C, and 100 MHz for ^{1}H, spectra. For proton-decoupled, F.t. measurements, spectral width: 4 kHz, pulse flipping-angle: 90°, acquisition time: 0.4 s, number of data points: 4096, transient time: 1–2 s, number of transients: 700–6,000. Conditions for $^{1}J_{C\text{-}1,H\text{-}1}$ measurements by gated decoupling, spectral width: 4 kHz, pulse flipping-angle: 90°, acquisition time: 0.2 s, number of data points: 2,000–40,000, computer-limited resolution: 2 Hz.

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