NEW SYNTHESES AND ^{13}C NMR SPECTRA OF THE METHYL ETHERS OF METHYL α-L-ARABINOPYRANOSIDE

E. V. Evtushenko and Yu. S. Ovodov

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A method is described for obtaining the methyl ethers of methyl α-L-arabinopyranoside that is based on the partial methylation of methyl α-L-arabinopyranoside followed by the liquid chromatography of the methyl ethers. The ^{13}C NMR spectra of the methyl ethers of methyl α-L-arabinopyranoside have been studied.

Syntheses of the methyl ethers of D- and L-arabinose, which are necessary standards in the structural study of polysaccharides, glycosides, and oligosaccharides were described long ago [1] but they are fairly laborious, with many stages. Alternative syntheses of the methyl ethers of L-arabinose that have been proposed recently [2] include a smaller number of stages but are still laborious. An approach based on the partial methylation of methyl glycosides followed by chromatography of the methylated sugars has proved to be exceptionally simple and useful for obtaining individual methyl ethers of monosaccharides. Syntheses of the methyl ethers of D-mannose [3, 4], D-xylose [5], L-rhamnose [6, 7], D-galactose [8], and D-glucose [9, 10] based on this approach have been described previously. The use of preparative GLC for the separation of mixtures of methylated sugars provides yields of the individual methyl ethers of up to 100 mg per cycle [5, 6]. The use of preparative liquid chromatography on silica gel gives yields of individual methyl ethers at the gram level [7, 9, 10]. An attempt was made previously [11] to synthesize methyl ethers of D-arabinose by the partial methylation of methyl β-D-arabinofuranoside and of methyl β-D-arabinopyranoside followed by thin-layer chromatography and paper electrophoresis of the mixtures of the methylated sugars formed. However, the yields of the individual ethers were fairly low.

In the present paper we describe a simple method of obtaining all the individual methyl ethers of methyl α-L-arabinopyranoside (I) based on the liquid chromatography on silica gel of the product of the partial methylation of (I). Partial methylation of (I) with methyl iodide and silver oxide gives a low yield of the 4-O-methyl ether [12], which is connected with the low reactivity of the axial hydroxyl under the conditions of this reaction. Consequently, to obtain a complete set of methyl ethers we used the partial methylation of methyl α-L-arabinopyranoside with dimethyl sulfate in alkali, leading to a more uniform distribution of the substituents. In view of the fact that the acetates of the 2,3- and 2,4-di-O-methyl ethers issue as a single peak under the conditions of GLC on a polyester phase, for the analysis of the methyl esters we used GLC of the unacetylated methyl ethers. In this case, complete separation of all the methyl ethers was observed. The considerable differences between the methyl ethers with respect to mobility in a thin layer has served as a basis for the use of liquid chromatography on silica gel for the preparative separation of the mixture of the methyl ethers of (I).

Below we give the R_f and R_T values of the methyl ethers of methyl α-L-arabinopyranoside (* — retention time relative to methyl 2-O-methyl-α-L-arabinopyranoside, 5.7 min; ** — retention time of the acetates of the methyl ethers):

	Position of the methyl groups							
	2	*3*	*4*	*2,3*	*2,4*	*3,4*	*2,3,4*	—
R_f	0,34	0,27	0,29	0,64	0.75	0,55	0,84	0,11
R_T^*	1.00	1,68	2,21	0,47	0.63	1,21	0,32	—
R_T^{**}	1.26	1,84	1,68	0,58	0.58	1,05	0,32	3.26

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When 7 g of a mixture of the methyl ethers of (I) in one portion was charged onto a column (45 × 3 cm) of silica gel, all the methyl ethers were separated. The total yield of individual methyl ethers was ≈80%. The yields and properties of the methyl ethers of (I) obtained (the methyl ethers were identified by comparison with authentic samples by the GLC method) were:

Positions of the methyl groups	Yield, g	mp, °C	$[\alpha]_D^{20}$, deg
2	1,9	93–94	−1,2
3	0,3	67–68	+24,0
4	0,2	75–76	+15,5
2,3	0,8	Syrup	+7,2
2,4	1,1	89–90	+12,3
3,4	0,3	44–46	+35,4
2,3,4	0,9	42–44	+19,5

^{13}C NMR spectroscopy is widely used for the structural study of oligo- and polysaccharides, but its use is usually preceded by the study of model compounds [13]. As the latter, it is customary to use the methyl ethers of methyl glycosides.

The assignment of the signals in the spectra of the monomethyl ethers was carried out by comparing them with the spectrum of (I) described previously [14], and those in the spectra of the di-O-methyl ethers by comparison of the spectra of the monomethyl ethers with allowance for the known effects of methylation [13]. The signals of the carbon atoms in the ^{13}C NMR spectra of the methyl ethers of methyl α-L-arabinopyranoside were as follows (δ, ppm):

Positions of the methyl groups	C-1	C-2	C-3	C-4	C-5	MeO-1	MeO-2	MeO-3	MeO-4
—	104,8	71,4	73,1	69,0	66,8	57,7			
2	104,3	81,1	72,3	68,8	66,3	57,7	60,4		
3	104,8	70,3	82,3	64,8	66,9	57,8		57,1	
4	104,6	71,7	72,7	78,5	62,7	57,7			57,7
2,3	104,3	79,9	81,6	64,8	66,4	57,2	60,6	57,0	
2,4	104,3	81,5	72,0	78,5	62,4	57,7	60,8		57,7
3,4	104,6	70,7	81,8	74,3	62,5	57,7		57,2	57,2
2,3,4	104,3	80,3	81,2	74,5	62,2	57,6	60,7	57,2	57,2

The following changes in the chemical shifts of the signals of the C atoms (δ, ppm) in the ^{13}C NMR spectra on the methylation of methyl α-L-arabinopyranoside and its monomethyl ethers are observed:

Transition	C-1	C-2	C-3	C-4	C-5
1→2	−0,5	+9,7	−0,8	−0,2	−0,5
1→3	0	−1,1	+9,2	−4,2	+0,1
1→4	−0,2	+0,3	−0,4	+9,5	−4,1
2→2,3	0	−1,2	+9,3	−4,0	+0,1
2→2,4	0	+0,4	−0,3	+9,7	−3,9
3→2,3	−0,5	+9,6	−0,7	0	−0,5
3→3,4	−0,2	+0,4	−0,5	+9,5	−4,4
4→2,4	−0,3	+9,8	−0,7	0	−0,3
4→3,4	0	−1,0	+9,1	−4,2	−0,2

From the facts given above, it can be seen that:

1) the magnitude of the α-effect amounts to 9.1-9.8 ppm;

2) in all cases, the β-effect is shown in an upfield shift of the signal. On the methylation of an equatorial hydroxy group, the β-effect on the neighboring carbon atoms amounts to 0.3-1.2 ppm if this atom bears an equatorial substituent, and 4.0-4.2 ppm if it bears an axial substituent. On the methylation of the axial hydroxyl at C-4 the β-effect amounts to 0.3-0.5 ppm for C3 and to 3.9-4.1 ppm for C5; and

3) the magnitudes of the γ-effects lie in the range of −0.2 to +0.4 ppm.

These results are in harmony with the known laws of methylation [13] and practically coincide with changes in the chemical shifts on the methylation of α-L-arabinose [15]. Small differences are observed between the changes in the chemical shifts for the 2,3-di-O-methyl ethers of methyl α-L-arabinopyranoside and of α-L-arabinose.

EXPERIMENTAL

Melting points were measured on a Boëtius instrument. Specific rotations were determined on a Perkin-Elmer M 141 automatic polarimeter. Chloroform was used as solvent. ^{13}C NMR spectra were obtained on a Bruker UX-90E spectrometer. Chemical shifts are given in ppm and were measured relative to CH_3OH as standard, taking δ_{CH_3OH} = 49.6 ppm. D_2O was used as solvent. TLC was performed on L 5/40 μ silica gel (Chemapol) in the chloroform—methanol (95:5) system. Silica gel L 100-160 μ (Chemapol) was used for column chromatography. Elution was performed with a gradient of methanol in chloroform, 50-ml fractions being taken. GLC was carried out on a Tsvet-106 instrument fitted with a flame-ionization detector and double column (200 × 0.3 cm). The packing was 1.5% of NPGS on Chromaton N-AW-HMDS (0.125-0.160 mm) (Chemapol). The rate of flow of argon was 60 ml/min. The temperature of the thermostat was 170°C.

Synthesis of the Methyl Ethers of (I). With stirring by means of a magnetic stirrer, dimethyl sulfate (25 ml) and a 30% solution of caustic soda (42 ml) were added over 2 h to a solution of 10 g of (I) in 15 ml of water. The solution was heated in the water bath for 0.5 h and it was then cooled and was deionized with ion-exchange resins. After evaporation of the solution the yield of faintly colored syrup amounted to 9.5 g.

SUMMARY

A method is described for obtaining methyl esters of methyl α-L-arabinopyranoside that is based on the partial methylation of methyl α-L-arabinopyranoside followed by the liquid chromatography of the methyl ethers. The ^{13}C NMR spectra of the methyl ethers of methyl α-L-arabinopyranoside has been studied.

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