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SYNTHESIS OF METHYL ETHERS OF METHYL (METHYL α-D-MANNOPYRANOSID)-URONATE

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Methyl (methyl α-D-mannopyranosid)uronate (I) has been obtained by the catalytic oxidation of methyl α-D-mannopyranoside with oxygen in the presence of platinum carbon with a yield of 20%. The partial methylation of (I) and preparative column chromatography on silica gel has provided a convenient method of obtaining all the methyl ethers of (I) in the individual state.

The methyl ethers of D-mannuronic acid are necessary in structural investigations of polysaccharides containing D-mannuronic acid residues. Directed syntheses of the methyl ethers of methyl (methyl α-D-mannopyranosid)uronate (I) described previously [1, 2] are fairly laborious with many stages.

In the present work we have used an approach that we have suggested previously [3] for obtaining methyl ethers of methyl (methyl α-D-glucopyranosid)uronate. The initial (I) was obtained with a yield of 20% by the catalytic oxidation of methyl α-mannopyranoside with oxygen in the presence of platinum on carbon followed by treatment with methanol. The mixture of methyl ethers of (I) obtained after the partial methylation of (I) was separated by liquid column chromatography into fractions with the same degree of substitution and, partly,

Position of the methyl groups	R_j	R_T, NPGS	R^*_T, NPGS	R^*_T, QF-1
—	0,08	—	2,40	2,37
2	0,16	2,00	1,96	1,70
3	0,16	1,74	1,36	1,00 (8,7 min)
4	0,23	2,29	1,36	1,30
2,3	0,31	1,00 (8,4 min)	1,00 (9,3 min)	0,74
2,4	0,38	0,74	0,85	0,67
3,4	1,36	0,64	0,50	0,33
2,3,4	0,51	0,32	0,36	0,22

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TABLE 1. ^{1}H Chemical Shifts and Spin–Spin Coupling Constants for Acetates of the Methyl Ethers of Methyl (Methyl α-D-Mannopyranosid)uronate

Protons	Positions of the methyl groups							
	–	2	3	4	2,3	2,4	3,4	2, 3, 4
H-1	4,84 d	4,92 d	4,86 d	4,75 d	4,97 d	4,87 d	4,77 d	4,88 d
H-2	5,26 t	3,63 t	5,30 m	5,24 m	3,52 m	3,61 t	5,23 t	3,55 m
H-3	5,40 m	5,30 dd	3,70 dd	5,24 m	3,68 dd	5,19 dd	3,60 dd	3,55 m
H-4	5,40 m	5,4 t	5,30 m	3,85 t	5,42 t	3,78 t	3,71 t	3,79 t
H-5	4,32 d	4,28 d	4,23 d	4,19 d	4,28 d	4,17 d	4,08 d	4,10 d
MeO	3,46 s	3,47 s (2)	3,37 s	3,44 s	3,44 s	3,47 s (2)	3,42 s	3,45 s
	3,78 s	3,77	3,45 s	3,46 s	3,50 s	3,82 s (2)	(2)	3,48 s
			3,77 s	3,85 s	3,53 s		3,51 s	3,50 s (2)
					3,77 s		3,83 s	3,80 s
AcO	2,02 s	2,05 s	2,10 s	2,07 s	2,10 s	2,15 s	2,15 s	
	2,06 s	2,11 s	2,16 s	2,16 s				
	2,17 s							
$J_{1,2}$	2,2	2,2	2,5	2,1	2,7	2,7	2,0	2,7
$J_{2,3}$	2,6	2,7	3,0	–	3,2	2,9	2,7	–
$J_{3,4}$	–	8,2	8,5	–	7,7	8,3	8,5	–
$J_{4,5}$	9,5	7,9	8,7	9,4	7,5	8,3	8,5	7,5

within the fractions. The R_f and R_T values of the methyl ethers are given on the previous page (* – values for the acetates).

The differences in the chromatographic mobilities of the methyl ethers of (I) in a thin layer enable us to obtain in the individual state with the aid of preparative liquid chromatography the 2,3,4-tri-O-methyl ether of (I) and the 2,3-di-O- and 4-O-methyl ethers of (I). Mixtures of the 2,4- and 3,4-di-O-methyl ethers of (I) and of the 2- and 3-O-methyl ethers of (I) were separated by liquid chromatography on silica gel in the form of their acetyl derivatives with practically quantitative yields. The separation was monitored with the aid of GLC. The ^{1}H NMR spectroscopy of their acetates was used to identify the methyl ethers of (I) (Table 1).

EXPERIMENTAL

Melting points were measured in a Boëtius instrument. Specific rotations were determined on a Perkin-Elmer M141 automatic polarimeter. ^{1}H NMR spectra were obtained on a Bruker WM-250 spectrometer in $CDCl_3$ solution with TMS as internal standard. TLC was performed on silica gel L (5-40 μ, Chemapol) in the hexane–acetone (12:8) system. Silica gel L (65-100 μ, Chemopol) was used for column chromatography. Analytical gas chromatography was performed on a Tsvet-106 instrument fitted with a flame-ionization detector and double columns (0.4 × 200 cm). The liquid phases used were 1.5% of NPGS and 2% of QF1 on Chromaton N-AW-HMDS (0.125-0.160 mm, Chemopol). The rate of flow of argon was 60 ml/min. The thermostat temperature for the NPGS column was 190°C and for the QF-1 column 170°C. Acetylation was performed with acetic anhydride in pyridine.

Methyl (Methyl α-D-Mannopyranosid)uronate [1]. Methyl α-D-mannopyranoside (10 g) was treated as described previously [3]. This gave (I) with a yield of 2.3 g (20%), syrup $[\alpha]_D^{20}$ +60.3° (c 0.8; methanol). The acetate of (I) was a syrup with $[\alpha]_D^{20}$ +109.3° (c 0.5; chloroform).

Partial Methylation of (I). Compound (I) (2.0 g) was dissolved in methanol (20 ml), and then silver oxide (4 g) and methyl iodide (4 ml) were added and the mixture was stirred in the dark with a magnetic stirrer for 1 h. It was filtered and the filtrate was evaporated to give 2.2 g of a mixture of methyl ethers in the form of a syrup.

Separation of the Methyl Ethers of (I). The mixture of methyl ethers of (I) (2.0 g) was deposited on a column (2 × 30 cm) of silica gel and was eluted with a gradient of acetone in hexane. This gave: 1) 0.2 g of the 2,3,4-Tri-O-methyl ether, syrup $[\alpha]_D^{20}$ +57.9° (c 1.0; methanol); 2) 0.21 g of the 2,3-di-O-methyl ether of (I), mp 94-95°C, $[\alpha]_D^{20}$ +58.0° (c 1.0; methanol). The acetate of the 2,3-di-O-methyl ether of (I) was a syrup with $[\alpha]_D^{20}$ +50.4 (c 0.9; chloroform); 3) 0.39 g of the 4-O-methyl ether of (I), mp 109-110°C, $[\alpha]_D^{20}$ +85.3° (methanol). The acetate of the 4-O-methyl ether had the form of a syrup with $[\alpha]_D^{20}$ +41.2° (c 1.9; chloroform); 4) 0.35 g of a mixture of the 2,4- and 3,4-di-O-methyl

ethers; and 5) 0.43 g of a mixture of the 2- and 3-O-methyl ethers. The mixture of di-O-methyl ethers (0.30 g) was acetylated and chromatographed on a column of silica gel (1.6 × 30 cm), using a gradient of ethyl acetate in hexane. The yield of the acetate of the 3,4-di-O-methyl ether of (I) was 0.15 g; syrup, $[\alpha]_D^{20}$ +35.9° (c 0.7; chloroform); R_f 0.56 (hexane–ethyl acetate (1:1)). The yield of the acetate of the 2,4-di-O-methyl ether was 0.14 g; syrup $[\alpha]_D^{20}$ +50.0° (c 0.6; chloroform); R_f 0.45 (hexane–ethyl acetate (1:1)).

The mixture of 2- and 3-O-methyl ethers of (I) (0.30 g) was acetylated and was chromatographed on a column of silica gel (1.6 × 30 cm) using a gradient of dioxane in hexane. The load on the column was 0.36 g of the mixture. The yield of the acetate of the 2-O-methyl ether of (I) was 0.08 g, mp 101-102°C, $[\alpha]_D^{20}$ +55.6° (c 0.8; chloroform); R_f 0.29 (dioxane–hexane (1:4)). The yield of the acetate of the 3-O-methyl ether of (I) was 0.27 g; syrup, $[\alpha]_D^{20}$ +30.7° (c 1.8; chloroform); R_f 0.23 (dioxane–hexane (1:4)).

SUMMARY

A convenient method is proposed for the synthesis of all the methyl ethers of methyl (methyl α-D-mannopyranosid)uronate, which consists in the catalytic oxidation of the initial glycoside followed by partial methylation and the preparative separation of the methyl ethers with the aid of chromatography on silica gel.

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POLYUNSATURATED FATTY ACIDS OF THE α-LINOLENIC SERIES FROM INSULIN PRODUCTION WASTES

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The following polyenic acids has been isolated from insulin production waste and have been determined quantitatively: eicosa-5Z,8Z,11Z,14Z-pentaenoic, docosa-7Z,10Z,13Z,16Z,19Z-pentaenoic, and docosa-4Z,7Z,10Z,13Z,16Z,19Z-hexaenoic acids. They were identified by PMR and ^{13}C NMR.

Higher fatty acids (HFAs) play an important physiological role in the normal vital activity of the organism. The greatest interest among them is presented by the polyunsaturated fatty acids (PUFAs) containing 20 and more carbon atoms in the chain and having more than two double bonds. One of the main functions of the PUFAs is participation in the synthesis of the prostaglandins – biologically active substances which already, today, are being used in obstetrics, gynecology, and veterinary medicine and have a great future [1-3]. PUFAs are also of independent interest, in particular, as agents for the treatment and prevention of a number of cardiovascular diseases. Thus, PUFAs of the ω-3 type and, namely, the isocosapentaenoic (I), docosapentaenoic (II), and docosahexaenoic (III) acids may prove to be promising for the prophylasis and treatment of atherosclerosis and myocardial infarct [4-8]; (I) [9-12] and (III) [13] for preventing the aggregation of thrombocytes and for the rapid dispersion of thrombi that have formed; and (I) [10, 14] and compounds including (I) and (III) with cyclodextrin [15] for lowering the cholesterol level in the blood serum.

The richest sources of PUFAs of the ω-3 type are fats of marine origin [16-18].

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