METHYLATION OF METHYL 6-O-TRITYL-α-D-MANNOPYRANOSIDE — A NEW ROUTE TO THE SYNTHESIS OF SOME METHYL ETHERS OF D-MANNOSE

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The partial methylation of methyl 6-O-trityl-α-D-mannopyranoside by Kuhn's method (BaO, $Ba(OH)_2 \cdot 8H_2O$, CH_3I) in dimethylformamide and dimethyl sulfoxide has been studied. Simple methods are proposed for obtaining the 3- and 4-mono-O-, the 2,3-, the 2,4- and 3,4-di-O-, and the 2,3,4-tri-O-methyl ethers of methyl 6-O-trityl-α-D-mannopyranoside.

The directed synthesis of methyl esters of D-mannose, which is used to determine the structures of glycosides and oligo- and polysaccharides containing D-mannose residues, presents certain difficulties in comparison with other monosaccharides.

Recently, considerable interest has been shown in methods for the selective methylation of carbohydrates and their derivatives. In particular, the partial methylation of methyl α-D-mannopyranoside has been studied [1] and the distribution of the methyl esters on methylation by the methods of Haworth, Kuhn, and Hakomori has been established. However, in spite of the large set of methyl ethers that can be obtained, the methylation of sugars and their glycosides is rarely used for preparative purposes because of the complexity of the distribution of the large number of products.

In view of this, interest is presented by the selective methylation of derivatives of methyl glycosides containing two or three free hydroxy groups. In this case, the reaction mixture is fairly simple, and the required compounds can be isolated chromatographically or by crystallization.

We have studied the methylation of methyl 6-O-trityl-α-D-mannopyranoside (I) by Kuhn's method (BaO, $Ba(OH)_2 \cdot 8H_2O$, CH_3I) in dimethylformamide (DMFA) and dimethyl sulfoxide (DMSO).

The methylation of (I) with two equivalents of methyl iodide (MeI) in DMFA gave a 45% yield of a mixture of mono-O-methyl ethers consisting of the 3- and 4-O-methyl ethers of (I) in a ratio of 5:1 which was separated chromatographically after acetylation. In addition, methyl 2,4-di-O-acetyl-3-O-methyl-6-O-trityl-α-D-mannopyranoside was obtained in the pure form by crystallizing an acetylated mixture of the 3'- and 4'-O-methyl ethers of (I) with a total yield of 30%. The methylation of (I) with three equivalents of MeI in DMFA gave 35% of methyl 2,3,4-tri-O-methyl-6-O-trityl-α-D-mannopyranoside and 37% of a mixture of diethers consisting of the 2,3-, 2,4-, and 3,4-di-O-methyl ethers of (I) in a ratio of 11:1:2. Methyl 4-O-acetyl-2,3-di-O-methyl-6-O-trityl-α-D-mannopyranoside was obtained by crystallizing an acetylated mixture of the diethers with an overall yield of 25%.

When (I) was treated with two equivalents of MeI in DMSO, 26% of methyl 2,3,4-tri-O-methyl-6-O-trityl-α-D-mannopyranoside and 48% of a mixture of the 2,3-, 2,4-, and 3,4-di-O-methyl ethers of (I) in a ratio of 1:3:2, respectively, was obtained. By chromatographic separation it was possible to obtain pure methyl 3,4-di-O-methyl-6-O-trityl-α-D-mannopyranoside and a mixture of the 2,3- and 2,4-di-O-methyl ethers of (I). The chromatographic separation of an acetylated mixture of the 2,3- and 2,4-di-O-methyl ethers of (I) enabled methyl 4-O-acetyl-2,3-di-O-methyl-6-O-trityl-α-D-mannopyranoside and methyl 3-O-acetyl-2,4-di-O-methyl-6-O-trityl-α-D-mannopyranoside to be obtained.

The complete compositions of the reaction mixtures are given in Table 1. It follows from these results that when (I) is methylated in DMFA its 2,3-di-O-methyl ether is formed predominantly, while the use of DMSO as a solvent leads to the formation of the 2,4-di-O-methyl ether of (I) as the main product. Furthermore, methylation in DMFA takes place more selectively than in DMSO both in the ratio of mono-, di-, and triethers and in those of the individual

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TABLE 1. Results of the Methylation of Methyl 6-O-Trityl-α-D-mannopyranoside (I) in DMFA and DMSO*

Compound	Yield, %			
	2 eq. of MeI	3 eq. of MeI	1 eq. of MeI	2 eq. of MeI
3-O-methyl-(I)	38	4	19	10
4-O-methyl-(I)	7	0	13	7
2,3-di-O-methyl-(I)	11	29	6	8
2,4-di-O-methyl-(I)	7	3	18	25
3,4-di-O-methyl-(I)	8	6	7	15
2,3,4-tri-O-methyl-(I)	8	35	5	26

*As in Russian original The first two columns under "Yield" presumably refer to DMFA, and the second two columns to DMSO.

mono- and diethers. However, methylation in DMFA takes place more slowly and incompletely, which gives rise to the necessity for using a larger amount of MeI, than for the case of DMSO, to achieve the same degree of methylation.

The positions of the methoxy groups in the methyl 3- and 4-O-methyl-6-O-trityl-α-D-mannopyranoside were shown after their detritylation by comparison with previously known methyl 2-, 3-, and 4-O-methyl-α-D-mannopyranosides. Since this was the first time that methyl 4-O-methyl-α-D-mannopyranoside had been obtained in the crystalline state and its specific rotation exceeded the values given in the literature, for additional confirmation it was synthesized independently from methyl 2,3-di-O-benzyl-6-O-trityl-α-D-mannopyranoside [2]. The two compounds were identical with respect to melting points, specific rotations, and IR spectra.

EXPERIMENTAL

Melting points were determined on a heated stage (and are uncorrected), specific rotations on a SM-1 polarimeter (Na lamp), and refractive indices on a IRF-22 refractometer. The specific rotations and refractive indices were determined at 20°C. Column chromatography was performed on silica gel L 100-250 μm, and thin-layer chromatography on Woelm TLC silica gel. The following solvent systems were used: 1) benzene–acetone (15:1); 2) benzene–acetone (5:1); 3) benzene–ethyl acetate (10:1); 4) carbon tetrachloride–benzene–acetone (6:3:1); and 5) benzene–acetone (1:1). The spots of the sugars on the plates were visualized with the aid of a 5-10% ethanolic solution of sulfuric acid, followed by heating. The microanalyses of the compounds synthesized coincided with the calculated figures.

General Method of Methylation. Over 10 h, with stirring, 1.1, 2.2, or 3.3 equivalents of methyl iodide was added to the solution of 5 g of methyl 6-O-trityl-α-D-mannopyranoside in 25 ml of DMFA or DMSO containing 6 g of barium oxide and 2.5 g of barium hydroxide octahydrate. The course of the reaction was monitored in system 2. The reaction mixture was stirred for another 10 h and was then diluted with a fivefold amount of benzene, the benzene extract was separated off, and the residue was washed twice with 50 ml of benzene. The combined benzene extracts were washed with water, with dilute acetic acid, with water, and with sodium bicarbonate solution, and were dried with anhydrous sodium sulfate and evaporated to dryness. The result of methylation, which are summarized in Table 1, were obtained by separating the reaction mixtures by column chromatograpy on silica gel in solvent systems 1 and 2. The 3- and 4-O-methyl, and also the 2,3- and 2,4-di-O-methyl ethers of (I) which were not separated in this way, were acetylated with acetic anhydride in pyridine and separated by column chromatography in solvent system 1 or 3 and system 1 or 4, respectively.

Methyl 2,4-Di-O-acetyl-3-O-methyl-6-O-trityl-α-D-mannopyranoside (II). The methylation of 5 g of (I) in DMFA with 2.2 equivalents of MeI and the chromatographic separation of the reaction products on SiO_2 in solvent system 2 gave 2.3 g of a mixture of monoethers. Acetylation of this mixture with acetic anhydride in pyridine and recrystallization of the mixture of acetates from 20 ml of ethanol–acetone (5:1) gave 1.75 g of pure (II) with mp 174-177°C, $[\alpha]_D$ +6.5° (c 1.5; chloroform).

Methyl 3-O-Methyl-6-O-trityl-α-D-mannopyranoside (III). The Zemplen deacetylation of (II) gave (III) with mp 135-136°C, (ethanol), $[\alpha]_D$ +24° (c 2.4; chloroform).

Methyl 3-O-Methyl-α-D-mannopyranoside (IV). The detritylation of (III) with 60% acetic acid led to (IV), $[\alpha]_D$ + 61°C (c 2.8; chloroform), n_D 1.478. According to the literature [3]: $[\alpha]_D$ + 59.6°.

Methyl 2,3-Di-O-acetyl-4-O-methyl-6-O-trityl-α-D-mannopyranoside (V). The mother solution after the isolation of (II) was evaporated to dryness, and the (II) and (V) present in the residue were separated chromatographically on SiO_2 with elution by solvent system 1 or 3. This gave 0.35 g of (V) and 0.35 g of (II). After (V) had been recrystallized from ethanol it had mp 153-153.5°C, $[\alpha]_D$ + 28° (c 2.3; chloroform).

Methyl 4-O-methyl-α-D-mannopyranoside (VI). The deacetylation of (V) followed by detritylation gave (VI). Treatment on SiO_2 in solvent system 5 gave pure (VI) with mp 100-101°C (ether), $[\alpha]_D$ + 84° (c 1.4; water), +94° (c 1.5; chloroform). According to the literature [4, 5]: $[\alpha]_D$ + 64° (water), +60.5° (water).

Methyl 4-O-acetyl-2,3-di-O-methyl-6-O-trityl-α-D-mannopyranoside (VII). The methylation of 5 g of (I) with 3.3 equivalents of MeI and separation of the reaction products on SiO_2 in solvent system 1 gave 1.9 g of a mixture of diethers. After this mixture had been acetylated and the acetates had been crystallized from ethanol—acetone—chloroform (2:2:1), 1.25 g of pure (VII) was obtained with mp 208-209°C (ethanol), $[\alpha]_D$ + 18° (c 2.4; chloroform).

Methyl 2,3-di-O-methyl-6-O-trityl-α-D-mannopyranoside (VIII). The Zemplen deacetylation of (VII) gave a quantitative yield of (VIII) with mp 172-174°C (ethanol), $[\alpha]_D$ + 8.5° (c 2.2; chloroform). According to the literature [6, 7]: mp 177-178°C, $[\alpha]_D$ + 76.1°, mp 172-174°C. For additional identification 4-O-tosyl-(VIII) was obtained, with mp 145°C, $[\alpha]_D$ + 32° (c 2.1; chloroform). According to the literature [6, 7]: mp 146-147°C, $[\alpha]_D$ + 35.1°, mp 144-145°C, $[\alpha]_D$ + 36.5°.

Methyl 3,4-Di-O-methyl-6-O-trityl-α-D-mannopyranoside (IX). The methylation of 5 g of (I) with 2.2 equivalents of MeI in DMSO and the separation of the mixture of methyl ethers on SiO_2 in solvent system 1 gave 0.8 g of (IX), and 1.6 g of a mixture of the 2,3- and 2,4-di-O-methyl ethers of (I). After additional purification of (IX) via the acetate, 0.6 g of pure (IX) was obtained with $[\alpha]_D$ + 46° (c 3.0; chloroform). According to the literature [6], $[\alpha]_D$ + 51.2°. The following crystalline derivatives were obtained: 2-O-acetyl-(IX), mp 155°C (ethanol), $[\alpha]_D$ + 18° (c 1.5; chloroform) and 2-O-tosyl-(IX) with mp 158-159°C (ethanol), $[\alpha]_D$ + 4° (c 4.5; chloroform). According to the literature [6, 8]: mp 160-161°C, $[\alpha]_D$ + 3.6°, mp 154-155°C, $[\alpha]_D$ + 3°.

Methyl 3-O-Acetyl-2,4-di-O-methyl-6-O-trityl-α-D-mannopyranoside (X). The mixture of the 2,3- and 2,4-di-O-methyl ethers of (I) [see the preparation of (IX)] (1.6 g) was acetylated with acetic anhydride in pyridine, and the resulting mixture of acetates was separated by chromatography on SiO_2 in solvent system 1 or 4. This gave 1.2 g of (X) and 0.4 g of (VII). Recrystallization from ethanol gave pure (X) with mp 141-142°C, $[\alpha]_D$ + 41° (c 1.8; chloroform).

Methyl 2,4-Di-O-methyl-6-O-trityl-α-D-mannopyranoside (XI). The Zemplen deacetylation of (X) gave a quantitative yield of (XI) with mp 166°C (ethanol), $[\alpha]_D$ + 26° (c 1.6; chloroform). According to the literature [9]: mp 167-168°C, $[\alpha]_D$ + 25.2°.

Methyl 2,3,4-Tri-O-methyl-6-O-trityl-α-D-mannopyranoside (XII). The methylation of (I) with 3.3 equivalents of MeI in DMFA or with 2.2 equivalents of MeI in DMSO followed by the separation of the methyl ethers on SiO_2 in solvent system 1 gave (XII). Recrystallization from ethanol or ether yielded pure (XII) with mp 154-155°C, $[\alpha]_D$ + 35° (c 2.3; chloroform). According to the literature [10, 11]: mp 149°C, $[\alpha]_D$ + 27°, mp 106-110°C, $[\alpha]_D$ + 33°.

SUMMARY

1. The partial methylation of methyl 6-O-trityl-α-D-mannopyranoside by Kuhn's method in dimethylformamide and dimethyl sulfoxide has been studied.

2. Simple methods have been proposed for obtaining the 3- and 4-mono-, the 2,3-, 2,4- and 3,4-di-, and the 2,3,4-tri-O-methyl ethers of methyl 6-O-trityl-α-D-mannopyranoside.

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LIPIDS OF COTTONSEED KERNELS

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The free, bound, and strongly bound lipids of the seed kernels of the cotton plant of variety 108-F have been studied. It has been shown that the free and bound lipids include 97.3% and 47.6% of neutral lipids, respectively. The polar lipids consist mainly of phospholipids and glycolipids. Two groups of glycolipids – sterol glycosides and glycosylglycerides – have been isolated and their compositions have been determined.

In order to obtain a food flour from cotton seeds, the kernels are dried to a moisture content of 2-3% [1]. In the drying process, the components of the kernel may change, and therefore for a comparison we first studied the compositions of the free (I), bound (II), and strongly bound (III) lipids of the initial kernels of the seeds of cotton plants of variety 108-F. The amount of (I) obtained by extraction with hexane in a Soxhlet apparatus was 39.7%; that of (II), extracted by Folch's method 6.3% [2], and that of (III) 0.3%. The amount of fraction (III) was judged from the amount of free fatty acids (FFAs) after alkaline hydrolysis [3]. By column chromatography (CC) with silicic acid, (I) and (II) were separated into polar lipids (PLs, yields 2.7 and 52.4%), and nonpolar or neutral lipids (NLs, yields 97.3 and 47.6%, respectively) [4]. The total yield of combined lipids from the column was 98-99%.

These figures indicate that the free lipids consist mainly of NLs, and the bound lipids contain almost equivalent amounts of NLs and PLs. A chloroform–methanol solution of fraction (II) was washed with 0.04% aqueous $CaCl_2$ to eliminate nonlipid components [5] and was then passed through a column; the NLs were eluted with chloroform, and the PLs, by successive elution first with acetone and then with methanol [6], were separated into glycolipids (GLs) and phospholipids (PhLs). The class composition of the NLs was determined by TLC on "Silufol" in solvent systems 1-4, and those of the GLs and PhLs in a thin layer of silica gel in system 5-7 (Table 1). Identification was carried out by specific reagents for individual groups of substances and from the R_f values, which corresponded to the rates of migration of known compounds.

In the neutral lipids of fractions (I) and (II) we detected carbohydrates, sterol esters, triacylglycerols (TAGs), FFAs, epoxyacylglycerols diacylglycerols (1,2- and 1,3-DAGs), oxyacylglycerols (OAGs), and traces of PhLs. The main component of fraction (I) consists of TAGs.

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