109. B. H. Toh and G. C. Hard, Nature (London), 269, 695 (1977).
110. D. B. Rifkin, R. M. Crowe, and R. Pollack, Cell, 18, 361 (1979).
111. J. Wehland, W. Herzog, and K. Weber, J. Mol. Biol., 111, 329 (1977).
112. J. Polonsky, J. Varenne, T. Prange, and C. Pascard, Tetrahedron Lett., 21, 1853 (1980).
113. G. H. Stout, W. G. Balkenhol, M. Poling, and G. L. Hickernel, J. Am. Chem. Soc., 92, 1070 (1970).
114. A. Szent-György, Proc. Natl. Acad. Sci. USA, 74, 2844 (1977).
115. C. W. J. Chang, Chem. Educat., 50, 260 (1973).
116. J. E. Casida, M. Eto, A. D. Mascioni, J. L. Engel, D. S. Mildbrath, and J. G. Verkade, Toxicol. Appl. Pharmacol., 36, 261 (1976).
117. D. E. Wright, Tetrahedron, 35, 1207 (1979).
118. S. M. Kupchan and R. M. Schubert, Science, 185, 791 (1974).
119. S. M. Kupchan, G. Tsou, J. Org. Chem., 38, 1055 (1973).
120. S. M. Kupchan, J. A. Lacadie, G. A. Gowie, and B. R. Sickles, J. Med. Chem., 19, 1130 (1976).
121. S. M. Kupchan, A. R. Branfman, and A. T. Sneden, J. Am. Chem. Soc., 97, 5294 (1975).
122. C. Paoletti, C. Lesca, S. Cros, C. Malvy, and C. Auclair, Biochem. Pharmacol., 28, 345 (1979).
123. R. W. Miller, R. G. Powell, C. R. Smith, E. Arnold, and J. Clardy, J. Org. Chem., 46, 1469 (1981).
124. T. Ebina, K. Ohtsuki, M. Seto, and N. Ishida, Eur. J. Cancer, 11, 155 (1975).
125. K. Linnainmaa, M. Sorsa, and T. Ilus, Hereditas, 90, 151 (1979).

SYNTHESIS OF SOME L-IDOSE DERIVATIVES

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UDC 547.917

The synthesis of 3-O-benzyl- and 3-O-mesyl-1,2-O-isopropylidene-β'-L-iodofuranose has been effected on the basis of the intramolecular nucleophilic exchange of a mesyloxy group at C_5 in derivatives of 1,2-O-isopropylidene-α-D-glucofuranose. It has been found that in a system of vicinal primary and secondary mesyloxy groups a selective replacement of the primary mesyloxy group by an acetyl group is possible. It has been shown in benzyl and mesyl ethers of 5,6-anhydro-1,2-O-isopropylidene-β-L-idofuranose the opening of the oxide ring under conditions of acid hydrolysis with the retention of the isopropylidene group is possible.

In the course of work on the synthesis of methyl ethers of monosaccharides, we have come up against the necessity of obtaining the difficulty accessible L-idose. We propose a new variant of the synthesis of some of its derivatives starting from D-glucose.

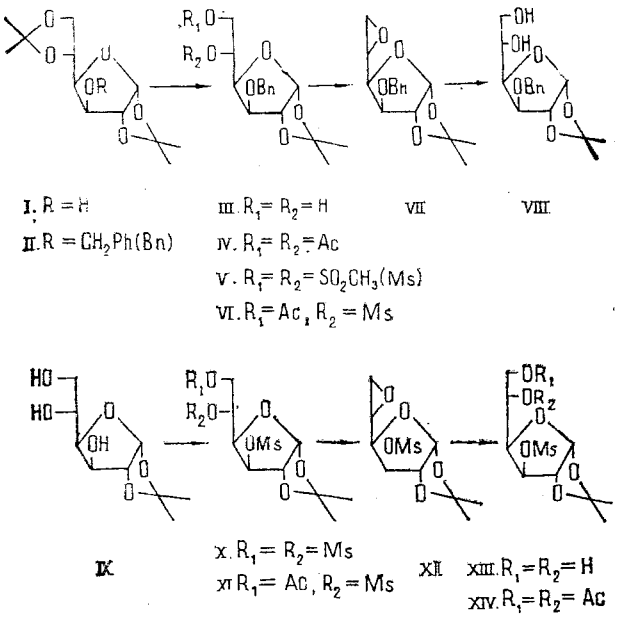
A number of methods of passing from the D-gluco- to the L-ido-configuration of sugars based on the nucleophilic replacement of C_5-O-sulfonic esters of the corresponding derivatives of 1,2-isopropylidene-α-D-glucofuranose with the isolation of 5-O-acyl- or 5,6-anhydro-derivatives of L-idose have been described in the literature. Potassium acetate in acetic anhydride [1, 2] and sodium benzoate in dimethyl formamide [3] have been proposed as nucleophilic agents for bimolecular substitution with the inversion of the configuration at C_5.

In recent years, in place of potassium acetate, an anion-exchange resin in the acetate form has been used [4, 5], which considerably increases the yield of L-idose derivatives. The synthesis of 5,6-anhydro derivatives of L-idose is based on intramolecular nucleophilic substitution on the treatment of the sulfonic esters having the D-gluco-configuration with

M. V. Frunze Simferopol' State University. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 422-426, July-August, 1982. Original article submitted September 22, 1981.

 0009-3130/82/1804-0388$07.50

sodium methanolate in methanol [6, 7]. The use of sodium isopropanolate [8] permits the exclusion of a side reaction leading to the formation of 6-O-methyl ether. A number of methods of synthesizing L-idose are based on the nucleophilic replacement of 5-O-ester groups in 1,2-O-isopropylidene-α-D-glucofuranurono-6,3-lactone [9].



We have developed and performed the synthesis of 3-O-benzyl- and 3-O-methylsulfonyl-1, 2-O-isopropylidene-β-L-idofuranose (see scheme). The starting material was diacetoneglucose (I). To obtain the 3-O-mesyl derivatives we used the readily accessible monoacetoneglucose (IX).

The benzylation of (I) with benzyl bromide in dimethyl sulfoxide (DMSO) in the presence of barium oxide and hydroxide gave a quantitative yield of 3-O-benzyl-(I) (II). The subsequent mild acid hydrolysis of (II) enabled 3-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranose (III) to be obtained in 88% yield, and this was purified through its crystalline 5,6-di-O-acetyl derivative (IV). The mesylation of (III) with methanesulfonyl chloride in pyridine at room temperature gave a high yield of the 5,6-di-O-mesyl ester (V), and its treatment with potassium acetate in DMSO led with a high degree of selectivity to the replacement of the primary mesyloxy groups by an acetoxy group. In this step, the yield of 6-O-acetyl-3-O-benzyl-5-O-mesyl-1,2-isopropylidene-α-D-glucofuranose (VI) amounted to more than 90%. The treatment of (V) with sodium isopropanolate in isopropanol permitted the synthesis of 3-O-benzyl-1,2-isopropylidene-5,6-anhydro-β-L-idofuranose (VII). Conditions for the acid hydrolysis of (VII) found experimentally led to the selective opening of the anhydro ring with the retention of the isopropylidene group.

In order to obtain 3-O-mesyl-1,2-isopropylidene-β-L-idofuranose (XIII), monoacetoneglucose (IX) was subjected to exhaustive mesylation. Then in the ester (X) so obtained, the primary mesyloxy group was replaced by an acetoxy group using potassium acetate in DMSO. The 6-O-acetyl-3,5-di-O-mesyl-1,2-O-isopropylidene-α-D-glucofuranose(XI) was then subjected to epoxidation with sodium isopropanolate in isopropanol. Subsequent mild acid hydrolysis of the oxide (XII) led to 3-O-mesyl-1,2-O-isopropylidene-β-L-idofuranose (XIII), which was purified in the form of the acetate (XIV).

The approach to the synthesis of L-idose derivatives that has been developed has a number of differences from the methods described in the literature. Instead of the tosylates usually used, we employed the mesyl esters, which are obtained faster and with higher yields and, moreover, take part in the nucleophilic substitution reaction considerably more readily. The known literature methods of synthesizing 6-O-acyl-5-O-sulfonyl derivatives of 1,2-O-isopropylidene-α-D-glucofuranose, which are direct precursors of the 5,6-anhydrosugars, are distinguished by their multistage nature and by low yields of the desired products. We have found that in a system of vicinal primary and secondary

methylsulfonyl groups, the selective replacement of the primary sulfo group with the formation of the required 6-O-acetyl derivatives is possible, which has considerably shortened and simplified the synthesis of these compounds. Furthermore, it has been established that in oxides of types (VII) and (XII), it is possible to open the anhydro ring and yet retain the 1,2-O-isopropylidene group, which is of practical interest for the synthesis of other derivatives of 3-O-benzyl- and 3-O-mesyl-L-idose.

EXPERIMENTAL

Melting points were determined on a heated stage, and specific rotations on a SM-1 polarimeter (Na lamp). Column chromatography was carried out on silica gel L (40-100 μ), and thin-layer chromatography on Woelm TLC silica gel. The following solvent systems were used: 1) benzene–acetone (5:1); 2) CCl_4–acetone (10:1); 3) benzene–ethanol (5:1); and 4) benzene–ethanol (3:1). The spots of the sugars on the plates were detected with the aid of a 5-10% ethanolic solution of H_2SO_4 followed by heating.

3-O-Benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (II). With vigorous stirring, 13 ml of benzyl bromide was added over 7 h to a solution of 26 g of diacetoneglucose [10] in 150 ml of DMSO containing 34 g of BaO and 14 g of $Ba(OH)_2 \cdot 8H_2O$. Then the reaction mixture was stirred for 16 h, diluted with 450 ml of $CHCl_3$, and centrifuged. The chloroform solution was washed with water to neutrality, dried with Na_2SO_4, and evaporated to dryness. This gave 33.1 g (95%) of (II) with n_D^{20} 1.497; $[\alpha]_D$ −25° (c 2.4; chloroform); according to the literature [11]: n_D^{20} 1.4985); $[\alpha]_D$ −24.8°.

3-O-Benzyl-1,2-O-isopropylidene-α-glucofuranose (III). To a solution of 33 g of (II) in 200 ml of methanol was added 33 ml of a 2% aqueous solution of H_2SO_4. After 48 h, the solution was neutralized with $BaCO_3$, the precipitate was centrifuged off, and the centrifugate was evaporated to dryness, giving 25.7 g (88%) of (III). For purification, the 25.7 g of (III) was acetylated with 150 ml of a mixture of acetic acid and pyridine (1:1) at room temperature for 20 h. The solution was evaporated and the residue was recrystallized from ethanol. This gave 24.3 g (75%) of the diacetate (IV). mp 120-121°C; $[\alpha]_D$ −53° (c 1.3; chloroform); according to the literature [12]: mp 120°C; $[\alpha_D]$ −50.8°. Zemplen deacetylation gave 19.1 g of (III) with $[\alpha]_D$ −43° (c 0.6; chloroform); according to the literature [12]: $[\alpha]_D$ −45.5°.

3-O-Benzyl-5,6-di-O-mesyl-1,2-O-isopropylidene-α-D-glucofuranose (V). At room temperature, 11 mg of mesyl chloride was added in portions over 4 h to a solution of 19.1 g of (III) in 95 ml of pyridine. After the end of the reaction (monitored by TLC in solvent system 1), the solution was poured into ice water with stirring, and the resulting precipitate was filtered off. This gave 22.8 g (80%) of (V). The recrystallization of (V) from ethanol–chloroform (9:1) yielded crystalline (V) with mp 125-126°C, $[\alpha]_D$ −20° (c 1.7; chloroform). Found, %: C 46.47; H 5.47. Calculated for $C_{18}H_{26}O_{10}S_2$, %: C 46.34; H 5.62.

6-O-Acetyl-3-O-benzyl-5-O-mesyl-1,2-O-isopropylidene-α-D-glucofuranose (VI). A solution of 17.1 g of (V) in 170 ml of DMSO containing 17.9 g of potassium acetate was heated for 4 h in the water bath at 78-80°C, the course of the reaction being monitored in solvent systems 1 and 2. Then the reaction mixture was poured with stirring into cold water, and the solid precipitate was filtered off. This gave 14.5 g (92%) of (VI). Recrystallization from ethanol yielded crystalline (VI) with mp 115-116°C; $[\alpha]_D$ −10° (c 2.1; chloroform). Found, %: C 52.77; H 5.84. Calculated for $C_{19}H_{26}O_9S_1$, %: C 53.01; H 6.09.

3-O-Benzyl-5,6-anhydro-1,2-O-isopropylidene-β-L-idofuranose (VII). A solution of sodium isopropanolate in isopropanol (1.54 g of Na in 87 ml of isopropanol) was added to a solution of 14.5 g of (VI) in 10 ml of methylene chloride. The reaction mixture was cooled to 0°C, and after 16 h it was neutralized with CO_2 and evaporated to dryness, the residue was extracted with chloroform, and the chloroform extract was washed with $NaHCO_3$ solution. Then it was dried with Na_2SO_4 and evaporated to dryness. The oxide (VII) was purified by chromatography on SiO_2 (column 3 × 15 cm) with elution by benzene–acetone (15:1). This gave 7.5 g (76%) of (VII). $[\alpha]_D$ − 81° (c 1.0; chloroform). Found, %: C 65.5; H 7.2. Calculated for $C_{16}H_{20}O_5$, %: C 65.74; H 6.9.

3-O-Benzyl-1,2-O-isopropylidene-β-L-idofuranose (VIII). A solution of 7.4 g of (VII) in 170 ml of a mixture of dioxane and water (4:3) was treated with 7.4 ml of 10% aqueous H_2SO_4, and the mixture was left at room temperature with periodic monitoring of the hydroly-

sis in solvent systems 1 and 2. After 6 days, the reaction mixture was neutralized with $BaCO_3$ and the precipitate was centrifuged off. The unchanged oxide (about 10%) was extracted from the aqueous dioxane solution with 70 ml of hexane. The aqueous dioxane layer was evaporated to dryness and chromatographed on a column of SiO_2 (3 × 30 cm), with elution by benzene–isopropanol (10:1). This gave 4.7 g (60%) of pure (VIII) which was converted by crystallization from ethyl acetate–petroleum ether into the crystalline compound, with mp 85-86°C; $[\alpha]_D$ −59° (c 3.4; chloroform); according to the literature [2]: mp 86-87°C $[\alpha]_D$ −61°; [13]: mp 89-90°C; $[\alpha]_D$ −48°.

3,5,6-Tri-O-mesyl-1,2-O-isopropylidene-α-D-glucofuranose (X). In portions over 5 h, 15 ml of methanesulfonyl chloride was added to a solution of 12.4 g of monoacetone glucose [10] in 60 ml of pyridine at room temperature. After the reaction had ended (monitoring by TLC in solvent system 3), the mixture was poured with stirring into ice water, and the solid product was filtered off. The yield of (X) was 19 g (75%). Recrystallization from chloroform–ethanol (2:1) gave crystalline (X) with mp 162-163°C; $[\alpha]_D$ −35° (c 1.6; chloroform). Found, %: C 31.4; H 4.8. Calculated for $C_{12}H_{22}O_{12}S_3$, %: C 31.72; H 4.88.

6-O-Acetyl-3,5-di-O-mesyl-1,2-O-isopropylidene-α-D-glucofuranose (XI). A solution of 18.3 g of (X) in 125 ml of DMSO containing 19.7 g of potassium acetate was heated on the water bath at 78-80°C for 4 h, the course of the reaction being monitored in solvent system 1. The reaction mixture was poured into cold water and extracted with chloroform. The organic layer was dried with Na_2SO_4 and evaporated to dryness. The residue (17.5 g) was recrystallized from ethanol, which gave 13 g (72%) of (XI) with mp 96-97°C; $[\alpha]_D$ −21° (c 1.7; chloroform); according to the literature [8]; mp 95-97°C; $[\alpha]_D$ −13°.

3-O-Mesyl-1,2-O-isopropylidene-5,6-anhydro-β-L-idofuranose (XII). A solution of 10 g of (XI) in 70 ml of methylene chloride was added to a solution of sodium isopropanolate in isopropanol (1.1 g of Na in 60 ml of isopropanol). The reaction mixture was cooled to 0°C and after 18 h it was neutralized with CO_2 and evaporated to dryness, the residue was extracted with chloroform, and the extract was washed with $NaHCO_3$ solution. Then it was dried with Na_2SO_4 and evaporated to dryness. The residue was recrystallized from ethanol, giving 5.5 g (82%) of (XII). mp 97-98°C; $[\alpha]_D$ −8° (c 2.2; chloroform); according to the literature [7]: mp 96.5-98.5°C; $[\alpha]_D$ −27.4°; [8]: mp 96-98°C; $[\alpha]_D$ −16°.

3-O-Mesyl-1,2-O-isopropylidene-β-L-idofuranose (XIII). A solution of 3.2 g of (XII) in 64 ml of dioxane–water (1:1) was treated with 3.2 ml of 10% aqueous H_2SO_4, and the mixture was left at room temperature with periodic monitoring in solvent system 4. After 6 days, the reaction mixture was neutralized with $BaCO_3$, and the precipitate was centrifuged off. The unchanged oxide (XII) (about 5%) was extracted from the aqueous dioxane solution with 50 ml of benzene–hexane (1:1). The aqueous dioxane layer was evaporated to dryness. The 2.9 g (85%) of (XIII) so obtained was acetylated with 30 ml of 1:1 mixture of acetic anhydride and pyridine overnight. Then the reaction mixture was evaporated, the residue was dissolved in chloroform, and the solution was washed with dilute H_2SO_4, with water, and with $NaHCO_3$ solution. The chloroform extract was dried with Na_2SO_4 and evaporated to dryness. Recrystallization of 3.3 g of the residue from ethanol gave 2.1 g (57%) of the crystalline diacetate (XIV). mp 114-115°C; $[\alpha]_D$ −27° (c 2; chloroform). Found, %: C 43.7; H 5.6. Calculated for $C_{14}H_{22}O_{10}S$, %: C 43.97; H 5.8. The Zemplen deacetylation of 1.8 g of the diacetate (XIV) gave 1.4 g (100%) of (XIII). Crystalline (XIII) was obtained by recrystallization from ethanol; it had mp 125-126°C; $[\alpha]_D$ −16° (c 2.9; methanol); according to the literature [5]: mp 129-129.5°C.

SUMMARY

1. A new route for the synthesis of 3-O-benzyl- and 3-O-mesyl-1,2-O-isopropylidene--β-L-idofuranose is proposed.

2. It has been found that in a system of vicinal primary and secondary methylsulfonyl groups the selective replacement of the primary mesyloxy group by an acetyl group is possible.

3. It has been shown in the benzyl and mesyl derivatives of 1,2-O-isopropylidene-5,6-anhydro-β-L-idofuranose that opening of the oxide ring with retention of the isopropylene group is possible under the conditions of acid hydrolysis.

LITERATURE CITED

1. L. Vargha, Ber., 87, 1351 (1954); T. H. Johnson and G. Rangarjan, J. Org. Chem., 45, 62 (1980).
2. J. Kiss and P. C. Wyss, Tetrahedron, 32, 1399 (1976).
3. D. H. Buss, L. D. Hall, and L. Hough, J. Chem. Soc., 1616 (1965).
4. P. Perchemlides, T. Osawa, E. A. Davidson, and R. W. Jeanloz, Carbohydr. Res., 3, 463 (1967); M. A. Miljovič and E. A. Davidson, Carbohydr. Res., 13, 444 (1970).
5. J. Kovar, Can. J. Chem., 48, 2383 (1970).
6. A. S. Meyer and T. Reinchstein, Helv. Chim. Acta, 29, 152 (1946); R. E. Gramera, T. R. Ingle, and R. L. Whistler, J. Org. Chem., 29, 878 (1964); U. G. Nayak and R. L. Whistler, J. Org. Chem., 34, 97 (1969).
7. J. Kovar and J. Jary, Collect. Czech. Chem. Commun., 33, 549 (1968).
8. N. A. Hughes and P. D. Tyson, Carbohydr. Res., 57, 317 (1977).
9. R. Cusk, H. Hönig, J. Nimpf, and H. Weidmann, Tetrahedron Lett., 21, 2135 (1980); I. Macher, K. Dax, E. Wanek, and H. Weidmann, Carbohydr. Res., 80, 45 (1980).
10. Methods of Carbohydrate Chemistry [in Russian], Moscow (1967), p. 165.
11. A. Goi, T. Bruzzese, A. F. Notarianii, M. Riva, and A. Ronchini, Arzneimittel-Forsch., 29, 986 (1979).
12. J. Kovar and H. H. Baer, Carbohydr. Res., 39, 19 (1975).
13. N. Baggett and W. Jeanloz, J. Org. Chem., 28, 1845 (1963).

HYDRODYNAMIC CHARACTERISTICS OF THE CAPSULAR POLYSACCHARIDES OF *Klebsiella*

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UDC 547.458+576.8/:542.66

Investigations of the acidic polysaccharides isolated from the capsules of *K. scleromatis* and *K. ozaenae* under the conditions of high-speed sedimentation and an approximation to equilibrium (Archibald's method) has made it possible to regard them as polydisperse homogeneous substances with different molecular masses and a nonspherical form of the molecules entering their composition.

The acidic polysaccharides of the capsules of klebsiellae *K. Scleromatis* and *K. ozaenae* (family Enterobacteriaceae) and their antigenic specificity is the main factor of the pathogenicity of this type of bacteria [1, 2]. This fact explains the considerable interest in the detailed study of these compounds.

We have considered the behavior of the capsular polysaccharides isolated from *K. scleromatis* and *K. ozaenae* (KPS-3 and KPS-4; serological types 3 and 4), in a centrifugal field. The experimental results are presented in Table 1. The sedimentation diagrams obtained in an ultracentrifuge (Fig. 1) each have a single peak for all concentrations of the polysaccharides under investigation. This indicates the existence of a polydispersity of these polysaccharides, as is confirmed by the considerable increase in the apparent coefficient of diffusion in high-speed sedimentation experiments, and also by the non-uniformity of the molecular masses at the meniscus and at the bottom of the cell in

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Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 427-428, July-August, 1982. Original article submitted October 12, 1981.

0009-3130/82/1804-0392$07.50