## Sorboses. I. Syntheses of 2, 3-O-Isopropylidene-6-amino-6-deoxy- $\alpha$ -L-sorbofuranoses<sup>1</sup>)

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Although 1- and 2-amino derivatives of Lsorbose (I) are known,<sup>2)</sup> the 6-amino derivative has not yet been described. In this paper we will report on the synthesis of 6-amino-6deoxy- and 1, 6-diamino-1, 6-dideoxy-2, 3-O-isopropylidene- $\alpha$ -L-sorbofuranoses.

The synthesis was achieved by the schemes outlined in Chart I. For the introduction of an amino group into the C-6 position of a sugar, the tosylation of the hydroxyl group at only this position was desired. At the outset, 1-O-acetyl-2, 3-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (IV) was prepared to protect all the other hydroxyl groups, and is stable under alkaline conditions and hydrolysable with acid.

The acetylation of 2, 3:4, 6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (II)<sup>3)</sup> with acetic an-

hydride in pyridine gave 1-O-acetyl-2, 3:4, 6-di-*O*-isopropylidene- $\alpha$ -L-sorbofuranose (III), which was hydrolyzed with 60% acetic acid to give IV. The tosylation of IV with one mole of tosyl chloride in pyridine gave a sirup mixture of the expected 6-tosylate, 1-O-acetyl-2, 3-O-isopropylidene-6-o-tosyl- $\alpha$ -L-sorbofuranose (V) and ditosylate, 1-O-acetyl-2, 3-O-isopropylidene-4, 6di-O-tosyl- $\alpha$ -L-sorbofuranose (VI). The latter was obtained from IV by treating it with more than 2 mol. of tosyl chloride. The separation of those two tosylates was achieved by alumina chromatography, but with poor yields. The purification of 2, 3-O-isopropylidene-6-anilino-6-deoxy- $\alpha$ -L-sorbofuranose (X), which was obtained by the treatment of V with aniline, was also difficult. The deacetylation of V by ethanolic sodium hydroxide gave 2, 3-O-isopropylidene-6-O-tosyl- $\alpha$ -L-sorbofuranose (VII) as silky crystals. The deacetylation of VI gave a

<sup>1)</sup> Presented at the Division of Organic Chemistry of the 16th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1963.

<sup>2)</sup> K. Heynes, H. Paulsen, R. Eichstedt and M. Rolle, Chem. Ber., 90, 2039 (1957).

<sup>3)</sup> T. Reichstein, Helv. Chim. Acta, 17, 311 (1934).



crystalline compound, the infrared spectrum of which exhibited no hydroxyl groups, suggesting that the compound is either 2, 3-Oisopropylidene-6-O-tosyl-1, 4-anhydro- $\alpha$ -L-sorbofuranose (VIII) or 1, 4-anhydro- $\alpha$ -L-psicose (VIII'). Therefore, the deacetylation of the mixture of V and VI, followed by either fractional crystallization or alumina chromatography, was carried out successfully to give two tosylates, VII and VIII (or VIII').

The heating of VII with aniline gave X, while that with liquid ammonia gave 2, 3-Oisopropylidene-6-amino-6-deoxy- $\alpha$ -L-sorbofuranose (XII) as a sirup, which was converted into a crystalline *p*-nitrobenzoate (XIII).

The structure of anhydrosugar (VIII or VIII') was also investigated. The deacetylation of VI with alcoholic sodium hydroxide gave an anhydrosugar (VIII or VIII'), while that with liquid ammonia at room temperature gave 2, 3-O-isopropylidene -4, 6-di-O-tosyl- $\alpha$ -L-sorbofuranose (IX), which was then easily converted

into the same anhydrosugar when treated with alcoholic sodium hydroxide. On the other hand, the partial hydrolysis of II to 2, 3-O-isopropylidene- $\alpha$ -L-sorbofuranose (XVI), followed by tosylation, gave 2, 3-O-isopropylidene-1, 6-di-O-tosyl- $\alpha$ -L-sorbofuranose (XVII).<sup>4,5)</sup> Reacting with alcoholic sodium hydroxide, XVII was converted into an anhydrosugar which showed an infrared absorption band identical with the above-described anhydrosugar. The latter course has no opportunities for Walden inversion. Therefore, the structure of anhydrosugar was established as VIII. It is noteworthy that no Walden inversion was observed in the reaction of VI to VIII.

The treatment of VIII with aniline gave dianilinosorbose. Under the same conditions, XVII gave the same product. From these results the dianilinosorbose was confirmed to be 2, 3-O-isopropylidene-1, 6-dianilino-1, 6-dideoxy- $\alpha$ -L-sorbofuranose (XI). Similarly, the treatment of VIII as well as of XVII with liquid ammonia gave 2, 3-O-isopropylidene-1, 6diamino-1, 6-dideoxy- $\alpha$ -L-sorbofuranose (XIV) as a sirup, which was then converted into a crystalline p-nitrobenzoate (XV). The two 1, 6-diamino-sorboses, XI and XIV, were also prepared from IX, with the amines via VIII as a probable intermediate.

The infrared absorption spectra of the abovedescribed sorbofuranoses are summarized in Table I. Previously, Barker and Stephens reported that the compounds containing a furanose or hydrofuranol ring exhibit infrared absosption of the A, B, C and D types at  $924\pm$ 

## TABLE I. INFRARED ABSORPTION BANDS OF SORBOFURANOSES

Frequencies  $(cm^{-1})$  of absolute bands

Compound	Type A	Type B	Type C	Type D	Other peaks
II	945	890	855	830	765
III	980	901	858	835	770
IV	985	888	860	828	770
VII	946	898	870	828	792
VIII	935	895	858	818	780
IX	977	900	865	827	770
x	938	892	866	823	760
XI	934	892	860	812	742
XIII	982	895	863	824	778
XV	944	880	855	830	720
XVI	980	891	864	830	750
XVII	958	890	856	818	765
Mean and standard derivation	958±24	895±7	864±6	823±7	

<sup>4)</sup> T. I. Temnikova and V. V. Sklyarava, Zh. Prikl. Khim., 27, 1131 (1954); Chem. Abstr., 49, 2952 (1955).
5) H. Ohle, Ber., 71, 562 (1938).

13,  $879\pm7$ ,  $858\pm7$  and  $799\pm17 \text{ cm}^{-1}$ , respectively.<sup>6</sup>) These four types of infrared absorption bands are also characteristic of sorbofuranoses, but their positions then shift to higher frequencies to some extent, appearing at  $958\pm24$ ,  $895\pm7$ ,  $864\pm6$  and  $823\pm7$  cm<sup>-1</sup> respectively. 1, 2-O-Isopropylidene- $\alpha$ -L-sorbopyranose<sup>5</sup>) and methyl  $\alpha$ -L-sorbopyranoside<sup>7</sup> showed no absorption bands of these four types. Instead, they exhibited absorptions at 910 and 902, 890 and 880, and 772 and  $792 \text{ cm}^{-1}$ , positions which were identical with those of D-glucopyranose as suggested by Barker et al.8) These facts are very useful in determining whether or not sorboses are of the furanose type.

## Experimental<sup>9)</sup>

1-O-Acetyl-2, 3: 4, 6-di-O-isoproylidene- $\alpha$ -L-sorbofuranose (III).—Into a cooled solution of 200 g. of 2, 3: 4, 6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (II) in 300 ml. of dry pyridine, 200 g. of acetic anhydride in portions were stirred. After having been stirred at  $0 \sim 5^{\circ}$ C for 4 hr. and after standing overnight at room temperature, the reaction mixture was poured onto 800 g. of ice. The product was then extracted with benzene, washed with a sodium bicarbonate solution, dried, and evaporated in vacuo. The residue was distilled to give a colorless sirup, which crystallized immediately. Yield: 204 g. (88%); b.p. 168°C/6 mmHg; m.p. 52°C  $[\alpha]_{D}^{19}$  -16.4 (c 1.038, acetone).

Found : C, 55.95 ; H, 7.51 ; CH<sub>3</sub>CO, 13.96. Calcd. for  $C_{14}H_{22}O_7$  (302): C, 55.63 ; H, 7.29 ; CH<sub>3</sub>CO, 14.23%.

**1-O-Acetyl-2, 3-O-isopropylidene-a-L-sorbofuranose** (**IV**). — A solution of 170 g. of 1-O-acetyl-2, 3: 4, 6-di-O-isopropylidene- $\alpha$ -L-sorbofuranose (**III**) in 200 ml. of 60% acetic acid was warmed at 80°C for 40 min. The reaction mixture was cooled, made alkaline with sodium carbonate, and then extracted with chloroform. After the removal of the solvent, the residue was distilled to give a colorless sirup. Yield: 88 g. (67.2%); b. p. 205°C/11 mmHg;  $[\alpha]_{\rm D}^{23}$ +7.3 (c 0.987, acetone).

Found : C, 50.41 ; H, 7.07 ; CH<sub>3</sub>CO, 16.26. Calcd. for  $C_{11}H_{18}O_7$  (262): C, 50.38 ; H, 6.87 ; CH<sub>3</sub>CO, 16.41%.

The Tosylation of 1-O-Acetyl-2, 3-O-isopropylidene- $\alpha$ -L-sorbofuranose (IV).—Into a solution of 100 g. of 1-O-acetyl-2, 3-O-isopropylidene- $\alpha$ -L-sorbofuranose (IV) in 300 ml. of dry pyridine, 73 g. of tosyl chloride in small portions were stirred while the mixture was being cooled in ice water. After having been stirred at room temperature for 4 hr., the reaction mixture was poured into 600 ml. of a saturated sodium carbonate solution and then extracted with chloroform, which had been washed with water, dried and evaporated to dryness in vacuo to a sirup (A). Yield: 118 g. i) Ten grams of the A sirup was fractionated by alumina chromatography with chloroform. The first fraction was 0.15 g. of 1-O-acetyl-2, 3-O-isopropylidene-4, 6-dio-tosyl- $\alpha$ -L-sorbofuranose (VI),  $[\alpha]_{D}^{23} - 3.8$  (c 1.03, acetone).

Found: C, 52.40; H, 5.64; S, 10.80. Calcd. for  $C_{25}H_{30}O_{11}S_2$  (570): C, 52.63; H, 5.26; S, 11.22%.

The other compound purely isolated was 0.18 g. of 1-O-acetyl-2, 3-O-isopropylidene-6-O-tosyl- $\alpha$ -L-sorbofuranose (V),  $[\alpha]_{D}^{23}$  +4.2 (c 0.790, acetone). Found: C, 52.35; H, 5.88; S, 7.90. Calcd. for

 $C_{19}H_{24}O_9S$  (416): C, 51.99; H, 5.77; S, 7.69%. ii) The 4,6-ditosylate VI was also obtained from

IV, along with more than 2 mol. of tosyl chloride, by using the same procedure.

iii) A solution of 50 g. of the A sirup in a solution of 8 g. of sodium hydroxide, 60 ml. of water and 280 ml. of ethanol was warmed at 50°C for 40 min. After the solvent had been removed, the residue was extracted with chloroform, which had been washed with water, dried and evaporated to dryness in vacuo to a sirup. a) Recrystallization from ethanol gave 12 g. of 2, 3-O-isopropylidene-6-Otosyl-1, 4-anhydro- $\alpha$ -L-sorbofuranose (VIII). The mother liquor was evaporated to dryness in vacuo. Recrystallization from petroleum ether and ethyl acetate gave 16 g. of 2, 3-O-isopropylidene-6-O-tosyl- $\alpha$ -L-sorbofuranose (VII). b) The sirup dissolved in chloroform was passed through an alumina column and evaporated to dryness. Recrystallization from ethanol gave 12 g. of 2, 3-O-isopropylidene-6-O-tosyl-1,4-anhydro- $\alpha$ -L-sorbofuranose (VIII). The column was eluted out with alcohol. The alcohol solution was evaporated in vacuo. Recrystallization of the residue from petroleum ether and ethyl acetate gave 10 g. of 2, 3-O-isopropylidene-6-O-tosyl- $\alpha$ -L-sorbofuranose (VII).

2, 3-O-Isopropylidene-6-O-tosyl- $\alpha$ -L-sorbofuranose (VII).—A solution of 2 g. of 1-O-acetyl-2, 3-O-isopropylidene-6-O-tosyl- $\alpha$ -L-sorbofuranose (V) in 20 ml. of 0.5 N ethanolic potassium hydroxide was warmed at 50°C for 1 hr. To the reaction mixture 100 ml. of chloroform were then added. The chloroform layer was washed with water, dried, and evaporated to dryness. Recrystallization from petroleum ether and ethyl acetate gave 1.1 g. (61.2%) of colorless needles; m. p. 105°C,  $[\alpha]_{2D}^{2D} + 15.1$  (c 1.075, acetone). Found: C, 51.70; H, 6.05; S, 8.55. Calcd. for

C<sub>16</sub>H<sub>22</sub>O<sub>8</sub>S (374): C, 51.34; H, 5.88; S, 8.56%. 2, 3-O-Isopropylidene-6-O-tosyl-1, 4-anhydro-α-L-

sorbofuranose (VIII).—This was prepared from 2g. of 1-O-acetyl-2, 3-O-isopropylidene-4, 6-di-O-tosyl- $\alpha$ -L-sorbofuranose (VI) and 20 ml. of ethanolic potassium hydroxide in a 62% yield by the abovedescribed procedure. M. p. 115°C (recrystallized from ethanol),  $[\alpha]_{24}^{24}$ —11.6 (c 1.035, acetone).

Found: C, 53.74; H, 5.62; S, 9.01. Calcd. for  $C_{16}H_{20}O_7S$  (356): C, 53.96; H, 5.62; S, 8.99%.

The anhydrosorbose VIII was also obtained from 2, 3-O-isopropylidene-4, 6-di-O-tosyl- $\alpha$ -L-sorbofuranose (IX) or 2, 3-O-isopropylidene-1, 6-O-tosyl- $\alpha$ -L-sorbofuranose (XVII) in a similar yield by the above-described procedure.

<sup>6)</sup> S. A. Barker and R. Stephens, J. Chem. Soc., 1954, 4550.

<sup>7)</sup> R. L. Whistler and R. M. Hixon, J. Am. Chem. Soc., 59, 2047 (1937).

<sup>8)</sup> S. A. Barker, E. G. Bourne, M. Stacy and D. H. Wiffen, J. Chem. Soc., 1954, 171.

<sup>9)</sup> All melting points are uncorrected.

2, 3-O-Isopropylidene-4, 6-di-O-tosyl- $\alpha$ -L-sorbofuranose (IX).—A solution of 10 g. of 1-O-acetyl-2, 3-O-isopropylidene-4, 6-di-O-tosyl- $\alpha$ -L-sorbofuranose (VI) in 10 ml. of liquid ammonia was allowed to stand overnight at room temperature. After the liquid ammonia had been removed, a brown sirup was obtained, the solution of which in 50 ml. of chloroform had been washed with water, dried, and evaporated to dryness in vacuo to a sirup. Alumina chromatography with chloroform gave 0.5 g. of colorless needles as a second fraction; m. p. 125°C (recrystallized from ethanol),  $[\alpha]_D^{23} + 8.4$  (c 1.003, acetone).

Found : C, 52.33; H, 5.48; S, 11.55. Calcd. for  $C_{23}H_{28}O_{10}S_2$  (528) : C, 52.23; H, 5.34; S, 12.14%.

2, 3-O-Isopropylidene-6-anilino-6-deoxy-a-L-sorbofuranose (X).—A solution of 2 g. of 2, 3-O-isopropylidene-6-o-tosyl- $\alpha$ -L-sorbofuranose (VII) and 2 g. of potassium carbonate in 20 ml. of aniline was heated while being stirred at 160~170°C for 20 hr. The reaction mixture was then cooled and extracted with three 60 ml. portions of chloroform, which had been washed with water, dried and evaporated in vacuo to get a dark brown sirup. Recrystallization from ethanol gave 0.7 g. of colorless needles; m. p. 140°C,  $[\alpha]_{24}^{24} + 32.6$  (c 0.859, acetone).

Found : C, 61.46 ; H, 7.35 ; N, 4.59. Calcd. for  $C_{15}H_{21}NO_5$  (295): C, 61.02 ; H, 7.12 ; N, 4.75%.

2, 3-O-Isopropylidene-1, 6-dianilino-1,6-dideoxy- $\alpha$ -L-sorbofuranose (XI).—This was obtained from 2g. of 2, 3-O-isopropylidene-6-O-tosyl-1, 4-anhydro- $\alpha$ -Lsorbofuranose (VIII) and 2 g. of potassium carbonate in 20 ml. of aniline by the above-described procedure for 2, 3-O-isopropylidene-6-anilino-6-deoxy- $\alpha$ -L-sorbofuranose (X). Recrystallization from ethanol gave 0.8 g. of the sample for analysis; m. p. 151°C,  $[\alpha]_{25}^{25}$  +10.3 (c 1.020, acetone).

Found: C, 68.36; H, 7.20; N, 7.78. Calcd. for  $C_{21}H_{26}N_2O_4$  (370): C, 68.11; H, 7.04; N, 7.57%.

The dianilino compound XI was also prepared in a similar yield from either 2, 3-O-isopropylidene-1, 6di-O-tosyl- $\alpha$ -L-sorbofuranose (XVII) or 2, 3-O-isopropylidene-4, 6-di-O-tosyl- $\alpha$ -L-sorbofuranose (IX) by the same procedure.

2, 3-O-Isopropylidene-6-amino -6- deoxy- $\alpha$ -L-sorbofuranose (XII).—A solution of 5 g. of 2, 3-O-isopropylidene-6- $\alpha$ -tosyl- $\alpha$ -L-sorbofuranose (VII) in 10 ml. of liquid ammonia was heated on a boiling waterbath for ten days. After the liquid ammonia had been removed, the residue, dissolved in 100 ml. of chloroform, was passed through an alumina column (50 g. of alumina was used) and evaporated to dryness in vacuo. A solution of 1 g. of the residue and 2 g. of *p*-nitrobenzoyl chloride in 15 ml. of dry pyridine was stirred at room temperature for 10 hr. The reaction mixture was poured into a saturated aqueous solution of sodium carbonate while being cooled and was extracted with chloroform which had been washed with water and evaporated to dryness in vacuo. Three recrystallizations from petroleum ether and ethyl acetate gave 1.4 g. of colorless needles (XIII); m. p. 235°C (decomp.),  $[\alpha]_{30}^{30} + 25.3$  (c 0.364, acetone).

Found : C, 54.22 ; H, 3.91 ; N, 8.32. Calcd. for  $C_{30}H_{26}N_4O_{14}$  (666) : C, 54.05 ; H, 3.91 ; N, 8.41%.

A solution of 1 g. of XIII in 50 ml. of 10% methanolic sodium hydroxide was refuxed for 1.5 hr. After the methanol had been removed, the residue was extracted with chloroform, and the extracts were washed with water saturated with sodium chloride, dried, treated with charcoal, and evaporated to dryness in vacuo to a sirup. Yield: 0.2 g,  $[\alpha]_{D}^{23} + 28.1$  (c 1.030, acetone).

Found: C, 49.63; H, 7.69; N, 6.07. Calcd. for  $C_9H_{17}NO_5$  (219): C, 49.32; H, 7.76; N, 6.39%.

2, 3-O-Isopropylidene-1, 6-diamino-1, 6-dideoxy- $\alpha$ -L-sorbofuranose (XIV).—This was prepared from 5 g. of 2, 3-O-isopropylidene-6-O-tosyl-1, 4-anhydro- $\alpha$ -L-sorbofuranose (VIII) and 10 ml. of liquid ammonia by the above-described procedure. *p*-Nitrobenzoate (XV): m. p. 110~115°C (decomp.) (by five recrystallizations from petroleum ether and benzene),  $[\alpha]_{2^{3.5}}^{2^{3.5}}$  -69.5 (*c* 0.243, acetone).

Found: C, 53.88; H, 4.24; N, 10.79. Calcd. for  $C_{30}H_{27}N_5O_{13}$  (665): C, 54.14; H, 4.06; N, 10.53%.

The 1,6-diaminosorbose (XIV) was obtained as colorless plates. M. p. 52°C,  $[\alpha]_D^{30} - 8.36$  (c 1.078, acetone).

Found : C, 49.80 ; H, 7.95 ; N, 13.01. Calcd. for  $C_9H_{18}N_2O_4$  (218): C, 49.54 ; H, 8.26 ; N, 12.84%.

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