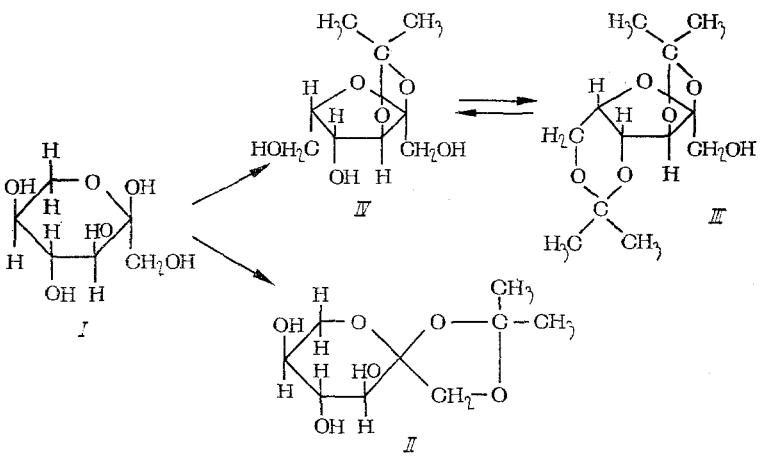
MECHANISM OF ACETONATION OF L-SORBOSE

L. O. Shnaidman and A. V. Fondarenko

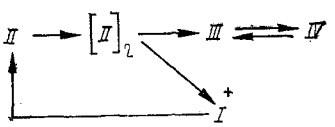
UDC 547.455.635'284.3

The mechanism of the acetonation of L-sorbose has been insufficiently studied. It is considered to be established that the keto group in the 2 position is affected in monoacetonation. This is demonstrated by the fact that monoacetonesorbose does not give the Fehling's test which is characteristic of ketoses. Then it was established [1, 2] that monoacetonation takes place on two adjacent hydroxyls (either 1,2 or 2,3), which is explained by the formation thereupon of the more stable five-membered ring (including the acetone residue) rather than a six-membered one upon acetonation of hydroxyls which are not adjacent. There exists an opinion [1-7] that the acetonation process goes mainly at the 2,3-hydroxyls, to form 2,3,O-isopropylidene-α-L-sorbofuranoside (IV), while 1,2,O-isopropylidene-α-L-sorbopyranose (II) is formed in low yield and is incapable of further acetonation.

Here it is assumed that L-sorbose (I) has the pyranoside structure, which is isomerized into the furanoside structure during acetonation. Hence the mechanism of the acetonation reaction was represented in the following form [1, 2].



However, the most recent studies by Japanese workers [8, 9] have not corroborated this mechanism for the acetonation reaction. By gas-liquid chromatography and paper chromatography they have shown that during the acetonation of II there is formed initially a dimer, $(II)_2$, which is converted into (2:3) (4:6)-diisopropylidene-α-L-sorbofuranose (III) and L-sorbopyranose (I). The latter undergoes acetonation to compound II, which is converted into the dimer $(II)_2$, etc. Compound III is partially hydrolyzed to IV. The reaction takes place according to the following scheme [8, 9]:



All-Union Scientific-Research Institute of Vitamins, Moscow. Translated from Khimiko-Farmatsevticheskii Zhurnal, Vol. 5, No. 1, pp. 55-59, January, 1971. Original article submitted November 5, 1969.

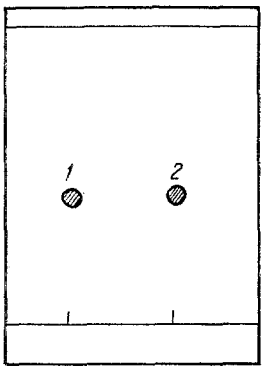


Fig. 1

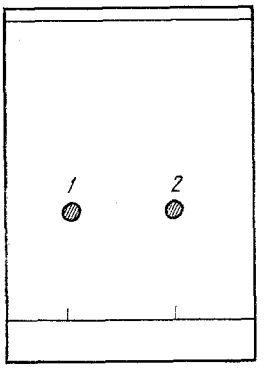


Fig. 2

Fig. 1. Chromatogram of 1,2-isopropylidene-α-L-sorbopyranose (II). 1) Compound II; 2) marker for II.

Fig. 2. Chromatogram of 2,3-isopropylidene-α-L-sorbofuranose (IV). 1) IV; 2) marker for IV.

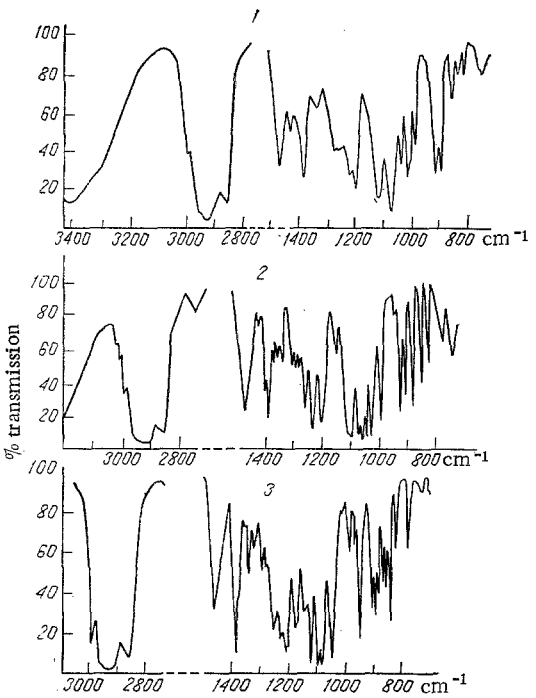
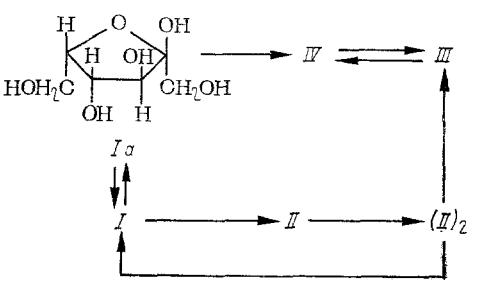


Fig. 3. IR spectra of acetone derivatives of L-sorbose. 1) II; 2) IV; 3) III.

The formation of III from II, in the opinion of the authors, is possible as a result of hydrolysis of the dimer. In other work [10] there is an indication that only II and III are formed during the acetonation process, and that IV is a hydrolysis product of III.

However, in our studies, already after 15 min from the beginning of the acetonation the following have been detected (in percent of theoretical yield) – II, 9.1; III, 18.2; and IV, 15.2 – which indicates that initially the process goes in the direction of forming IV with simultaneous formation of II. We have also confirmed that, upon acetonation of II and IV as isolated in pure form, both of these compounds give III, in yields of 70 and 78.7%, respectively. It must be assumed that in explaining the mechanism of the acetonation reaction one must take into account the existence of L-sorbose in two forms – the furanoside (Ia) and the pyranoside (I) – and hence the existence of two independent reaction directions, according to the following chemical scheme:



EXPERIMENTAL

1,2,-Isopropylidene-α-L-sorbopyranose (II) [4, 10]. A mixture of 10 g of anhydrous sorbose and 850 ml of dry acetone with 100 g of anhydrous copper sulfate was kept at 50° for 5 h, with vigorous shaking. The cooled reaction mixture was filtered, and the precipitate was washed with acetone. The slightly acid filtrate was basified to pH 7.5-8.0. The acetone was distilled off and the syrupy residue was treated with dry ether, as a result of which it crystallized, giving crystals of mp 142° (from ethyl acetate). The purity of the substance obtained was also confirmed by elemental analyses and chromatographically (Fig. 1). Found %: C 49.25; H 7.20. $C_9H_{16}O_6$. Calculated %: C 49.10; H 7.27.

TABLE 1. Results of a Study of the Kinetics of the Acetonation of L-Sorbose (I)

Compound formed	Time of sample withdrawal, from start of acetonian (in min)							
	15		30		45		60	
	content (in %)	yield (in %)	content (in %)	yield (in %)	content (in %)	yield (in %)	content (in %)	yield (in %)
III	2,19	18,2	5,6	46,7	7,2	60,0	7,2	60,0
	2,0	18,0	5,2	46,2	6,8	59,2	7,5	61,0
Average	9,09	18,1	5,4	46,45	7,0	59,6	7,35	6,05
IV	1,55	15,2	0,28	2,8	0,28	2,8	0,62	6,1
	1,7	15,6	0,25	2,7	0,22	2,5	0,71	6,5
Average	1,62	15,4	0,26	2,75	0,25	2,65	0,67	6,3
II	0,92	9,1	1,67	16,4	0,85	8,4	1,57	15,4
	0,9	9,0	1,8	16,9	0,8	8,3	1,62	15,6
Average	0,91	9,05	1,73	16,6	0,82	8,35	1,59	15,5

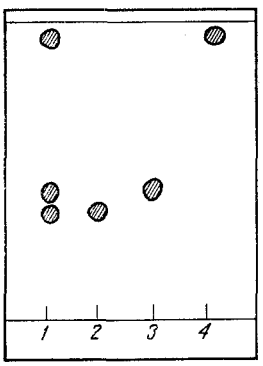


Fig. 4. Chromatogram of acetone derivatives obtained in acetonation of L-sorbose. 1) Reaction mixture; 2) mark for II; 3) mark for IV; 4) mark for III.

2,3-Isopropylidene-α-L-sorbofuranose (IV) [3]. Diacetone-L-sorbose (50 g) was dissolved in 800 ml of water containing 0.4 g of hydrochloric acid (d. 1.19), and the solution was allowed to stand for 2 h at 50°. Then the solution was neutralized with a saturated potassium carbonate solution until there was no acid reaction to Congo paper, and it was evaporated under vacuum (water bath temperature not over 50°); the residue was extracted with boiling ethyl acetate. After the larger part of the solvent had been distilled and the extract had been cooled, a precipitate of IV fell; it consists of colorless needles having a mp of 92-93° (from ethyl acetate). The purity of the substance obtained was also confirmed by elemental analyses and chromatographically (Fig. 1). Found %: C 49.2; H 7.25. $C_9H_{16}O_6$. Calculated %: C 49.1; H 7.27. In the IR spectra of compounds II, III, and IV (Fig. 3) absorption bands with the following frequencies are observed: 3580 cm^{-1} (valence stretching vibrations of a free OH group); 1460 cm^{-1} (CH_2 group); 1380 cm^{-1} [the $C(CH_3)_2$ group]; and 1250 cm^{-1} (the C–O group). The absorption intensity at 3580 cm^{-1} for IV and the very low one for III correspond to their chemical structures.

Identification of Acetone Derivatives Obtained in the Process of Acetonating L-Sorbose. For this purpose we used chromatography in a thin layer of adsorbent [11]. On a 9 × 12 cm plate, coated with silica gel bonded with gypsum, was applied the solution; it was dried, and the plate was placed in a chamber with the solvent (acetone–hexane, 3 : 2). Then the plate was dried again, and the spots were developed with an alcoholic phosphomolybdic acid solution. The acetone derivatives showed up in the form of blue-violet spots on a green background. To determine quantitatively the acetone derivatives, half of the plate was not developed, and the appropriate part of the silica gel was removed from it and the compound was eluted with acetone. The acetone eluates were evaporated on a water bath (at 80-90°), and the residue was dried for 3 or 4 min in a drying oven at 100-105°. To the dry residue was added 1 ml of water, 1 ml of 5% phenol solution, and 5 ml of concentrated sulfuric acid, and the mixture was allowed to stand for 30 min at 20°. The color intensity was measured in a photocolorimeter, and from a calibration curve the percent content of the acetone derivatives was calculated [12].

Investigation of the Process of Acetonation of L-Sorbose. (I). To a mixture of 125 ml of dry acetone and 10 g of dried sorbose, cooled to −4 to −6°, was added 5 ml of oleum, and the mixture was stirred for an hour while the temperature was maintained at 12-14°. Periodically, after every 15 min, samples of the reaction mixture were withdrawn and their solution was neutralized with sodium hydroxide to a weakly alkaline reaction. A 0.01-ml sample of the solution was withdrawn with a micropipette and was deposited on a plate. Using the method indicated above we were able to separate the acetone derivatives (Fig. 4) and then to determine the quantitative ratio in the reaction mixture in various stages of the acetonation. Results are given in Table 1.

Investigation of the Process of Acetonation of Individual 2,3-Isopropylidene-α-L-sorbofuranose (IV) and 1,2-Isopropylidene-α-L-sorbopyranose (II). To a mixture of 125 ml of dry acetone and 10 g of IV, cooled to −4 to −6°, 5 ml of oleum was added dropwise so that the temperature of the mixture did not rise above 10°. Acetonation was carried out for 2 h at 12-14°. At the end of the acetonation process the reaction mixture was rapidly cooled to −15° and was kept at this temperature for 1 h; then an inverse neutralization with a 14% sodium hydroxide solution was carried out, to a weakly alkaline medium. The precipitated sodium sulfate crystals were filtered off and the acetone and mesityl oxide were distilled off. Compound III was isolated from the syrup obtained by treatment with a 42% sodium hydroxide solution; yield 78.65%.

The acetonation of II was carried out similarly to give III in 70% yield.

LITERATURE CITED

1. V. M. Berezovskii, Vitamin Chemistry [in Russian], Moscow (1959), p. 61.
2. L. O. Shnaidman, Vitamin Production [in Russian], Moscow (1968), p. 246.
3. T. Reichstein and A. Grüssner, Helv. Chim. Acta, 17, 311 (1934); 21, 254 (1938).
4. H. Ohle, Chem. Ber., 71, 562 (1938).
5. T. I. Temnikova and V. V. Sklyarova, Zh. Prikl. Khim., No. 21, 1131 (1954).
6. V. M. Berezovskii and L. N. Strel'chunas, Zh. Organ. Khim., No. 1, 453 (1953).
7. A. A. Beér and I. A. Rubtsov, Synthesis of Vitamins [in Russian], Moscow (1956), p. 5.
8. K. Toknyama, E. Honda, and N. Hoki, J. Org. Chem., 29, 133 (1964).
9. K. Toknyama and E. Honda, Bull. Chem. Soc. Japan, 37, 591 (1964).
10. Y. Patil and J. Bose, J. Indian Chem. Soc., 43, (3), 161 (1966).
11. V. A. Devyatnin, V. M. Svetlaeva, L. O. Shnaidman, et al., Khim.-Farm. Zh., No. 5, 39 (1967).
12. M. Dubois and K. Gilles, Anal. Chem., 28, 350 (1956).