SYNTHESIS OF AN ESTER OF DEXTRAN AND PELENTANIC ACID

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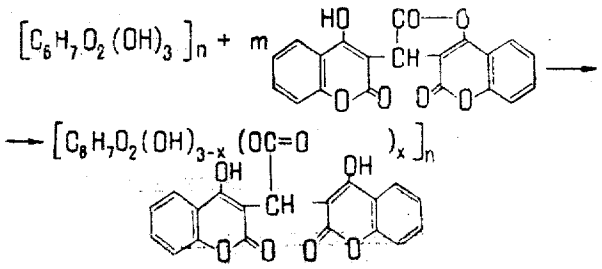
Khimiya Prirodnykh Soedinenii, Vol. 1, No. 4, pp. 245-246, 1965

One of the interesting trends developing at the present time in the chemistry of polymers is the synthesis of polymeric medicinal substances by the addition to polymers, by means of ionic, coordination, or covalent bonds, of low-molecular-weight medicinal compounds. This synthesis is generally carried out in order to prolong the action of the low-molecular-weight medicinal substances and to improve other properties – for example, their solubility [1].

A large number of polymeric medicinal substances has been obtained by S. N. Ushakov and his colleagues from poly-(vinyl alcohol) and copolymers of vinyl alcohol and also of vinylpyrrolidone [1, 2]. Of these preparations, considerable interest is attached to the ester of poly-(vinyl alcohol) and pelentanic acid, which possesses the properties of an anticoagulant [3].

When synthetic polymers foreign to the organism are used for the addition of low-molecular-weight medicinal substances, the assimilability of the latter and their excretion from the organism are of fundamental importance. Consequently, it is necessary to use carefully fractionated synthetic polymers, since when their molecular weight is too high the danger of their deposition in various organs arises. The use of the addition of low-molecular-weight medicinal substances of natural polymers – polysaccharides and proteins – which are gradually hydrolysed by enzymes in the organism would appear to be advantageous. In this case, it is probably possible to use polymers with a high molecular weight without fearing the possibility of their deposition in the organism. Among polysaccharides, the most interesting is dextran, which is widely used as a blood substitute [4].

In the present paper we consider the problem of the preparation of an ester of dextran and pelentanic acid. In the synthesis of this ester, as in the synthesis of the pelentanic ester of poly-(vinyl alcohol), the lactone of pelentanic acid was used as the acylating agent. The pelentanic ester of dextran was synthesized by the following route:



The reaction was carried out in aqueous pyridine solution containing 95% of pyridine for various periods of time at 20°C. The concentration of dextran in the solution was 4%. The pelentanic esters of dextran were obtained in the form of the pyridinium salts, readily decomposed by sodium bicarbonate, the degree of esterification of the dextran scarcely decreasing at all during this process. The pelentanic ester of dextran is readily soluble in water.

To characterize the composition of the products synthesized, their content of ester groups was determined from the bromine number [5] (see Table).

The results of the experiment show that the esterification reaction takes place at a high velocity during the first three hours, after which the velocity falls off. When more than 1.33 mole of pelentanic acid lactone per elementary unit of the dextran macromolecule was added to the reaction mixture, the degree of esterification rose only slightly, which may apparently be explained by steric factors.

The dextran ester synthesized has been sent for pharmacological testing.

Experimental

Cautiously, with cooling to +5°C and stirring, 4 ml of pyridine was added to a solution of 1 g of dry dextran in 1 ml of water. The necessary amount (0.1-6 g) of pelentanic acid lactone was dissolved in 15 ml of pyridine, after which this solution was added slowly, with cooling to +5°C and stirring, to the dextran solution. The mixture was left at 18°C for 3-27 hr.

The ester of pelentanic acid and dextran obtained was precipitated with acetone. The purification of the ester from unchanged lactone was carried out by reprecipitating it four times from pyridine in acetone. Then the product was

washed with acetone.

The products obtained (pyridine salt of the ester of pelentanic acid and dextran) contained from 1 to 6% of pyridine, depending on the degree of esterification.

Influence of the Esterification Conditions on the Compositions of the Ester of Pelentanic Acid and Dextran

Amount of pelentanic acid lactone used per elementary unit of the dextran, mole	Reaction time, hours	Composition of the pelentanic ester of dextran	
		Pelentanic acid residue, % by weight of the ester	Degree of esterification of the hydroxyl groups of the dextran, γ*
1.33	1	39.1	27.5
1.33	3	60.5	65.0
1.33	8	69.5	95.0
1.33	27	73.6	125.0
0.044	24	5.0	2.5
0.22	24	20.0	11.0
0.44	24	34.7	22.5
2.66	24	76.6	140.0

*γ represents the number of ester groups per 100 elementary units of the dextran macromolecules.

To eliminate the pyridine, the ester was dissolved in water and the solution was made alkaline to pH 7.5-8 with sodium bicarbonate. The sodium hydrogen salt of the pelentanic ester of dextran was precipitated with acetone, washed with it, and dried under vacuum over P_2O_5.

Summary

1. The ester of dextran and pelentanic acid with a maximum γ value of 140 has been synthesized.
2. The influence of some reaction conditions on the composition of the esters obtained has been investigated.

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29 March 1964

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