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BRIEF COMMUNICATIONS

Intramolecular Esters of Alginic Acid

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Abstract—The intramolecular ester (lactone) of alginic acid and of the polyuronide obtained on its fractionating were synthesized, and the effects of temperature and reaction duration on the number of ester groups formed in the polymer were studied.

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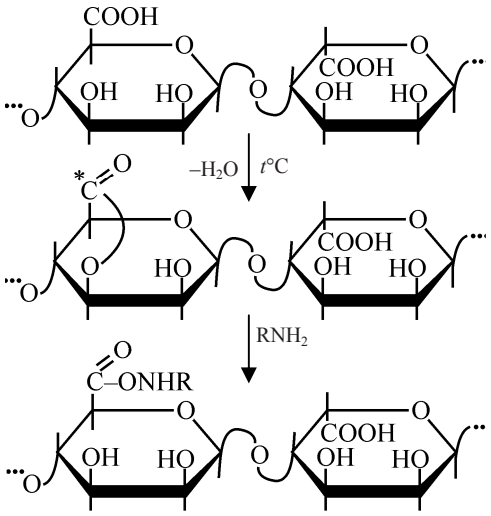
When certain carboxymethylpolysaccharides are heated their intramolecular esterification occurs [1] to form lactones, which in some cases are more accessible than esters and can be used as acylating agents in creating physiologically active polymers (PAP).

In this connection the aim of our work was to study the lactone-forming ability of alginic acid, which possesses a wide spectrum of biological activity [2]. It is accessible and can serve as a relatively low-cost raw material for the PAP synthesis, however its intermolecular and intramolecular esterification is poorly studied [3].

EXPERIMENTAL

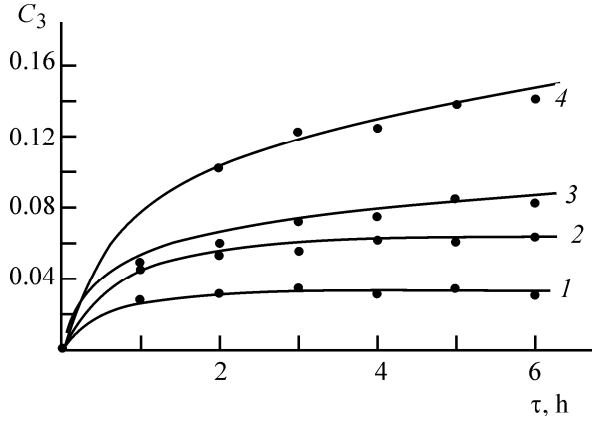
Chemical modification of alginic acid was carried out according to the scheme:



Here R is OH, NH_2; an asterix implies that the position of an ester group is shown arbitrarily.

Alginic acid is insoluble in aqueous solutions of acids that hinders the quantitative determination of ester groups in a polymer by means of the fast and convenient procedure based on their transformation to complexes of hydroxamic acid with iron(III) [4]. At the same time a fraction soluble in water at pH < 7 was found in the course of the fractionation of alginic acid (technical specifications 6-09-10-535-76). For its isolation we added concentrated hydrochloric acid to pH 2 to an alginic acid solution in 1 N aqueous NaOH, filtered off the resulting precipitate, and neutralized the filtrate up to pH 7, concentrated it in vacuum (20–25 mm Hg), removed low-molecular impurities by dialysis, concentrated the solution once more, and precipitated a polymer by alcohol. The precipitate was filtered off and washed with the alcohol. Yield 15–20%.

Thus isolated polymer is a white amorphous powder, soluble in aqueous solutions of acids and alkalis and insoluble in alcohol, acetone and some other organic solvents. On adding to it phenol and concentrated sulfuric acid a colored solution (a color reaction toward carbohydrates [5]) is formed. The conductometric titration analysis of the sample has shown that each monosaccharide fragment of the polymer contains a carboxyl group. In the IR spectrum of the isolated polyuronide in the H^+ form we have detected absorption bands at 1735 cm^{-1}, which are characteristic of carboxy group (C=O) stretching vibrations, and in the spectra of the Na^+ form,



Effect of reaction duration τ on the number of intramolecular ester groups C_3 in the polyuronide under study heated in vacuum at (*1*) 61, (2) 83, (*3*) 100, and (*4*) 117°C.

absorption bands at 1616 cm^{-1}, which can be assigned to the stretching vibrations of carboxylate ions [6]. It has appeared that the IR spectra of alginic acid and the polyuronide practically coincide. Having assumed that the isolated polysaccharide is a low-molecular fraction of alginic acid or a polyuronide related to it, we used it to determine conditions of the formation of intramolecular esters.

Polyuronide lactones were prepared by heating its H^+ form either in vacuum at 61–117°C from 1 up to 6 h or in boiling dioxane or toluene for 6–8 h. On the reaction termination the product was filtered off, washed with alcohol, and dried in a vacuum at 60°C. When using toluene the reaction was carried out with the azeotropic water distillation.

The resulting samples of the polyuronide lactone are amorphous powders insoluble in alcohol and acetone and soluble in water and aqueous solutions of alkalis and acids.

Table 1. Degree of conversion of carboxy groups of certain polysaccharides to intramolecular esters on heating in vacuum (20 mm Hg, 110°C, 4 h)

Polysaccharide	C_3, %
Carboxymethyldextrane	25.1
Carboxymethylamylose	16.0
Carboxymethylcellulose	12.5
Polyuronide under study	12.3[a]
Carboxymethylrhodexman	11.5
Carboxyethyldextrane	7.4

[a] Temperature 117°C.

In the IR spectra of samples of lactones preliminarily treated by sodium alcoholate or reprecipitated from a sodium carbonate solution to convert carboxy groups to carboxylate ions we detected absorption bands at 1777 cm^{-1} characteristic of ν(C=O) of a pentatomic lactone, which are absent from the spectra of the initial polyuronide, and also absorption bands ν ($RCOO^-$) of the carboxylate ion at 1616 cm^{-1} [6].

The samples obtained were characterized by a degree of substitution C_s that is a number of the ester groups per a monosaccharide fragment.

Ester groups in a polymer were determined by the hydroxamic reaction. We used gluconic acid lactone, which we have synthesized, as a model compound for constructing a calibration plot. To obtain it, we passed a 10% aqueous solution of calcium gluconate through KU-2×8 ion-exchange resin and distilled off water from the resulting solution up to formation of a syrup. The residue was mixed with dioxane and boiled for 8 h. After cooling the reaction mixture we filtered off the precipitated lactone, washed it with cold dioxane and alcohol, and dried at 60°C. Melting point of the product obtained was 134–136°C.

The study of the reaction of lactone formation on heating the polyuronide in vacuum has shown that the number of ester groups increases as temperature and reaction duration increase (see the figure), the greatest number of lactones (C_s = 0.142) being formed in samples at 117°C in 6 h. However the further temperature increase is not rational as it can lead to the polymer decomposition.

The data on the ability of other polysaccharides to form intramolecular esters [7] are presented in Table 1 in comparison to the polyuronide. As it has appeared, its ability to lactonization is comparable with the activity of carboxymethylrhodexman and carboxymethylcellulose.

The alternative procedure for obtaining lactones is heating of a polyuronide in an inert organic solvent. It has appeared in this case (Table 2) that the number of ester groups in samples is practically independent of reaction medium type. Heating in dioxane or toluene under equal conditions results in the formation of approximately equal number of lactones. The reaction temperature is of the greatest importance for the lactonization process: the higher it is, the greater is the degree of substitution on ester groups.

It has also appeared that on heating in alcohols (ethanol, propanol, butanol, and benzyl alcohol) the

Table 2. Synthesis of polyuronide lactones in organic solvents (6 h)

Solvent	bp	C_3, %	
		1[a]	2[a]
Ethanol	78.3	0.043	–
Dioxane	100.8	0.076	0.126[b]
Toluene	110.6	0.085	0.141[b]
1-Butanol	117.7	–	0.149

[a] (1, 2) are polyuronides isolated from alginic acids of different batches. [b] Holding time 8.5 h.

polyuronide under study, unlike other carboxylated polysaccharides, forms not intermolecular esters, but lactones.

No absorption maxima at 256 nm corresponding to the absorption by benzyl ester were found in the UV spectra of samples synthesized on heating the polyuronide in benzyl alcohol. At the same time in the IR spectra of all synthesized samples in the Na^+ form absorption bands at 1777 cm^{-1} characteristic of ν(C=O) of a pentatomic lactone and bands at 1616 cm^{-1} characteristic for the carboxylate ion were found, whereas absorption bands at 1745 cm^{-1} characteristic of ν(C=O) of the Alk–COO–Alk group were not detected.

It was also found (Table 2) that the number of ester groups in a polyuronide strongly depends on a particular batch of alginic acid. Within the limits of one batch the dependence of the process of lactones formation on the reaction duration and temperature is obeyed, however polyuronides isolated from different batches of alginic acid have different ability to lactonization. It is known that alginic acids can differ by the sequence and relation of mannuronic and guluronic units [8] that, probably, is responsible for different ability to form intramolecular esters.

Thus, the most convenient method of the synthesis of lactones of the polyuronide under study is its heating in vacuum at 110–120°C or in boiling toluene. Therewith the second procedure is more convenient in certain cases, as the reaction can be carried out up to the termination of water liberation, which is distilled off from the reaction medium in the azeotrope form.

The results obtained in studying the ability of a polyuronide to form lactones were further used in the synthesis of lactones of alginic acid itself.

The lacronization of alginic acid was carried out in toluene with the azeotropic distillation of water within 6–8 h.

In the IR spectra of alginic acid lactones (as well as in the IR spectra of polyuronide lactones) we have detected absorption bands at 1777 cm^{-1}, which are characteristic of ν(C=O) of a pentatomic lactone.

The number of ester groups in alginic acid lactones was determined by the results of their reactions with hydroxylamine and hydrazine [4]. The synthesized hydroxamic acid and alginic acid hydrazide were analyzed by the elemental analysis for nitrogen and by the iodometric titration [9].

Thus it was found that the lactones obtained by heating alginic acid in toluene (from 6 up to 8 h) react with hydroxylamine to form hydroxamic acids with a substitution degree (a number of hydroxamic acids per a monosaccharide fragment of a polymer) from 0.085 up to 0.141.

The analysis of the products of the reaction between lactones of alginic acid and hydrazine hydrate has shown that the number of hydrazide groups in a polymer is about 0.15 mol per a monosaccharide fragment, hence the number of ester groups in the lactone of alginic acid was no less than this value.

CONCLUSION

On heating alginic acid in vacuum or in organic solvent up to 15% of its carboxy groups form intramolecular esters (lactones), which give the corresponding hydroxamic acid and hydrazide upon the reaction with hydroxylamine or hydrazine.

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