Preparation of *O*-(3-formylmethoxy-2-hydroxypropyl)cellulose

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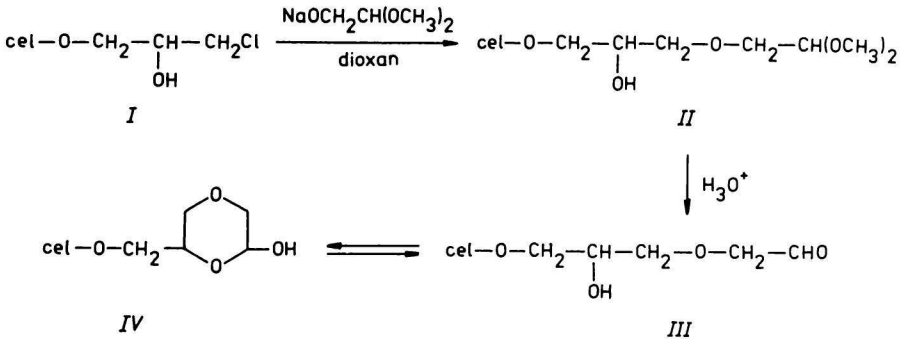
O-[3-(2,2-Dimethoxyethoxy)-2-hydroxypropyl]cellulose has been prepared by the reaction of bead *O*-(3-chloro-2-hydroxypropyl)cellulose with sodium 2,2-dimethoxyethoxide in dioxan. On partial acid hydrolysis this derivative afforded *O*-(3-formylmethoxy-2-hydroxypropyl)cellulose. Under the conditions of alkylation partial crosslinking of cellulose by transverse 2-hydroxy--1,3-propylene bonds took place. The prepared new aldehyde derivative of bead cellulose retained the spheric shape of the particles.

Реакцией гранулированной *O*-(3-хлор-2-гидроксипропил)целлюлозы с натриевым 2,2-диметоксиэтоксидом в диоксане была получена *O*-[3-(2,2-диметоксиэтокси)-2-гидроксипропил]целлюлоза. В результате частичного кислого гидролиза этого соединения была получена *O*-(3-формилметокси-2-гидроксипропил)целлюлоза. В условиях алкилирования имело место частичное межцепочечное связывание целлюлозы поперечными 2-гидрокси-1,3-пропиленовыми мостиками. Полученное новое альдегидное производное гранулированной целлюлозы сохраняло сферическую форму частиц.

One of the most important types of chemically modified celluloses utilizable as polymeric reagents or carriers of covalently bound biochemicals are aldehyde derivatives. From the point of view of accessibility of the reacting functional groups as well as hydrodynamic properties, bead cellulose is most suitable for these purposes. In the previous work [1] we published the classification of these derivatives according to the origin of their carbonyl carbon. The present work deals with preparation of another aldehyde derivative of different substitutional type, *i.e.* such one where the aldehyde group is bound to the basic chain of the polysaccharide through a side chain.

The starting derivative of bead cellulose, *O*-(3-chloro-2-hydroxypropyl)cellulose (*I*; Scheme 1), was prepared in suspension to retain the physicochemical properties of bead cellulose [2]. In the reaction of the derivative *I* with sodium 2,2-dimethoxyethoxide in anhydrous dioxan 50 % conversion to *O*-[3-(2,2-dimethoxyethoxy)-2-hydroxypropyl]cellulose (*II*) has been achieved. In the subse-



Scheme 1

quent step, *i.e.* on partial acid hydrolysis, this derivative was converted to the final product, bead *O*-(3-formylmethoxy-2-hydroxypropyl)cellulose (*III*). The presence of the formylmethoxy group in the obtained aldehyde derivative *III* was proved by means of IR spectrometry on the basis of the intensive broad band appearing at

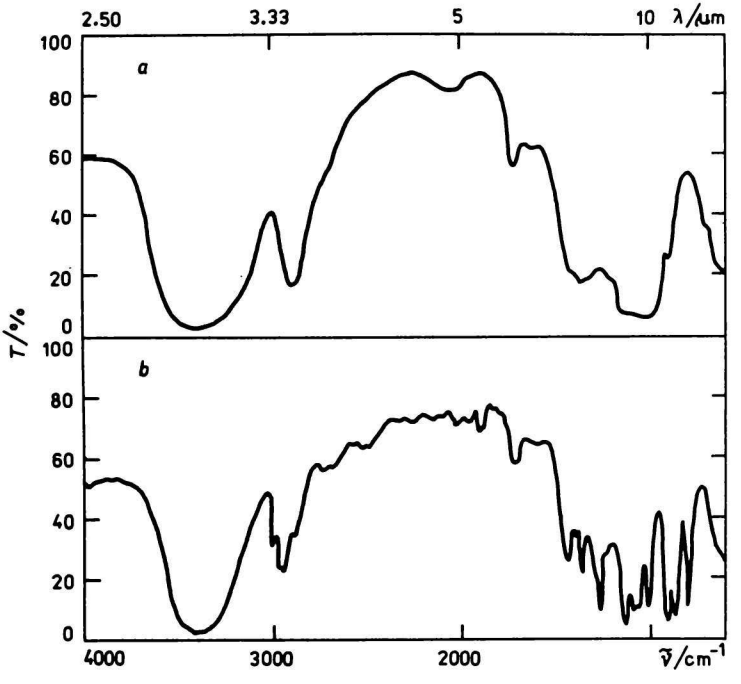


Fig. 1. Infrared spectra (KBr) of *O*-(3-formylmethoxy-2-hydroxypropyl)cellulose (*a*) and glycolaldehyde (*b*).

$\tilde{\nu} = 1720\ cm^{-1}$, present also in the spectrum of glycolaldehyde (Fig. 1). The content of aldehyde groups was established from the nitrogen content after converting *III* to its 4-nitrophenylhydrazone. By the described procedure the required cellulose derivative was prepared with the degree of substitution by 3-formylmethoxy-2-hydroxypropyl groups of about 0.1. Due to the presence of the δ-hydroxyl group in the spacer of the prepared derivative *III*, there is a possibility of formation of the 1,4-dioxanoide structure of the substituent with hemiacetal hydroxyl group (*IV*), stabilizing thus its aldehyde group. Therefore, this derivative may be described also as *O*-[6-hydroxy-1,4-dioxan-2-yl)methyl]cellulose.

The attempts to dissolve the prepared *O*-(3-formylmethoxy-2-hydroxypropyl)-cellulose as well as the intermediate, *O*-[3-(2,2-dimethoxyethoxy)-2-hydroxy-propyl]cellulose, in cadoxene [3] were unsuccessful. With regard to the fact that modification reactions of bead cellulose can be practically performed only in a heterogeneous phase, it is necessary to use manifold excess of the reactants. From the same reason we used excess amount of the nucleophile, *i.e.* sodium 2,2-dimethoxyethoxide. The reason why the derivatives mentioned above were insoluble lies evidently in the displacement reaction of the nucleophile with hydroxyl groups of cellulose leading to concurrent reactions, *i.e.* crosslinking of the cellulose chains with transverse 2-hydroxy-1,3-propylene bonds similarly as in the crosslinking reaction of alkali cellulose with chloromethyloxirane [4]. Crosslinking of the tertiary structure of the newly prepared aldehyde derivative of cellulose, proceeding simultaneously, prevented its decomposition which might occur during partial acid hydrolysis of the dimethyl acetal-protected intermediate. Owing to this fact, the product obtained in quantitative yield retained the spheric shape of the particles.

Utilization of the prepared cellulose derivative for binding of biochemicals and evaluation of its structural features will be the subject of our next work.

Experimental

O-(3-Chloro-2-hydroxypropyl)cellulose (*I*) was prepared from bead cellulose (Institute of Macromolecular Chemistry, Prague) according to [2] and glycolaldehyde dimethyl acetal according to [5]. 4-Nitrophenylhydrazone derivatives of *O*-(3-formylmethoxy-2-hydroxy-propyl)cellulose were obtained by the similar procedure as the same derivative of *O*-(formylmethyl)cellulose [1]. Elemental analyses were performed on a Perkin—Elmer 240 analyzer and infrared spectra were recorded with a Perkin—Elmer 457 spectrometer. Degrees of substitutions *S* of the cellulose derivatives were calculated after the relationship $S = 162/(M_x/w_x - \Delta M_r)$, where M_x is the relative atomic or molecular mass, w_x is the mole ratio of the element or group determined, ΔM_r is the increment of relative molecular mass of the glucose residue in cellulose brought about by substitution.

O-[3-(2,2-Dimethoxyethoxy)-2-hydroxypropyl]cellulose (II)

In the sucked bead *O*-(3-chloro-2-hydroxypropyl)cellulose (5.7 g, dry mass = 17.5 %, Cl 4.1 %, *i.e.* 1.15 mmol, *S* (3-chloro-2-hydroxypropyl groups) = 0.21) water was replaced with anhydrous dioxan through methanol. Then it was added into the freshly prepared dioxan suspension of sodium 2,2-dimethoxyethoxide, obtained from glycolaldehyde dimethyl acetal (1.3 g; 12.3 mmol), sodium hydride (0.3 g; 12.5 mmol), and anhydrous dioxan (20 cm^3; 50 °C, 3 h), and the reaction mixture was shaken for 24 h at room temperature. Then the mixture was diluted with methanol (20 cm^3), sucked, and washed with water until negative reaction for alkalis and chlorides. White bead *O*-[3-(2,2-dimethoxyethoxy)-2-hydroxypropyl]cellulose (yield = 7.0 g, dry mass = 16.9 %) insoluble in cadoxene was obtained.

O-(3-Formylmethoxy-2-hydroxypropyl)cellulose (III)

a) To the sucked bead *O*-[3-(2,2-dimethoxyethoxy)-2-hydroxypropyl]cellulose (1.5 g) 0.05 M-hydrochloric acid (3 cm^3) was added and the mixture was heated at 100 °C. After 30 min, 60 min, and 120 min samples were withdrawn (*ca.* 0.5 g), washed with water to neutral reaction, and converted to 4-nitrophenylhydrazone derivatives. The content of aldehyde groups was calculated from the determined nitrogen (Table 1).

Table 1

Hydrolysis of bead *O*-[3-(2,2-dimethoxyethoxy)-2-hydroxypropyl]cellulose to *O*-(3-formylmethoxy-2-hydroxypropyl)cellulose (100 °C, 0.05 M-HCl (3 cm^3) + cellulose derivative (1.5 g, dry mass = 16.9 %))

t/min	*w*(N)/%	*S*
30	1.99	0.09
60	2.18	0.10
120	2.14	0.10

w(N) — Mass ratio of nitrogen in 4-nitrophenylhydrazone derivative.
S — Degree of substitution by 3-formylmethoxy-2-hydroxypropyl groups.

b) Suspension of the sucked bead *O*-[3-(2,2-dimethoxyethoxy)-2-hydroxypropyl]-cellulose (5 g) in 0.05 M-hydrochloric acid (10 cm^3) was heated at 100 °C for 1 h. After washing the solid phase with water to neutral reaction, white bead *O*-(3-formylmethoxy-2-hydroxypropyl)cellulose (yield = 4.4 g, dry mass = 16.5 %, *w* = 2.24 % nitrogen in the 4-nitrophenylhydrazone derivative, *S* (3-formylmethoxy-2-hydroxypropyl groups) = 0.10) insoluble in cadoxene was obtained.

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