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LETTERS
TO THE EDITOR

Synthesis of Hydroxamic Derivatives of Carboxymethyl- and Carboxyethyldextran

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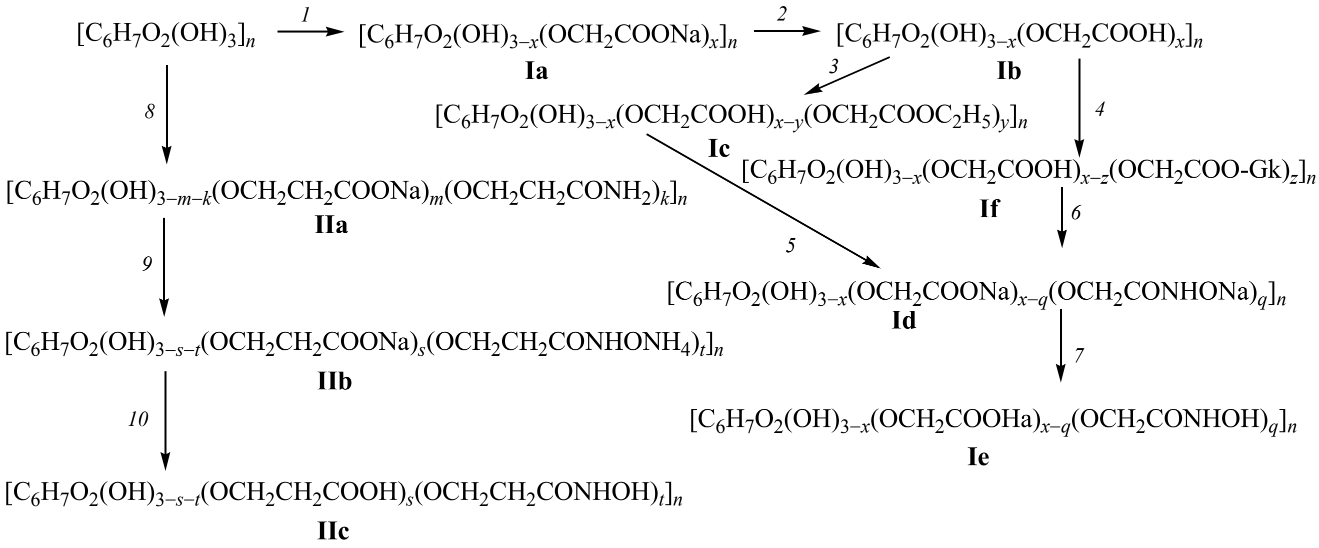
Synthesis of polyligands and chemisorbents is of particular interest in the chemistry of modified natural polysaccharides. The cross-linked chitosan derivatives were proposed as complexing agents [1]. Derivatives of the starch dialdehyde dioximes and dihydrazones show high chelating ability in relation to a number of metals [2, 3].

In the present work the chemical modification of the microbial polysaccharide dextran was carried out in order to obtain hydroxamic derivatives carboxymethyl- (**Ie**) and carboxyethyldextran (**IIb**). Many compounds containing hydroxamic groups are known to be strong chelating agents and are widely used in analytical chemistry [4].



1, $ClCH_2COOH$, NaOH, 60°C, 3 h; *2*, *7*, *10*, cation-exchange resin KU-2-8; 3, EtOH, reflux, 10 h; *4*, 100°C, vacuum; *5*, *6*, $NH_2OH{\cdot}HCl$, NaOH, 20°C, 20 min or NH_2OH, 20°C, 16 h; *8*, $CH_2{=}CHCONH_2$, NaOH, 40°C, 3 h or $CH_2{=}CHCONH_2$, $(Et)_4N^+OH^-$, dioxane, 40°C, 3 h; *9*, $NH_2OH{\cdot}HCl$, K_2CO_3, 90°C, 1 h.

We used for further transformations the synthesized by us carboxymethyldextran derivatives **Ia** (**Ib**) with carboxymethylation degree of 1.2–1.47 and carboxyethyldextran **IIa** amides derivatives with carboxyethylation degree of 0.53–1.48 per monosaccharide unit. Esterification degrees of carboxymethyldextran **Ic** ethyl esters obtained by the autocatalysis reaction were 31–32%. Lactonization degree of the corresponding carboxymethyldextran **If** lactones was 22–24%. According to the elemental analysis data, the conversion of ester groups into hydroxamic moieties reaches up to 90%. Thus, we obtained dextran **Id** derivatives containing carboxymethyl and carboxymethylhydroxamic groups whith the (*N*-hydroxy)amidation degree 0.34–0.42. The conversion of amide groups into the hydroxamic ones in derivatives **IIb** was 45–51%, and the corresponding (*N*-hydroxy)amidation degree 0.24–0.76 per the monosaccharide unit.

We used a commercial dextran [linear 1,6(1,3)-polyglucan produced by *Aureobasidium pullulans*] with *M* 60000. The ^{13}C NMR spectra were recorded in a pulse mode on a Bruker AM-500 spectrometer with the operating frequency of 50.32 MHz in D_2O. The IR spectra were recorded on a FSM 1201 Fourier spectrometer from KBr pellets. The UV spectra of aqueous solutions of hydroxamic derivatives were recorded on an Ocean Optics PX-1 spectrometer using 1 cm cuvettes at room temperature. The photometric measurements were performed on a KFK-3-01 spectrophotometer.

(1→6)-2(3)-*O*-(*N*-Hydroxy)ethanamido-2(3)-*O*-carboxymethyl-α-*D*-glucan sodium salt (Id). *a.* 1 g of the powdered compound **Ic** or **If** was dissolved in aqueous alkaline solution of hydroxylamine (10 ml of 2 M $NH_2OH \cdot HCl$ and 10 ml of 3 M NaOH) and the reaction mixture was kept under stirring for 20 min at 20°C.The resulting solution was dialyzed against distilled water for 24 h, then evaporated in a vacuum evaporator to form a film. The film was triturated in acetone to obtain a powder, which was filtered off and dried in a vacuum desiccator at 20°C.

b. To 1 g of the powdered of compound **Ic** was added 10% aqueous solution of hydroxylamine (10 ml). The solution was stirred at 20°C for 16 h. The desired product was isolated as described above.

The (*N*-hydroxy)amidation degree 0.36, yield 95%, white powder. The IR spectrum (KBr), ν, cm^{-1}: 3425, 2925, 1675 (CONH), 1600 (COO^-), 1418, 1323, 1150, 1100, 1015, 707, 588. UV spectrum: λ_{max} 225 nm. ^{13}C NMR spectrum (50.32 MHz, D_2O), δ_C, ppm: 177 (COO^-), 169 (CONH).

(1→6)-2(3)-*O*-(*N*-Hydroxy)propanamido-2(3)-*O*-carboxyethyl-α-*D*-glucan sodium salt (IIb). To a solution of 1 g of compound **Ib** in 10 ml of H_2O were added aqueous solutions of hydroxylamine and potassium carbonate (10 ml 2 M $NH_2OH \cdot HCl$ and 4 ml of 2 M K_2CO_3), and the reaction mixture was kept under stirring at 90°C in a water bath for 1 h. After cooling, the solution was dialyzed against distilled water for 24 h. The solution was filtered and evaporated in a vacuum evaporator to form a film. The resulting film was triturated in acetone to obtain a powder, which was filtered off and dried in a vacuum desiccator at 20°C.

The (*N*-hydroxy)amidation degree 0.71, yield 90%, pale yellow powder. IR spectrum (KBr), ν, cm^{-1}: 3425, 2928, 1665 (CONH), 1575 (COO^-), 1422, 1367, 1154, 1107, 1012, 765, 538. UV spectrum: λ_{max} 235 nm. ^{13}C NMR spectrum (50.32 MHz, D_2O), δ_C, ppm: 177 (COO^-), 170 (CONH).

Synthesis of compounds (Ie) and (IIc). A solution of 0.95 g of compound **Id** or **IIb** in 25 ml of H_2O was transferred into a chromatography column with a cation exchange resin KU-2-8. The eluate and washings were collected in a flask (0.5 l) and evaporated to dryness in a vacuum evaporator. The precipitate was triturated in acetone and dried in a vacuum desiccator at 20°C.

(1→6)-2(3)-*O*-(*N*-Hydroxy)ethanamido-2(3)-*O*-carboxymethyl-α-*D*-glucan (Ie). (*N*-Hydroxy)amidation degree 0.36, yield 91%, pink powder. IR spectrum (KBr), ν, cm^{-1}: 3435, 2928, 1740 (COOH), 1645 (CONH), 1442, 1357, 1242, 1154, 1117, 1008, 762, 663. UV spectrum: λ_{max} 212 nm.

(1→6)-2(3)-*O*-(*N*-Hydroxy)propanamido-2(3)-*O*-carboxyethyl-α-*D*-glucan (IIc). (*N*-Hydroxy)amidation degree 0.71, yield 89%, pink powder. IR spectrum (KBr), ν, cm^{-1}: 3435, 2928, 1723 (COOH), 1655 (CONH), 1438, 1357, 1272, 1201, 1157, 1114, 1012, 917, 843, 762. UV spectrum: λ_{max} 215 nm.

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