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Sulfation of Diethylaminoethyl Cellulose with Chlorosulfonic Acid in 1,4-dioxane

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Abstract. Sulfation of diethylaminoethylcellulose with chlorosulfonic acid in 1,4-dioxane was studied. It is shown that with an increase in the amount of chlorosulfonic acid and the duration of the process, an increase in the sulfur content in diethylaminoethylcellulose sulfate is observed. The maximum sulfur content (13.8 wt.%) in DEAE-cellulose sulfate is observed at a ratio of $ClSO_3H$:(DEAEC) of 20.22:1 (mmol: g) and a process duration of 180 min. The introduction of a sulfate group into the DEAEC molecule was confirmed by elemental analysis and FTIR spectroscopy. In the FTIR spectra of ethylaminoethylcellulose sulfate there are absorption bands related to stretching vibrations υ(C–O–S) at 810–815 cm^{-1} and asymmetric stretching vibrations υas(O=S=O) at. 1249–1254 cm^{-1}. Using X-ray phase analysis and optical microscopy, it was shown that during the sulfation of diethylaminoethylcellulose, amorphization of the material is observed. It has been shown by gel permeation chromatography that with an increase in the duration of the sulfation process, glycosidic bond cleavage reactions are also observed with the formation of products with a lower molecular weight and greater polydispersity.

Keywords: cellulose, DEAE-cellulose, 1,4-dioxane, chlorosulfonic acid, sulfation.

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Сульфатирование диэтиламиноэтилцеллюлозы хлорсульфоновой кислотой в 1,4-диоксане

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Аннотация. Изучено сульфатирование диэтиламиноэтилцеллюлозы хлорсульфоновой кислотой в 1,4-диоксане. Показано, что с увеличением количества хлорсульфоновой кислоты и продолжительности процесса наблюдается увеличение содержания серы в сульфате диэтиламиноэтилцеллюлозы. Максимальное содержание серы (13.8 мас.%) в сульфате ДЭАЭ-целлюлозы наблюдается при соотношении $ClSO_3H$:(ДЭАЭЦ) 20,22:1 (ммоль: г) и продолжительности процесса 180 мин. Введение сульфатной группы в молекулу ДЭАЭЦ-подтверждено данными элементного анализа и ИК-Фурье-спектроскопии. В ИК-спектрах сульфата этиламиноэтилцеллюлозы присутствуют полосы поглощения, относящиеся к валентным колебаниям υ(C–O–S) при 810–815 $см^{-1}$ и асимметричным валентным колебаниям υas(O=S=O) при 1249–1254 $см^{-1}$. Методами рентгенофазового анализа и оптической микроскопией показано, что в процессе сульфатирования диэтиламиноэтилцеллюлозы наблюдается аморфизация материала. Методом гель-проникающей хроматографии показано, что с увеличением продолжительности процесса сульфатирования также наблюдаются реакции разрыва гликозидных связей с образованием продуктов с меньшей молекулярной массой и большей полидисперсностью.

Ключевые слова: целлюлоза, ДЭАЭ-целлюлоза, 1,4-диоксан, хлорсульфоновая кислота, сульфатирование.

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Introduction

Modern polymer chemistry is focused on the creation of biodegradable materials that meet increasingly stringent economic and environmental requirements. In this regard, special attention has been paid to natural biopolymers from renewable raw materials, such as cellulose, starch, and chitin [1]. Such raw materials are the basis for biodegradable and biocompatible materials that can become an alternative to synthetic polymers obtained from petrochemical raw materials.

Cellulose is the main structural component of lignocellulosic biomass and a valuable chemical raw material from which valuable chemical compounds can be obtained [2]. Cellulose, as the most widespread, renewable biopolymer resource, attracts a lot of attention from researchers for the production of new cellulose materials. Such unique properties of cellulose as biocompatibility, non-toxicity, polychirality, multifunctionality, mechanical strength, high crystallinity, the ability to form certain superstructures. determine its use to create materials with a variety of properties. Cellulose derivatives are widely used in the food, pharmaceutical, and chemical industries [3–6]. Thus, cellulose acetate sulfates can also have mitogenic activity [7]. Among mixed cellulose esters, carboxymethyldiethylammoniummethyl cellulose and carboxymethyl-2-diethylaminoethyl cellulose can be distinguished, which are used to separate gold, platinum, and palladium [8].

Among cellulose derivatives, special attention is paid to products containing a sulfate group. Cellulose sulphation is a new way to obtain water-soluble products with demanded quality characteristics, in particular, the ability to enzymatically decompose compared to native cellulose. Cellulose sulfates are used in various industries as thickeners, sorbents, ion exchange materials, etc. [five]. In addition, cellulose sulfates have anticoagulant activity [6], and the presence of various functional groups can significantly expand the scope of their application. Sulfuric anhydride complexes with various bases are widely used as sulfating reagents for hydroxyl-containing organic compounds, which are used not only to obtain a sulfating mixture, but also as a reaction medium [10].

Previously [9], we were the first to obtain a new derivative, diethylaminoethyl cellulose sulfate, using sulfamic acid in 1,4-dioxane and in a eutectic mixture with urea. It has been shown that when using a eutectic mixture of sulfamic acid-urea, side reactions of carbaming occur.

Diethylaminoethylcellulose is a positively charged resin commonly used in ion exchange chromatography to separate biomolecules and, in particular, to purify proteins and nucleic acids [11]. Diethylaminoethylcellulose is a commercially available compound. As a derivative of cellulose, it is environmentally friendly and easily decomposed. The study of other areas of use of diethylaminoethylcellulose and its derivatives, in addition to simple use in chromatographic technologies, is of particular interest. For example, its modification with sulfate groups leads to the formation of a

material whose surface contains both cationic and anionic groups. Such materials can be used as a basis for microcarriers in biomedical technologies [12].

In order to obtain water-soluble multifunctional cellulose with the simultaneous presence of cationic and anionic functional groups, the process of sulfation of diethylaminoethylcellulose with chlorosulfonic acid in 1,4-dioxane was studied. The structure and composition of the sulfation products were studied by FTIR spectroscopy, X-ray diffraction, optical microscopy, gel permeation chromatography, and elemental analysis.

Experimental part

We used diethylaminoethylcellulose (DEAE-Cellulose) (Reakhim, Russia).

The sulfur trioxide complex with 1,4-dioxane used for sulfation of DEAE-cellulose was obtained by the reaction of 1,4-dioxane with chlorosulfonic acid [10]. To do this, 25 ml of 1,4-dioxane were placed in a three-necked flask equipped with a thermometer, a mechanical stirrer, and a dropping funnel, and 1–4 ml (15.2–60.8 mmol) chlorosulfonic acid.

Sulfation of DEAE cellulose with the previously prepared sulfur trioxide complex was carried out according to a modified procedure [13]. 2.5 g of DEAE-cellulose was added to the complex of sulfur trioxide and 1,4-dioxane with stirring at a temperature of 20–22 °C, and the reaction mixture was stirred at this temperature for 60–180 min. Upon completion of the sulfation process, the reaction mixture was neutralized with an aqueous ammonia solution to pH 8–9. To remove inorganic salts and other low molecular weight compounds, the neutralized reaction mixture was subjected to dialysis against water. Dialysis was carried out in a cellophane dialysis bag brand MF-503–46 MFPI (USA) with a pore size of 0.1 μm for 10–15 hours, changing the water every hour. After dialysis, an aqueous solution of sulfated DEAE-cellulose was evaporated to dryness in a vacuum on a rotary evaporator and a solid residue was obtained – sulfated DEAE-cellulose in the form of an ammonium salt containing 6.3–13.8 wt.% sulfur.

Elemental analysis of DEAE-cellulose sulfate was performed on a Flash EA-1112 elemental analyzer (Thermo Quest Italia).

The FTIR spectra of DEAE-cellulose and DEAE-cellulose sulfate were recorded using a Shimadzu IR Tracer-100 IR Fourier spectrometer (Japan) in the wavelength range of 400–4000 cm-1. The spectral information was processed using the OPUS program (version 5.0). Solid samples for analysis were prepared as tablets in a KBr matrix (2 mg sample/1000 mg KBr).

Optical microscopy data were acquired with an OSEELANG OSL-017 microscope (Wuyi, Zhejiang, China) and processed with S-Viewer 1.0 software.

Weight average molecular weight (Mw), number average molecular weight (Mn) and polydispersity of liquid product samples were determined by gel permeation chromatography using an Agilent 1260 Infinity II Multi-Detector GPC / SEC System with triple detection: refractometer (RI), viscometer (VS) and light scattering (LS). Separation was carried out on 2xAquagel-OH mixed M and Aquagel OH-30 columns using a 0.1 M aqueous solution of LiNO3 as a mobile phase. The column was calibrated using polydisperse PEG / PEO standards (Agilent, USA). The flow rate of the eluent was 1 (ml / min), the volume of the injected sample was 100 μl. Before analysis, the samples were dissolved in the mobile phase (5 mg / ml) and filtered through a 0.45 μm PTFE membrane filter (Millipore). Data collection and processing was performed using Agilent GPC / SEC MDS software.

Results and Discussions

A well-known method for the sulfation of hydroxy-organic compounds is the use of complexes of sulfur trioxide with organic solvents [10, 14], which can also be obtained by reacting chlorosulfonic acid with the corresponding bases. The use of 1,4-dioxane in the sulfation of polymers with chlorosulfonic acid has a number of advantages. First, 1,4-dioxane is a less toxic organic solvent than pyridine, which is often used in sulfation reactions. Second, sulfation by the complex of 1,4-dioxane with sulfur trioxide proceeds in a lower temperature range than during sulfation with other reagents [13]. The SO_3–1,4-dioxane complex is unstable when the temperature rises above 30 °C; therefore, DEAEC was sulfated with this complex at a temperature of 20–22 °C.

In Table 1 presents the results of a study of the effect of the ratio of reagents on the sulfur content in DEAE-cellulose sulfate during sulfation with chlorosulfonic acid in 1,4-dioxane.

According to the data presented in Table 1, with an increase in the amount of chlorosulfonic acid and the duration of the process, the formation of a more sulfated product occurs, reaching the maximum value of sulfur (13.8 wt.%) at a ratio of $ClSO_3H$: (DEAEC) 20.22: 1 (mmol: g) and process duration 180 min. Moreover, for a given ratio of reagents, with a decrease in the duration of the process from 180 to 60 min, a symbatic decrease in the sulfur content in the target product, DEAE-cellulose sulfate, is observed.

In comparison with the results obtained during sulfation of microcrystalline cellulose (MCC) under similar conditions [15], sulfation of DEAE-cellulose made it possible to synthesize a water-soluble sulfated product with a high sulfur content (13.8 % versus 9.3 %). The greater reactivity of DEAE cellulose compared to MCC in the sulfation reaction may be due to the different morphology of the initial objects, and hence the greater availability of reactive hydroxyl groups.

The embedding of a sulfate group into the DEAE-cellulose molecule was confirmed by FT-IR spectroscopy (Fig. 1). In the FTIR spectra of ethylaminoethylcellulose sulfate there are absorption bands related to stretching vibrations υ(C–O–S) at 810–815 cm^{-1} and asymmetric stretching vibrations υ_{as}(O=S=O) at. 1249–1254 cm^{-1}.

Comparison of X-ray diffraction patterns of initial diethylaminoethyl cellulose and sulfated DEAE cellulose (Fig. 2) shows that amorphization of the material is observed, which occurs as a result of a decrease in the number of –OH groups and the destruction of ordered polysaccharide during

Table 1. Effect of the reagents ratio on the sulfur content in DEAE-cellulose sulfate upon sulfation with chlorosulfonic acid in 1,4-dioxane

№	$ClSO_3H$:(DEAEC), mmol: g	Time, min	Sulfur content S, wt.%
1	5,04:1	60	6.3
2	5,04:1	120	6.6
3	12,63:1	60	8.4
4	12,63:1	120	9.0
5	12,63:1	180	9.5
6	20,22:1	60	12.6
7	20,22:1	120	13.2
8	20,22:1	180	13.8

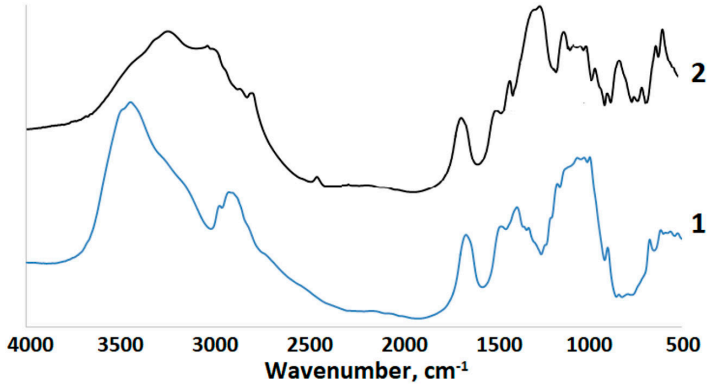

Fig. 1. FTIR spectra: 1 – DEAE-cellulose, 2 – DEAE-cellulose sulfate

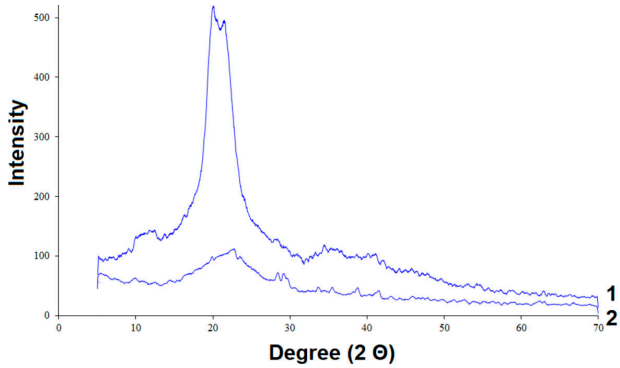

Fig. 2. XRD diffraction patterns: 1 – DEAE-cellulose, 2 – DEAE-cellulose sulfate

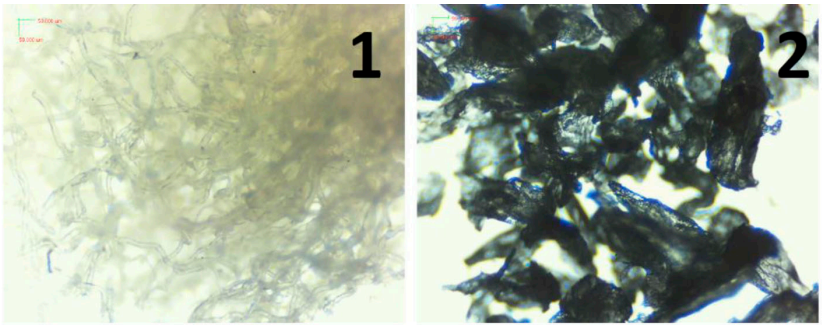

Fig. 3. Optical microscopy data: 1 – DEAE-cellulose, 2 – DEAE-cellulose sulfate

sulfation. On the X-ray diffraction pattern of the DEAE-sulfate sample, there is a noticeable smoothing of the peaks in the range of angles from 15 to 25°q, which confirms the amorphization of the material structure that has occurred [16–18].

The obtained XRD data are consistent with the data of optical microscopy (Fig. 3). In accordance with the data of optical microscopy (Fig. 3), it is shown that the fibrous structure of DEAE-cellulose is disordered during sulfation.

According to optical microscopy (Fig. 3), DEAE cellulose consists of filamentous tubular structures of various sizes. Sulfation of DEAE cellulose leads to the formation of particles of various shapes and sizes, which form aggregates, which, in turn, agrees with the data of [9].

On Fig. 4 shows the molecular weight distribution curves (Mw) of DEAE-cellulose samples sulfated with a sulfur trioxide complex with 1,4-dioxane at different process times.

According to GPC data, the duration of the process significantly affects the profile of the MWD curve of sulfated DEAE cellulose. The product obtained after 60 min treatment of DEAE-cellulose with a complex of sulfur trioxide with 1,4-dioxane is characterized by low polydispersity (1.88) and Mw 26133 Da. A similar profile of the curve was observed in [9], while chlorosulfonic acid is a more aggressive sulfating agent, which leads to an acceleration of the breaking of glycosidic bonds [19] in the polymer chain of DEAE-cellulose. As a result, with an increase in the duration of the process, the MWD curve gradually shifts to the low molecular weight region with a simultaneous increase in the polydispersity of the samples. On the MWD curves of DEAE-cellulose sulfates, three main regions are clearly distinguishable: 1) 30–60 kDa, which refers to a low-substituted polymer; 2) 10–30 kDa, corresponding to a modified partially depolymerized product; 3) the region below 10 kDa is represented by oligomeric hydrolysis products, partially removed during product dialysis.

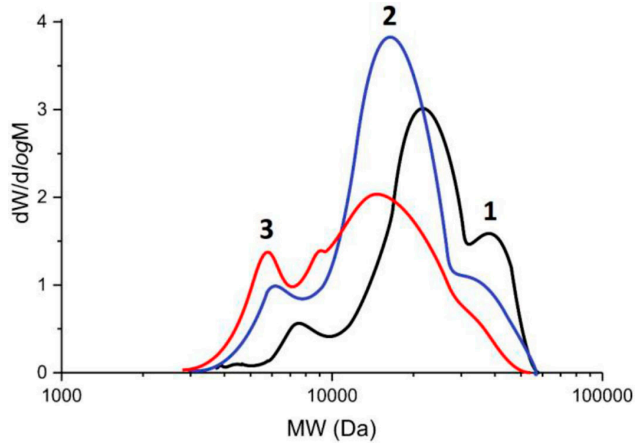

Fig. 4. Curves of molecular weight distribution of samples of DEAE-cellulose sulfates (at the ratio $ClSO_3H$:(DEAEC), 20,22:1 mmol: g): 1 – at a duration of 60 min, 2 – at 120 min, 3 – at 180 min

Table 2. Molecular weight characteristics of DEAE-cellulose sulfate samples (at the ratio $ClSO_3H$:(DEAEC), 20,22:1 mmol: g): 1 – at a duration of 60 min, 2 – at 120 min, 3 – at 180 min.

Sample	Mn (Da)	Mw (Da)	PD
1	13901	26133	1,88
2	8619	19478	2,26
3	5316	14885	2,8

Conclusions

This paper presents the results of a study of the process of sulfation of DEAE-cellulose with chlorosulfonic acid in 1,4-dioxane. The influence of the ratio of reagents on the sulfur content in DEAE-cellulose sulfate has been established.

The embedding of a sulfate group into the DEAE-cellulose molecule has been proven by IR spectroscopy. In the FTIR spectra of diethylaminoethylcellulose sulfate there are absorption bands related to stretching vibrations υ(C–O–S) at 810–815 cm^{-1} and asymmetric stretching vibrations υ_{as}(O=S=O) at. 1249–1254 cm^{-1}.

It was shown by XRD that the introduction of a sulfate group leads to amorphization of DEAE cellulose due to a decrease in its order. This is also indicated by optical microscopy data. According to optical microscopy, DEAE-cellulose consists of filamentous tubular structures of different sizes. Sulfation of DEAE-cellulose leads to the production of particles of various shapes and sizes, forming aggregates.

It has been shown by gel permeation chromatography that the duration of the process significantly affects the profile of the MWD curve of sulfated DEAE cellulose. With an increase in the duration of the process, the MWD curve gradually shifts to the low molecular weight region with a simultaneous increase in the polydispersity of the samples.

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