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Synthesis of bismuth (III) oxofumarate and its solubility in organic solvents

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ABSTRACT

This paper present the synthesis of bismuth (III) oxofumarate $(BiO)_2C_4H_2O_4$ by solution-solid reaction due to the interaction of basic bismuth nitrates $[Bi_6O_5(OH)_3](NO_3)_5$ - $3H_2O$ and $[Bi_6O_4(OH)_4](NO_3)_6$ - H_2O with aqueous solutions of fumaric acid $C_4H_4O_4$. Solubility of $(BiO)_2C_4H_2O_4$ in various organic solvents has been investigated. The morphology and phase composition of the samples was established by X-ray diffraction, scanning electron microscopy, thermogravimetric and chemical analyzes. © 2020 Elsevier Ltd. All rights reserved.

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1. Introduction

According to statistics from the World Health Organization, more than 750 thousand people die every year from stomach cancer. The precipitation of bismuth on the surface of the ulcer and the subsequent formation of a glycoprotein complex that provides bactericidal activity against *Helicobacter pylori* explains the pharmacodynamics of bismuth-containing drugs.

The current outbreak of the coronavirus disease COVID-19 (COronaVIrus Disease), which occurred in Wuhan (China) in December 2019 and was recognized by the World Health Organization as a pandemic on March 11, 2020, has become a global burden on the health system. It is known that some bismuth salts can effectively inhibit both the NTPase and RNA helicase activities of SARS-CoV-2 nsp13, which are responsible for the replication of the coronavirus genome material [1]. SARS-CoV-2 could be found in the rectal swabs even when the testes for throat swabs turned negative. It means that coronavirus remains in the gastrointestinal tract much longer than in the respiratory tract. This fact makes the gastrointestinal tract the most attractive target for ther-

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apeutic intervention to prevent the further spread of the virus in the body and by the faecal-oral route in the population. An eventual gastroprotective agent is bismuth oxofumarate,

since fumaric acid (FA), being one of the intermediates of the Krebs and Krebs-Henseleit cycles, regulates metabolic processes and because of that is used in oral and parental therapy [2]. Usually, metallic bismuth and its oxide are used as precursors

for the preparation of bismuth and its oxide are used as precursors for the preparation of bismuth compounds. Nitric acid is the best solvent for granules of metallic bismuth and bismuth oxide. Therefore, the industrial and common method for producing bismuth compounds (III) is based on hydrolytic precipitation by the treating of bismuth-containing nitric acid solutions [3]. It is well known that the main requirements for the resulting compounds for medicine and technology are high purity and reactivity.

The purpose of this work is synthesis of bismuth (III) oxofumarate (**BOF**) by treating of solid basic bismuth nitrates (BBN) with fumaric acid solutions. And also the study of solubility of **BOF** in organic solvents at the temperature of 22 °C.

2. Experimental

All chemicals were of analytical grade and used as received without further purification. Ethyl alcohol, benzyl alcohol, ethylene glycol, o-xylene, *n*-hexane were analytical grade. The $[Bi_6O_5(OH)_3]$ (NO₃)₅·3H₂O (**BBN-I**) and $[Bi_6O_4(OH)_4](NO_3)_6$ ·H₂O (**BBN-II**) were

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Fig. 1. SEM images of the as-prepared precursors (a) BBN-I, (b) BBN-II, and the samples obtained from BBN-I (c) and BBN-II (d) after retreatment of FA.



Fig. 2. XRD patterns of C4H4O4 (1), BBN-I (2), BBN-II (4) and the samples obtained from BBN-I (3) and BBN-II (5) by the treatment of FA solutions.

Table 1Solubility of BOF in organic solvents.

Solvent	Concentration of Bi ³⁺ (mol/L)
Ethyl alcohol Benzyl alcohol Ethylene glycol o-xylene n-hexane	$\begin{array}{c} 2,5\cdot10^{-6} \\ 2,5\cdot10^{-5} \\ 3,2\cdot10^{-5} \\ 9,5\cdot10^{-7} \\ 1,36\cdot10^{-6} \end{array}$

made by the hydrolysis of nitric acid solutions in the following way: 38 g of α -Bi₂O₃ (MCP HEK, GmbH) was dissolved in 100 ml HNO₃ (1:1). The resulting clear solution was diluted with water (1:40) and stirred at room temperature for 1 h. The white precipi-

tate of **BBN-I** was formed, isolated by filtration, washed with water and dried in air at room temperature. The solid **BBN-II** was precipitated from the above solution by adding distilled water (1:20) at 60 °C, and constant stirring for 1 h. The obtained sample was filtered, washed with water ($60 \circ C$) for one time, and dried at room temperature in air. **BOF** was synthesized by the treatment of 10 g BBN-I and BBN-II with 0.19 M FA solutions with stirring at 70 °C for 1 h. The as-prepared white precipitates were filtered, washed by distilled water ($60 \circ C$), and dried at room temperature in air.

The phase content of the products was characterized by X-ray powder diffraction (XRD), which was recorded on a D8 Advance powder X-ray diffractometer using Cu K α radiation. Phase identification was performed using the powder database ISDD PDF-4+ (2011 г.). The morphology observation was performed on the scanning electron microscope (SEM, Hitachi TM1000). To determine the solubility of BOF in organic solvents an extraction method was applied. The solution of HNO₃ (1:1) was used as an extractant. Chemical analyzes were made by photocalorimetry with using KJ and C7H5O3Na solutions.

3. Results and discussion

For the synthesis of **BOF** the solid precursors **BBN-I** and **BBN-II** were chosen because of the special morphology. These compounds are plane prismatic crystals, that is why they well separated from the mother liquid and precipitates will have less impurities. According to chemical analysis, after adding **BBN-I** to a FA solution and stirring for 1 h, the content of NO³⁻ in the sample was 2.8%. However, after rewashing with FA solution at 70 °C, the content of NO³ can be reduced to 1.73%. In the sample obtained from **BBN-II**, before washing with acid, the content of NO³ was 2.44%,

and after washing, it was 1.24%. Chemical analysis of the samples showed that the experimental bismuth content in the solid product $\omega(Bi^{3+}) = 73.6 \text{ wt\%}$ is in fair agreement with the calculated value of 74.1 wt% for **BOF** with the composition (BiO)₂C₄H₂O₄.

SEM was used to characterize the morphologies of the precursors (Fig. 1a, b). As shown in Fig. 1c, the as-precipitated **BOF**, obtained from **BBN-I**, has an average particle size of $3-30 \mu m$, consisting of small plates. The sample obtained from **BBN-II** is the spherical particles with an average size of $5-12 \mu m$ also consisting of small plates (see Fig. 1d). This flakes have a thickness of up to 100 nm.

The phase composition and crystallinity of the as-synthesized precursors were examined by powder XRD, see Fig. 2. A comparison of diffraction peaks of the obtained BOF-s were carried out with the main peaks of the solid FA and initial BBN-s. Three diffraction patterns can be attributed to FA [4], **BBN-I** (PDF #70–1226), **BBN-II** [3] and the new compounds with the main d (Å): 10.47; 3.57; 3.47; 3.36; 2.98; 2.82; 1.99; 1.76. XRD patterns of the obtained powders contain broadened peaks of **BOF** with the one intensified peak at 10.47 Å. It is known that the most of sheet-like or plate-like bismuth compounds have a layered structure with the (001) basal plane, containing Bi-O layers. Moreover, the SEM images (Fig. 1c, d) confirm a plate-like morphology, which can indicate on the preferred [001] orientation and that the wide surface of the plates can be indexed as (001) plane.

Bismuth compounds usually have low solubility in most solvents. Studies on the treatment of **BOF** with various organic solvents at 22 $^{\circ}$ C showed that the solubility in non-polar solvents has a minimum value (Table 1).

The quantitative interpretation of Bi^{3+} concentration data is that the higher solubility of **BOF** in ethylene glycol can be described by the possible complex formation, as shown in Eq. 1. A similar complex was observed in [5] with using a nickel formate as the precursor.

$$(BiO)_2C_4H_2O_4 + nHOCH_2CH_2OH \rightarrow |(BiO)_2(HOCH_2CH_2OH)_n|C_4H_2O_4$$

4. Conclusions

In summary, the bismuth (III) oxofumarate $(BiO)_2C_4H_2O_4$ can be obtained by treating of solids basic bismuth (III) nitrates

 $[Bi_6O_5(OH)_3](NO_3)_5 \cdot 3H_2O$ and $[Bi_6O_4(OH)_4](NO_3)_6 \cdot H_2O$ of the fumaric acid solutions. Bismuth (III) oxofumarate is spherical particles with sizes up to 30 µm, which consist of thin nanoplates up to 100 nm in size. The content of nitrate ions in the precipitate is more than 1.73%, after rewashing with fumaric acid, this value decreases to 1.24%. The highest solubility of the bismuth (III) oxofumarate is achieved in the ethylene glycol solution.

CRediT authorship contribution statement

Evgeniia E. Luneva: Investigation, Writing - original draft. **Kseniya V. Mishchenko:** Conceptualization, Investigation, Visualization, Writing - review & editing. **Yurij M. Yukhin:** Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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