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**Experimental part.** The series of 2-amino-4-alkyl-4,6-dihydropyrano[3,2-c][2,1]benzoxathiin-3-carbonitrile 5,5-dioxides and triethylammonium 3-[1-(4-hydroxy-2,2-dioxido-1,2-benzoxathiin-3-yl)alkyl]-1,2-benzoxathiin-4-olate 2,2-dioxides was synthesized. The antimicrobial activity of the compounds obtained was determined by the agar "well" diffusion method.

**Conclusions.** It has been shown that 1,2-benzoxathiin-4(3H)-one 2,2-dioxide as a structural analog of 1H-2,1-benzothiazin-4-one 2,2-dioxide can be used in similar three- and two-component reactions, but its reactivity is less due to the replacement of the 1-N-R-group with an O-atom. The novel compounds obtained exceeded the antimicrobial activity of the reference drugs, and were more active against gram-positive bacteria in contrast to isosteric derivatives of 1H-2,1-benzothiazin-4-one 2,2-dioxide that were active against gram-negative strains and fungi.

**Key words:** 1,2-benzoxathiin-4(3H)-one 2,2-dioxide; 2-amino-4H-pyrane; three-component interaction; ammonium salt; antimicrobial activity

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Цель данной работы была изучить взаимодействие 1,2-бензоксатиин-4(3H)-он 2,2-диксида с метиленактивными нитрилами и аллифатическими альдегидами и оценить антимикробную активность полученных соединений.

Результаты и их обсуждение. 1,2-Бензоксатиин-4(3H)-он 2,2-диксид как структурный аналог 1,3-дикарбонильных соединений был использован в трехкомпонентном взаимодействии с аллифатическими альдегидами и метиленактивными нитрилами. В случае малаонодинитрила образовывались целевые производные. При использовании этилцианата и диметиламина единственным изолированным продуктом было триэтиламмониевая соль, получение которой возможно также в случае двухкомпонентного взаимодействия. Изучение антимикробных свойств показало более высокую активность, чем у препаратов сравнения, особенно в отношении грамположительных штаммов.

Экспериментальная часть. Был синтезирован ряд 2-амино-4-алкил-4,6-дигидропирано[3,2-c][2,1]бензоксатиин-3-карбонитрилов 5,5-диоксидов и 3-[1-(4-гидрокси-2 2-диоксидо-1,2-бензоксатиин-3-ил)алкил]-1,2-бензоксатиин-4-опат 2,2-диксидов. Для полученных соединений было проведено определение антибактериальной активности методом диффузии в агар.

Выводы. 1,2-Бензоксатиин-4(3H)-он 2,2-диксид как структурный аналог 1Н-2,1-бензотиазин-4-он 2,2-диксида был использован в трех- и двухкомпонентных реакциях, но его реакционная способность оказалась меньше за счет замены 1-N-R-группы на атом кислорода. Полученные соединения по антибактериальной активности превысили препараты сравнения и проявили активность в отношении грамположительных бактерий, в отличие от изостерных производных 1Н-2,1-бензотиазин-4-он 2,2-диксида, антибактериальные свойства которых были связаны с ингибирующим влиянием на грамотрицательные штаммы и грибы.

Ключевые слова: 1,2-бензоксатиин-4(3H)-он 2,2-диксид; 2-амино-4-Н-пиран; трехкомпонентное взаимодействие; триэтиламмониевая соль; антимикробная активность.

The results of the studies in different countries all over the world indicate the growth of the antimicrobial resistance (AR) and, particularly the multiple drug resistance in numerous microorganisms that are the main cause of growth of different infectious sickness rate [1, 2, 3]. The obvious consequences of this process include an increase in morbidity and mortality, prolongation of the disease time and a greater risk of complications [4]. AR becomes also the cause for the greater economic burden for the population due to decrease in their labor productivity and increase of the costs for diagnosis and treatment of such disease type [5]. Altogether the impact of AR on the health and economic system can be estimated as extremely negative. Therefore, the synthesis of new efficient biologically active compounds with the promising antimicrobial properties still remains one of the topical issues in development of new drugs [6]. The World Health Organization is also encouraging works in this direction. According to this the Global Strategy on Containment of Antimicrobial Resistance (2001) [7] was worked out. It contains a complete list of recommendations for AR combating. In particular, the strategy to promote the creation of new drugs and vaccines with the necessary properties was proposed, especially with novel chemical core-structures, which were not earlier utilized as antimicrobial substances.

In our previous works we used 1H-2,1-benzothiazin-4-one 2,2-dioxide as a core-structure to obtain its new pyran-annulated derivatives, as well as novel ammonium salts and consequently to assess their antimicrobial activity [8, 9]. These studies allowed us to find the substances with a moderate activity against P. aeruginosa and C. albicans. In this regard, aiming to obtain new effective antimicrobial agents we continued our investigations in this field by modifying of the abovementioned core-structure via isosteric replacement of the 1-N-R group with an O-atom, resulting in 1,2-benzoxathiin-4(3H)-one 2,2-dioxide (Fig.).

This idea has marked the beginning of new research of our scientific group dedicated to revealing the synthetic and pharmacological potential of 1,2-benzoxathiin-4(3H)-one 2,2-dioxide. It is also targeted on determination of the general regularities on the structure-bioactivity relationships in series of SO₂-containing heterocycles and subsequently on purposeful construction of drugs with a desired activity.

Therefore, the present article describes the synthesis of new 2-amino-4-alkyl-4-H-pyran-3-carbonit-
riles and triethylammonium 3-[1-(4-hydroxy-2,2-dioxido-1,2-benzoxathiin-3-yl)alkyl]-1,2-benzoxathiin-4-olate 2,2-dioxides based on 1,2-benzoxathiin-4(3H)-one 2,2-dioxide.

The starting 1,2-benzoxathiin-4(3H)-one 2,2-dioxide 4 was synthesized according to Scheme 1. At the first stage methyl salicylate 1 reacted with methanesulfonyl chloride 2 yielding methanesulfonate 3. The latter was next cyclized under the action of sodium hydride in DMF solution at 0 °C producing sulphone 4 [10, 11].

It is well known that 2-amino-4H-pyrans can be easily obtained via three-component domino-type interaction of 1,3-dicarbonyl compounds with aldehydes and active methylene nitriles using a wide range of bases as a catalyst [12]. Since 1,2-benzoxathiin-4(3H)-one 2,2-dioxide 4 can be considered as a structural analog of 1,3-dicarbonyl compounds, according to the task set it was introduced into the three-component interaction with aliphatic aldehydes 5 and malononitrile 6 (Scheme 2) which resulted in formation of the target 2-amino-4-alkyl-4,6-dihydropyrano[3,2-c]2,1-benzoxathiin-3-carbonitrile 5,5-dioxides 7 as precipitates that did not require further purification. The reaction readily proceeded when using equimolar quantities of the initial reagents in ethanol in the presence of the catalytic amount of triethylamine to promote the interaction. As it was additionally determined, this three-component reaction did not require heating and proceeded smoothly under the room temperature. It is in a full agreement with the previously regularities found [8]. Performing the reaction under reflux affected neither the product obtained nor the yield.

The yields of 2-amino-4H-pyrans 7 (Tab. 1) in the range from formaldehyde to butyraldehyde were average. However, in the case of valeric aldehyde the yield of 7e turned out to be poor – only approximately 10 %. The solvent replacement of ethanol to methanol gave its increase up to 45 %, which might be due to lower solubility of the product. It is interesting that the fused derivative 7h was obtained for α-methylcinnamaldehyde, whereas despite of our efforts, involvement of cinnamaldehyde often used in the 2-amino-4H-pyran synthesis [13] was not successful. Presumably, the α-methylgroup in this case may act as a steric hindrance and avoids formation of undesirable by-products.

In the three-component reaction glutaraldehyde 5i as a bifunctional representative was also introduced. This gives a chance to obtain two types of 2-amino-4H-pyran depending on the number of aldehyde equivalents applying in the reaction, namely 2-amino-4H-pyran with a free aldehyde group and the corresponding bis-derivative of 2-amino-4H-pyran. Thus, using glutaraldehyde in the amount of 1 equiv in the three-component interaction did not result in the desired reaction product. At the same time, application of 0.5 equiv of 5i led to isolation of bis-2-amino-4H-pyran 7i, but unfortunately, in an extremely poor yield (Scheme 2).

In continuation of the current study we then applied other possible representative of active methylene nitrile – ethyl cyanoacetate 8 – in the three-component interaction with a view to introduce the ester group in position 3 of the 2-amino-4H-pyran ring. Nevertheless our efforts appeared to be unsuccessful since any desired ethyl 2-amino-4H-pyran-3-carboxylate was not isolated during these attempts. At the same time, the corresponding triethylammonium salt of bis-1,2-benzoxathiin-4(3H)-one 2,2-dioxide derivative 9g was isolated in 6% yield as the single
product when isobutyric aldehyde was applied in the three-component interaction (Scheme 3). Taking into account the known mechanism of 2-amino-4H-pyran formation [14] and the regularities previously found [8] this fact can be explained by two ways depicted in Scheme 3. The first way implies the direct interaction of 1,2-benzoxathiin-4(3H)-one 2,2-dioxide 4 with aldehyde 5g with formation of a highly reactive intermediate A. Then this intermediate reacts not with ethyl cyanoacetate 8, but with the second molecule of 4 forming a symmetrical bis-derivative isolated in the form of triethylammonium salt 9g. Besides this, we can assume the second way involving the yield is primary Knoevenagel condensation between ester 8 and aldehyde 5g resulted in intermediate B. The subsequent Michael addition of the latter to 1,2-benzoxathiin-4(3H)-one 2,2-dioxide 4 gives adduct C, which loses the molecule of ester 8 and is converted into enone A. Thereafter, enone A reacts as described above giving salt 9g. In our opinion, both of these routes are equiprobable.

Triethylammonium salts similar to 9 are new derivatives of 1,2-benzoxathiine 2,2-dioxide. In this regard, we set the task of the purposeful obtaining of salts 9 based on the two-component approach described previously on the example of 1H-2,1-benzothiazin-4(3H)-one 2,2-dioxide [15]. According to this procedure the target salts 9 were obtained by the interaction of 1,2-benzoxathiin-4(3H)-one 2,2-dioxide 4 with aliphatic aldehydes in the molar ratio of 2:1 in the presence of the equimolar amount of triethylamine in i-PrOH for 1 hour (Scheme 4).

The data for the compounds obtained are presented in Tab. 1 and 2. The 1H NMR data are given in Tab. 3.

The study of the antimicrobial properties of the compounds obtained was performed according to the international standards, 16] by the agar “well” diffusion method against the standard test-strains of gram-positive and gram-negative bacteria and fungi. The results revealed the higher antimicrobial activity than those of the reference drugs. The activity against the gram-positive strains was a little higher than moderate compared to gram-negative bacteria and fungi. The most active were samples with propyl, isopropyl and butyl substituents in position 4 of the pyran core, the activity increased along with the prolongation of the chain. Furthermore, triethylammonium salts corresponding to 2-amino-4H-pyran-3-carbonitriles showed higher antimicrobial properties. Thereby, utilization of long-chain aliphatic aldehydes along with the synthesis of the corresponding triethylammonium salts may be considered as a promising way for further construction of the narrow spectrum antibiotics.

For similar derivatives of 1H-2,1-benzothiazin-4(3H)-one 2,2-dioxide the moderate activity against P. aeruginosa and C. albicans was revealed [8]. Thus, the isosteric replacement of the 1-N-R-group to O-atom caused alteration of the antimicrobial activity.

The results of studying the antimicrobial properties are presented in Tab. 4.

**Experimental Part**

**Chemistry**

The starting aldehydes and active methylene nitriles were obtained from commercial sources and used without further purification. Melting points were determined on a Gallenkamp melting point apparatus, Model MFB-595 in open capillary tubes. The 1H NMR-spectra were recorded on a Varian WXR-400 spectrometer using DMSO-d6 as a solvent and TMS as an internal standard. Elemental analyses were carried out using a Carlo Erba CHNS-O EA 1108 analyzer.

The procedure for the synthesis of 1,2-benzoxathiin-4(3H)-one 2,2-dioxide 4. To the ethereal solution (200 mL) of methylsalicylate 1 (25.8 mL, 0.2 mol) and triethylamine (31 mL, 0.22 mol) add methane-
Melting points, elemental analysis and yields for 2-amino-4-alkyl-4,6-dihydropyran-3,2-c][2,1]benzoxathiin-3-carbonitrile 5,5-dioxides (7a-i)

| No. | Alk  | M. p., °C | Molecular formula, M. m. | Elemental analysis, % | Yield, % |
|-----|------|-----------|--------------------------|----------------------|---------|
| 7a  | H    | 258-260   | C₆H₆N₉O₅S₂ 276.27        | calc 52.15          | 55      |
|     |      |           |                          | exp 52.17           |         |
| 7b  | Me   | 241-243   | C₆H₆N₉O₅S₂ 290.29        | calc 53.75          | 36      |
|     |      |           |                          | exp 53.79           |         |
| 7c  | Et   | 217-219   | C₆H₆N₉O₅S₂ 304.32        | calc 55.21          | 48      |
|     |      |           |                          | exp 55.25           |         |
| 7d  | n-Pr | 208-209   | C₆H₆N₉O₅S₂ 318.35        | calc 56.55          | 75      |
|     |      |           |                          | exp 56.59           |         |
| 7e  | n-Bu | 222-224   | C₆H₆N₉O₅S₂ 332.37        | calc 57.79          | 45      |
|     |      |           |                          | exp 57.82           |         |
| 7f  | i-Pr | 201-203   | C₆H₆N₉O₅S₂ 318.35        | calc 56.55          | 46      |
|     |      |           |                          | exp 56.59           |         |
| 7g  | i-Bu | 205-207   | C₆H₆N₉O₅S₂ 332.37        | calc 57.79          | 39      |
|     |      |           |                          | exp 57.82           |         |
| 7h  | Ph   | 230-233   | C₆H₆N₉O₅S₂ 392.43        | calc 64.24          | 46      |
|     | Me   |           |                          | exp 64.27           |         |
| 7i  | (CH₂)₃ | 257-259  | C₆H₆N₉O₅S₂ 592.60        | calc 54.70          | 6       |
|     |      |           |                          | exp 54.72           |         |

Sulfonyl chloride 2 (15.4 mL, 0.22 mol). Stir the reaction mixture for 18 h when cooling. Then wash it with the saturated solution of sodium carbonate (50 mL) and water (100 mL). Evaporate the ethereal layer after drying with sodium sulfate to give a light yellow solid; the yield is 39.0 g (85 %). M. p. – 45-50 °C.

Dissolve methansulfonate 3 (39.0 g, 0.17 mol) in dry DMF (100 mL), and cool the solution to 0 °C. Then add it to the cooled suspension of sodium hydride (19.55 g, 0.51 mol) in dry DMF (100 mL) and mix for 1 h at 0-5 °C. Pour the reaction mixture into ice, acidify with diluted HCl to pH 3-4, filter the white precipitate obtained and recrystallize from ethanol; the yield is 22.0 g (67 %). M. p. – 80-85 °C.

The general procedure for the synthesis of 2-amino-4-alkyl-4,6-dihydropyran-3,2-c][2,1]benzoxathiin-3-carbonitrile 5,5-dioxides (7a-h). To the solution of 1,2-benzoxathiin-4(3H)-one 2,2-dioxide 4 (0.198 g, 0.001 mol), malononitrile 6 (0.066 g, 0.001 mol) and the appropriate aliphatic aldehyde 5a-h (0.001 mol) in ethanol (5-10 mL) add the catalytic amount of triethylamine. Allow the mixture to stand for 24 h at the room temperature. Filter the resulting precipitates of 7a-h, wash with ethanol and then dry on air.

Melting points, elemental analysis and yields for triethylammonium 3-[(4-hydroxy-2,2-dioxido-2,1-benzo[xathiin-3-yl)alkyl]-2,1-benzo[xathiin-5-olat 2,2-dioxides (5c,d,f,g)

| No. | Alk  | M. p., °C | Molecular formula, M. m. | Analysis, % | Yield, % |
|-----|------|-----------|--------------------------|-------------|---------|
|     |      |           |                          | calc        |         |
|     |      |           |                          | exp         |         |
| 9c  | Et   | 151-153   | C₆H₆N₉O₅S₂ 537.65        | calc 55.81  | 37      |
|     |      |           |                          | exp 55.85  |         |
| 9d  | n-Pr | 130-132   | C₆H₆N₉O₅S₂ 551.67        | calc 56.57  | 45      |
|     |      |           |                          | exp 56.61  |         |
| 9f  | i-Pr | 188-190   | C₆H₆N₉O₅S₂ 551.67        | calc 56.58  | 69      |
|     |      |           |                          | exp 56.61  |         |
| 9g  | i-Bu | 153-155   | C₆H₆N₉O₅S₂ 565.70        | calc 57.31  | 45      |
|     |      |           |                          | exp 57.33  |         |
The 1H NMR spectral data (δ, ppm; J, Hz) of the compounds obtained

| 7a  | 7.78 (d, J = 7.93 Hz, 1H, Ar); 7.60-7.70 (m, 1H, Ar); 7.46-7.57 (m, 2H, Ar); 7.35 (br. s., 2H, N(CH3)2) | 3.33 (s, 2H, CH2 pyran) |
| 7b  | 7.77-7.82 (m, 1H, Ar); 7.61-7.73 (m, 1H, Ar); 7.45-7.55 (m, 2H, Ar); 7.32 (s, 2H, NH2); 3.59 (q, J = 6.70 Hz, 1H, CH pyran); 1.37 (d, J = 6.26 Hz, 3H, CH3) |
| 7c  | 7.76-7.91 (m, 1H, Ar); 7.62-7.72 (m, 1H, Ar); 7.44-7.56 (m, 2H, Ar); 7.37 (br. s., 2H, NH2); 3.69 (t, J = 3.91 Hz, 1H, CH pyran); 1.69 (dt, J = 7.43, 3.72 Hz, 2H, CH(CH3)); 0.83 (t, J = 7.43 Hz, 3H, CH3CH2) |
| 7d  | 7.79 (d, J = 7.83 Hz, 1H, Ar); 7.61-7.71 (m, 1H, Ar); 7.44-7.55 (m, 2H, Ar); 7.36 (br. s., 2H, NH2); 3.64 (t, J = 4.11 Hz, 1H, CH pyran); 1.57-1.72 (m, 2H, CH2CH2CH2); 1.20-1.37 (m, 3H, CH2CH2CH2); 0.86 (t, J = 1.00 Hz, 3H, CH3CH2CH2) |
| 7e  | 7.79 (d, J = 7.83 Hz, 1H, Ar); 7.61-7.70 (m, 1H, Ar); 7.46-7.55 (m, 2H, Ar); 7.36 (br. s., 2H, NH2); 3.66 (t, J = 1.00 Hz, 1H, CH pyran); 1.66 (m, 2H, CH2CH2CH2); 1.25 (m, 4H, CH2CH2CH2); 0.81 (t, J = 1.00 Hz, 3H, CH3CH2CH2) |
| 7f  | 7.81 (d, J = 7.83 Hz, 1H, Ar); 7.66 (d, J = 8.22 Hz, 1H, Ar); 7.49-7.57 (m, 2H, Ar); 7.45 (s, 2H, NH2); 3.50 (d, J = 2.74 Hz, 1H, CH pyran); 2.04 (d, J = 2.35 Hz, 1H, CH(CH3)); 1.01 (d, J = 7.04 Hz, 3H, CH(CH3)) |
| 7g  | 7.81 (d, J = 7.83 Hz, 1H, Ar); 7.59-7.72 (m, 1H, Ar); 7.46-7.55 (m, 2H, Ar); 7.39 (s, 2H, NH2); 3.55 (t, J = 5.87 Hz, 1H, CH pyran); 1.87 (m, 1H, CH2CH2CH2); 1.56 (t, J = 6.26 Hz, 2H, CH2CH2CH2); 0.91 (d, J = 6.62 Hz, 3H, CH3CH2CH2); 0.85 (d, J = 6.65 Hz, 3H, CH3CH2CH2) |
| 7h  | 7.82 (d, J = 7.43 Hz, 1H, Ar); 7.64-7.72 (m, 1H, Ar); 7.43-7.57 (m, 4H, Ar, NH2); 7.30-7.37 (m, 2H, Ar); 7.21-7.29 (m, 3H, Ar); 6.55 (s, 1H, CH); 4.32 (s, 1H, CH pyran); 1.76 (s, 3H, CH3) |
| 7i  | 7.59-7.72 (m, 4H, Ar); 7.40-7.48 (m, 4H, Ar); 7.30-7.35 (m, 4H, NH2, NH2); 3.62 (t, J = 1.00 Hz, 2H, CH2CH2) |

The procedure for the synthesis of 1,3-bis(2-amino-4,6-dihydropyran-3,2-cyano-2,1-benzoxathine-3-carbonitrile-4-y1,5,5-dioxide)propan (7i).

To the solution of 1,2-benzoxathiin-4-(3H)-one 2,2-dioxide 4 (0.198 g, 0.001 mol), malononitrile 6 (0.066 g, 0.001 mol) and 50 % solution of glutaraldehyde 5i (0.100 g, 0.0005 mol) in ethanol (5-10 mL) add the catalytic amount of triethylamine. Allow the mixture to stand for 24 h at the room temperature. Filter the resulting precipitate of 7i, wash with ethanol and then dry on air.

The general procedure for the synthesis of triethylammonium 3-[(4-hydroxy-2,2-dioxide-2,1-benzoxathin-3-yl)alkyl]-2,1-benzoxathiin-5-olat 2,2-dioxides (9c,d,f,g). To the solution of 1,2-benzoxathiin-4-(3H)-one 2,2-dioxide 4 (0.198 g, 0.001 mol) and the appropriate aliphatic aldehyde 3c,d,f,g (0.0005 mol) in propan-2-ol (10 mL) add triethylamine (0.13 mL, 0.001 mol). Mix the solution for 1 h under reflux. After cooling filter the resulting precipitates of 9c,d,f,g, wash with propan-2-ol and dry on air.

Microbiology

According to the WHO recommendations the following test-strains were used: *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudo- monas aeruginosa* ATCC 27853, *Bacillus subtilis* ATCC 6633, *Proteus vulgaris* ATCC 4636, *Candida albicans* ATCC 653/885. The inoculum suspension was prepared using a Densi-La-Meter apparatus (made by PJI-VA-Lachema, Czech Republic; 540-nm wavelength).

The suspension was prepared according to the manual for the device and the information sheet No.163-2006 “Standardization for preparation of microbial suspen-
The antimicrobial activity of compounds 7b-7h, 9c-9g

| Table 4 | Diameter of the growth inhibition zones (the average for three experiments), mm |
|---------|--------------------------------------------------------------------------------|
| No.     | Gram-positive bacteria | Gram-negative bacteria | Fungi |
|         | S. aureus | E. coli | B. subtilis | P. aeruginosa | P. vulgaris | C. albicans |
| 7b      | 14        | 14      | 17        | 17           | 17         | 17         |
| 7c      | 17        | 16      | 18        | 14           | 14         | 15         |
| 7d      | 21        | 22      | 15        | 16           | 16         | 16         |
| 7e      | 21        | 22      | 16        | 15           | 16         | 16         |
| 7f      | 18        | 20      | 17        | 16           | 17         | 16         |
| 7g      | 18        | 20      | 18        | 18           | 18         | 17         |
| 7h      | 17        | 17      | 19        | 16           | 16         | 16         |
| 9c      | 20        | 21      | 21        | 17           | 17         | 18         |
| 9d      | 19        | 20      | 21        | 17           | 18         | 17         |
| 9f      | 21        | 20      | 22        | 18           | 17         | 17         |
| 9g      | 19        | 21      | 21        | 18           | 18         | 18         |

**Metronidazole**

**Synthomycin**

**Conclusion**

1. The series of 2-amino-4-alkyl-4,6-dihydropyran-3,2-c[2,1]benzoxathiin-3-carbonitrile 5,5-dioxides has been synthesized based on the three-component interaction of 1,2-benzoxathiin-4(3H)-one 2,2-dioxide with malonaldehyde and aliphatic aldehydes.

2. Using ethyl cyanoacetate in the same interaction did not lead to the desired ethyl 2-amino-4H-pyran-3-carboxylates and in the case of isobutyric aldehyde resulted in formation of triethylammonium salt. It is explained by two equiprobable reaction pathways.

3. By means of the two-component approach based on the interaction of 1,2-benzoxathiin-4(3H)-one 2,2-dioxide and aliphatic aldehydes the series of triethylammonium 3-[1-(4-hydroxy-2,2-dioxido-1,2-benzoxathiin-3-yl)alkyl]-1,2-benzoxathiin-4-olate 2,2-dioxides has been synthesized.

4. The assessment of the antimicrobial properties of the compounds obtained has revealed the higher activity than those of the reference drugs, especially against the gram-positive strains, and the activity against gram-negative bacteria and fungi is slightly less.

Conflict of Interests: authors have no conflict of interests to declare.

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