suppressing the signs of pain remains one of the interests of physicians today. And, accordingly, this is a matter of great interest to synthetic chemists, pharmacists, clinical specialists, and ordinary patients, which are finally the most important group of consumers.

Aim. The development of scheme of synthesis in the range of N-hetaryl-4-methyl-2,2-dioxo-1H-2$^{\lambda}$6,1-benzothiazine-3-carboxylic acid derivative, elaboration of methods for confirmation their quality and elaboration of techniques for their quantification, applied for purposes of pharmaceutical analysis.

Materials and methods. N, N-carbonyldiimidazole, 4-methyl-2,2-dioxo-1H-2 of 6,1-benzothiazine-3-carboxylic acid, dimethylformamide, derivatives of hetarylalkylamine, physico-chemical methods (determination of the melting point, elemental and biological analysis, chemical reaction for identification, titrimetric method for quantification).

Results and discussion. As it has been stated after biological investigations, the most potent representative in the range of amides of N-hetaryl-4-methyl-2,2-dioxo-1h-2$^{\lambda}$6,1-benzothiazine-3-carboxylic acid is N-(Pyridin-3-ylmethyl)-4-methyl-2,2-dioxo-1H-2*l*6,1-benzothiazine-3-carboxamide, which has shown the most potent analgesic activity comparatively with the Control.

Conclusions. The mentioned procedures of synthesis and methods for qualification and quantification will be worked out and improved on experimental samples of a newly synthesized substance.

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 2-AMINO-4-(4-CHLORO-1-ETHYL-2,2-DIOXIDO-1*H*-BENZO[*C*][1,2]THIAZIN-3-YL)-4*H*-PYRAN-3-CARBONITRILES

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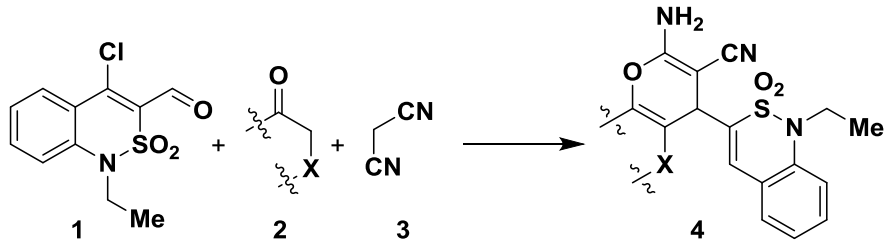
Introduction. Construction of the molecules comprising several pharmacophores is a promising way for development of new bioactive substances. 2,1-benzothiazine 2,2-dioxide and 2-amino-4*H*-pyrane cores are examples of such fragments. Derivatives of these heterocyclic systems have proven to be effective agents with antimicrobial, anti-inflammatory, analgesic and other activities. Owing to this we decided to join abovementioned pharmacophores in one framework and to examine microbiological activity of the products synthesized.

Aim. To synthesize derivatives containing both 1*H*-2,1-benzothiazine 2,2-dioxide and 2-amino-4*H*-pyrane cores and to study their antimicrobial activity.

Materials and methods. Standard methods of organic synthesis were applied in the research. Agar well diffusion method was used for evaluation of antimicrobial activity. 4-Chloro-1-ethyl-1*H*-2,1-benzothiazine-3-carbaldehyde 2,2-dioxide, malononitrile and CH_2CO-containing compounds were used as starting materials.

Results and discussion. Target compounds **4** were obtained by a three-component reaction of 4-chloro-1-ethyl-1*H*-2,1-benzothiazine-3-carbaldehyde 2,2-dioxide **1** with carbonyl compounds **2** and malononitrile **3** in moderate to high yields. Structure and purity of the products were proved by ^{1}H and ^{13}C NMR spectroscopy as well as HPLC-MS. The reactions were carried out in refluxing propan-2-ol in the presence of catalytic amount of a base for 1-4 hours. Strains of *S. aureus ATCC 25923, E. coli ATCC 25922, P. aeruginosa ATCC 27853, B. subtilis ATCC 6633, P. vulgaris ATCC 4636, C. albicans ATCC 885/653* were used for the activity evaluation. Tested compounds appeared to be active against all the strains. It should be noted that the highest activity was revealed against *C. albicans* and *B. subtilis* strains.



Conclusions. The simple synthetic procedure allowed to obtain complex heterocyclic compounds comprising 2,1-benzothiazine 2,2-dioxide and 2-amino-4*H*-pyrane moieties. 2-Amino-4-(4-chloro-1-ethyl-2,2-dioxido-1*H*-benzo[*c*][1,2]thiazin-3-yl)-4*H*-pyran-3-carbonitrile framework has certain prospects in further search of antimicrobial substances of heterocyclic structure.

THE OPTIMIZATION OF 3-DICHLOROMETHYL-1,2,2-TRIMETHYLCYCLOPENTANCARBOXYLIC ACID SYNTHESIS

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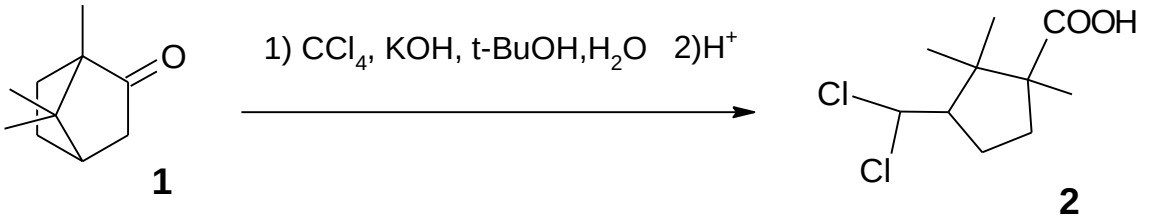
Introduction. Previously we have used 3-dichloromethyl-1,2,2-trimethylcyclopentanecarboxylic acid (**2**) (scheme) for synthesis of biologically active compounds. For the first time the acid **2** was synthesized by Meyers in 1970. It was obtained via chlorination of camphor **1** by tetrachloromethane and following splitting of semi-product by potassium hydroxide.

Scheme



Aim. The aim of this work was to optimize method of synthesis of 3-dichloromethyl-1,2,2-trimethylcyclopentanecarboxylic acid (**2**).

Results and discussion. We used the technique suggested by Meyers for racemic camphor **1**. We eliminated the stage of distillation of solvent excess in vacuum, as well as the stage of extraction of impurities and product by ether. Thus, we simplified the procedure and avoided using of precursors.

The optimization of the synthesis of acid **2** was carried out by using the method of mathematical planning of the experiment. The most significant parameters that affect the yield of the target product have been determined. They are the amounts of potassium hydroxide, tert-butanol, tetrachloromethane, water and the temperature of the reaction mixture.

The maximum and minimum values of the parameters were established experimentally. The optimal amounts of reagents and their combination was determined using the steepest ascent method according to the regression equation. Mathematical calculations were performed using the STATISTICA 10 StatSoft Inc. system and Excel spreadsheet processor of MS Office 2019.

It has been possible to increase the acid yield from 67 to 74% using the calculated amounts of reagents.

Conclusion. The methods of synthesis of 3-dichloromethyl-1,2,2-trimethylcyclopentanecarboxylic acid have been optimized. The effectiveness of the selected method of mathematical planning has been shown.