SYNTHESIS OF NONSYMMETRICAL 1,4-DIHYDROPYRIDINES CONTAINING PYRIMIDINE-2,4(1*H*,3*H*)-DIONE AND 2,1-BENZOTHIAZINE 2,2-DIOXIDE MOIETIES BY HANTZSCH REACTION

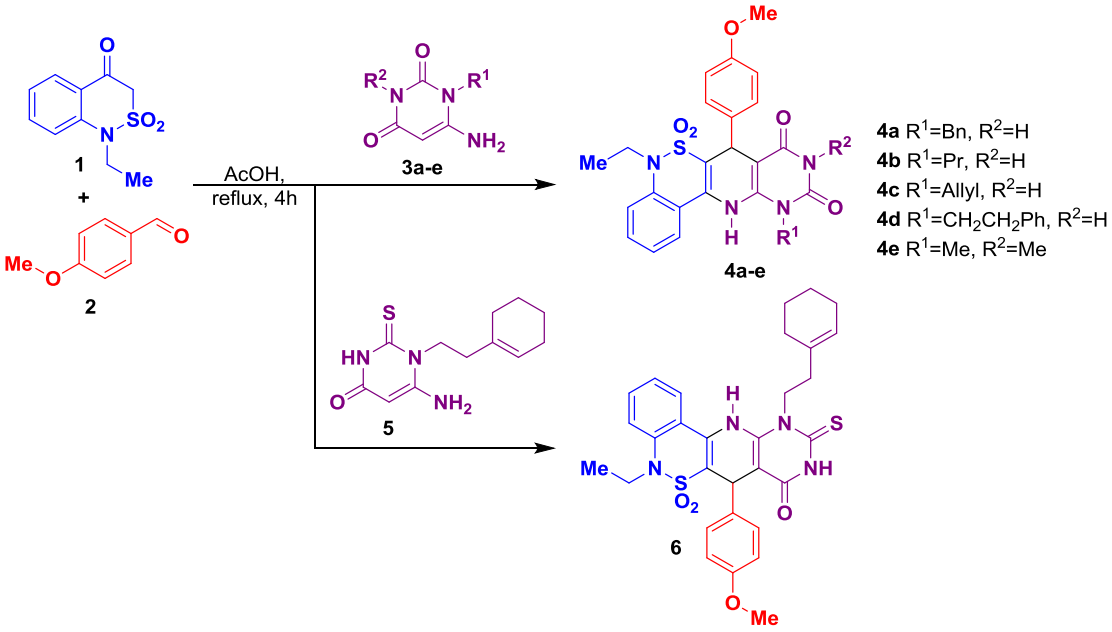
Dorofieiev M. D., Sytnik K. M., Shemchuk L. A.
Scientific supervisor: ass. prof. Lega D. A.
National University of Pharmacy, Kharkiv, Ukraine
legus.211288@gmail.com

Introduction. Hantzsch reaction is a famous reaction which allows to construct 1,4-dihydropyridine core. Originally this reaction was reported in 1881 by A.R. Hantzsch by a multi-component interaction between an aldehyde, 2 equiv of a β-ketoester and ammonia or its donors leading to symmetrical 1,4-dihydropyridines. This approach was subsequently modified in order to obtain nonsymmetrical derivatives of the latter, which are quite interesting for medicinal chemistry since may include several different pharmacophore fragments. One of these methods consists in interaction of a methylene active carbonyl compound with an aldehyde and an enamine. Considering 2,1-benzothiazin 2,2-dioxide and pyrimidine-2,4-dione fragments as pharmacologically attractive we set the task to join them in one molecular framework using modified Hantzsch reaction.

Aim. To synthesize nonsymmetrical 1,4-dihydropyridines containing pyrimidine-2,4(1*H*,3*H*)-dione and 2,1-benzothiazine 2,2-dioxide moieties by Hantzsch reaction.

Materials and methods. A set of chemicals either synthesized by known procedures or obtained from commercial sources were used. During research standard methods of organic synthesis were also applied.

Results and discussion. Aiming to obtain the target nonsymmetrical 1,4-dihydropyridines we examined three component interaction of 1-ethyl-1*H*-2,1-benzohiazin-4(3*H*)-one 2,2-dioxide **1** with 4-methoxybenzaldehyde **2** and series of mono- and disubstituted 6-aminouracils **3**. It was found that heating of the equimolar mixture of the starting compounds in acetic acid leads to formation of polycondensed derivatives **4** in good yields. Utilizing 6-amino-1-(2-(cyclohex-1-en-1-yl)ethyl)-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-one **5** in the reaction allowed us to obtain corresponding thioxo derivative **6**. Structure and purity of the products were proved by ^{1}H and ^{13}C NMR spectroscopy as well as HPLC-MS.



Conclusion. The simple synthetic procedure allowed to obtain polycondensed heterocyclic compounds containing pyrimidine-2,4(1*H*,3*H*)-dione and 2,1-benzothiazine 2,2-dioxide fragments.