Research of the three-component reaction [3+2] cycloaddition and study of synthesized compounds as potential inhibitors of proteinkinases

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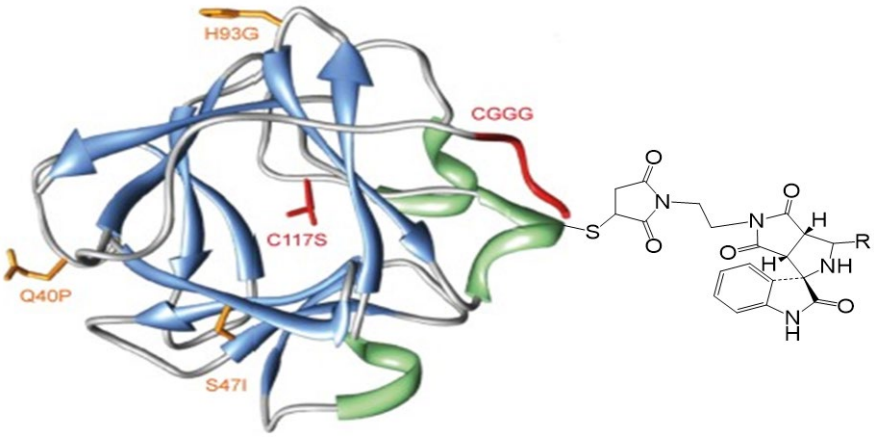
Introduction. One of the most important tasks of modern synthetic organic chemistry is the synthesis of new biologically active substances (BAS) in order to create new drugs based on them, which have a high therapeutic effect and minimal side effects. Among modern drugs are dominated molecules of heterocyclic structure. One of the directions in the synthesis of such substances is the creation of new spirooxindole. The nucleus of these BAS is the basis of many natural alkaloids with wide biological activity [1] and the synthesis of compounds containing maleimide linker allows us to consider them as potential inhibitors of proteinkinases [2].

Materials and methods. The starting isatin and α-amino acids were obtained from commercial sources and used without further purification. Dipolarophile used, *N,N*'-ethylene-*bis*-maleimide, was prepared according to the known method [2]. The structure of received compounds was confirmed by IR- and ^{1}H NMR- spectroscopy, mass-spectrometry and elemental analysis. Computer molecular modeling of the binding of synthesized compounds with proteinkinase FGFR1 *in silico* was performed using the program Autodock4 (http://autodock.scripps.edu/).

Results and discussion. A series of new derivatives of spiroindole-3,3'-pyrrolo[3,4-c]pyrrole were synthesized via three-component domino-interaction. For the synthesized compounds, molecular modeling of their binding to the protein kinase FGFR1 was performed.



Conclusions. Series of derivatives 1'-ethylene-*N*-maleimide-2a',5a'-dihydro-1'H-spiroindole-3,3'-pyrrolo[3,4-*c*] pyrrole-2,2',6'(1H,1'H,5'H)-trione were synthesized. The synthesis of the studied derivatives is promising for further search for new biologically active substances.

References

1. Ball-Jones R. B., Badillo J. J., Franz A. K. Strategies for the enantioselective synthesis of spirooxindoles. Organic & Biomolecular Chemistry. 2012;10(27):5165–5181.
2. Red`kin R. G., Siumka Ye. I., Shemchuk L. A., Chernykh, V. P. 1' (hexamethylene-N-maleimide) 2a',7a' dihydro 1'H spiro[indole 3,3' pyrrolo[3,4 c]pyrrolisidine] 2,2',7'(1H,3'H,5'H) trione, containing maleinimide linker, exhibits inhibitory properties against of receptor factor growth fibroblast and has antimicrobial action: pat. 124687 Ukraine. № u201707279; stated 10.07.2017; published 25.04.2018, bull. № 8/2018.