SYNTHESIS AND EVALUATION OF HYDRAZONE COMPOUNDS AS CARBONIC ANHYDRASE INHIBITORS

Liucija Urbelytė[1], Martynas Bagdonas[2], Birutė Grybaitė[1], Rita Vaickelionienė[1], Daumantas Matulis[2], Asta Zubrienė[2], Vytautas Mickevičius[1]

[1]*Department of Organic Chemistry, Kaunas University of Technology, Kaunas, Lithuania*
[2]*Department of Biothermodynamics and Drug Design, Institute of Biotechnology, Life Sciences Center, Vilnius University, Saulėtekio 7, Vilniu, Lithuania*
birute.grybaite@ktu.edu

Carbonic anhydrases (CAs) are enzymes implicated in a wide range of diseases, including epilepsy, obesity, glaucoma and cancer. Selective inhibition of CAs by synthetic inhibitors-drugs could be used for their treatment. Primary sulfonamides are the most important class of CA inhibitors [1–2]. In this study a group of 4-substituted-benzensulfonamides bearing hydrazone moieties (Fig. 1) was synthesized and compound binding affinity to CA isozymes was evaluated.

In the synthesis, compound **1** was alkylated with methyl bromoacetate in ethanol to give ester **2**. Ethyl 2-[(2,6-dichloro-4-sulfamoylphenyl)amino]acetate **(3)** was synthesized by treating **2** with HCl in the presence of hydrogen peroxide. The obtained esters **2, 3** were converted to the hydrazides **4, 5**. The prepared starting compounds **4**, **5** were treated with various aldehydes or ketones and hydrazone-type compounds **6-13** were obtained.

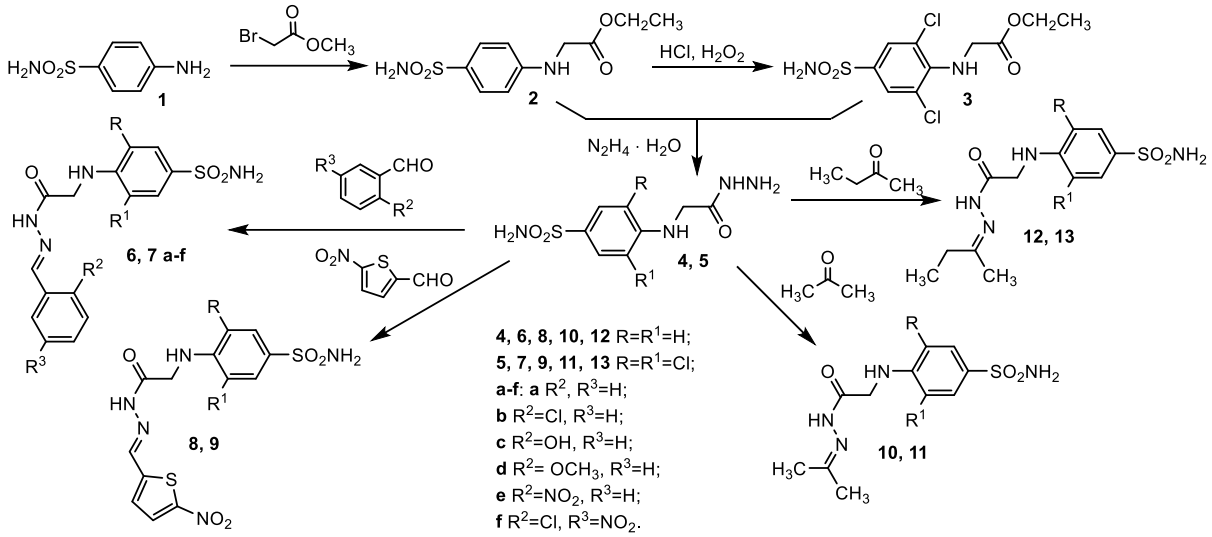

Fig. 1. Synthesis of substituted benzenesulfonamides **2-13**

The binding affinity of synthesized hydrazone-bearing derivatives for eight carbonic anhydrase isozymes was determined. Several compounds exhibited low nanomolar dissociation constants for isozyme CA VB, which is implicated in diseases of the central nervous system and obesity.

References

1. Linkuvienė V, Zubrienė A, Manakova et al. *Quarterly Reviews of Biophysics*. 2018. **51**. e10.
2. Frost S., McKenna R. (Ed.) Subcellular Biochemistry. 2014. Springer Netherlands, p. 430.