Thematic Section: Preparative Chemistry.

Full Paper

Reference Object Identifier – ROI: jbc-02/17-51-9-115 Subsection: Organic Chemistry. Publication is available for discussion in the framework of the on-line Internet conference "Butlerov readings". http://butlerov.com/readings/

Submitted on September 06, 2017.

Synthesis, the structure of arylsalicylic amides, which have anthelmintic activity

© Dmitry P. Sevbo, Anna Yu. Malakhova, and Vladimir N. Kuklin⁺*

Department of Pharmaceutical Chemistry. St. Petersburg Chemical and Pharmaceutical Academy. Prof. Popova St., 14, Lit. A. St. Petersburg, 197376. Russia. Phone: +7 (812) 234-13-59, (812) 499-39-00 ext. 4080. E-mail: kuklin-prof@yandex.ru

*Supervising author; ⁺Corresponding author

Keywords: arylsalylamides, production methods, structure and biological activity.

Abstract

For the first time, 11 new arylsalicylamides with higher anthelmintic activity were synthesized compared to fenasal [5-chloro-N-(2-chloro-4-throprophenyl)-2-hydroxybenzamide], for which, using modern physicochemical methods of analysis (IR, NMR spectroscopy, UV spectrophotometry, and chromium-mass spectrometry), their structure, purity by chromatographic methods, and the authenticity of colored and sedimentary reactions have been proved. A technological method for the synthesis of new acetoxy derivatives of aryl salicylamides was developed. Their acute toxicity (LD50) on white mice (males) was determined and it was shown that the newly synthesized derivatives of aryl salicylamides according to the Hodge and Sterner classification refer to low-toxic compounds. The association of anthelmintic activity with the structure of the new salicylamides obtained was established. It has been shown that aryl salicylamides obtained on the basis of 3,5-dichlorosalicylic acid have greater anthelmintic activity than the corresponding bromine-containing analogs; substitution of methyl for alkoxy group in the aromatic amine fragment of arylsalicylamides leads to a decrease in acute toxicity, and anthelmintic activity also increases for the propoxy derivative.

References

- [1] N. Punegova, I.I. Kurbanova, T.S. Shitova, O.G. Sinyashin, and V.A. Alfonsov. Effect of structure and physico-chemical characteristics of veterinary medicines Vetameks and Melapol plus containing synthetic melatonin on their ability to prolonged action. Butlerov Communications. 2014. Vol.38. No.5. P.13-18. ROI: jbc-02/14-38-5-13
- [2] T.V. Bolotova, V.A. Ermokhin, E.A. Mikha, A.S. Gilmutdinova, and P.P. Purygin. Synthesis of amino acid acetylsalicylates. Butlerov Communications. 2017. Vol.49. No.3. P.114-118. ROI: jbc-02/17-49-3-114
- [3] N.M. Storozhok, and N.P. Medyanik. Amid derivatives of salicylic acid effective inhibitors of UV initiated oxidation of organic substrates. Butlerov Communications. 2017. Vol.50. No.6. P.22-29. ROI: ibc-02/17-50-6-22
- [4] N.M. Storojok, N.P. Medyanik, S.A. Krekov, and A.P. Krisin. The supramolecular organization Nreplaced amides of salicylic acid. Butlerov Communications. 2011. Vol.24. No.3. P.109-112. ROI: jbc-02/11-24-3-109
- [5] S. Sharma, N. Anand Approaches to design and synthesis of antiparasitic drugs. *Pharmacochemistry* Library. 1997. Vol.25. P.239-257.
- [6] R.S. Vartanyan Synthesis of essential medicines. *Moscow: Medical Information Agency.* 2004. 845p. (russian)
- [7] B.P. Pilugin. Synthesis and biological activity of 2-amino-benzimidazole derivatives. *Moscow:* Chemistry. 2003. 298p. (russian)
- [8] A.Yu. Malakhova, F.S. Mikhaylitsyn, D.P. Sevbo, S.N. Trusov. Salicylanilides as promising compounds for the creation of new medicines. A collection of materials from the II All-Russian Scientific and Practical Conference with international participation "Innovations in the Health of the Nation", St. Petersburg, November 17, 2014. SPb.: SPXFA Publishing House. 2014. P.448-451. (russian)
- [9] A. Imramovsky, K. Pauk, V. Pejchal, J. Hanusek. Salicylanilides and their derivates as perspective antituberculosis drugs: synthetic routes and biological evaluations. Journal of Organic Chemistry. 2011. Vol.8. P.211-220.

Kazan. The Republic of Tatarstan. Russia. © Butlerov Communications. 2017. Vol.51. No.9. 115

- Full Paper
 D.P. Sevbo, A.Yu. Malakhova, and V.N. Kuklin

 [10] A.V. Buryakina, F.S. Mikhaylitsyn, D.P. Sevbo, S.N. Trusov, A.Yu. Malakhova. Acute toxicity of
 salicylanilides with anthelmintic activity. Honey Parasitology and Parasitic Diseases. 2012. No.2. P.53-54. (russian)
- [11] G.A. Gitsu, A.Yu. Malakhova, F.S. Mikhaylitsyn, D.P. Sevbo, S.N. Trusov, A.Ya. Safarova. Comparative evaluation of the antimino-lipidic activity of compounds of a number of salicylanilides (benzamides). Honey Parasitology and Parasitic Diseases. 2014. No.1. P.44-45. (russian)