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Investigation of Alkylation Reaction of 2-Arylsubstituted Pyrimidine-4(*3H*)-ones and Screening of Anticonvulsant Activity of Alkylated Products

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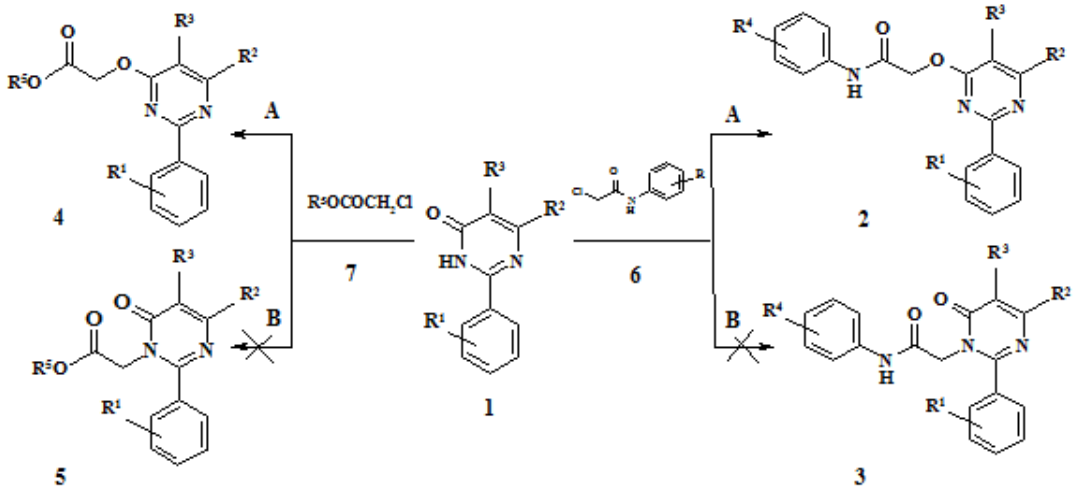
Currently pyrimidine derivatives are known by their broad spectrum of biological activity including a significant effect on the CNS. Thus, among pyrimidines there were found the compounds with sedative, anxiolytic [1], antipsychotic [2] and anticonvulsant effects [3].

Consequently, our study aimed to synthesize a series of O-alkylated pyrimidine-4(*3H*)-one derivatives and investigate their anticonvulsant activity. Based on the PASS-prediction data which showed a high possibility of antiepileptic and neuroprotecive activity of the planned compounds we performed an alkylation of 2-aryl-6-methylpyrimidine-4(*3H*)-ones by N-arylsubstituted α-chloroacetamides **(6)**, chloroacetic acid and its ester **(7)**. The reaction was carried out while heating in dioxane medium in the presence of sodium bicarbonate. Planning the synthesis we divined the possibility of two directions of the reaction due to the presence of a few reactive centers in molecules of initial pyrimidine-4(*3H*)-ones. This reaction could result into the formation of N- and O-alkylation products or their mixture (Scheme).



The data of NMR ^{1}H and ^{13}C-spectroscopy confirmed the formation of O-alkylated products **(2, 4).**

For screening the anticonvulsant activity of synthesized compounds the pentylenetetrazole-induced seizure model was used. The results of the study revealed a pronounced antiepileptic activity among compounds of this series.

[1] S. Selleri, F. Bruni, C. Costagli [et al.] J. Med. Chem., 2005, Vol. 48, №21, pp. 6756-6760.
[2] H.B. Simpson, E.B. Foa, M.R. Liebowitz [et al.] JAMA Psychiatry, 2013, Vol. 70, №11, pp.1190-1198.
[3] S.B. Wang, X.Q. Deng, Y.P. Yuan [et al.] Eur. J. Med. Chem., 2012, Vol.56, pp. 139-144.