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New methoxy and ethoxy arylpiperazines from hexyl-1,2,4-triazolo[4,3-a]pyridin-3(2H)-ones as dual 5-HT1A / D2 ligands

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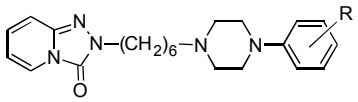

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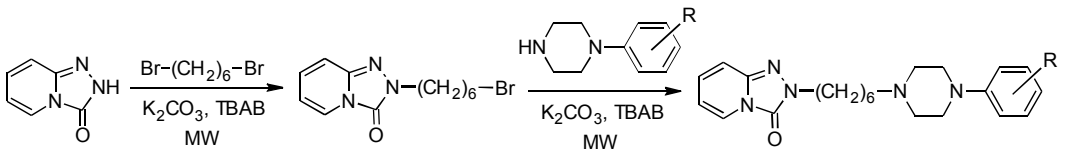
R = OCH_3, OC_2H_5

Figure 1. General structure of ligands

It is now known that many neurotransmitter systems are responsible for diseases of the central nervous system. Very important role in the pathogenesis and treatment of depression and anxiety is played by 5-HT_{1A} receptors [1,2] and D_2 dopamine receptors [3]. The high efficacy of dual 5-HT_{1A} / D_2 ligands has been proven in the fight against depression, therefore it seems reasonable to look for new compounds with this profile of action [4].



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R = OCH_3, OC_2H_5

Figure 2. Synthesis plan

The aim of the conducted research was to search for ligands for dual 5-HT_{1A} / D_2 receptors. The activity of four compounds belonging to the 2-[6-(4-arylpiperazin-1-yl)hexyl]-1,2,4-triazolo[4,3-a]pyridin-3(2H)-one group with the methoxy and ethoxy substituent at arylpiperazine ring were tested. Compounds were synthesized by a two-step synthesis involving *N*-alkylation of 1,2,4-triazolo[4,3-a]pyridin-3(2H)-one (**2**) by 1,6-dibromohexane (**3**) followed by condensation with selected arylpiperazine (**4**). Reactions were carried out in the presents of microwave radiation. The synthesized compounds were tested in *in-vitro* studies. Among the tested combinations, compounds showing high affinity for the tested receptors were found.

[1] Moses-Kolko E.L. et. al. *Fertil. Steril*. 89 (2008) 685-692
[2] Savitz J. et. al. *Prog Neurobiol*. 88 (2009) 17-31
[3] Chen Z. et. al. *Receptors Channels* 4 (1996) 1-8
[4] Ullah N. *Med Chem*. 10 (2014) 484-96

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