Ural Branch
of the Russian Academy
of Sciences

MedChem Russia 2019

4th Russian Conference
on Medicinal Chemistry
with international participants

June 10-14, 2019
Ekaterinburg, Russia

Abstract book

4th Russian Conference on Medicinal Chemistry with international participants. MedChem Russia 2019
Abstract book – Ekaterinburg : Ural Branch of the Russian Academy of Sciences, 2019. – 512 p.
ISBN 978-5-7691-2521-8

Abstract book includes abstracts of plenary lectures, oral and poster presentations, and correspondent presentations of the Conference

Novel bivalent AMPA-receptor ligands of bis(pyrimidine) series

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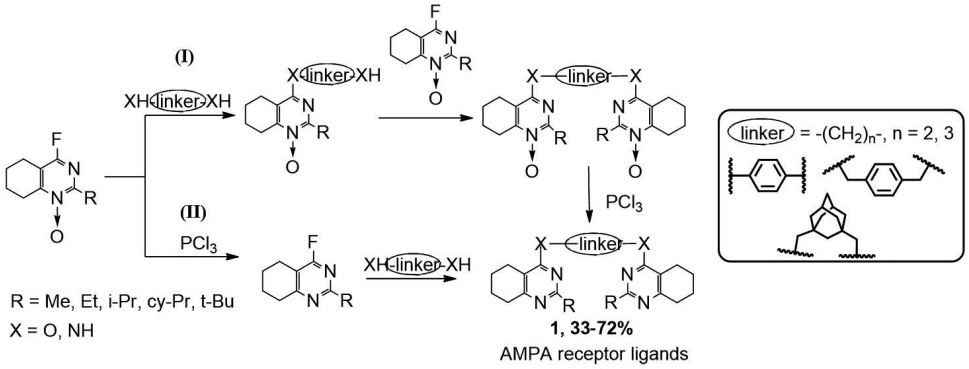
AMPA-receptors are the attractive targets for treatment of a series of neurological disorders. Positive AMPA-receptors modulators can be useful for treatment of the cognitive impairments improving learning and memory, whereas in contrast negative modulators (or blockers) are perspective agents for treatment of epilepsy. Here we present the synthesis of a novel series of bispyrimidines **1** which were supposed to act as bivalent AMPA-receptors ligands. Based on our previously described synthetic approaches [1] we obtained the targeted heterocycles **1** using two routes: (I) double S_NAr reaction of 4-fluoropyrimidine *N*-oxides with different bisnucleophiles and subsequent reduction of *N*-oxide fragment, or (II) reduction of starting 4-fluoropyrimidine *N*-oxides and subsequent S_NAr reaction with bisnucleophiles.



Obtained compounds **1** were tested in patch-clamp experiments for the influence on the kainate-induced currents recorded for the Purkinje cells extracted from the rat cerebellum. Several compounds **1** showed high positive (increase of the kainate-induced currents for 35-60% at 0.001-0.1 μM) or negative modulating effect [2].

This work was supported by the Russian Science Foundation, grant no. 17-15-01455.

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