

# Synthesis and Evaluation of Artificial Glutamate Analogs

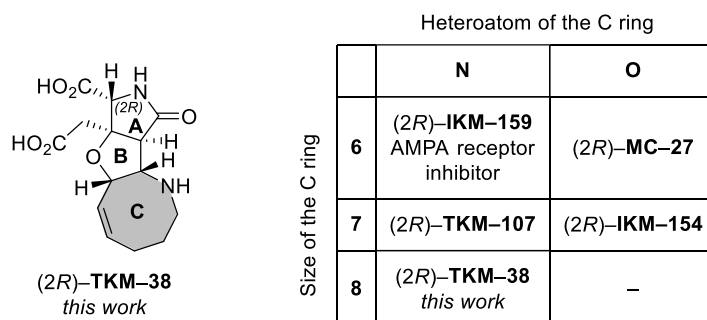
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Ionotropic glutamate receptors (iGluRs) mediate excitatory neurotransmission in the central nervous system. We here report collective synthesis and biological evaluation of both enantiomers of artificial glutamate analogs as a ligand for iGluRs.

We have previously synthesized both enantiomers of IKM-159, employing enantiomerically pure amine as a chiral building block in the first multi-component coupling reaction.<sup>1,2</sup> In the present study, we synthesized other analogs (IKM-154, MC-27, TKM-38, and TKM-107), by optical resolution strategy employing menthol as a chiral auxiliary, to improve the overall efficiency in the synthesis.



Starting from oxanorbornene derivative readily available by multi-component coupling reaction, optically pure artificial glutamate analogs shown in the Table as well as the antipodes were successfully synthesized in total 9 steps for each. Mice in vivo assay indicated the heteroatom and the size play an important role in the neuroactivities.<sup>3</sup>

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