SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF NEW 1-PHENYL-1,3,8-TRIAZASPIRO[4.5]DECAN-4-ONE DERIVATIVES AS NEW POTENTIAL SELECTIVE NOP LIGANDS

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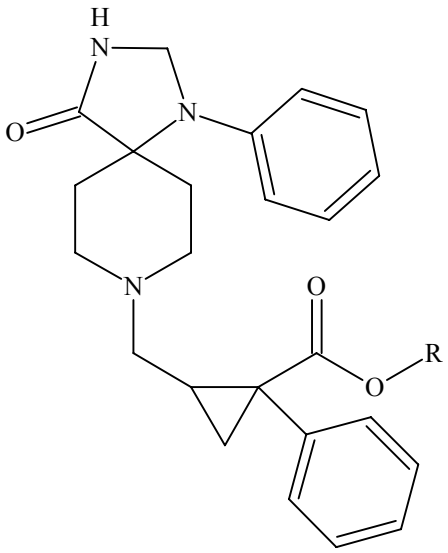
Recently reported as the fourth member of the opioid receptor family, NOP receptor [also called opioid receptor-like (ORL_1) or nociceptin receptor (OP_4)] is a G-protein-coupled receptor closely related to KOP, MOP and DOP opioid receptors. The endogenous ligand is a 17-amino acid neuropeptide, named nociceptin or orphanin FQ.
NOP receptor and nociceptin are widely distributed in the central nervous system as well as in the periphery and are involved in several physiological effects including nociception, attenuation of anxiety, modulation of learning and memory, stimulation of food intake, diuresis, hypotension and bradycardia, inhibition of reward pathways in drug addiction.
Thus, considering the number of modulatory effects in which nociceptin is involved, the synthesis of selective non-peptide NOP agonists or antagonists represent an interesting target for the development of novel therapeutics for several neurological conditions.
In this work we present the design, synthesis and preliminary pharmacological data of methyl, ethyl, propyl and isopropyl 2-[(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-8-yl)methyl]-1-phenylcyclopropanecarboxylate enantiomers as new potential selective NOP ligands useful to provide new insights in the binding to this subtype of opioid receptor.



R = CH_3, C_2H_5, C_3H_7, i-C_3H_7