SYNTHESIS OF LIGANDS OF THE PURINERGIC RECEPTORS P1 AND P2

The purinergic receptors are widely distributed in body. There are two big families: P1 and P2. The P1 family includes four receptor subtypes named A1, A2A, A2B and A3. They are G-protein coupled receptors and the physiological ligand is adenosine. A2A receptors, in particular, are coupled to the dopamine D2 receptors: A2A adenosine receptors antagonists induce a better interaction of dopamine with its D2 receptors improving the dopaminergic cerebral functions, which are highly compromised in the Parkinson's disease due to the dopamine depletion. Drug development is limited by the presence of the blood-brain barrier (BBB), so there is need to obtain new compounds that can penetrate the BBB through chemical modifications of known scaffolds or the synthesis of molecular hybrids.
In addition, in recent years it has become increasingly clear that these receptors are involved in antitumor treatment options. In this light, further development of adenosine receptors antagonists could give access to new candidates in this area.
The big P2 family is divided in two subfamilies named P2Y and P2X, whose physiological ligands are ATP or ADP. The P2Y receptors are G protein coupled receptors, whereas the P2X ones are ion channel receptors. These subfamilies include several subtypes usually ubiquitarious in the body. Among all of the P2Y receptors subfamily, P2Y12 receptors are G protein coupled receptors involved in the process of platelet aggregation, and they are relatively present only on the platelets. Their physiological agonist is ADP, while ATP is the antagonist. The development of P2Y12 antagonists may represent a good biological target in the field of cardiovascular diseases in which the platelets aggregation is one of the major problems.

GOALS
Synthesis and biological evaluation of new purinic or pyrimidinic derivatives as ligands for the purinergic receptors.

INSTRUMENTS AND METHODS
Common equipment of a synthetic organic laboratory. Use of chromatographic (preparative HPLC, flash chromatography) and analytic (NMR, HPLC-mass spectrometry, IR) techniques for the purification, identification and characterization of the synthesized compounds.

MAIN SUBJECTS
Medicinal chemistry

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