Molecular Tools for the Cellular Study of Adenosine A_1 Receptors

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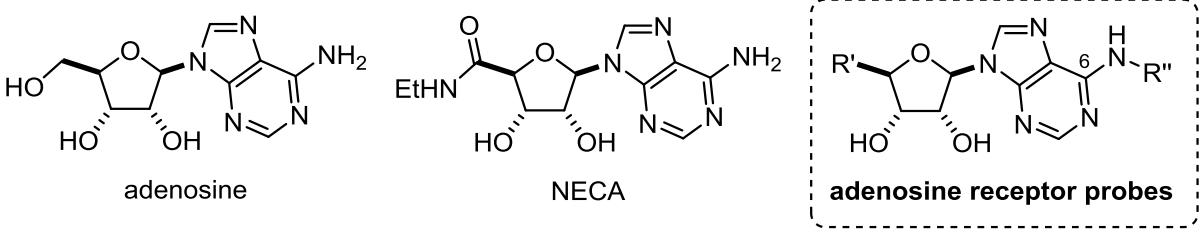
The purine nucleoside adenosine is not only an important building block for nucleic acids but also acts as an important signalling molecule by exerting its agonist activity at four known adenosine receptor subtypes: A_1, A_{2A}, A_{2B} and A_3. Adenosine receptors (ARs) belong to the family of G-protein coupled receptors (GPCRs) and have a wide and varying tissue distribution. Whilst implication in cardiovascular, respiratory, inflammatory and neurological disorders have emphasised their therapeutic potential on the one hand [1], understanding their cellular trafficking and agonist-induced internalisation [2] is equally important from a basic research point of view.

We have previously discovered several potent and A_1R-selective agonists that are based on the adenosine and NECA structures. [3] Here, we present the improved synthesis of some of these A_1R-selective agonists. In particular, we have optimised the key S_NAr-reaction to introduce substituents at the purine C-6 position by using microwave chemistry among other things. Furthermore, we also present some fluorescent adenosine and NECA derivatives that might be interesting tools to study the trafficking and activation of A_1R.



[1] S. Sachdeva et M. Gupta, Saudi Pharm. J. 2013, 21, 245. [2] A. E. Baines et al., Neuropharmacology 2011, 61, 1. [3] A. Knight et al., J. Med. Chem. 2016, 59, 947.