

New library of 3-Mercaptopyruvate Sulfurtransferase inhibitors

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In a wide variety of multicellular organisms, cells must be able to communicate with one another. This communication is made through the use of signalling molecules carrying specific information from cell to cell. Some of these molecules are endogenously produced and can be proteins, lipids or gases. In mammals and plants, they participate in biological processes such as vasodilation, the regulation of cardiovascular, nervous and immune systems and cytoprotection.

Gasotransmitters are signalling molecules, they include Hydrogen sulphide (H₂S), Carbon monoxide (CO) and Nitric oxide (NO). H₂S has been assigned to this family by Wang in 2002 and is subject to lots of scientific experimentation since then, although, its exact biological role remains unknown.

In mammals, three different enzymes are responsible for the production of H₂S. Cystathionine- β -synthase (CBS), cystathionine- γ -lyase (CSE) and 3-mercaptopyruvate sulfurtransferase (3-MST). Inhibiting these three enzymes will give some information about their physiological role. Thus, inhibitors have to be designed and synthesized. CBS and CSE have already been investigated and working inhibitors have already been reported (they include aminooxyacetic acid (AOAA) for CBS one and propargylglycine (PAG) and β -cyano-L-alanine (BCA) for CSE). The synthesis of a potent, selective and biologically suitable inhibitor for 3-MST is still at its beginning. Hanaoka et al., in 2017, reported four inhibitors, however, their poor solubility in water makes them less usable in a biological medium. C. Szabo's and C. G. Bochet's groups have reported a library of inhibitors based on one of Hanaoka's molecules as well.

This work revolved around building a library of potential inhibitors based on one reported by Hanaoka (shown below). In particular, functional groups were added to the naphthalene rings on the left-hand side of the molecule.

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