Synthesis and Antiproliferative Properties of Tryptamine Derivatives

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It is known that branching in aliphatic amines reduces their degradation in an organism by MAO enzymes. The main target of our project was to reveal the influence of carbon chain branching in tryptamines onto their antiproliferative activity against both tumor and normal cell lines. In this project we have synthesized several derivatives of tryptamine substituted at position 5 using the rearrangement of cyclopropyl ketone arylhydrazones to form either branched or unbranched products. This method assumes the use of cyclopropyl methyl ketone or its derivative with a phenyl group at position 2 in the small cycle as starting compounds. The mechanism includes a cyclopropane ring-opening, a pyrroline ring-closure and a subsequent Fischer-type rearrangement. The derivatives obtained were subsequently modified using the two following ways. The first one included the mono benzylation at the aliphatic nitrogen atom via the reductive amination reaction. The second type of modification required the introduction of a protecting group onto the more reactive aliphatic nitrogen atom and subsequent benzylation at the indol ring nitrogen and deprotection. Thus, we have synthesized 15 previously unknown tryptamine hydrochlorides which have been submitted for the biological investigation of their antiproliferative activity versus four different cell lines (three tumor and one normal). The IC50 values obtained have been analyzed in terms of the structure–activity relationship. To sum up, the products obtained were found effective in inhibiting the vital activity of tumor cells with IC50 values down to 1.5 μM. Keywords: tryptamine, antitumor activity, cyclopropyl ketones

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