Synthesis of Enantiomerically Pure Tryptamine Derivatives, Potential Antitumour Drugs

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Tryptamine derivatives are well-known bioactive compounds. For example, serotonin, which is 5-hydroxytryptamine, is an important neurotransmitter. Various drugs based on the tryptamine core cure different diseases including tumors. However, there is a problem in using amines in pharma connected with their fast degradation catalysed by enzyme monoamine oxidase. The problem can be solved by branching tryptamines at the alpha-position to amino group. This approach leads to the formation of a chiral center and previously antitumor activity of tryptamines with a chiral center was tested in racemic mixtures. The aim of our research was to synthesize enantiomerically pure tryptamines which had been known previously as racemic mixtures and demonstrated improved antitumour activity. Our approach to tryptamine derivatives was based on asymmetric Grandberg rearrangement of cyclopropylketone arylhydrazones. Enantiomerically pure ketones were obtained in high yields from corresponding enantiomers of trans-2-phenylcyclopropanecarboxylic acid which in turn were obtained via optical resolution of racemic acid. Finally, we obtained enantiomerically pure tryptamine derivatives and performed indole ring modifications. We also developed various approaches to increase water solubility of tryptamines. The first and the main approach included modification of tryptamine molecule, the second one was connected with changing anion from chloride to organic one so it could form intimate ionic pair with tryptamine molecule. Obtained tryptamine derivatives were given to biological laboratory to test their bioactivity against different cell lines. Finally, enantiomerically pure tryptamines were found to show better results than cisplatin which is widely used for treating cancer.