How to Stop the "Walking" Protein?

Vekhova, Darina

An effective method to stop a tumor growth is inhibition of the mitotic kinesin, that is a protein, which moves along microtubules and transport substances necessary for cancer cells division. 1,2,3,4-tetrahydropyrimidine-2-thione derivatives can bind to the kinesin inside a cancer cell and form a stable complex which discontinue moving along the microtubule. So, the process of cancer cell’s mitosis and tumor growth stops. Steric shielding of the kinesin molecule by the system of aromatic circle and heterocycle in such derivatives does not affect the polymerization of microtubules and prevents severe side effects. The basis of the new compound synthesis was Biginelli condensation. The selected components were thiourea and benzaldehyde. To embed necessary functional groups into the compound’s structure I took benzoylacetonitril as a third component. To choose relevant conditions we did 3 series of synthesis. Reactions with hydrochloric acid and thiourea sulfate as catalysts did not lead to new products. Polar solvent dimethylformamide and catalyst trimethylchlorosilane supposedly activated the iminium mechanism of the condensation at room temperature. As a result, 4,6-diphenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile was synthesized. Its yield was 55 %. The substance is dissolvable in isopropyl alcohol and dimethyl sulfoxide (DMSO). The melting temperature is about 221 degrees Celsius. The structure was confirmed by the IR and NMR spectroscopies. The molecular docking demonstrated that the values of binding constants of the synthesized compound and the extant prototype of anti-cancer drug monastrol to mitotic kinesin Eg5 are approximately equal. It proves that our compound is perspective for inventing an anti-cancer drug with minimal side effects.

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