SYNTHESIS OFNEW 1-3-(1H-BENZODIMIDAZOL-2-YL)-4-HYDROXYPHENYL-5-OXOPYRROLIDINE-3-CARBOXYLICACID DERIVATIVES

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Various nitrogen-containing heterocyclic compounds have been widely identified for their broad spectrum of biological activity and have become a focal point of extensive research due to their frequent occurrence as naturally existing bioactive compounds, including benzimidazole, naphthalimide, pyrrolidine [1]. Pyrrolidine is a well-known molecular fragment given its pharmacological diversity of activity, including antiproliferative effects as one outcome. It has also been investigated as a potential small molecule with broad-spectrum antitumour activity against various cancer cell lines [2, 3]. Cancer represents a significant global health challenge, emphasizing the critical need for the discovery of effective anticancer agents. Consequently, this paper delves into the discussion of synthesizing derivatives of these compounds.

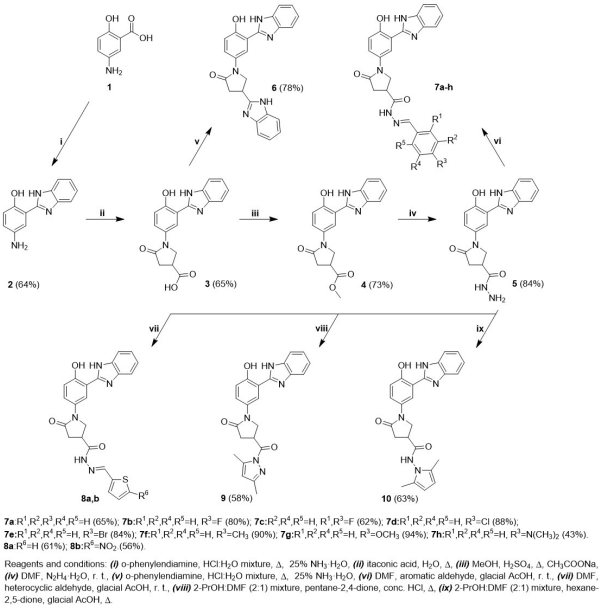

Fig. 1. Synthesis of hydrazide 5 and its derivatives 6–10

4-Amino-2-(1H-benzo[d]imidazol-2-yl)phenol (2) was synthesized in the Phillips reaction by reacting 5-aminosalicylic acid 1 with 1,2-phenylenediamine in a mixture of hydrochloric acid and water (1:2). Acid 3 was obtained by the reaction of compound 2 and itaconic acid in the water. Then this acid 3 was esterified with methanol using catalytic amount of sulfuric acid. The obtained methyl ester 4 reacted with hydrazine monohydrate in N,N-dimethylformamide (DMF) at room temperature, and the corresponding hydrazide 5 was synthesized. To find out the effect of the benzimidazole fragment on the biological properties the first target product compound 6 containing two benzimidazole rings is obtained again by the following Phillips reaction. By the reaction of hydrazide 5 and heterocyclic or aromatic aldehydes in DMF hydrazones 7 and 8 were prepared. Pyrazole ring containing derivative 9 was synthesized by reaction with acetylacetone in DMF catalyzing by hydrochloric acid while pyrrole derivative 10 was obtained by the hydrazide 5 condensation reaction with 2,5-hexanedione in the presence of a catalytic amount of acetic acid in the reaction mixture. The structure of the obtained compounds was confirmed based on the data of 1H NMR, 13C NMR, and IR spectra. All compounds will be tested to measure their potential antitumor activity at Weill Cornell Medicine of Cornell university, New York, USA.

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