SYNTHESIS OF 3-(24-DIHIDROXY-5-BENZYL)ALKYL CARBOXYLIC ACIDS AND THEIR DERIVATIVES

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HSP90 (Heat Shock Protein 90) is a chaperone protein that belongs to the heat shock protein class and has a mass roughly equal to 90 kDa. The protein is found in most animal kingdoms and accounts for 1-2% of all proteins located inside human cells. The chaperone is responsible for proper protein folding, their stabilization during heat stress conditions and assistance during degradation [1]. Cancer cells contain elevated levels of HSP90, which is vital to their migration, metastasis, proliferation and other processes occurring during tumor growth [2]. According to the data presented by the World Health Organization in 2022, cancer is a leading case of deaths globally, responsible for around 10 million deaths annually [3]. Consequently, HSP90 has been subject to numerous studies over the last decade as a potential target for anti-cancer and anti-neurodegenerative medications [2].

The studies of radicicol (a natural product that binds competitively to HSP90) have shown that a resorcinol fragment with its hydroxy groups is crucial to the inhibition of the N-terminal domain, which contains the preeminent region of the protein — the ATP binding pocket [4]. Further studies revealed that for a drug molecule to bind effectively to the active site of the protein, it needs to contain an aromatic ring situated near the resorcinol moiety [5].

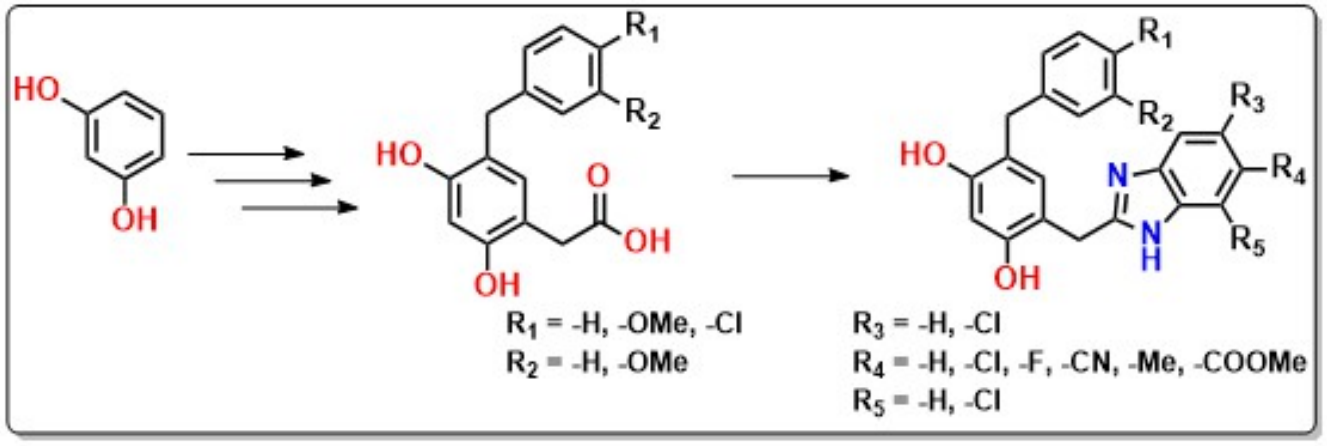

Fig. 1. Synthesis of benzimidazoles using resorcinol as a starting compound

The objective of this work is to synthesize various 3-(2,4-dihidroxy-5-benzyl)alkyl carboxylic acids and use them in the synthesis of potential resorcinol-based HSP90 inhibitors containing a benzimidazole moiety. The ten-step synthesis, it's challenges and results as well as more details about HSP90 will be discussed during the presentation.

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