SYNTHESIS OF 4-((BENZIMIDAZOL-2-YL)THIO)-6-ISOPROPYLRESORCINOLS

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An increasing number of cancer cases are being observed worldwide.Therefore, Hsp90 inhibitors are among the most promising approaches for cancer treatment. Hsp90 is a molecular chaperone expressed in a variety of cells and plays a critical role in regulating the cell cycle, including processes such as cell proliferation, signal transduction, and transcription [1]. Under environmental stress conditions such as high temperature and hypoxia, Hsp90 is overexpressed in cells [2], especially in tumor cells [3], to maintain a dynamic balance between protein folding and degradation. Due to the presence of mutated and unstable client proteins, cancer cells exhibit a greater dependence on Hsp90 than normal cells. This increased reliance renders Hsp90 an attractive therapeutic target as its inhibition can selectively disrupt oncogenic signaling pathways and reduce tumor development. The aim of this work is to synthesize variously substituted sulfur-containing resorcinol compounds that could act as Hsp90 inhibitors and inhibit cancer progression.

For the synthesis of targeted compounds, 1-isopropyl-2,4-dimethoxybenzene was selected as the starting material. Structural modification was introduced at the fifth position of aromatic ring, where thiobenzimidazoles moieties, were attached. Hydroxy groups were protected with methoxy groups to avoid additional reactions. The isopropyl substituent was obtained after the Wittig reaction with carbonyl and reduction. For the addition of sulfur-containing compounds, a Ullmann-type reaction was performed with iodinated and isopropyl-substituted dimethoxybenzene. Finally, the protecting groups were removed to yield the desired target compounds.

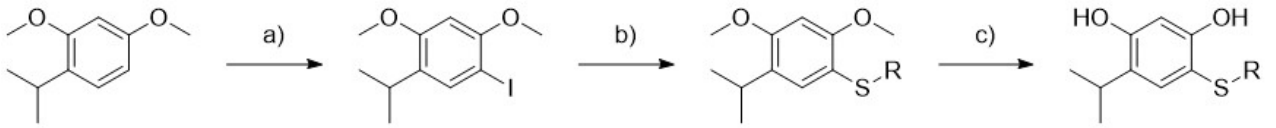

Fig. 1. Scheme of targeted compounds, a) NIS, CH_3CN; b) CuI, 2,9-dimethyl-1,10-phenanthroline hydrate, *t*-BuOK, DMF, 110°C, Ar; c) BBr_3, DCM, 0°C, Ar.

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