4-ISOPROPYL-6-(1-SUBSTITUTED 1*H*-IMIDAZOL-5-YL)BENZENE-1,3-DIOLS AS POTENTIAL HSP90 INHIBITORS

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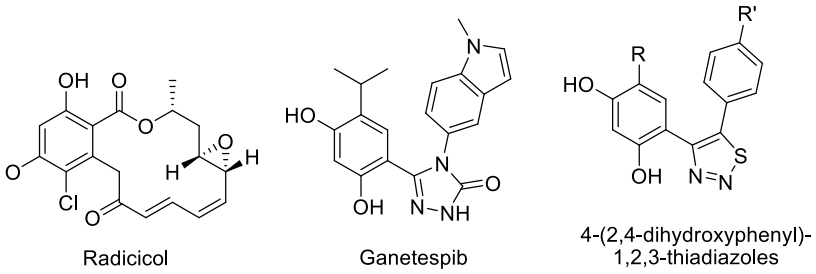
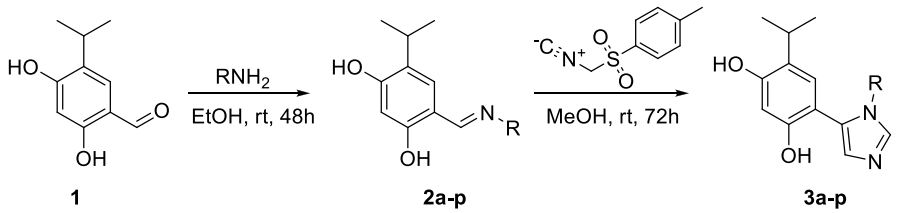
Heat shock protein 90 (Hsp90) is an ATP-dependent molecular chaperone responsible for maintaining the conformation, stability and function of its client proteins. It constitutes 1-2% of total cell proteins and the amount is doubled in cellular stress conditions [1]. Hsp90 clients include many oncogenic proteins responsible for cell cycle progression, cellular proliferation, invasion and metastasis. Moreover, studies show that Hsp90 shows a higher affinity to small-molecule inhibitors in malignant cells than in normal cells [2]. Hence making Hsp90 a promising target for cancer therapy.

Hsp90 inhibitors may be categorized according to their structure. The major class under investigation is molecules containing resorcinol moiety, that are based on the natural compound Radicicol. Active synthetic structures usually contain an alkyl group in the 4th position and a 5-membered ring in the 6th position, connected to another substitute, such as in compound Ganetespib, currently undergoing clinical trials [3].



In continuance to our work where a set of 4-(2,4-dihydroxyphenyl)-1,2,3-thiadiazoles were studied [4], we designed a synthetic pathway to obtain 4-isopropyl-6-(1-substituted 1*H*-imidazol-5-yl)benzene-1,3-diols. 2,4-dihydroxy-5-isopropylbenzaldehyde **1** and primary amines gave imines **2a-p**, which were used in cyclization with 1-(isocyanomethanesulfonyl)-4-methylbenzene to form imidazoles **3a-p**. The biological activity is to be discussed in the poster presentation.



References

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