INVESTIGATION OF 2-((SUBSTITUTED IMINO)METHYL)PHENOLS 1,3-CYCLOADDITION REACTIONS

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Hsp90 (heat shock protein) – chaperone protein, responsible for folding and stabilization of client proteins. Although it is important in normal cell regulation processes, the amount of Hsp90 is significantly larger in malignant cells. Continuing our research on potential Hsp90 inhibitors [1], we decided to synthesize compounds, containing two known pharmacophores – 4-isopropyl-1,3-diol fragment, affined to Hsp90 binding center, and imidazole ring, which has antimicrobial, antiviral and anticancer properties [2]. In our efforts to obtain 4-isopropyl-6-(1-(4-methoxyphenyl)-1*H*-imidazol-5-yl)benzene-1,3-diol (**4**, fig. 1) by van Leusen imidazole synthesis [3] we isolated unexpected by-product **5** with condensed heterocyclic system never described in literature.

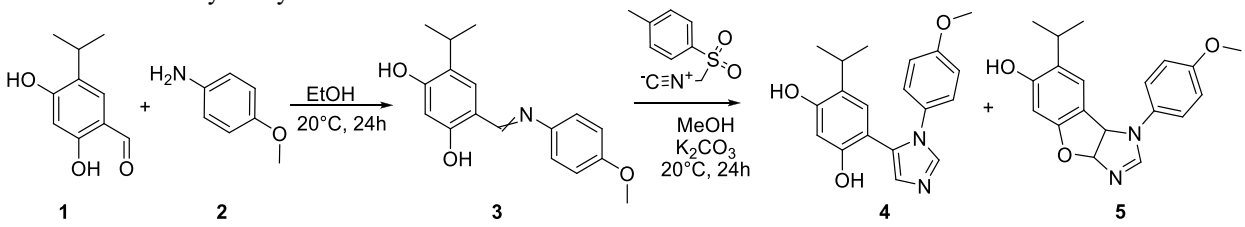

Fig. 1. Synthesis of 4-isopropyl-6-(1-(4-methoxyphenyl)-1*H*-imidazol-5-yl)benzene-1,3-diol.

In order to investigate the formation of 3a,8b-dihydro-1*H*-benzofuro[3,2-*d*]imidazole fragment we decided to explore other imines with *ortho*-hydroxysubstituted aromatic rings. Firstly, we optimized conditions of the reaction with toluenesulfonylmethyl isocyanide (TosMIC). Best solvent proved to be polar protic methanol. Organic bases such as triethylamine and pyridine did not favor the reaction and inorganic base K_2CO_3 gave the best total yield as well as the best yield of compound with fused three-ring moiety. Secondly, we decided to investigate the impact of various substitutes R and R' (fig. 2). We prepared different Shiff's bases (**6a-o**) according to known procedures. Then imines reacted with TosMIC and K_2CO_3 in methanol to give compounds **7a-o** and **8a-o**. Further results will be discussed in the poster presentation.

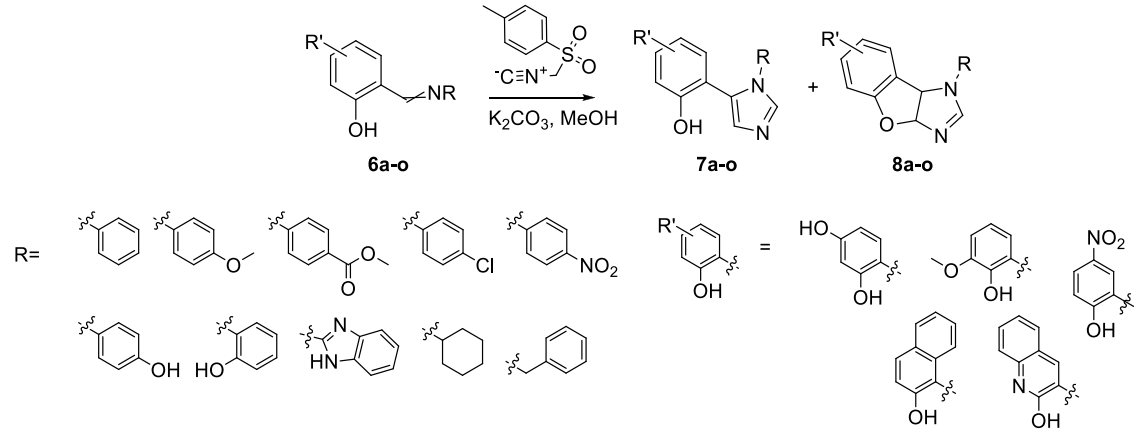

Fig. 2. Investigation of 1,3-cycloaddition reactions.

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