DESIGN AND SYNTHESIS OF NOVEL DERIVATIVES BASED ON1-(NAPHTHALEN-1-YL)-4-PHENYL-1H-IMIDAZOLE-2-THIOL

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Hydrazide–hydrazone derivatives represent an important class of bioactive compounds and have shown promising anticancer activity against a wide range of human cancer cell lines. Their structural versatility and ability to interact with multiple biological targets make them attractive scaffolds for further drug development.[1] Likewise, aminoketone derivatives have been reported to exhibit in vitro anticancer activity against selected cancer cell lines, suggesting their potential relevance in anticancer drug research.[2]

The starting compound **2** was prepared by the reaction of 1-naphthylamine **(1)** with 2-bromo-1-phenylethan-1-one at room temperature. Compound **3** was obtained by the reaction of aminoketone **2** with KSCN in 10% HCl under reflux. Methyl 2-((1-(naphthalen-1-yl)-4-phenyl-1H-imidazol-2-yl)thio)acetate **(4)** was obtained via S-alkylation of compound **3** with methyl bromoacetate. The reaction of ester **4** with hydrazine hydrate in 2-propanol under reflux gave 2-((1-(naphthalen-1-yl)-4-phenyl-1H-imidazol-2-yl)thio)acetohydrazide **(5)**, which crystallized from the reaction mixture after cooling it down. Condensation of hydrazide **5** with heterocyclic aldehydes gave hydrazones **6a-d**. The condensation of hydrazide **5** with 2,5-hexanedione in 2-propanol in the presence of a catalytic amount of acetic acid resulted in the formation of N-(2,5-dimethyl-1H-pyrrol-1-yl)-2-((1-(naphthalen-1-yl)-4-phenyl-1H-imidazol-2-yl)thio)acetamide **(7)**. The interaction of hydrazide **5** with 2,4-pentanedione in 2-propanol, in the presence of a catalytic amount of hydrochloric acid, resulted in the formation of pyrazole **8**.

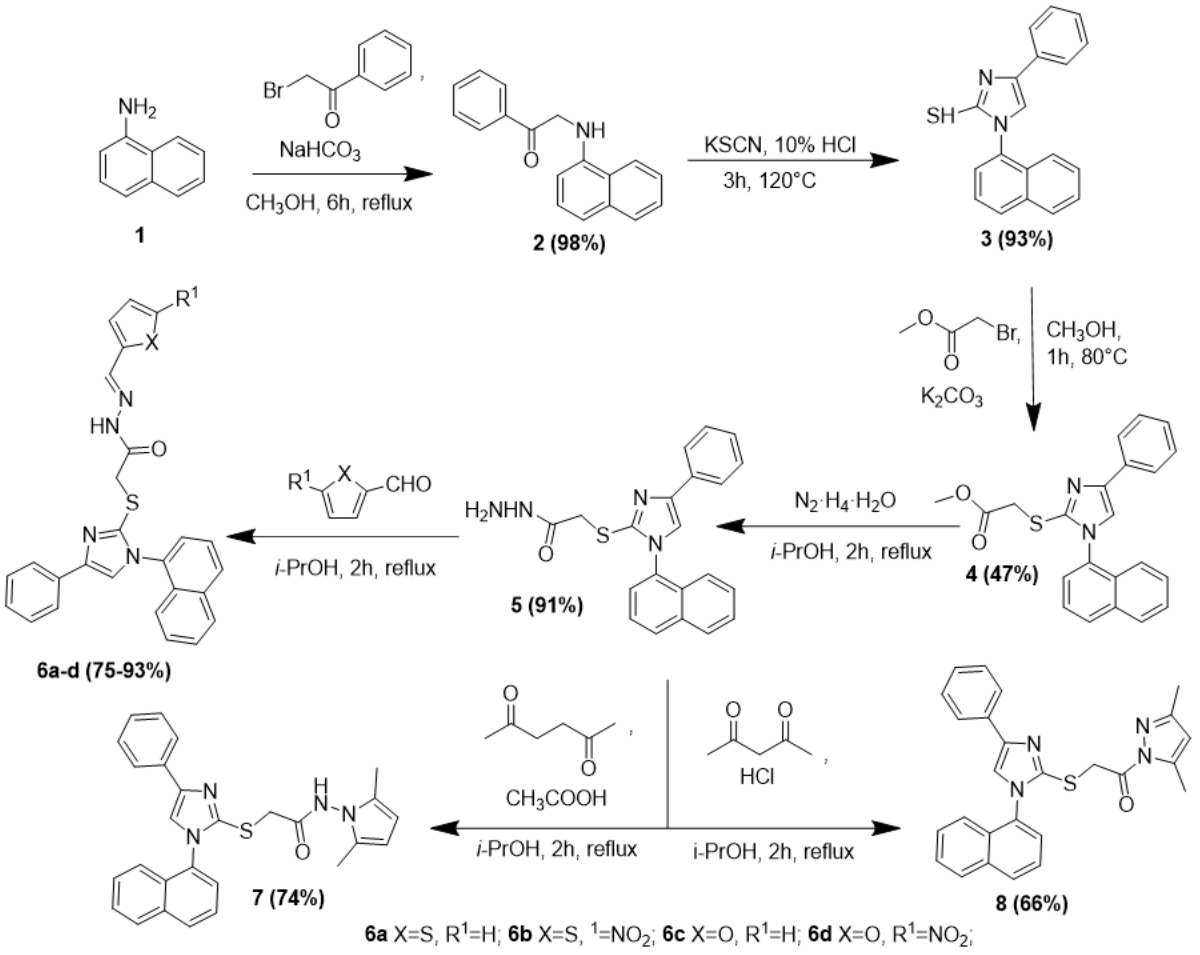

Fig. 1. Synthesis of compounds **2-8**.

The structure of the synthesized compounds was characterized by spectral data (IR, NMR spectra, and elemental analysis).

[1] S. Karakuş, F. Tok, B. İ. Abas, E. Tütüncü, and Ö. Çevik, "Synthesis and in vitro anticancer activity of some new hydrazide-hydrazones derived from articaine," J. Res. Pharm., vol. 28, no. 6, pp. 1901–1910, Jan. 2024, doi: 10.29228/jrp.863.

[2] W. Seebacher et al., "Formation of 5-Aminomethyl-2,3-dihydropyridine-4(1H)-ones from 4-Amino-tetrahydropyridinylidene Salts," Molecules, vol. 28, no. 19, art. no. 6869, Sep. 2023, doi: 10.3390/molecules28196869