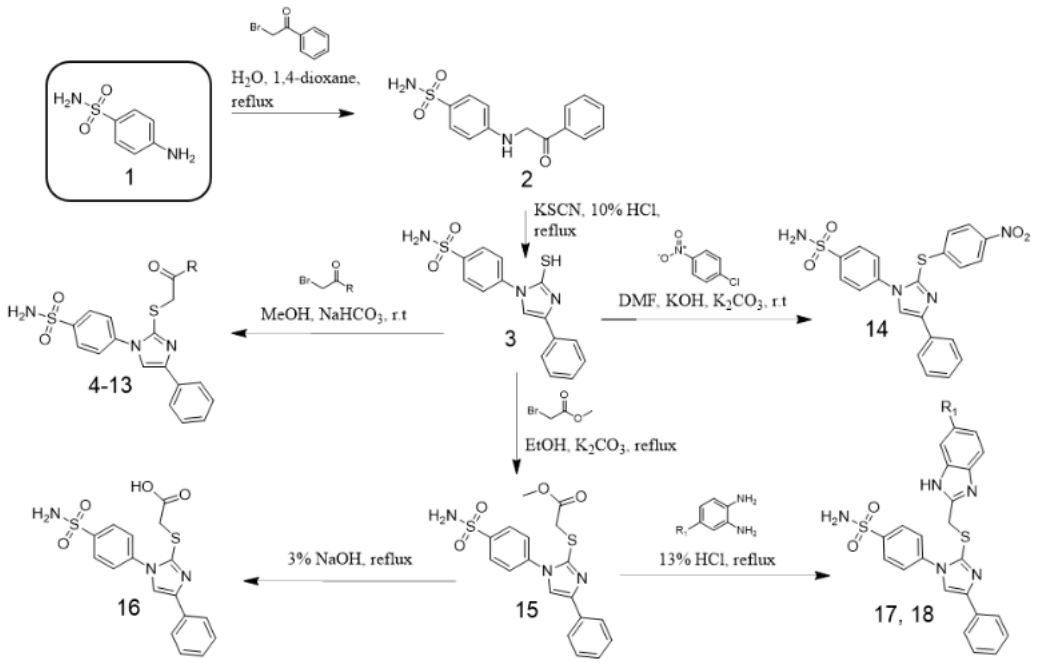
Synthesis and biological evaluation of alkylated 2-mercaptoimidazoles bearing a benzenesulfonamide moiety

Benzenesulfonamides are widely explored due to their wide range of potential pharmaceutical uses as anticancer, antibacterial drugs [1]. As well as functionalized 2-mercaptoimidazoles which present potent anticancer activity [2]. In this present study, α-aminoketone **2** was obtained by reacting the primary amine **1** with bromoacetophenone, which in turn was reacted with potassium thiocyanate in the presence of hydrochloric acid to obtain 2-mercaptoimidazole **3**. Compounds **4-13** were synthesized by alkylating 2-mercaptoimidazole **3** with a corresponding bromoacetophenones in methanol at reflux, using sodium bicarbonate as a weak base. Similarly, compound **14** was yielded by performing an alkylation with 4-nitrochlorobenzene in dimethylformamide using potassium hydroxide as a strong base, as well as potassium carbonate. Ester **15** was obtained by alkylating 2-mercaptoimidazole **3** with methyl bromoacetate in ethanol in presence of potassium carbonate and in turn was hydrolyzed with a sodium hydroxide solution to obtain carboxylic acid **16**. Benzimidazoles **17**, **18** were prepared by condensing corresponding benzenediamines with an ester in presence of hydrochloric acid. The structure of the synthesized compounds was characterized by spectral data (IR, NMR spectra, and elemental analysis).



4 R = Ph; **5** R = 4-OHPh; **6** R= 4-ClPh; **7** R = 4-FPh; **8** R = 1-naphthyl; **9** R = 4-NO_2Ph; **10** R = 4-triFMePh; **11** R = 2,4-diFPh; **12** R = 4-CNPh; **13** R = 2,3,4-triMeOPh; **17** R_1 = Cl; **18** R_1 = F

Synthesized compounds were tested against H69, H69AR and A549 human lung carcinoma cells bearing promising results, especially compounds **8** and **10**.

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2. AL-BLEWI, Fawzia, SHAIKH, Salma Akram, NAQVI, Arshi, ALJOHANI, Faizah, AOUAD, Mohamed Reda, IHMAID, Saleh and REZKI, Nadjet. Design and Synthesis of Novel Imidazole Derivatives Possessing Triazole Pharmacophore with Potent Anticancer Activity, and In Silico ADMET with GSK-3β Molecular Docking Investigations. Online. 25 January 2021. MDPI AG.