ABSTRACT

This Ph.D. thesis comprises several chapters focused on the synthesis of various derivatives containing ketene dithioacetal, including thiazole, thiazole hydrazide, and thiophene derivatives, as well as the synthesis of Thiazolo[3,2-a]pyrimidine and its further cyclization to form pyrazolo[3,4-d]thiazolo[3,2-a]pyrimidine derivatives.

Chapter 1 describes the synthesis and characterization of a diverse range of thiazole derivatives containing ketene dithioacetal. The synthetic methodologies involve multistep reactions, leading to the formation of structurally diverse compounds. A series of novel ethyl (*E*)-2-cyano-3-((4-methyl-5-(arylcarbamoyl)thiazol-2-yl)amino)-3-(methylthio) acrylate have been synthesized starting from various 2-amino-*N*-aryl-4-methylthiazole-5-carboxamide. The significant features of this reaction procedure are novel, modest and short time. Synthesized molecules were evaluated *in vitro* for their α-amylase inhibitory activity and displayed moderate to excellent inhibition with IC_{50} values varying from 12.55 μg/mL to 69.47 μg/mL using acarbose as control. Moreover, a molecular docking study was carried out for synthesized molecules against human pancreatic α-amylase (2QV4) via utilizing the Autodock technique. The docking outcomes of some molecule showed very good cytotoxic activity.

Chapter 2 focuses on the cyclization of ketene dithioacetal to synthesize Thiazolo [3,2-a]pyrimidine, a heterocyclic framework with promising properties. The synthesis route is optimized to provide a concise and efficient method for accessing this valuable scaffold. A series of novel *N*-aryl-6-cyano-5-imino-3-methyl-7-(methylthio)-5*H*-thiazolo[3,2-*a*]pyrimidine-2-carboxamide has been synthesized starting from various 2-amino-*N*-aryl-4-methylthiazole-5-carboxamide. The important characteristics of this reaction technique are new, easy and less time-consuming. Molecules were assessed for cytotoxic activity against human breast carcinoma cell line (MCF-7), human lung adenocarcinoma cell line (A549) and human cervical cancer cell line (HeLa). Tested molecules showed moderate to excellent anticancer activity against various cell lines compared to doxorubicin. Moreover, a molecular docking study was carried out for synthesized molecules against topoisomerase-II via utilizing the Autodock technique. The docking outcomes of three molecule showed an excellent cytotoxic activity.

Chapter 3 specifically focuses on the synthesis and characterization of thiazole hydrazide derivatives containing ketene dithioacetal. A series of novel compounds are synthesized through efficient synthetic routes, utilizing ketene dithioacetal as a key building block. The synthesized derivatives are thoroughly characterized using spectroscopic techniques. Furthermore, the antibacterial properties of the thiazole hydrazide derivatives are evaluated against a panel of bacterial strains. The compounds exhibit significant antibacterial activity, demonstrating their potential as promising agents in combating bacterial infections. This research contributes to the development of novel derivatives containing ketene dithioacetal, expanding the scope of thiazole hydrazide derivatives, and providing valuable insights into their antibacterial properties. The findings of this study pave the way for further exploration of these compounds in the field of medicinal chemistry and antimicrobial drug discovery.

Chapter 4 of this thesis presents the synthesis and characterization of thiophene derivatives containing ketene dithioacetal. A series of novel compounds is synthesized using efficient synthetic methodologies, incorporating ketene dithioacetal. The synthesized thiophene derivatives are extensively characterized using spectroscopic techniques. Moreover, the antibacterial properties of the synthesized thiophene derivatives are evaluated against a range of bacterial strains. The compounds exhibit significant antibacterial activity, showcasing their potential as a possible effective agent in combating bacterial infections. This research contributes to the expanding knowledge of thiophene derivatives containing ketene dithioacetal, providing insights into their synthetic strategies and highlighting their promising antibacterial properties. The findings of this study pave the way for further exploration and application of these compounds in the field of medicinal chemistry and antimicrobial drug development.

Chapter 5 focuses on the synthesis of pyrazolo[3,4-*d*]thiazolo[3,2-*a*]pyrimidine derivatives from thiazolo[3,2-*a*]pyrimidine. The synthesis of pyrazolo[3,4-*d*]thiazolo[3,2-*a*]pyrimidine compounds is relatively rare in the literature, making this research particularly significant. A novel synthetic approach is developed to efficiently cyclize thiazolo[3,2-*a*]pyrimidine compounds and transform them into pyrazolo[3,4-*d*]thiazolo[3,2-*a*]pyrimidine derivatives. The synthesis involves specific reaction conditions and appropriate functional group modifications to achieve the desired cyclization process. The synthesized pyrazolo[3,4-*d*]thiazolo[3,2-*a*]pyrimidine derivatives are characterized using various spectroscopic techniques to confirm their

structures and purity. The importance of this synthesis lies in the limited reported examples of these compounds, thereby expanding the knowledge and potential applications of this class of molecules. The findings of this study contribute to the synthetic methodologies for pyrazolo[3,4-*d*]thiazolo[3,2-*a*]pyrimidine derivatives and offer new possibilities for their utilization in various fields, including medicinal chemistry, materials science, and drug discovery.