RESEARCH ARTICLE

Synthesis of New Benzimidazole Derivatives Containing Azoles Ring Moiety and Study their Biological Activity

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ABSTRACT

This study provides a new library of benzimidazole derivatives containing azole ring moiety was synthesized *via* 1,3-dipolar cycloaddition. The obtained compounds were characterized by FT-infrared, ^{1}H- and ^{13}C- NMR spectroscopy. The biological activity was tested for most of the synthesized compounds against four types of bacteria two of them are gram-ve [*Escherichia coli* (*E. coli*) and *Pseudomonas aeruginosa* (*P. aeruginosa*)] and two gram+ve [*Bacillus subtilis* (*B. subtilis*) and *Staphylococcus aureus* (*S. aureus*)]. Indeed, the synthesized compounds show a good to moderate effect on both types of bacteria.

Keywords: Benzimidazole, 1,3-dipole cycloaddition, Antibacterial, Isoxazolidine.

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INTRODUCTION

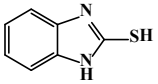
Out of many heterocyclic compounds, benzimidazole is widely used in synthetic organic chemistry. These structures are crucial due to the wide existence in medicinal compounds.[1] It is a heterocyclic compound that exists in nature as an core structure of cyanocobalamin and has been incorporated into pharmaceutical agents to form enzyme inhibitors and DNA intercalators.[2] Benzimidazole is a versatile core ring producing a diverse range of pharmaceutical uses such as anti-inflammatory and analgesic,[3]2,4-triazolo[2,3-a] benzimidazoles were synthesized through the reaction of 1,2-diaminobenzimidazole with carbon disulfide. The resulting 1,2,4-triazolo[2,3-a]benzimidazole-2-thione intermediate reacted with one equivalent of the alkyl halide to give the corresponding 2-alkylthio derivative 3a-g. The latters were acylated to afford the 1-acyl-2-alkylthio-1,2,4-triazolo[2,3-a]-benzimidazole derivatives 4–10 in good yields. Structures of the new compounds were verified on the basis of spectral and elemental methods of analyses. Fourteen of the prepared compounds were tested for their possible antifungal activities. Most of the tested compounds showed activity against Candida albicans and Fusarium oxysporum comparable to that of fluconazole as a reference drug. Compounds 8a, 9a, and 10d are the most active ones against most of the fungi used. Compounds 3e, 4d, 5d, 6d, 7d, 8c, 8d, 9d, and 10d were tested for their anti-inflammatory and analgesic effects; most of these compounds showed potent and significant results compared to indomethacin. Moreover, ulcerogenicity and the median lethal dose (LD50 anti-Tubercular,[4] antifungal,[5] antimicrobial,[6] anthelmintic,[7]and anticancer.[8]

Azoles are a pentatomic heterocyclic which play a crucial role in organic chemistry as constituents of biologically interesting compounds and as valuable intermediates in many synthetic processes. Such heterocyclic rings can be obtained via the 1,3-dipolar cycloaddition, which provides quick access to a huge number of natural compounds. This strategy has been used to generate an isoxazolidine ring that might not be made by classical chemistry. The isoxazolidine moiety rarely exists in the natural compounds but still represents a valuable intermediate in synthesis.[9] Compounds containing isoxazolidine ring possess crucial and interesting pharmacological effects such as antioxidant,[10] antibacterial,[11] antiviral,[12] antifungal,[13] and antiretroviral activities.[14]

MATERIALS AND METHODS

Stuart SMP3 electronic apparatus was used for melting points, FT-IR spectrums were taken using Shimadzu FT-IR spectrophotometer, ^{1}H and ^{13}C –NMR spectrums have obtained from (Brucker 400 MHz) spectrometer, (DMSO) was used as a solvent. The completion of the reaction was followed using TLC silica gel plates and the visualization using $KMnO_4$ dip and UV light.

Synthesis of 2-mercapto benzimidazole[15]



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