Development of Substituted Diazoles with Potential Pharmacological Activities

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***Abstract*—Diazole derivatives are an important class of heterocyclic compounds known for their wide-ranging pharmacological properties, including antimicrobial, anticancer, anti-inflammatory, and enzyme inhibitory activities. In this study, a series of substituted diazoles were designed and synthesized using efficient synthetic methodologies to introduce structural diversity. The structures of the synthesized compounds were confirmed through spectroscopic techniques such as NMR, IR, and mass spectrometry. Preliminary biological evaluations were performed to assess their pharmacological potential, including antimicrobial screening and cytotoxicity assays. Several derivatives demonstrated significant biological activity, and structure–activity relationship (SAR) analysis suggested that the type and position of substituents critically influenced bioactivity. These findings highlight substituted diazoles as promising scaffolds for further drug development and provide valuable insights into the relationship between molecular structure and pharmacological efficacy.**

***Index Terms*—Substituted Diazoles, Heterocyclic Compounds, Chemical Synthesis, Biological Evaluation, Pharmacological Activity**

I. INTRODUCTION

The ring of diazole and imidazole is the most prevalent heterocycle in medicinal chemistry, and it has the most variety of biological activity. Antimicrobial [1,2], antiulcer [3], anthelmintic [4], anticancer [5-7], anti-inflammatory [8], anti-tubercular [9–11], antimalarial [12], antihistaminic [13], and antioxidant [14] properties were demonstrated for the substituted benzimidazoles. A review of the literature revealed that one of the primary pharmacophores for anti-tubercular action is the benzimidazole ring [9–11]. The most prevalent infectious disease in the world, tuberculosis (TB), is brought on by the Mycobacterium tuberculosis bacteria and is a major global health concern. A third of the world's population is infected with Mycobacterium tuberculosis, according to recent epidemiological data. Infection with this bacillus is directly responsible for three million deaths and eight million illnesses annually (WHO, 2002) [15]. Resistance to existing anti-tuberculosis medicines is another significant problem. The situation has gotten considerably worse with the rise of multidrug-resistant tuberculosis (MDR-TB). Up to 4% of all TB patients worldwide are resistant to multiple anti-tubercular therapies due to inadequate or partial treatment resistance [16–20].

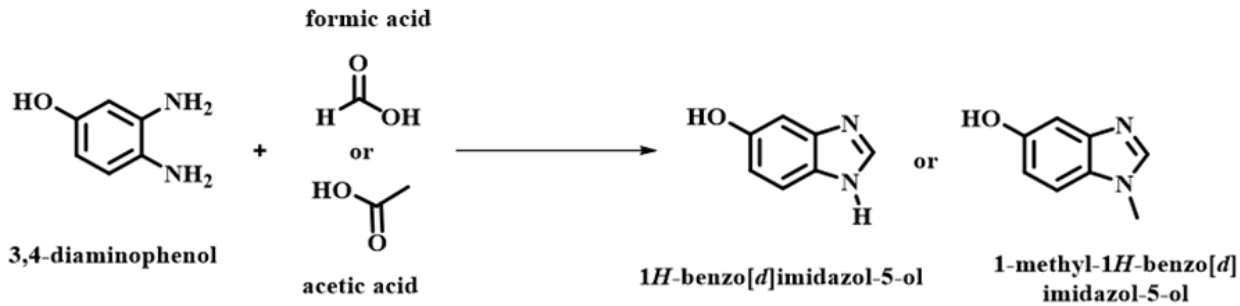
II. MATERIAL AND METHODS

All chemicals used in the experiments were of analytical reagent (AR) grade. Analytical thin-layer chromatography (TLC) was carried out on Merck pre-coated silica gel 60 F254 aluminium sheets. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded in $CDCl_3$ on a 500 MHz spectrometer with tetramethylsilane (TMS) serving as the internal standard.

III. CHARACTERIZATION TECHNIQUES

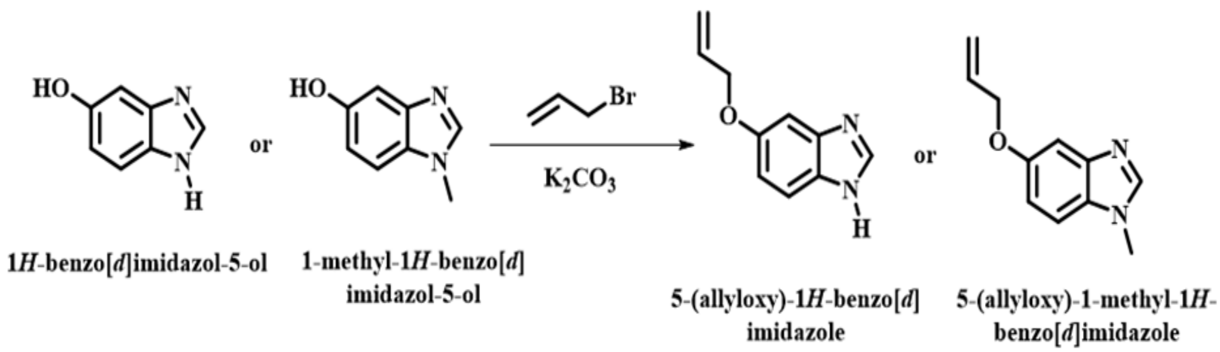
The structure of synthesized compounds was determined by chemical properties elemental analysis and spectral data. ^{1}H-NMR spectra were recorded on Bruker Avance Neo 500 MHz spectrometer using $CDCl_3$ solvent and TMS as internal standards at SAIF, Punjab University, Chandigarh (India). Chemical shifts are expressed in ppm. Mass spectrums were recorded on Thermo Scientific TSQ 8000 Gas Chromatogram.

General Reaction for Synthesis of substituted diazoles
Well-proportioned reaction mixture of substituted diamineacetophenone and formic acid or acetic acid with resin-based catalyst at suitable temperature for suitable time. The reaction will be monitored by TLC. After reaction is completed, it is poured in cold water and product will be crystallized by column chromatography with ethyl acetate and ethanol
.



Scheme 1. Synthesis of substituted diazoles

General Reaction for Synthesis of substituted 5-(allyloxy)-1H-benzo[d]imidazole
Well-proportioned reaction mixture of substituted diazole and Allyl bromide in presence of catalyst and in solvent at suitable temperature for suitable time will be refluxed. The reaction is monitored by TLC. The product is recrystalised by column chromatography.



Scheme 2. Synthesis of substituted 5-(allyloxy)-1H-benzo[d]imidazole

Table 1. Scope of Synthesis of substituted diazoles

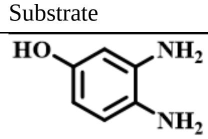
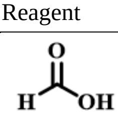
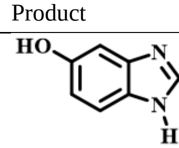
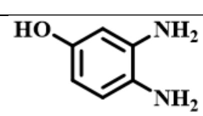
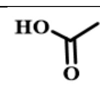
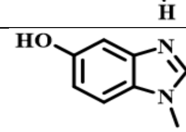
Sr.No	Substrate	Reagent	Product	Time in Hrs.	Yield
1				7	78
2				7	83

Table 2. Scope of Synthesis of substituted 5-(allyloxy)-1H-benzo[d]imidazole

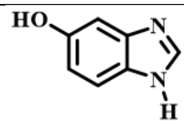
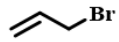
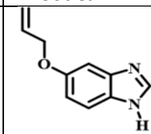
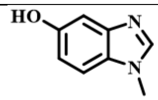
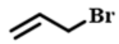
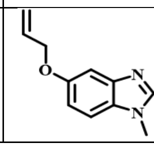
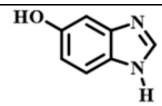
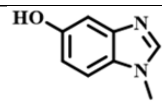
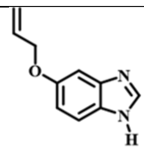
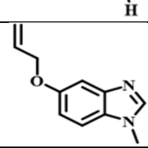
Sr. No	Substrate	Reagent	Product	Time in Hrs.	Yield
1				7	78
2				7	83

Table 3. Structural Analysis

Sr. No	Structure of Products	Structural analysis by ^{1}HNMR and GCMS
1		^{1}HNMR (500MHz, $CDCl_3$):δ 12.30 (s,1H), 9.20 (s,1H), 8.19 (s,1H), 7.39-6.99 (m, 3H) GCMS: Cal m/z:134.14, Found m/z: 134.10
2		^{1}HNMR (500MHz, $CDCl_3$):δ):δ 9.18 (s,1H), 8.11 (s,1H), 7.31-6.91 (m, 3H),3.71 (s,3H) GCMS: Cal m/z: 148.16 Found m/z:148.11
3		^{1}HNMR (500MHz, $CDCl_3$):δ 12.36 (s,1H), 8.14 (s,1H), 7.38-6.96 (m, 3H), 6.0 (m,1H), 5.43-5.30 (m,2H), 4.6 (d,2H) GCMS: Cal m/z:174.20, Found m/z: 174.15
4		^{1}HNMR (500MHz, $CDCl_3$):8.10 (s,1H), 7.32-6.90 (m, 3H), 5.8 (m,1H), 5.40-5.28 (m,2H), 4.6 (d,2H), 3.69 (s,3H) GCMS: Cal m/z: 188.23 Found m/z: 188.20

IVCONCLUSION

In present work, synthesized the series of substituted diazole's structure and 5-(allyloxy)-1H-benzo[d]imidazole is promising moiety that are able to shows the strong biological activity. Furthermore, the benzo ring inflection of the structure intentionally incorporation of hydroxyl (-OH) group over the ring. Which shows the promising and the strong biological activities. As a conclusion, our results revels and participate significantly to create a structural moiety and interactive relationship shows strong activity against microbes. Which is useful in drug design strategy in future. Conflict of Interest: Authors have declared that no competing interests exist.

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