

Allylation of Substituted Diazoles: Synthesis and Biological Evaluation of Allyl-Functionalized Diazole Derivatives

Jaydeep V. Rathod

Research centre, Department of Chemistry G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati

M.M. Kodape

Department of Chemistry, Sant, Gadge Baba Amravati University, Amravati

A. B. Gajbhiye

Research centre, Department of Chemistry G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati

N.D. Gawhale

Department of Chemistry, G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati

Abstract

By allylating substituted diazoles, a practical synthetic method for the synthesis of allyl-functionalized diazole derivatives was synthesized. The purpose of the study was to examine the addition of an allyl group to the diazole framework and the impact of structural alteration on the biological characteristics of the resultant derivatives. Under appropriate reaction conditions, a number of substituted diazole compounds were allylated to produce the corresponding allyl-functionalized derivatives in acceptable yields. The synthesized compounds were analyzed using ¹H NMR spectroscopy and gas chromatography mass spectrometry (GC-MS), which verified the synthesis of the desired products and supported the proposed molecular structures. The biological activity of the produced compounds against particular bacteria strains was then assessed. The results of the biological screening showed that the synthetic compounds' antibacterial activity varied depending on the kind and location of substituents on the diazole nucleus. The current study shows that allylation offers a straightforward path toward novel allyl-functionalized diazole derivatives with possible biological importance as well as a helpful structural modification of substituted diazoles.

Keywords: Allylation; Substituted Diazoles; Allyl-Functionalized Diazoles; Heterocyclic Synthesis; ¹H NMR; GC-MS; Biological Evaluation; Antimicrobial Activity.

Introduction

In the 1840s, imidazole-based compounds have been the subject of much research and development due to their numerous applications, including medicinal medicines, agrochemicals, ligands, synthetic acceptors, catalysts, and more. [1-4]. Imidazole-based molecules hold a unique position in the pharmaceutical industry [5]. Numerous imidazole derivatives, including 1) 1H-imidazole, 2) (z)-N-(cyclohexa-2,4 dieny)-N-methylformamidine, 3) 4,5-dihydro-1H imidazole, 4) 2,5-dihydro-1H imidazole, 5) 2,3-dihydro 1H-imidazole, and 6). Researchers are utilizing new imidazole derivatives with medical applications.

Because of its unique structural characteristics, the imidazole ring can interact with a variety of biotic enzymes and receptors via ion-dipole, hydrogen bonds, π - π stacking, coordination, cation- π , van der Waals forces, and more [8-10]. The imidazole ring found in many essential biological components, including deoxyribonucleic acid (DNA), histamine, vitamin B12, and hemoglobin, is responsible for the different biological functions of imidazole derivatives [11-13].

Synthesizing the derivatives of substituted *o*-allyl of substituted diazoles is the next step. The synthesis of *o*-allyl of substituted diazoles and a knowledge of substituted molecules with interesting antimicrobial properties are the goals of this study. It might result in the synthesis of novel therapeutic approaches in the future.

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 (¹H NMR) spectra were recorded in CDCl₃ on a 500 MHz spectrometer with tetramethylsilane (TMS) serving as the internal standard.

Characterization Techniques

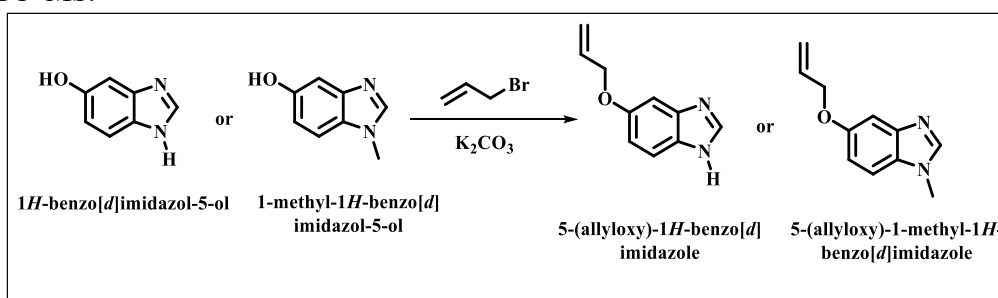
The structure of synthesized compounds was determined by chemical properties elemental analysis and spectral data. ¹H-NMR spectra were recorded on Bruker Avance Neo 500 MHz spectrometer using CDCl₃ solvent and TMS as internal standards at SAIF, Punjab University,

Chandigarh (India). Chemical shifts are expressed in ppm. Mass spectrums were recorded on Thermo Scientific TSQ 8000 Gas Chromatogram.

Experimental

General Reaction for Synthesis of substituted *O*-Allyl of Substituted Diazoles

N-Allylimidazole can be synthesized by the N-allylation of imidazole using allyl bromide in the presence of a suitable base. In a typical procedure, imidazole is dissolved or suspended in a suitable solvent acetonitrile followed by the addition of potassium carbonate as a base. Allyl bromide is then added gradually to the reaction mixture, which is stirred at room temperature for 7h under mild heating until completion of the reaction. The reaction proceeds through deprotonation of the imidazole N-H group followed by an SN2 reaction with allyl bromide to afford N-allylimidazole [14]. The progress of the reaction can be monitored by TLC. After completion, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is separated, washed with water or brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product is purified by column chromatography when necessary, and the purified N-allylimidazole is characterized by ¹H NMR spectroscopy and GC-MS.



Scheme 1. Synthesis *O*-Allyl of Substituted Diazoles

Table 1. Scope of Synthesis of substituted *O*-Allyl of Substituted Diazoles

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

**Table 2. Structural Analysis
Biological Activity**

Sr. No	Structure of Products	Structural analysis by ¹ HNMR and GCMS
1		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
2		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

Antimicrobial Properties

The synthesized *O*-allyl substituted diazole derivatives were evaluated for their antimicrobial properties against selected Gram-positive and Gram-negative bacterial strains and fungal strains

using an appropriate in vitro antimicrobial assay. The compounds were tested at selected concentrations, and their antimicrobial activity was assessed by measuring the zone of inhibition around the respective samples. A standard antimicrobial agent was used as a reference for comparison, while the solvent was employed as a negative control. The synthesized *O*-allyl diazole derivatives exhibited varying degrees of antimicrobial activity against the tested microorganisms [15]. The observed differences in activity may be associated with the nature and position of substituents present on the diazole framework and the incorporation of the allyloxy functionality. The results indicate that structural modification through *O*-allylation can influence the antimicrobial properties of substituted diazole derivatives.

Compound	Microorganism	Concentration (µg/mL)	Zone of inhibition (mm)	Activity
1. 5-(allyloxy)-1H-benzo[d]imidazole	<i>Staphylococcus aureus</i>	100	18	Good
2. 5-(allyloxy)-1-methyl-1H-benzo[d]imidazole	<i>Escherichia coli</i>	100	14	Moderate

Conclusion

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 allyl group over the ring. Which shows the promising and the strong anti-microbial activities. As a conclusion, our results revels and participate significantly to synthesis a structural moiety and interactive relationship show 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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