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Research Article

SILICA SULFURIC ACID CATALYZED MICROWAVE-ASSISTED SYNTHESIS OF SUBSTITUTED BENZOXAZOLES AND THEIR ANTIMICROBIAL ACTIVITY

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ABSTRACT
Substituted Benzoxazoles were synthesized by using microwave assisted treatment of orthoesters with o-aminophenols in presence of silica sulfuric acid to get the target compound. The structure of the synthesized compounds was characterized by ^{1}H and Mass spectral analysis. All the synthesized compounds were screened for their antibacterial and antifungal activities.
KEYWORDS: Benzoxazoles, Microwave assisted synthesis, Orthoesters, Silica sulfuric acid, Antibacterial and antifungal activities.

INTRODUCTION

Benzoxazole moiety has attracted special attention in chemistry[1] and biochemistry[2-4]. Extensive literature survey has been carried out on this heterocyclic moiety which exhibited various pharmaceutical properties such as antiviral[5], antibiotic[6], antimicrobial[7], anticancer[8], antitumor[9] and anti-inflammatory[10] activities. Interestingly Mohammadpoor-Baltork *et al*[11] had reported synthesis of substituted Benzoxazoles under conventional method. By keeping these observations in mind, in this current paper we report the synthesis of substituted Benzoxazoles by using non-conventional method and carried out antimicrobial studies for the synthesized compounds.

MATERIALS AND METHODS

Microwave oven (LG Smart Chef MS-255R operating at 2450 MHz having maximum output power of 960 W) was used for microwave irradiation. ^{1}H NMR spectra were recorded on Brucker at 500 MHz in $CDCl_3$ as a solvent and TMS as an internal standard. FTIR spectra were recorded on a Avatar 330 FTIR using KBr discs. Mass spectra were recorded on JEOL-GC Mate using electron Ionization technique.

Synthesis of substituted Benzoxazoles

A mixture of trialkyl orthoester (1.1 mmol), *o*-aminophenol, (1 mmol) and silica sulfuric acid (50 mg) were taken in a beaker (50mL). The reaction mixture was mixed properly with the help of glass rod and irradiated in a microwave oven at 45W, for 1-3min. The time taken for the completion reaction is indicated in Table-1. The progress of the reaction was monitored by TLC (ethyl acetate: hexane, 7:3). After completion of the reaction, the reaction mixture was cooled and dichloromethane (25mL) was added. The catalyst was filtered from the reaction mixture, it was then washed with water and dried over anhydrous $CaCl_2$. The filtrate was concentrated under vacuum to obtain the product **3(a-f)**.

Antimicrobial activity

The isolated components were screened for their Antimicrobial activity by using standard protocol, *Staphylococcus aureus, E.Coli, Candida albicans and Candida glabrata* were used for this antimicrobial activity determination. The test material (10mg) was dissolved in DMSO (Dimethyl Sulfoxide) to prepare a stock solution of 1000 mcg/ml from which concentrations of 25,50,100 and 200 mcg/ml were prepared for the determination of minimum inhibitory concentration (MIC). The standard control comprises of the medium, organism culture and dilution of similar order of standard drug.

Antibacterial Testing

For antibacterial testing the tube dilution technique was used. Muller Hinton Broth (pH-7.4) was used as a culture medium. This was sterilized and suspended in series of borosilicates test tubes. The test solution was then added, so as to attain a final concentration of 200, 100, 50 and 25 mcg/ml. Then 0.1ml of test organism strain 10^6 cfu/ml was added. These tubes were incubated at 37^0C for 48hrs and then examined, for the presence (or) absence of

growth of microorganisms. For Comparison, Trimethoprim (MIC – 1mcg/ml) was used as a standard drug.

Antifungal Testing

For antifungal testing, Saboraud Dextrose Agar medium (pH-6.0) was employed for growth. The sterile medium was dispensed in a series of borosilicates test tubes. This was sterilized and suspended in series of borosilicates test tubes. The test solution was then added, so as to attain a final concentration of 200, 100, 50 and 25 mcg/ml. Then 0.1ml of test organism strain was added. These tubes were incubated at 28-30^{0}c in a dark place. Visual examination was carried out for determining the presence (or) absence of growth of microorganisms. For Comparison, Miconazole (MIC – 6.25mcg/ml) was used as a standard drug.

Spectral Data

3a: Molecular Formula: $C_9H_9NO_2$ Molecular Weight: 163.06.^{1}H-NMR ($CDCl_3$) ppm): 7.26 (d, -2H, Ar-H); 7.21 (d, -2H, Ar-H); 2.59 (q, -CH_2, -2H); 1.32 (t, -CH_3, -3H). HRMS (EI; m/z): 163.2819.

3b: Molecular Formula: $C_{10}H_{11}NO_2$ Molecular Weight: 177.08.^{1}H-NMR ($CDCl_3$) ppm): 7.25 (s, -2H, Ar-H); 7.22 (d, -1H, Ar-H); 2.57 (q, -CH_2, -2H); 2.36 (d, -3H, -CH_3); 1.34 (t, -CH_3, -3H). HRMS (EI; m/z): 177.0000.

3c: Molecular Formula: $C_9H_8ClNO_2$ Molecular Weight: 197.026.^{1}H-NMR ($CDCl_3$) ppm): 7.20 (d, -2H, Ar-H); 7.22 (1, -2H, Ar-H); 2.56 (q, -CH_2, -2H); 1.33 (t, -CH_3, -3H). HRMS (EI; m/z): 197.1709.

3d: Molecular Formula: $C_8H_7NO_2$ Molecular Weight: 149.05.^{1}H-NMR ($CDCl_3$) ppm): 7.24 (d, -2H, Ar-H); 7.22 (d, -2H, Ar-H); 2.56 (q, -CH_3, -3H). HRMS (EI; m/z): 149.1678.

3e: Molecular Formula: $C_9H_9NO_2$ Molecular Weight: 163.06.^{1}H-NMR ($CDCl_3$) ppm): 7.26 (s, -2H, Ar-H); 7.21 (d, -1H, Ar-H); 2.57 (q, -CH_3, -3H); 2.36 (d, -3H, -CH_3). HRMS (EI; m/z): 163.0236.

3f: Molecular Formula: $C_8H_6ClNO_2$ Molecular Weight: 183.01.^{1}H-NMR ($CDCl_3$) ppm): 7.22 (d, -2H, Ar-H); 7.22 (d, -1H, Ar-H); 2.56 (q, -CH_3, -3H). HRMS (EI; m/z): 183.0921.

RESULTS AND DISCUSSION

All the compounds were successfully synthesized in good yields. The synthesized compounds were characterized by ^{1}H NMR and Mass spectral analysis. All the synthesized compounds had shown potent antibacterial and antifungal activities. In all the synthesized compounds, the ethoxy and methoxy group attached to Benzoxazoles ring will act as a pharmacophores based on the SAR studies.

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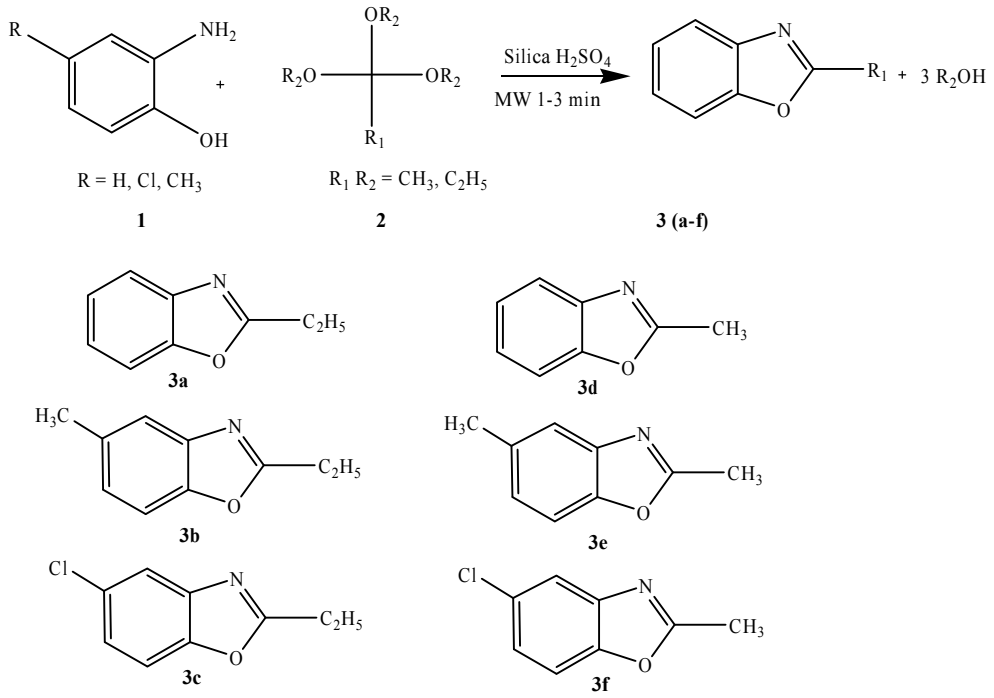
Table: 1 Physical data of the synthesized compounds [3(a-f)]

Synthesized compounds	Melting point (^{0}C)	% Yield	Microwave Time (min)
2-ethoxybenzo[d] oxazole	Colourless oil	97	2-3
2-ethoxy-5-methylbenzo[d] oxazole	58-60	95	1.5
2-ethoxy-5-chloro-benzo[d] oxazole	28-30	98	3
2-methoxybenzo[d] oxazole	Colourless oil	97	2
2-methoxy-5-methyl-benzo[d] oxazole	Colourless oil	98	2.5
2-methyoxy-5-chlorobenzo[d] oxazole	57-59	95	3

Table: 2 Antimicrobial activity of the synthesized compounds [3(a-f)]

Synthesized Compounds	Microorganisms			
	Zone of Inhibition (mm)			
	S.aureus	*E.Coli*	*C.albicans*	*C.glabrata*
2-ethoxybenzo[d] oxazole	18	15	14	16
2-ethoxy-5-methylbenzo[d] oxazole	16	17	14	15
2-ethoxy-5-chloro-benzo[d] oxazole	17	14	19	18
2-methoxybenzo[d] oxazole	16	15	18	20
2-methoxy-5-methyl-benzo[d] oxazole	15	17	17	19
2-methyoxy-5-chlorobenzo[d] oxazole	18	16	19	16
Trimethoprim (Standard)	25	23	-	-
Miconazole (Standard)	-	-	26	15



REACTION SCHEME 1

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