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Synthesis and Antimicrobial Evaluation of Some New Benzimidazolechalcones under Microwave Irradiation Method

Balasaheb B. Musle [1] and Subhash M. Lonkar [*]
[1]Shri Guru Buddhiswami Mahavidhyalaya, Purna (Jn.), Dist: Parbhani. M.S. (India)
[*] P.G.Research Center, Department of Chemistry, Shri Shivaji College, Parbhani. M.S. (India)
Email: *balasahebmusle@gmail.com*

Abstract

A simple and convenient route is described for the synthesis of a series of benzimidazolechalcones **(3a-3i)** from benzimidazole-2-carbaldehyde and substituted acetophenones by using microwave irradiation method. Chalcones had been synthesizing by conventional way of heating which were taking a long time. To improve the yield and to minimize the reaction time, Benzimidazolechalcones were synthesized by Microwave irradiation method (MWI) and elucidated on the basis of spectral analysis such as IR, ^{1}HNMR, and Mass spectroscopy. Synthesized chalcones were shown the moderate to good antibacterial and antifungal activity against all used strains.

KEYWORDS: Benzimidazole-2-carbaldehyde,Substitutedacetophenones,MWI, Benzimidazolechalcones, Antimicrobial activity.

Introduction

There is growing interest in the pharmacological potential of natural products. Chalcones (1,3-diaryl-2-propen-1-ones) constitute an important class of natural products belonging to the flavonoid family having a wide spectrum of biological activities. Chemically, they consist of open chain flavanoids in which the two aromatic rings are joined by a three carbon α,β- unsaturated carbonyl system. The presence of a reactive α, β unsaturated keto function in chalcones is found to be responsible for their antimicrobial activity [1]. Chalcones show antibacterial, antifungal, antitumor and anti-inflammatory properties. They are also intermediates in the biosynthesis of flavonoids, which are substances wide spread in plants and with an array of biological activities [2].

Heterocyclic compounds containing nitrogen have been described for their biological activity against various microorganisms. The indole unit is the key building block for a variety of compounds, which have crucial roles in the functions of biologically important molecules [3,4]. Chalcones present great interest as compounds exhibiting antimalarial, antifibrogenic, anticancer, antitrichomonal, antileishmanial and cytotoxic activities.

The flavonoid compounds are a group of natural products found in fruits, vegetables, nuts, seeds and flowers as well as in teas and are important constituent of human diet. They have been demonstrated to possess antioxidant, antihypertensive, anti-allergic, antinocicepative, trypsin inhibitors, plant growth regulator [5,6,7].

The usage of microwave energy to accelerate organic reactions is of increasing interest and offers several advantages over conventional techniques [8,9]. In the earlier part of our research work we reported synthesis of substituted 2-hydroxyaryl aldehydes by the microwave-induced Reimer-Tiemann reaction [10].Synthesis of molecules, which normally require a long time, can be achieved

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conventionally and rapidly in a microwave oven. An attempt was made to synthesize coumarinyl chalcones both by conventional and microwave method [11,12]. In one half of the century microwave energy had been used for the heating of food material. (Rajendra S. Verma) but now the application of microwave energy has been utilized in organic synthesis [13]. In 1855, Robert Bunsen invented the burner which acts as energy source for heating a reaction vessel and synthesis of organic compound by heating on burner was become a traditional method [14]. Therefore we thought worthwhile to synthesize some new chalcones which may shows higher antimicrobial activity.

Experimental

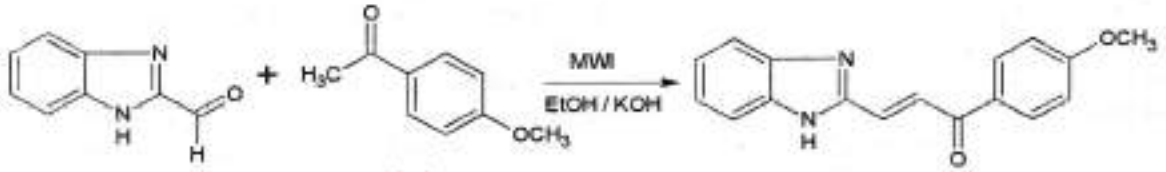
The melting points were recorded in open capillary and were uncorrected. IR spectra were recorded using Perkin-Elmer FTIR-RX1 spectrophotometer. ^{1}HNMR spectrum was recorded using $CDCl_3$ on Bruker Advance (400 MHz) and their chemical shifts are recorded in δ (parts per million) units with respect to tetramethyl silane (TMS) as internal standard. Mass spectra were recorded on a Waters Q-T of micro MS. All the reagents and solvents used were of AR grade. Progress of the reactions was monitored using TLC, performed on silica gel, using ethyl acetate: benzene as the solvent system.

General procedure

An equimolar mixture of Benzimidazole 2-Carbaldehyde **(1a)** (1.46gm, 0.01 mol) and 4-Methoxy Acetophenone **(2a)** (1.50 ml, 0.01 mol) were dissolved in 25 ml of ethanol with stirred and aqueous solution of 20 ml 40 % potassium hydroxide were added dropwise. Resulting reaction mixture was irradiated in microwave for 5 to 10 min. with short interval of time for 30 sec. to avoid evaporation excess solvent. Reaction progress was monitored on TLC using benzene/ethyl acetate combination (1:1, V/V) as mobile Phase. On completion of reaction, the reaction mixture was poured on crushed ice cold water and acidified with HCl. The separated solid was filtered and recrystallized from absolute alcohol.

All the benzimidazolechalcones **(3b-3i)** were synthesized by same procedure.

Scheme:



(1a) (2a) (3a)

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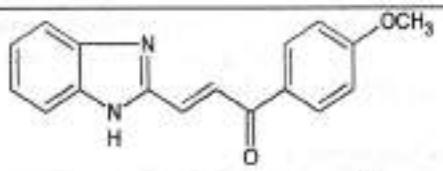
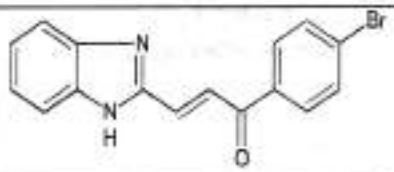
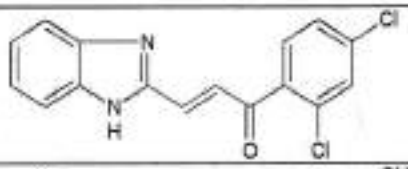
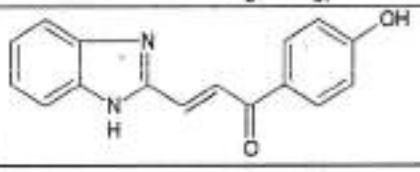
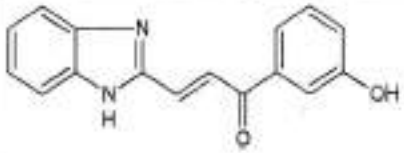
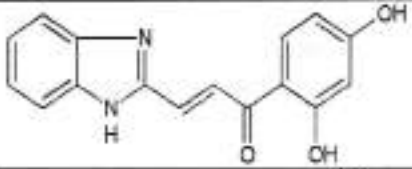
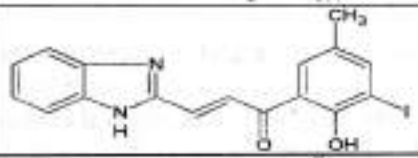
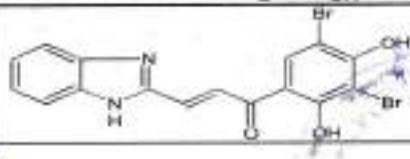
Table.1: Physical and analytical data of synthesized Benzimidazolechalcones:

Sr. No.	Synthesized Compounds	Reaction Time (in Minutes)	Yield (%)	Melting Point (°C)
3a		6.5	75	171
3b		7.0	78	183
3c		7.5	84	215
3d		7.5	76	140
3e		8.0	72	165
3f		8.0	76	155
3g		9.5	80	182
3h		9.5	78	194

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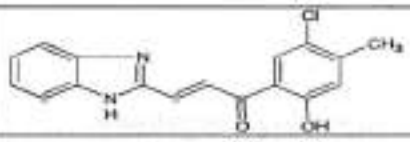
3i		8.5	84	147

Antimicrobial activity

The synthesized Benzimidazolechalcones were tested for their antibacterial and antifungal activity by measuring zone of inhibition on agar plates by disc diffusion method[15] with *E. coli* and *Aspergillus nigar*. All these compounds possess moderate to good activity against all stains used in comparison with Tetracycline and Griseofulvin which are listed in Table.2.

Table 2: Zone of Inhibition (mm) of Benzimidazolechalcones

Entry	Antibacterial *E.coli*	Antifungal Aspergillus *nigar*
3a	12	14
3b	11	13
3c	18	15
3d	14	12
3e	15	13
3f	19	17
3g	15	18
3h	17	15
3i	14	19
Control	00	00
Tetracycline	20	00
Griseofulvin	00	20

Result and discussion

In continuation of research work we report here a simple and efficient microwave assisted synthesis of benzimidazolechalcones in one step with high yield, simple procedure, no need of purification, save time as well as heat energy.They were fully characterized and evaluated for their antibacterial and antifungal activity. Benzimidazolechalcones are readily used synthons for preparation of different type of heterocyclic compounds like Pyrazole,Pyrimidins and Flavonones.Therefore it can be concluded that the benzimidazolechalcones will be great importance in medicinal chemistry as antibacterial and antifungal agents.

Spectral Analysis

3a) 3-(1H-benzimidazol-2-yl)-1-(4-methoxyphenyl)prop-2-en-1-one:

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IR (KBr): ν (cm^{-1}) 1663, 1580, 1530, 3285, 1019.
^{1}H-NMR δ= 7.78 (d, 1H), 7.86 (d, 1H), 7.62 (d, 1H, Ar-H), 7.58 (d, 1H, Ar-H), 6.65-7.12(m, 4H, Ar-H), 3.72 (s, -OCH_3), 12.38 (s, N-NH).
Mass (m/z): 278, 247, 118, 107, 54, 31.

3b) 3-(1*H*-benzimidazol-2-yl)-1-(4-bromophenyl)prop-2-en-1-one:
IR (KBr): ν (cm^{-1}) 1660, 1578, 1530, 3286.
^{1}H-NMR δ= 7.72 (d, 1H), 7.86 (d, 1H), 7.62 (d, 1H, Ar-H), 7.58 (d, 1H,Ar-H), 6.63-7.15 (m, 4H,Ar-H), 12.40 (s, N-NH).
Mass (m/z): 327, 248, 194, 79, 54.

3c) 3-(1*H*-benzimidazol-2-yl)-1-(2,4-dichlorophenyl)prop-2-en-1-one:
IR (KBr): ν (cm^{-1}) 1657, 1575, 1530, 3280.
^{1}H-NMR δ= 7.72(d, 1H), 7.86(d, 1H), 7.62-6.72 (dd, 1H,Ar-H), 7.58 (s, 1H,Ar-H), 6.86-7.12 (m, 4H,Ar-H), 12.49 (s, N-NH).
Mass (m/z): 317, 119, 84, 79, 54

3d) 3-(1*H*-benzimidazol-2-yl)-1-(4-hydroxyphenyl)prop-2-en-1-one:
IR (KBr): ν (cm^{-1}) 3350, 3285, 1658, 1580, 1530, 1022.
^{1}H-NMR δ= 7.92 (d, 1H), 7.81(d, 1H), 7.64 (d, 1H,Ar-H), 7.58(d, 1H,Ar-H), 6.65-7.22 (m, 4H,Ar-H), 4.57 (s,-OH), 12.43 (s, N-NH).
Mass (m/z): 264, 117, 93, 79, 54, 28

3e) 3-(1*H*-benzimidazol-2-yl)-1-(3-hydroxyphenyl)prop-2-en-1-one:
IR (KBr): ν (cm^{-1}) 3348, 3289, 1658, 1584, 1530, 1052.
^{1}H-NMR δ= 7.80 (d, 1H), 7.86 (d, 1H), 7.62 (d, 1H, Ar-H), 7.58 (d, 1H, Ar-H), 6.65-7.22 (m, 4H, Ar-H), 4.58 (s,-OH), 12.60 (s, N-NH).
Mass (m/z): 264, 117, 93, 79, 54, 28.

3f) 3-(1*H*-benzimidazol-2-yl)-1-(2,4-dihydroxyphenyl)prop-2-en-1-one:
IR (KBr): ν (cm^{-1}) 3340, 3285, 1650, 1580, 1530, 1022.
^{1}H-NMR δ=7.73(d, 1H), 7.86 (d, 1H), 7.62 (d, 1H,Ar-H), 7.54 (d, 1H,Ar-H), 6.67-7.20 (m, 4H,Ar-H), 4.55 (s,-OH), 12.48 (s, N-NH).
Mass (m/z): 280, 198, 97, 82,79, 54, 28.

3g) 3-(1*H*-benzimidazol-2-yl)-1-(2-hydroxy-3-iodo-5-methylphenyl)prop-2-en-1-one :
IR (KBr): ν (cm^{-1}) 3345, 3275, 1658, 1580, 1530, 1030,
^{1}H-NMR δ= 7.76 (d, 1H), 7.86(d, 1H), 7.62(d, 1H, Ar-H), 7.60(d, 1H, Ar-H), 6.65-7.22(m, 4H, Ar-H),4.52 (s,-OH), 12.40 (s, N-NH).
Mass (m/z): 404, 322, 243, 82, 79, 54, 28

3h) 3-(1*H*-benzimidazol-2-yl)-1-(3,5-dibromo-2,4-dihydroxyphenyl)prop-2-en-1-one:
IR (KBr): ν (cm^{-1}) 3349, 3285, 1658, 1582, 1530, 1025,
^{1}H-NMR δ= 7.80 (d, 1H), 7.86(d, 1H), 7.67(d, 1H, Ar-H), 7.58(d, 1H, Ar-H),7.52(s,1H,Ar-H), 6.65-7.22(m, 4H,Ar-H),4.52 (s,-OH), 12.40 (s, N-NH).
Mass (m/z):438, 359, 356, 82, 79, 54, 28

3i) 3-(1*H*-benzimidazol-2-yl)-1-(5-chloro-2-hydroxy-4-methylphenyl)prop-2-en-1-one:

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IR (KBr): ν (cm-^{1}) 3350, 3285, 1658, 1580, 1540, 1037.
^{1}H-NMR δ= 7.78(d, 1H), 7.86(d, 1H), 7.65(d, 1H,Ar-H), 7.58(d, 1H,Ar-H), 6.65-7.22(m, 4H,Ar-H),4.52 (s,-OH), 12.40 (s, N-NH).
Mass (m/z): 312, 233, 82, 79, 54, 28

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