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Research Article

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Synthesis, characterization and antimicrobial activity of N-substituted 2-substituted-benzimidazole derivatives

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ABSTRACT

A series of some novel benzimidazole was synthesized and evaluated for antimicrobial activity. The reaction of o-phenylenediamine with dicarboxylic acid(malonic acid, succinic acid, salicylic acid, phthalic acid) yield 2-substituted-benzimidazoles.The title compounds were synthesized by treating 2-substituted-benzimidazole with benzoyl chloride and sodium hydride.Their structures were confirmed by IR,^{1}H-NMR and ^{13}C-NMR Antimicrobial activity against Pseudomonas aeruginosa was studied for the synthesized compounds.

Keywords: Benzimidazole, o-phenylenediamine,benzoyl chloride

INTRODUCTION

Benzimidazole is a heterocyclic compound consisting of benzene ring fused with imidazole ring. The chemistry and pharmacology of benzimidazoles have been of great interest to medicinal chemistry[1], because its derivatives possessed various biological activites[2] such as anticancer[3-5], antihypertensive[6], antimicrobial[7-9], Moreover benzimidazoles[10] are important intermediates in organic reaction.

The title compounds were synthesized by treating 2-substituted-benzimidazole with benzoyl chloride and sodium hydride. Their structures were confirmed by IR,^{1}H-NMR and ^{13}C-NMR,Antimicrobial activity against *Pseudomonas aeruginosa*[11] was studied for the synthesized compounds.

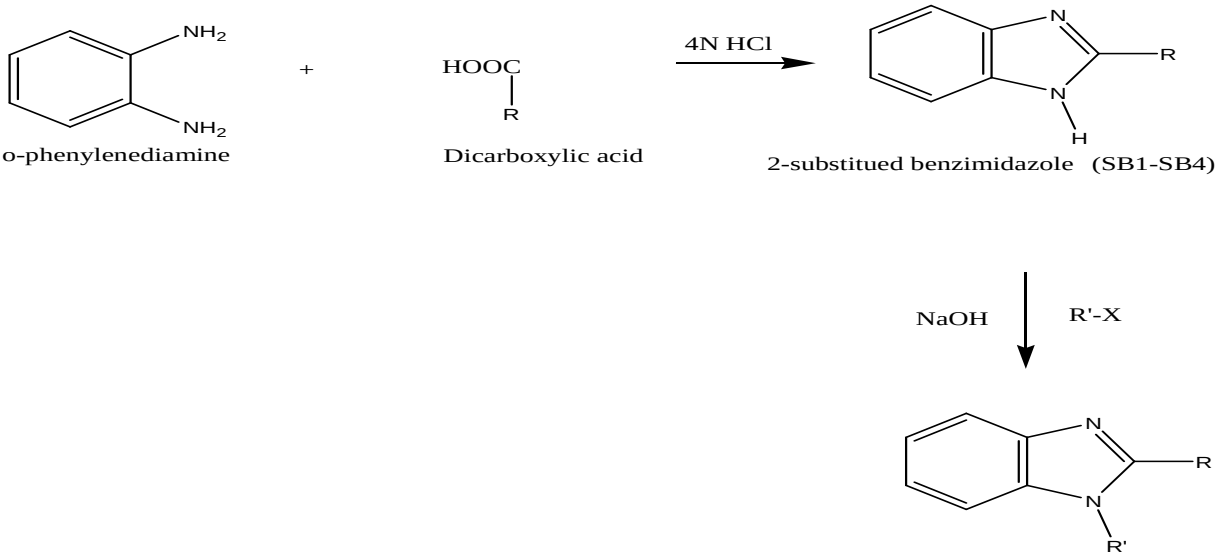
EXPERIMENTAL SECTION

All melting points were taken in open capillaries and are uncorrected.IR spectra were recorded in KBr on Shimadzu spectrometer. ^{1}H-NMR and ^{13}C-NMR in DMSO-d6 on Bruker AC-400 spectrometer using MeOD as an internal standard. The microorganisms were obtained from National Chemical Laboratory, Pune.

Preparation of 2-substituted-benzimidazole (SB1-SB4)

Procedure: o-phenylenediamine (4.0 g) was condensed with carboxylic acids(malonic acid, succinic acid, salicylic acid, phthalic acid) in 50ml of 4N HCl. The reaction mixture was stirred for about 4hours with magnetic stirrer at 80°C. The product were precipitated by adding concentrated ammonia solution, filtered through suction and washed with cold water. The Synthesized compounds were recrystallized from water and ethanol.

Scheme I



COMPOUNDS	R	R'
SB1	$-CH_2COOH$	-
SB2	$-CH_2CH_2COOH$	-
SB3	$-C_6H_5-OH$	-
SB4	$-C_6H_5-COOH$	-
BB1	$-CH_2COOH$	$-COC_6H_5$
BB2	$-CH_2COOH$	$-COCH_3$
BB3	$-CH_2CH_2COOH$	$-C0C_6H_5$
BB4	$-CH_2CH_2COOH$	$-COCH_3$
BB5	$-C_6H_5-OH$	$-COC_6H_5$
BB6	$-C_6H_5-OH$	$-COCH_3$
BB7	$-C_6H_5COOH$	$-COC_6H_5$

Preparation of 1-benzyl 2-substituted-benzimidazole (BB1-BB8)

Procedure: 2-substituted-benzimidazole (0.02 mol) was treated with benzoyl chloride (2.5 mol g) in the presence of a little quantity of sodium hydride (2.0 mol g). The reaction mixture was stirred for 8-12 hours at 40°C. Excess solvent was removed by distillation and crude product was washed with water, extracted with ethyl acetate and finally recrystallized from water and ethanol.

Table 1 Analytical data of 2-substituted-benzimidazole

compounds	Yield(%)	Molecular formula	M.wt
SB1	61	$C_9H_8N_2O_2$	176
SB2	68	$C_{10}H_{10}N_2O_2$	190
SB3	74	$C_{13}H_{11}N_2O$	211
SB4	79	$C_{14}H_{11}N_2O_2$	239

IR SPECTRAL ANALYSIS

Spectral data for the compounds (SB1-SB4)

SB1: (1H-benzoimidazol-2-yl)-acetic acid: IR(cm^{-1}) : 2958(C=C-H str), 1671(C=Cstr), 3192(O-Hstr), 3443(N-Hstr), ^{1}H NMR : δ7.2(aromatic proton), 4.9(C-NH)proton. ^{13}C NMR : δ 178.34(COOH), δ47.5(C=C).

SB2: 3-(1H-benzoimidazol-2-yl)-propionic acid: IR(cm^{-1}) : 2849(C=C-Hstr), 1708(C=Ostr), 3137(N-Hstr).

SB3: (1H-benzoimidazol-2-yl)-benzoyl alcohol: IR(cm^{-1}) : 2862(C=C-Hstr), 3385(N-Hstr),

SB4: (1H-benzoimidazol-2-yl)-benzoic acid: IR(cm^{-1}) : 2675(C=C-Hstr), 3120(O-Hstr), 3458(N-Hstr).

Table 2 Analytical data of 1-benzoyl 2-substituted-benzimidazole (BB1-BB8)

Compounds	Yield(%)	Molecular formula	M.wt
BB1	65	$C_{16}H_{12}N_2O_3$	280
BB2	71	$C_{11}H_{10}N_2O_3$	218
BB3	68	$C_{17}H_{14}N_2O_3$	294
BB4	81	$C_{12}H_{12}N_2O_3$	232
BB5	85	$C_{20}H_{15}N_2O_2$	315
BB6	58	$C_{15}H_{13}N_2O_2$	253
BB7	75	$C_{21}H_{15}N_2O_3$	343
BB8	60	$C_{16}H_{13}N_2O_3$	281

IR SPECTRAL ANALYSIS (SB1-SB2)

BB1: (1-acetyl-1H-benzoimidazol-2-yl)-acetic acid: IR(cm^{-1}) : 2960(C=C-Hstr), 1179(N-Cstr), 3070(O-Hstr), ^{1}H NMR : δ7.12(aromatic proton) δ 0.8(CH_3)proton. ^{13}C NMR : δ 60.0(C=C)group.

BB2:(1-benzoyl-1H-benzoimidazol-2-yl)-acetic acid: IR(cm^{-1}): 2959(C=C-Hstr), 1118(N-Cstr), 3192(O-Hstr). ^{1}H NMR : δ7.596(aromatic proton).

BB3: 3-(1-benzoyl-1H-benzoimidazol-2-yl)-propionic acid: IR(cm^{-1}): 2835(C=C-Hstr), 1118(N-Cstr), 2835(O-Hstr).

BB4: 3-(1-acetyl-1H-benzoimidazol-2-yl)-propionic acid: IR(cm^{-1}): 2921(C=C-Hstr), 1155(N-Cstr), 3385(O-Hstr).

BB5: (1-acetyl-1H-benzoimidazol-2-yl)-benzoyl alcohol: IR(cm^{-1}): 2837(C=C-Hstr), 1183(N-Cstr), 3272(O-Hstr).

BB6: 3-(1-acetyl-1H-benzoimidazol-2-yl)-benzoyl alcohol: IR (cm^{-1}): 2856(C=C-Hstr), 1155(N-Cstr), 3237(O-Hstr).

BB7: 1-benzoyl-(1H-benzoimidazol-2-yl)-benzoic acid: IR (cm^{-1}): 2826(C=C-Hstr), 1585(N-Cstr), 3349(O-Hstr).

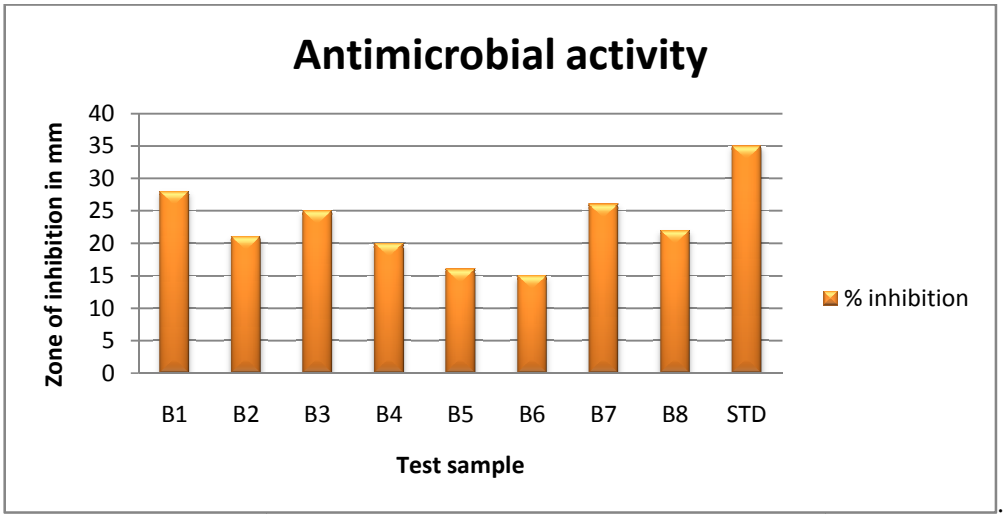
BB8:(1-acetyl-1H-benzoimidazol-2-yl) - benzoic acid: IR (cm^{-1}): 2856 (C=C-Hstr),1158 (N-Cstr).

RESULTS AND DISCUSSION

The anti-microbial activity for the given sample was carried out by disc diffusion technique[12-15]. The test microorganisms of *pseudomonas aeruginosa* were obtained from National Chemical Laboratory(NCL) Pune and maintained by periodical sub culturing on nutrient agar medium for bacteria. The effect produced by the sample was compared with the effect produced by the positive control(reference standard ciprofloxacin 5 µg/disc.

The obtained results are tabulated as follows:

S. No	Name of the microorganisms	Zone of Inhibition in mm								
		BB1	BB2	BB3	BB4	BB5	BB6	BB7	BB8	Std
1.	*Pseudomonas aeruginosa*	28	21	25	20	16	15	26	22	35



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DISCUSSION

The reaction of o-phenylenediamine with dicarboxylic acids (malonic acid, succinic acid, salicylic acid, phthalic acid) yield 2-substituted-benzimidazoles.The title compounds were synthesized by treating 2-substituted-benzimidazole with benzyl chloride and sodium hydride. Their structures were confirmed by IR,^{1}H-NMR and ^{13}C-NMR.Antimicrobial activity against *Pseudomonas aeruginosa* was studied for the synthesized compounds. The purity and homogeneity of all the synthesized compounds were confirmed by their column chromatography. The aromatic stretching frequencies for all the derivatives were found to be at the range of 2900-3100 cm^{-1}.The presence of NH stretching was confirmed by the peaks at 3500-3300cm^{-1}. Also ^{1}H-NMR spectra were useful for identifying protons. The peaks at the frequency range 6.0 – 9.0 confirms the aromatic protons and 2.2-5.8 confirms the NH_2 protons. From the microbiological studies, the antimicrobial activity of BB1(1-acetyl-1H-benzoimidazol-2-yl)-acetic acid was found to be the highest among the other compounds.

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