



## SYNTHESES OF SOME NEW 1, 2, 3-BENZOTRIAZOLES AS ANTIMICROBIAL AGENTS

Ram Janam Singh<sup>\*1</sup>

<sup>\*</sup> Quality Control Laboratory, IOCL, Panipat Refinery Panipat, Haryana-132140 (India)

<sup>1</sup> Synthetic Research Laboratory, Department of Chemistry, T.D.P.G.College Jaunpur,(U.P.)

\*E-mail:drjsinghtdc@rediffmail.com

### ABSTRACT

Several 1, 2, 3-benzotriazoles were prepared as possible biologically active agents. The compounds (**3a-e**) were characterized by spectral and elemental analyses. All newly synthesized compounds have been assayed for their antifungal activity against *P. oryzae*, *B. cinerea*, *A. nigar*, *C. albicans* and *T. rubrum*.

**Keywords:** Sodium amide, benzimidazoles, 1, 2, 3-benzotriazoles, Triazoles, antifungal activity.

### INTRODUCTION

The importance of triazole- derivatives lie in the field that these have occupied an unique position in heterocyclic chemistry due to their agricultural, industrial and biological activities<sup>1</sup>. The 1, 2, 3-triazole system has wide spread uses, and it has been considered as an interesting component in terms of antimicrobial activity<sup>2</sup>. Compounds containing benzotriazole moieties attached to a heterocyclic system are of wide interest because of their diverse biological activities<sup>3</sup>. In views of these observations and in continuation of our earlier work<sup>4-9</sup> on the syntheses of some 1,2,4- & 1,2,3- triazole derivatives, we now report the syntheses of some more 1,2,3-benzotriazole derivatives derived from benzimidazoles with 1-chloromethyl benzotriazoles and their antifungal activities.

### EXPERIMENTAL

Melting and boiling points were determined on a Gallen Kamp apparatus in open capillaries and are uncorrected. IR spectra (KBr in cm<sup>-1</sup>) were recorded on a Jasco FT-IR 5300 spectrophotometer and Proton magnetic resonance (PMR) spectra (DMSO-d<sub>6</sub>) on a Varion EM 390 spectrophotometer using TMS as an internal standard (chemical shift in  $\delta$  ppm). Mass spectra were recorded on Jeol JMS-D 300 mass spectrophotometer operating at 70 eV. The Purity of the compounds was checked by TLC using silica gel G and purified by column chromatography. All compounds showed satisfactory elemental analyses.

#### General Procedure for the preparation of 1,2,3-Benzotriazoles:

A mixture of sodium amide (0.01 mol) and the corresponding benzimidazole (0.01 mol) in dry toluene (15 mL) was refluxed for 05 hours. Chlororomethylbenzotriazole (0.01 mol) was added to hot suspension and refluxed for 10 hours, cooled and poured on crushed ice. The crude solids were separated and filtered. The crude solids were recrystallized from water.

#### 1-[(2, 5-Dimethyl)-1H-1, 3-benzimidazole-1-yl] methyl]-1H-1, 2, 3-benzotriazole (**3a**):

(Yield 72 %), m.p. 232 °C. Anal.Calc. for C<sub>16</sub>H<sub>15</sub>N<sub>5</sub>, C, 69.28; H, 5.46; N, 25.26 %; Found C, 69.05; H,5.19; N, 25.39% ; IR (KBr) : 3050 (aromatic C–H stretching), 2980 (aliphatic C–H stretching), 1676 (C=C, C=N) and 1442,740 cm<sup>-1</sup> (monosubstituted benzene); PMR:  $\delta$  2.52 (3H,s, CH<sub>3</sub>), 6.82 (2H,s, CH<sub>2</sub>) and 7.12-7.65ppm (7H, m, aromatic); MS: m/z 295 (M<sup>+</sup>) other peaks observed at 144, 132, 120, 105, 88, 66, 54 and 46.

**1-[(2-Ethyl-5-methyl)-1H-1, 3-benzimidazole-1-yl] methyl]-1H-1, 2, 3-benzotriazole (3b):**

(Yield 70 %), m.p. 245 °C. Anal.Calc. for C<sub>17</sub>H<sub>17</sub>N<sub>5</sub>, C, 70.06; H, 5.89; N, 24.05 %; Found C, 70.20; H,6.05; N, 23.82% ; IR (KBr) : 3051 (aromatic C–H stretching), 2988 (aliphatic C–H stretching), 1612, 1680 ( C=C, C=N) and 1439, 838, 795 cm<sup>-1</sup> (monosubstituted benzene); PMR: δ 2.16-2.20 (3H, t, CH<sub>3</sub>), 2.50-2.52 (2H, q, CH<sub>2</sub>), 2.48 (3H, s, CH<sub>3</sub>), 6.88 (2H,s, CH<sub>2</sub>) and 7.12-7.66 ppm (7H, m, aromatic); MS: m/z 285 (M<sup>+</sup>) other peaks observed at 166, 138, 110, 104, 68, 59, and 39.

**1-[[5-Methyl-2-(trichloromethyl)-1H-1,3-benzimidazole-1-yl]methyl]-1H-1,2,3-benzotriazole (3c):**

(Yield 70 %) m.p. 267 °C. Anal.Calc. for C<sub>16</sub>H<sub>12</sub>Cl<sub>3</sub>N<sub>5</sub>, C, 50.46; H, 3.19; N, 18.40 %; Found C, 50.15; H,3.27; N, 18.70% ; IR (KBr) : 3020 (aromatic C–H stretching), 2792 (aliphatic C–H stretching), 1672 ( C=C, C=N) and 1484, 811, 705 cm<sup>-1</sup> (monosubstituted benzene); PMR: δ 2.48 (3H, s, CH<sub>3</sub>), 7.09 (2H,s, CH<sub>2</sub>) and 7.40-8.05 ppm (7H, m, aromatic); MS: m/z 286 (M<sup>+</sup>) other peaks observed at 197, 172,159, 127, 105, 78, 55 and 41.

**1-[[5-Methyl-2-(2-pyridyl)-1H-1, 3-benzimidazole-1-yl] methyl]-1H-1, 2, 3-benzotriazole (3d):**

(Yield 72 %) m.p. 245 °C. Anal.Calc. for C<sub>20</sub>H<sub>16</sub>N<sub>6</sub>, C, 70.55; H, 4.75; N, 24.70 %; Found C, 70.33; H,4.98; N, 24.40% ; IR (KBr) : 3028 (aromatic C–H stretching), 2850-2972 (aliphatic C–H stretching), 1645, 1691 ( C=C, C=N) and 1457, 805, 785 cm<sup>-1</sup> (monosubstituted benzene); PMR: δ 2.52 (3H,s, CH<sub>3</sub>), 7.14 (2H, s, CH<sub>2</sub>) and 7.41-8.02 ppm (11H, m, aromatic); MS: m/z 302 (M<sup>+</sup>) other peaks observed at 234,230,188, 165,137, 95, 77, 55, and 38.

**1-[[5-Methyl-2-(3-pyridyl)-1H-1, 3-benzimidazole-1-yl] methyl]-1H-1, 2, 3-benzotriazole (3e):**

(Yield 72 %) m.p. 253 °C. Anal.Calc. for C<sub>20</sub>H<sub>16</sub>N<sub>6</sub>, C, 70.55; H, 4.75; N, 24.70 %; Found C, 70.63; H,4.91; N, 24.91% ; IR (KBr) : 3092 (aromatic C–H stretching), 2992 (aliphatic C–H stretching), 1665, 1688 ( C=C, C=N) and 1471, 625 cm<sup>-1</sup> (monosubstituted benzene); PMR: δ 1.65 (3H,s, CH<sub>3</sub>), 7.07 (2H, s, CH<sub>2</sub>) and 7.33, 9.33 ppm (11H, m, aromatic); MS: m/z 299 (M<sup>+</sup>) other peaks observed at 235,231,187, 166,135, 94, 78, 56, and 37.

**Antifungal Activity:**

Five compounds were evaluated for their fungicidal activity against *P.oryzae*, *B.cinerea*, *A. niger*, *C.albicans* and *T.rubrum* at 1000 ppm, 500 ppm and 100 ppm concentrations, respectively by food poisoning of solidified agar technique<sup>10-12</sup>. The inhibitory activities were compared with commercial fungicide Griseofulvin (standard drug) under similar conditions. The mould cultures used were 7 days old. The results are presented in **Table-1**.

The percentage inhibition after the incubation for 24, 48 and 72 hours was calculated by following equation:

$$\text{Percentage inhibition} = \frac{(C-T) \times 100}{C}$$

Where, C= Diameter of Fungus colony (mm) in control plates

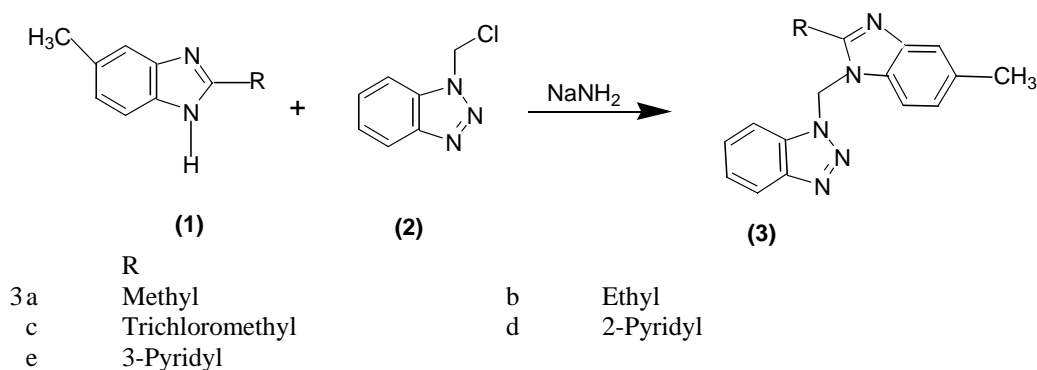
T= Diameter of Fungus colony (mm) in treated plates

It is obvious from the fungicidal screening results that the most of compounds have significant fungi toxicity at 1000 ppm against all of five fungi, but the fungi toxicity decreases considerably upon dilution. All the five compounds showed good activity against *P. oryzae*, *B. cinerea*, *A. nigar*, *C. albicans* and *T. rubrum*. It is quite evident from fungi toxicity data that methyl, ethyl, trichloromethyl, 2-pyridyl and 3-pyridyl group in benzimidazole-substituted benzotriazoles (**3a-e**) is responsible to enhance the antifungal activity.

## RESULTS AND DISCUSSION

In the present work, nucleophilic addition reaction of benzimidazoles to 1-chloromethyl benzotriazole in presence of a strong base, NaNH<sub>2</sub> under reflux conditions afforded the 1,2,3- benzotriazole (**3a-e**). (Scheme 1).

The five membered rings in compound (**3a-e**) exhibits an envelop confirmation with the NH<sub>2</sub> group lying out of the molecular plane. The attack of the second nitrogen atom on the first nitrogen of the adjacent azide with displacement of N<sub>2</sub> is the easiest way to visualize product formation. PMR spectra of the synthesized compounds support the structures and the expected reactions. The absorption peak for the characteristic methylene group between the benzimidazole and the benzotriazole ring for (**3a-e**) appears as a singlet in the region of δ 6.82–7.14 ppm. The absence of the NH proton absorption δ 6.65–9.33 ppm in the PMR spectra for the benzotriazoles in (**3a-e**) confirms the nucleophilic addition of benzimidazoles to 1-chloromethyl benzotriazole.



Scheme-1

Table-1. Evaluation of Antifungal Activity of the compounds (3a-e)

Compd.	Average percentage inhibition after 72 hours														
	<i>P. oryzae</i>			<i>B. cinerea</i>			<i>A. niger</i>			<i>C. albicans</i>			<i>T. rubrum</i>		
	1000 ppm	500 ppm	100 ppm	1000 ppm	500 ppm	100 ppm	1000 ppm	500 ppm	100 ppm	1000 ppm	500 ppm	100 ppm	1000 ppm	500 ppm	100 ppm
3a	88	80	68	77	59	52	74	53	38	69	51	36	62	56	36
3b	92	80	79	65	52	44	65	43	24	62	51	27	80	66	48
3c	92	84	79	91	82	74	91	67	37	69	54	34	66	60	46
3d	92	80	68	91	82	74	90	63	62	64	56	31	60	53	37
3e	92	80	66	65	48	39	70	46	37	66	46	35	72	49	24
Standard (Griseofulvin)	100	84.6	66.3	99.4	84.6	71.0	98.8	84.6	71.0	99.6	84.6	68.3	99.8	82.5	71.0
Control	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00

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