



## **SYNTHESIS AND ANTIMICROBIAL EVALUATION FOR CERTAIN 1-(1H-BENZOTRIAZOL-1-YL)-1-SUBSTITUTED PHENYL METHANAMINE**

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### **ABSTRACT**

The various derivatives of 1-(1H-benzotriazol-1-yl)-1-substituted phenyl methanamine (**3a-e**) were synthesized by refluxing benzotriazole with different substituted aldehydes (**2a-e**) and ammonium chloride in ethanol. The structures of the synthesized compounds have been characterized by IR and <sup>1</sup>H NMR spectral data. The title compounds were evaluated for their antibacterial and antifungal activities and found to exhibit a variable degree of activity.

**Keywords:** Benzotriazole, Mannich base, Antifungal, Antibacterial

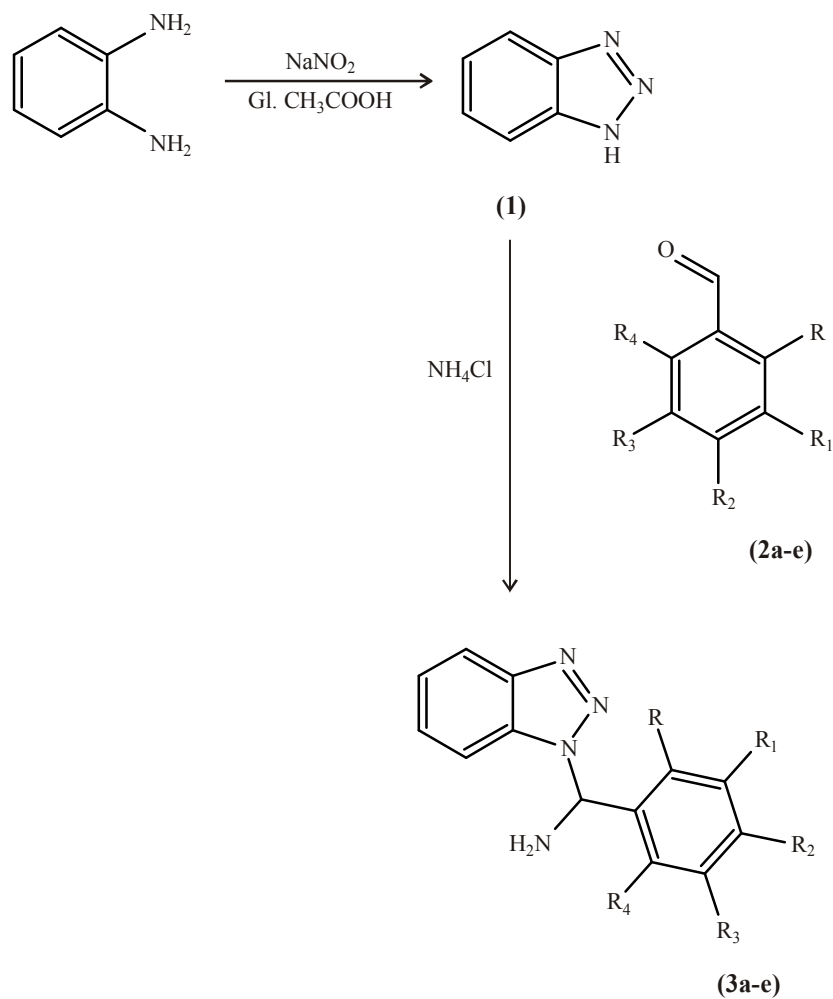
### **INTRODUCTION**

Azoles have played a crucial role in the history of heterocyclic chemistry and also been used extensively as important synthons in the organic synthesis. Owing to the versatile chemotherapeutical activities of azoles, a significant amount of research activity has been directed towards this class. Benzotriazole, a five membered heterocyclic system with three nitrogen atoms at 1, 2, 3 positions contains an active hydrogen atom to nitrogen atom. Benzotriazole are found to possess various biological activities like analgesic<sup>1</sup>, antimicrobial<sup>2</sup>, anticonvulsant, anti-inflammatory<sup>3</sup> and antitumour<sup>4</sup>. Several derivatives of benzotriazoles are reported as agonists of peroxisome proliferator activated receptors<sup>5</sup>. In view of the above biological importance, we now report the synthesis of some of 1-(1H-benzotriazol-1-yl)-1-substituted phenyl methanamine and antibacterial and antifungal

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activities associated with them.



**Scheme 1**

The title compounds (**3a-e**) were synthesized by treating benzotriazole with the substituted aromatic aldehydes (**2a-e**) and ammonium chloride in ethanol. The structures of the products were confirmed by the spectral analysis. Derivatives of benzotriazole are listed in Table 1.

**Table 1: Various substituents in the titled compounds**

Compound	R	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>
<b>3a</b>	H	H	H	H	H
<b>3b</b>	Cl	H	H	H	H
<b>3c</b>	H	OCH <sub>3</sub>	OCH <sub>3</sub>	OCH <sub>3</sub>	H
<b>3d</b>	H	H	NO <sub>2</sub>	H	H
<b>3e</b>	H	H	CH <sub>3</sub>	H	H

## EXPERIMENTAL

Melting points were determined by open capillary method and were uncorrected. The IR spectra were recorded on a JASCO FTIR -420 series using KBr pellet. The <sup>1</sup>H NMR were recorded at Uwin Life Sciences, Bangalore using TMS as standard. Purity of the synthesized compounds was checked by TLC using silica gel G plates using benzene –ethyl acetate (6 : 4) as developing solvent and the spots were exposed in iodine chamber.

### Synthesis of 1-(1H-benzotriazol-1-yl)-1-substituted phenyl methanamine (**3a**)

A mixture of aromatic aldehydes (**2a**) (1 mmol) and ammonium chloride was refluxed for 30 min in absolute ethanol (10 mL) until the aldehyde was completely soluble. The benzotriazole (**1**) (4 mmol) was heated in absolute ethanol (10 mL) and then it was added to the reaction mixture, which was then refluxed for 2 hrs. The reaction mixture was concentrated and the separated product was filtered off and recrystallised with the suitable solvent. (**3a**) Yield 72%. m.p. 298<sup>0</sup>C. The physical and analytical data of the compounds are given in Table 2.

### Biological evaluation

#### Antibacterial activity<sup>7</sup>

Antibacterial activity of the newly synthesized compounds was screened using *Bacillus subtilis*, *Staphylococcus aureus* and *E.Coli* by the cup plate method. Bacteria were cultured in nutrient agar medium and the solution of the compounds was made in DMSO at

100 µg/mL concentration. The bacteria were precultured overnight in nutrient broth at  $37 \pm 1^\circ\text{C}$ . After incubation period, the inhibition zone was measured in mm. The antifungal activity of the compounds was evaluated against *Candida albicans*. Dimethyl sulphoxide was used as a solvent. Known antibiotics like ampicillin and griseofulvin were used for comparison at the same concentration. The activity of the data is presented in Table 3.

**Table 2: Physical and analytical data of compounds**

Compd.	Mol.formula (Mol.wt)	m.p. ( $^\circ\text{C}$ )	Yield (%)	IR (KBr) ( $\text{cm}^{-1}$ )	$^1\text{H}$ NMR ( $\delta$ ppm) (TMS)
<b>3a</b>	$\text{C}_{13}\text{H}_{12}\text{N}_4$ (224)	298	72	3485, 3018, 2975, 1604, 1565, 1355	5.78 (s, 1H, CH-Ar), 6.4-8 (m, 9H, ArH), 9.27 (s, 2H, NH).
<b>3b</b>	$\text{C}_{13}\text{H}_{11}\text{ClN}_4$ (259)	299	68	3479, 3011, 2981, 1611, 1555, 1348, 1209	5.75 (s, 1H, CH-Ar), 6.42-8.23 (m, 8H, ArH), 9.22 (s, 2H, NH).
<b>3c</b>	$\text{C}_{16}\text{H}_{18}\text{N}_4\text{O}_3$ (314)	>300	67	3481, 3019, 2974, 1618, 1559, 1341,	3.83 (s, 9H, $\text{OCH}_3$ ), 5.73 (s, 1H, CH-Ar), 6.41-8.24 (m, 6H, ArH), 9.24 (s, 2H, NH).
<b>3d</b>	$\text{C}_{13}\text{H}_{11}\text{N}_5\text{O}_2$ (269)	297	60	3481, 3028, 2990, 1619, 1571, 1340	5.74 (s, 1H, CH-Ar), 6.37-7.97 (m, 8H, ArH), 9.26 (s, 2H, NH).
<b>3e</b>	$\text{C}_{14}\text{H}_{14}\text{N}_4$ (238)	285	62	3479, 3031, 2985, 1624, 1574, 1354	2.14 (s, 3H, $\text{CH}_3$ ), 5.81 (s, 1H, CH-Ar), 6.39-8.2 (m, 8H, ArH), 9.23 (s, 2H, NH).

**Table 3: Anti-bacterial and anti-fungal activity of the title compounds: (Expressed in mm)**

Compd	Antibacterial activity			Antifungal activity
	<i>B. subtilis</i>	<i>P. aureginosa</i>	<i>E. coli</i>	<i>C. albicans</i>
<b>3a</b>	09	08	15	10
<b>3b</b>	10	07	10	12
<b>3c</b>	09	08	12	10
<b>3d</b>	18	11	11	11
<b>3e</b>	09	10	12	10
<b>Ampicillin</b>	15	21	18	--
<b>Griseofulvin</b>	--	--	--	15

## RESULTS AND DISCUSSION

The main aim of this work was to synthesize few derivatives of 1-(1H-benzotriazol-1-yl)-1-substituted phenyl methanamine. These were confirmed by IR (KBr) spectral data by the presence of a peak in the range of 2990-2950  $\text{cm}^{-1}$ . This was supported from  $^1\text{H}$  NMR spectral data as a sharp singlet was observed at around 5.73-5.81  $\delta$  ppm assigned for 1H of CH-Ar formed at the junction. Purified final compound yielded moderate yields. Table 2 summarizes the physical and analytical data of the compounds. Derivatives (**3a**) and (**3d**) exhibited activity against *E.coli*, *B. subtilis* and *P. aureginosa* at 100  $\mu\text{g/mL}$  which showed the importance of nitro compounds, while (**3b**) exhibited activity at 100  $\mu\text{g/mL}$  which showed the importance of chloro group. Hence, from these findings, it was found that electron withdrawing group is necessary to exhibit such activity. All other compounds show mild activity against the selected strains.

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