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Synthesis and Antibacterial Activity of 1-[N-Substituted Aminobenzothiazolyl] Methylbenzimidazoles

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The Mannich bases of the benzimidazoles were prepared by using formaldehyde and amino benzothiazoles in the presence of traces of conc. HCl. These prepared compounds were tested for their antibacterial activity against gram(+ve) and gram(-ve) bacteria. Some of the compounds show remarkable activity.

INTRODUCTION

Benzothiazole compounds have a wide spectrum of biological activities like fungicides[1]. The 2-arylbenzothiazoles have nematocidal activity and protocidal activity[2]. The substituted benzothiazole shows a wide variety of biological activities such as anthelmintic[3], antibacterical[4,5], antitubercular[6], anaesthetic[7,8] and immunosuppressive agents[9]. While benzimidazole derivatives attract wide interest on account of their herbicidal[10], antimicrobial[11] and antiviral activity.

Benzimidazole on Mannich reaction with appropriate aminobenzothiazole and paraformaldehyde in the presence of traces of conc. HCl gave the title compounds (I) (Scheme-I). Antimicrobial evaluation of the synthesised compounds was carried out by standard method against gram(+ve) and gram(-ve) bacteria.

Antibacterial Activity

All the compounds were screened for their antibacterial activity against *S. aureus*, *B. mega* and *E. coli* by cup-plate method[13] at a concentration of 100 mg using DMF as solvent. After 24 h of the inhibition at 37°C, the zones of inhibition were measured in mm. The activity was compared with known antibiotics, *i.e.* ampicillin (*S. aureus* 18, *B. mega* 24, *E. coli* 22) and chloroamphenicol (*S. aureus*, 28; *B. mega*, 16, *E. coli* 20).

All compounds showed moderate to good antibacterial activity against *S. aureus* (14–25), *B. mega* (12–18), *E. coli* (11–12) mm zone of inhibition at same concentration.

EXPERIMENTAL

The instrumental details are same as in previous papers.

Substituted 2-aminobenzothiazoles[14] were prepared according to the procedure recorded in the literature.

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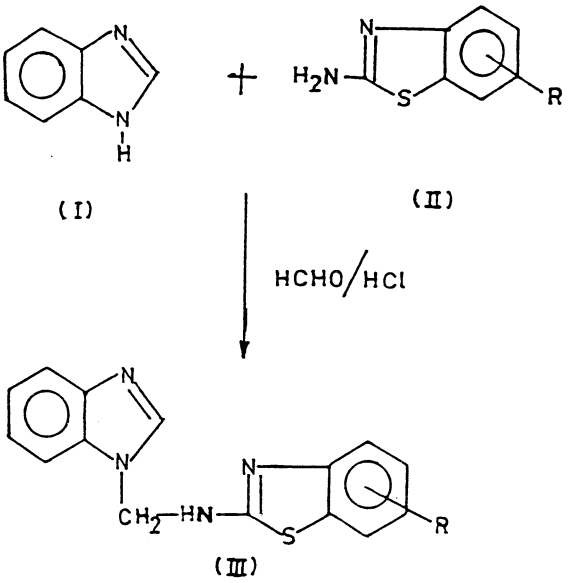

SCHEME I

1-N[6′-Chloro-2′-amino benzimidazolyl] methyl benzimidazole (12)

Benzimidazole (0.01 mol) in 20 mL ethanol was stirred with paraformaldehyde (0.011 mol) and 2-amino 6-chlorobenzothiazole (0.01 mol) was added slowly for 10 min in the presence of conc. HCl. The reaction mixture was refluxed for 1 h. The refluxed reactants were cooled and poured on crushed ice and neutralised by 10% $NaHCO_3$ solution; the separated solid was filtered, washed with cold water, dried and recrystallised from aq. ethanol to give (12). m.p. 194°C; yield: 62%; IR: ν_{max}1280 (C—N), 1615 (C=C), 1630 (C=N), 2910 (—CH_2) and 3340 cm^{-1} (—NH). PMR: δ 5.40 (S, 2H, N—CH_2—N), 6.7–7.8 (m, 10H, aromatic —H and —NH).

Similarly all compounds of the series were prepared. The IR and NMR spectra of other members of the series were also in agreement with their structures assigned. The physical data were recorded in Table-1.

TABLE-1
PHYSICAL DATA OF THE SYNTHESISED COMPOUNDS

Comp. No	Substitutent R	m.p.* (°C)	Yield (%)	Mol. formula	% of Nitrogen	
					Calcd.	Found
1	H	110	67	$C_{15}H_{12}N_4S$	20.00	19.79
2	4′-CH_3	189	70	$C_{16}H_{14}N_4S$	19.04	18.92
3	5′-CH_3	212	72	$C_{16}H_{14}N_4S$	19.04	18.90
4	6′-CH_3	230	70	$C_{16}H_{14}N_4S$	19.04	18.82
5	4′-OCH_3	196	65	$C_{16}H_{14}N_4OS$	18.06	17.79
6	5′-OCH_3	224	68	$C_{16}H_{14}N_4OS$	18.06	17.56

7	6′-OCH_3	246	66	$C_{16}H_{14}N_4OS$	18.06	17.69
8	4′-OC_2H_5	140	72	$C_{17}H_{16}N_4O$	17.28	17.20
9	5′-OC_2H_5	149	75	$C_{17}H_{16}N_4O$	17.28	17.18
10	6′-OC_2H_5	162	71	$C_{17}H_{16}N_4O$	17.28	17.00
11	4′-Cl	180	60	$C_{15}H_{11}N_4Cl$	17.80	17.76
12	5′-Cl	194	62	$C_{15}H_{11}N_4Cl$	17.80	17.60
13	6′-Cl	209	66	$C_{15}H_{11}N_4Cl$	17.80	17.56
14	5′-Br	182	69	$C_{15}H_{11}N_4Br$	15.59	15.42
15	6′-Br	198	64	$C_{15}H_{11}N_4Br$	15.59	15.20
16	4′-NO_2	140	78	$C_{15}H_{11}N_5O_2$	21.53	21.50
17	5′-NO_2	154	74	$C_{15}H_{11}N_5O_2$	21.53	21.34
18	6′-NO_2	160	70	$C_{15}H_{11}N_5O_2$	21.53	21.12
19	5′-OH	132	75	$C_{15}H_{12}N_4O$	18.91	18.70
20	6′-OH	176	71	$C_{15}H_{12}N_4O$	18.91	18.78

*All compounds crystallised from aq. ethanol and give C and H analysis satisfactorily.

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