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NOTE

Synthesis of Aniline Substituted Benzimidazole Derivatives

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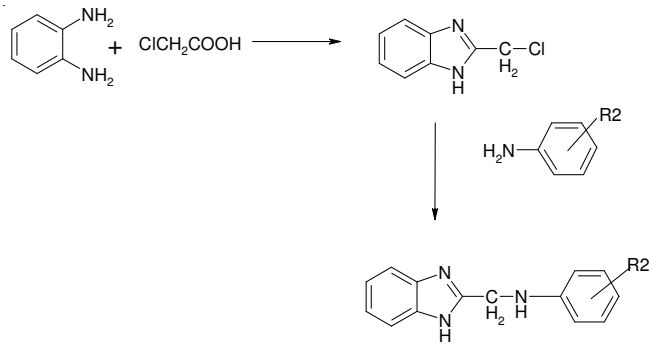
2-Chloromethyl benzimidazole can be synthesized by the reaction of *o*-phenylene diamine with chloroacetic acid. This on reaction with substituted anilines in presence of ethanolic KOH gives corresponding benzimidazole derivatives. The synthesized compounds were characterized by IR, ^{1}H NMR and mass spectral data.

Key Words: 2-Chloromethyl benzimidazole, *o*-Phenylene diamines, Chloroacetic acid, Aniline.

Benzimidazole is a aromatic heterocyclic compound having imidazole ring fused to benzene. The most prominent benzimidazole compound in nature is N-ribosyl-dimethyl-benzimidazole, which serves as an axial ligand for cobalt in vitamin B_{12}[1]. The nucleus is present in some drugs such as proton pump inhibitors and anthelmintic agents[2]. Mebendazole and thiabendazole which have anthelmintic and antifungal properties are benzimidazole class of compounds[3]. Benzimidazole and its derivatives are widely used as intermediates in synthesis of organic target compounds including pharmaceuticals, agrochemicals, dyes, photographic chemicals, corrosion inhibitors, epoxy curing agents, adhesives and plastic modifiers. Benzimidazole is a white to slightly beige solid; melting at 145-150 ºC, boils at 360 ºC, slightly soluble in water, soluble in ethanol. Benzimidazole and its derivatives are used in organic synthesis and as vermicides or fungicides[4,5].

Melting points of the synthesized compounds were determined by open capillary method and were uncorrected. IR spectral analysis was carried out using FTIR-8400S, Shimadzu at M.S. Ramaiah College of Pharmacy, Bangalore. ^{1}H NMR spectral data was obtained from Indian Institute of Sciences, Bangalore. The instrument used was Amx-400 and the solvent used was deuterated chloroform.

General procedure for synthesis of 1*H*- benzimidazol-2-yl-methyl)-phenyl-amine derivatives[6-13]: In the ethanolic KOH solution 2-chloromethyl benzimidazole (0.02 mol) and substituted anilines (0.0217 mol) were added and it was refluxed for 5 h. Hot mixture was poured in crushed ice with constant stirring. Separated solid was filtered, dried and recrystallized from ethanol. The yields ranged from 30-45 %. The spectral data are given below:



2a: R^2 = H; **2b:** R^2 = -4-NO_2; **2c:** R^2 = -2,4-NO_2; **2d:** R^2 = -4-Cl

Scheme-I

Compound 2a: IR (KBr, ν_{max}, cm^{-1}): 3450, 3320 (N-H str.), 1545 (N-H bend), 3040 (Ar, C-H str.), 2870 (CH_2 str.), 1450, 1420 (C=C str.). ^{1}H NMR ($CDCl_3$): 3.6 (2H, CH_2), 5.2 (1H N-H aniline), 12.7 (1H, NH Ar-benzimidazole), 8.7 (4H Ar-benzimidazole), 8.3 (5H, phenyl).

Compound 2b: IR (KBr, ν_{max}, cm^{-1}): 3350, 3325 (N-H str.), 1575 (N-H bend), 3120 (Ar, C-H str.), 2820 (CH_2 str.), 1475, 1420 (C=C str.). ^{1}H NMR ($CDCl_3$): 3.5 (2H, CH_2), 4.5 (1H N-H aniline), 12.3 (1H, NH Ar-benzimidazole), 7.9 (4H Ar-benzimidazole), 8.1 (4H, phenyl).

Compound 2c: IR (KBr, ν_{max}, cm^{-1}): 3475 (N-H str.), 1523 (N-H bend), 3020 (Ar, C-H str.), 2875 (CH_2 str.), 1456 (C=C str.). ^{1}H NMR ($CDCl_3$): 3.9 (2H, CH_2), 5.7 (1H N-H aniline), 11.7 (1H, NH Ar-benzimidazole), 9.2 (4H Ar-benzimidazole), 8.6 (3H, phenyl).

Compound 2d: IR (KBr, ν_{max}, cm^{-1}): 3375, 3323 (N-H str.), 1523 (N-H bend), 3075 (Ar, C-H str.), 2800 (CH_2 str.),

1475, 1435 (C=C str.). ^{1}H NMR ($CDCl_3$): 2.7 (2H, CH_2), 4.9 (1H N-H aniline), 11.7 (1H, NH Ar-benzimidazole), 7.5 (4H Ar-benzimidazole), 7.9 (4H, phenyl).

2-Chloromethyl benzimidazole can be synthesized by the reaction of *o*-phenylene diamine with chloroacetic acid. This on reaction with substituted anilines in presence of ethanolic KOH gives corresponding derivatives (**Scheme-I**).

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