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Research Article

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Facile and efficient one-pot synthesis of benzimidazoles using Boron trichloride

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ABSTRACT

We report the synthesis of benzimidazoles using Boron trichloride as an efficient catalyst. One-pot synthesis of 2-substituted benzimidazole derivatives from o-phenylenediamine and a variety of aldehydes were developed under mild reaction conditions. On completion of reaction the products were characterized by IR, NMR and Mass Spectra. These methods are more convenient and reactions can be carried out in higher yield.

Keywords: Benzimidazoles, Aldehydes, o-Phenylenediamine, Boron trichloride

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INTRODUCTION

The development of an efficient synthesis of bioactive compounds in an ecologically and economically favourable way is a great challenge in modern chemistry. Benzimidazole moiety is a bicyclic compound having an imidazole ring containing two nitrogen atoms at nonadjacent positions, fused to benzene. It has been useful intermediates in the development of molecules of pharmaceutical and biological interest. The chemistry and pharmacology of benzimidazoles have been of great interest to medicinal chemistry [1-2], because its derivatives possessed various biological activities such as anticancer [3], antihypertensive [4], anthelmenthic [5- 7], anti-protozoal [8-9], antimicrobial [10-15], antioxidant [16-17], anti-inflammatory [18-19], analgesic [20] and anti-hepatitis-B-virus [21]. Due to the high importance of 2-aryl-1H-benzimidazoles for the preparation of biologically active molecules, their synthesis has been received considerable attention.

In such consequence we have developed a new protocol for the preparation of Benzimidazole moiety with short times and high yields. In our present work, we unzip our results for preparation of Benzimidazole moiety with high yields which is superior to other methods.

EXPERIMENTAL SECTION

Melting points were measured by using the capillary tube method with an electrothermal method 9200 apparatus. ^{1}H NMR spectra were recorded on BRUKER ADVANCE II 400 NMR Spectrometer using TMS as internal standard. The mass spectra were obtained on a JEOL 5x102/DA-6000 mass spectrometer. The IR spectra were recorded on Perkin-Elmer spectrum RX IFT-IR System using KBr pellets. Chemical shifts are given in ppm (δ) and are referenced to the residual proton resonances of the solvents. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$-*d* or DMSO-*d*6 as the internal standard (^{1}H NMR: TMS at 0.00 ppm, $CDCl_3$ at 7.26 ppm, DMSO at 2.50 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm, DMSO at 40.00 ppm.

***General procedure for the synthesis of benzimidazoles* (2a-m)**

A mixture of o-phenylenediamine (1.0 mmol) and aldehyde (1.2 mmol) in the presence of Boron trichloride was stirred in DCM (5 ml) at room temperature up to 1-2 hr. The progress of the reaction was monitored by TLC. After

completion of the reaction as indicated by TLC, the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate and washed with water and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude products were purified by column chromatography. All the products were identified by spectral (IR, ^{1}H NMR, ^{13}C NMR and mass) and analytical data.

Scheme I: The synthetic route was depicted in scheme I

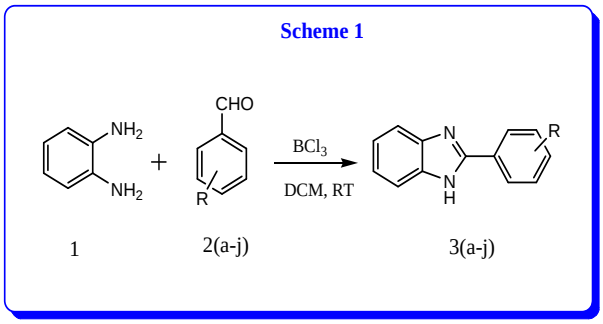
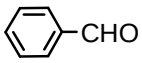
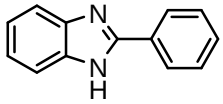
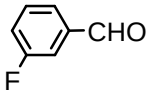
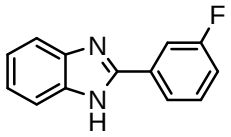
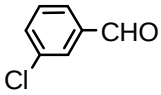
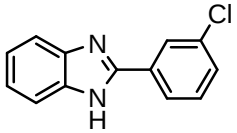
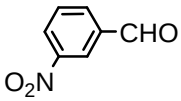
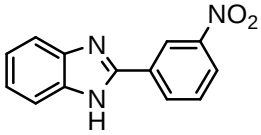
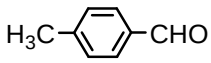
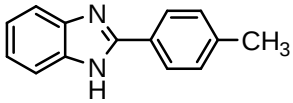
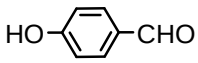
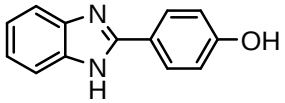
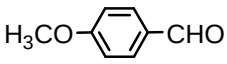
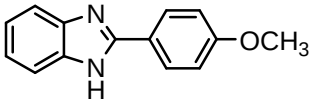
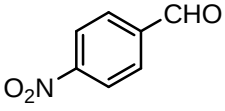
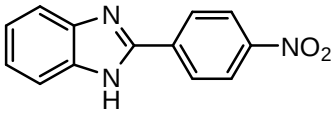
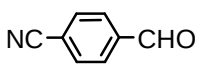
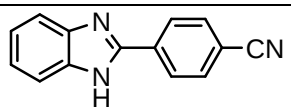
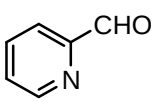
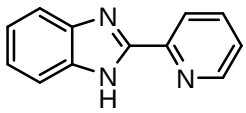


Table 1: Boron tribromide-catalyzed synthesis of benzimidazoles 3(a-j)

Entry	Aldehyde	Product	Yield(%)
1			85
2			91
3			90
4			88
5			93
6			83
7			84
8			85
9			86
10			84

Spectral data for selected compounds

2-Phenyl-1H-benzimidazole(3a): white powder, mp 295°C. ^{1}H NMR (DMSO-*d6*):
12.96 (s, 1H), 8.21-8.20 (t, *J* = 9.0 Hz, 2H), 7.62-7.49 (m, 5H), 7.23-7.20 (m, 2H). ^{13}C NMR (DMSO-*d6*): δ 151.70, 130.65, 130.31, 129.42, 126.91, 122.58. IR (cm^{-1}, KBr): 3500, 1718, 1600, 948, 740 cm^{-1}.

2-(3-fluorophenyl)-1*H*-benzimidazole(3b): White solid, mp 115-116°C. ^{1}H NMR (DMSO-*d6*): δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.81-7.78 (m, 1H), 7.67-7.65 (m, 2H), 7.46-7.42 (m, 1H), 7.32-7.29 (m, 2H), 7.17-7.14 (m, 1H). ^{13}C NMR (DMSO-*d6*): δ 162.92, 150.39, 144.08, 135.41, 132.93, 131.64, 123.41, 122.97, 119.54, 117.08, 113.46, 111.96. IR (cm^{-1}, KBr): 3422, 2994, 1770, 1618, 1383, 1246, 1050 cm^{-1}.

2-(3-Chlorophenyl)-1H-benzimidazole(3c): White powder, mp 232-234°C. ^{1}H NMR (DMSO-d6 MHz): δ 13.05 (s, 1H), 8.24 (s, 1H), 8.16-8.15 (m, 1H), 7.61-7.56 (m, 4H), 7.24 (s, 2H). ^{13}C NMR (DMSO-*d6*): δ 150.20, 134.24, 132.68, 131.41, 130.01, 126.49, 125.48. IR (cm^{-1}, KBr): 3538, 1720, 1600, 1450, 1550, 748 cm^{-1}.

2-(3-Nitrophenyl)-1H-benzimidazole(3d): Yellow powder, mp 306°C. ^{1}H NMR (DMSO-d6 MHz): δ 13.31 (s, 1H), 8.44-8.41 (m, 4H), 7.73-7.66 (m, 2H), 7.28 (s, 2H). ^{13}C NMR (DMSO-*d6*): δ 149.46, 148.26, 136.50, 127.85, 124.76. IR (KBr): 3436, 1607, 1516, 1338, 950 cm^{-1}.

2-(4-Methylphenyl)-1*H*-benzimidazole(3e): white solid, mp 275°C. ^{1}H NMR (DMSO-d6): δ 12.83 (s, 1H), 8.08 (d, *J* = 8.4 Hz, 2H), 7.58 (s, 2H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.20 (dd, *J*=6.0 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (DMSO-*d6*): δ 151.84, 140.04, 129.98, 127.90, 126.87, 122.43, 21.44. IR (KBr): 3397, 3027, 2922, 2858, 1813, 1514, 1481, 1452, 1412, 1383, 1348, 1282, 1157, 1021, 987, 746, 612 cm^{-1}.

2-(4-Hydroxyphenyl)-1*H*-benzimidazole(3f): white powder, mp 229-230°C. ^{1}H NMR (DMSO-d6): δ 12.65 (s, 1H), 9.96 (s, 1H), 8.01 (d, *J* = 2.4 Hz, 2H), 7.53 (s, 2H), 7.16 (dd, *J1* = 6.0 Hz, *J2* = 3.0 Hz, 2H), 6.92 (d, *J* = 3.6 Hz, 2H). ^{13}C NMR (DMSO-*d6*): δ 159.59, 152.25, 128.62, 122.07, 121.62, 116.15. IR (KBr): 3376, 3290, 3027, 2807, 1697, 1611, 1591, 1443, 1394, 1268, 839, 745cm^{-1}.

2-(4-methoxyphenyl)-1H-benzimidazole(3g): Solid, mp 285°C. ^{1}H NMR (DMSO-d6): δ 12.76 (s, 1H), 8.13 (d, *J* = 3.0 Hz, 2H), 7.56 (s, 2H), 7.18 (dd, *J*=5.4 Hz, 2H), 7.13 (d, *J* =2.4 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (DMSO-*d6*): δ 161.07, 151.82, 128.48, 123.18, 122.21, 114.83, 55.79. IR(KBr): 3544, 1724, 1610, 1450, 1100, 1200, 950 cm^{-1}.

2-(4-Nitrophenyl)-1H-benzo[d]imidazole(3h): yellow powder, mp 314°C. ^{1}H NMR (DMSO-d6): δ 13.31 (s, 1H), 8.44-8.41 (m, 4H), 7.73-7.66 (m, 2H), 7.28 (s, 2H). ^{13}C NMR (DMSO-*d6*): δ 149.46, 148.26, 136.50, 127.85, 124.76. IR (KBr): 3436, 1607, 1516, 1338, 950 cm^{-1}.

4-(1H-Benzo[d]imidazole-2yl) benzonitrile(3i): white crystal, mp 262°C. ^{1}H NMR (DMSO-d6): δ 5.50 (brs, 1H), 7.45-7.60 (m, 2H), 7.82-7.90 (m, 2H), 8.05 (d, 2H), 8.50 (d, 2H). ^{13}C NMR (DMSO-*d6*): δ 151.70, 132.77, 132.17, 129.12, 126.91, 118.85, 122.5, 118.45. IR (KBr): 3417, 3047, 2912, 1605, 1454, 1408, 748 cm^{-1}.

2-(Pyridine-2-yl)-1H-benzo[d]imidazole (3j): solid, mp 245-248°C. ^{1}H NMR (DMSO-d6): δ 6.85 (m, 2H), 7.00 to 7.10 (m, 1H), 7.45 to 7.55 (m, 1H), 7.80 to 7.90 (m, 2H), 8.10 (t, 1H), 8.65 (d, 1H). ^{13}C NMR (DMSO-*d6*): δ 112.3, 122.6, 12.6, 12.6, 34.3, 147.9, 149.3, 151. IR (KBr) υ values: 3068, 1449, 1402, 1280, 746 cm^{-1}.

CONCLUSION

In conclusion, Boron trichloride has been employed as a novel and efficient catalyst for the synthesis of benzimidazoles in good yields from o-phenylenediamine and a wide variety of aldehydes. All of the reactions were carried out in the presence of Boron trichloride in DCM at room temperature.

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