Synthesis, molecular docking, molecular dynamic simulation studies, and anti-tubercular activity evaluation of substituted benzimidazole derivatives

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A. IR graph of compound ST02 to ST04

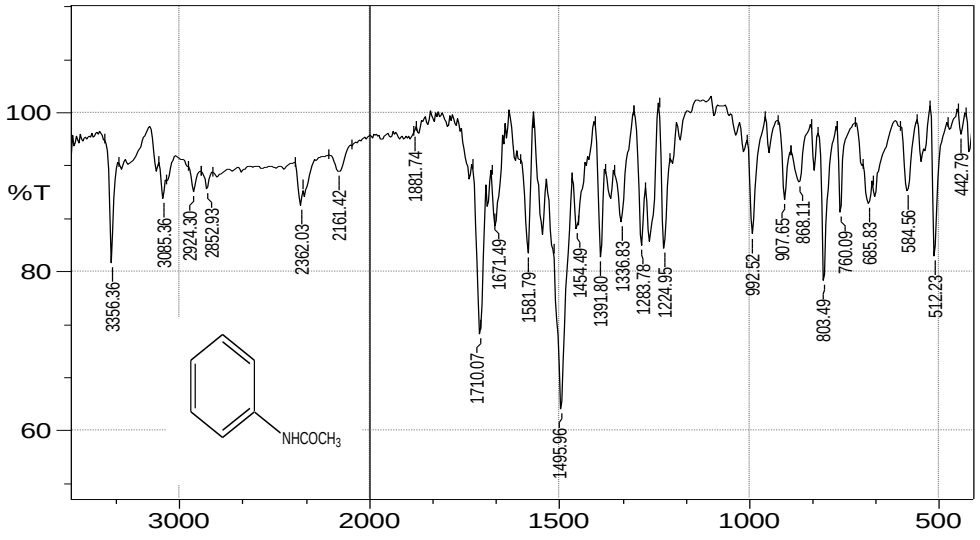


Figure 1: FTIR spectra of ST02

FT-IR range: 3356 cm^{-1} (NH str primary amine), 2923 cm^{-1} (CH str aromatic), 3085 cm^{-1} (CH_3 str), 1771 cm^{-1}(C=O str carbonyl).

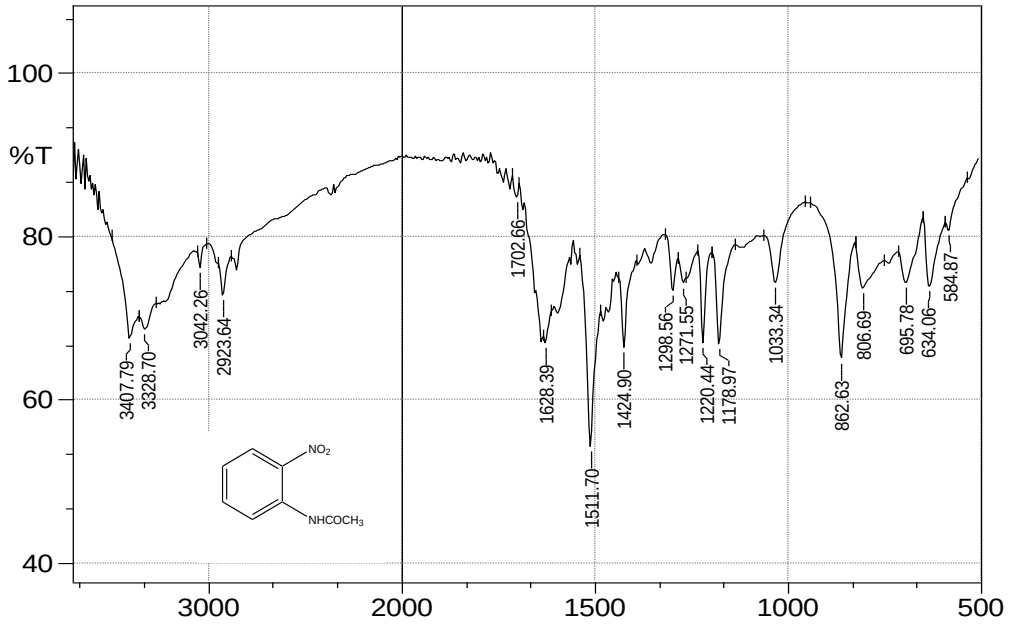


Figure 2: FTIR spectra of ST03

FT-IR range: 3407 cm^{-1} (NH str secondary amine), 2923 cm^{-1} (CH str aromatic), 1628 cm^{-1}(C=C str aromatic), 1511 cm^{-1}(N=O str carbonyl).

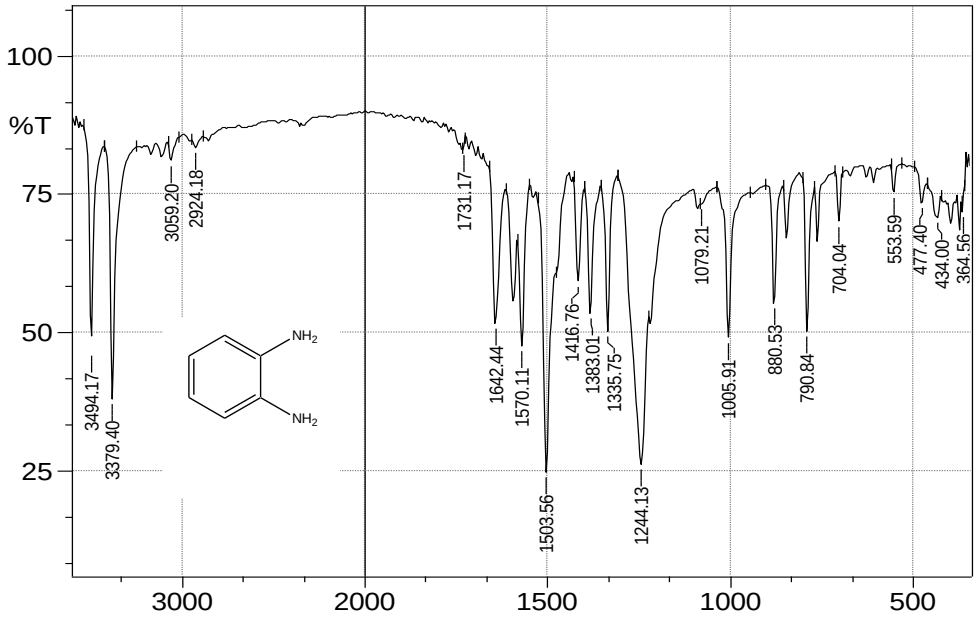


Figure 3: FTIR spectra of ST04

FTIR Range: 3494 and 3379 cm^{-1} (NH str secondary amine), 2924 cm^{-1} (CH str aromatic), 1642 cm^{-1}(C=C str aromatic), 1503 cm^{-1}(N=C str).

B. IR and NMR spectra of synthesized substituted compounds (1-12)

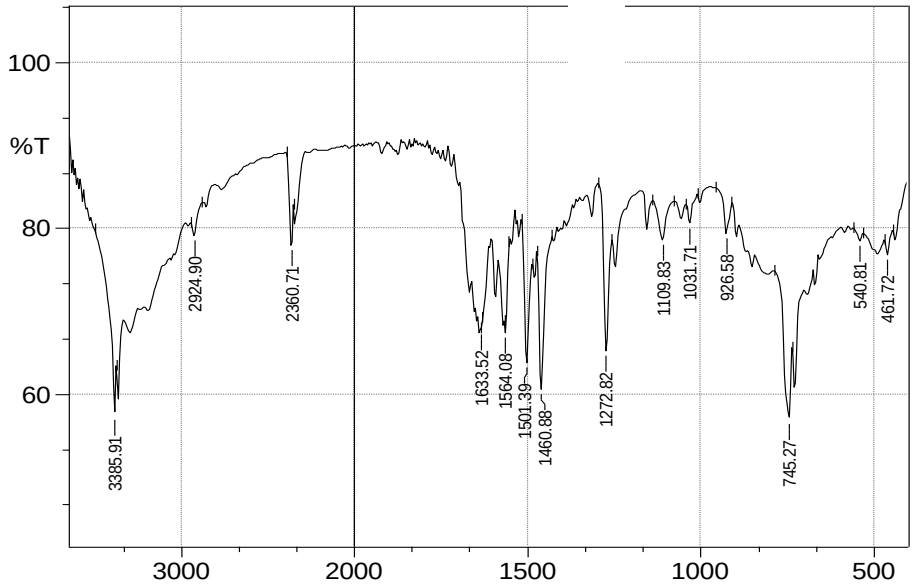


Figure 4: FT-IR spectra of compound **1**

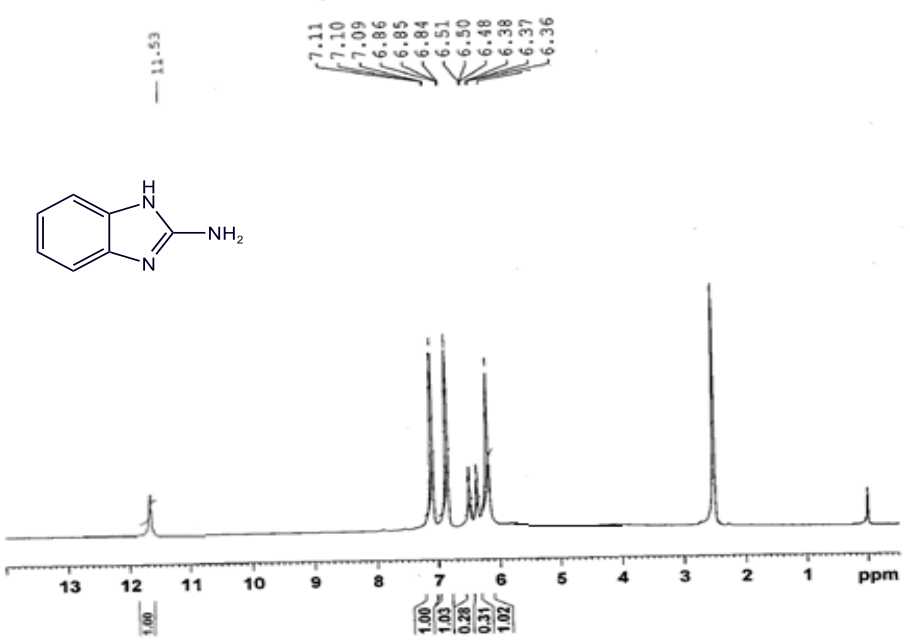
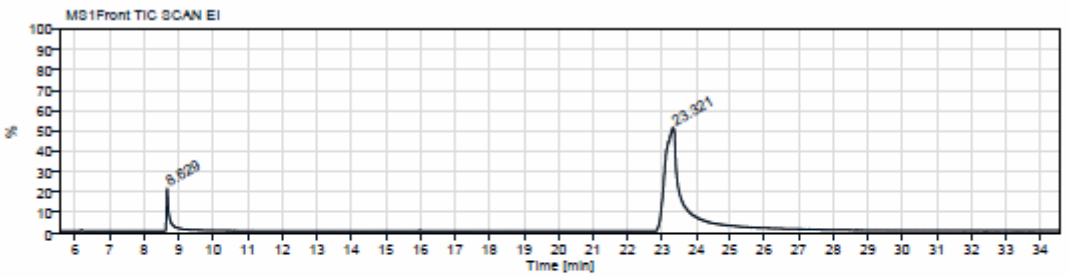


Figure 5: 1H-NMR of compound 1



Peak Results (Area Percent at least 1%)

RT (min)	Signal Description	Width (min)	Area	Height	Area%
8.629	MS1Front TIC SCAN EI	0.519	1773577.1	330572.8	9.93
23.321	MS1Front TIC SCAN EI	0.877	16091746.7	697951.1	90.07
	Sum MS1Front TIC SCAN EI		17865323.8		

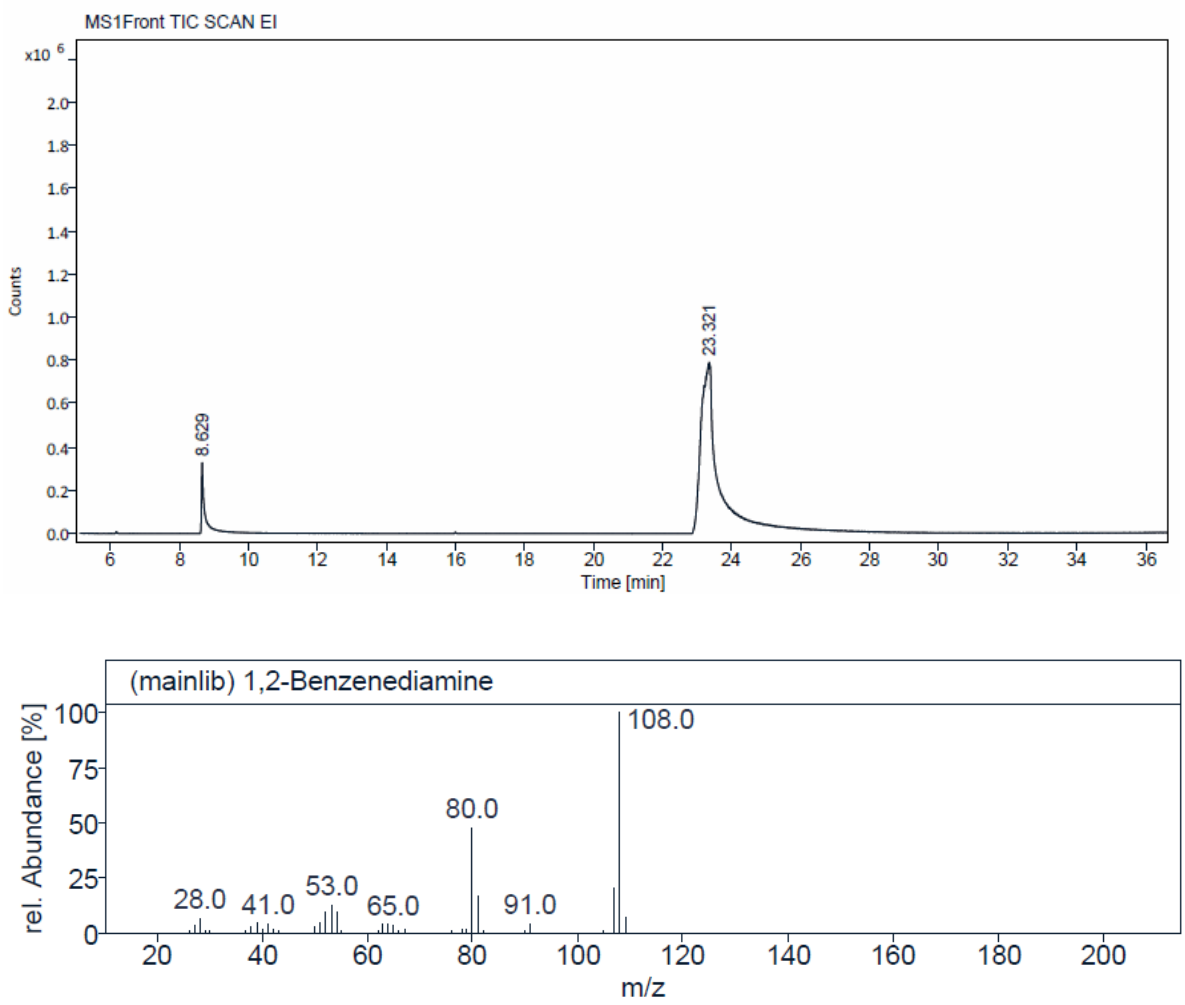


Figure 6: GCMS data with library search results for compound **1**.

1H-1,3-benzodiazol-2-amine **(1)**. White powder. Yield: 60%; MP: 180-182℃; R_f: 0.76 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}):), 3429 cm^{-1} (N-H primary amine str), 3371 cm^{-1} (NH str secondary amine), 3140 cm^{-1} (CH str heterocyclic ring), 2945 cm^{-1} (CH str aromatic), 1700 cm^{-1}(C=C str aromatic), 1697 cm^{-1}(N=C str); ^{1}H NMR (400 MHz, DMSO) δ ppm 6.36−7.11 (m, 4H, aromatic-H), 11.53 (s, 2H, amine-NH_2); GCMS, m/z =133 $(M+H)^+$.

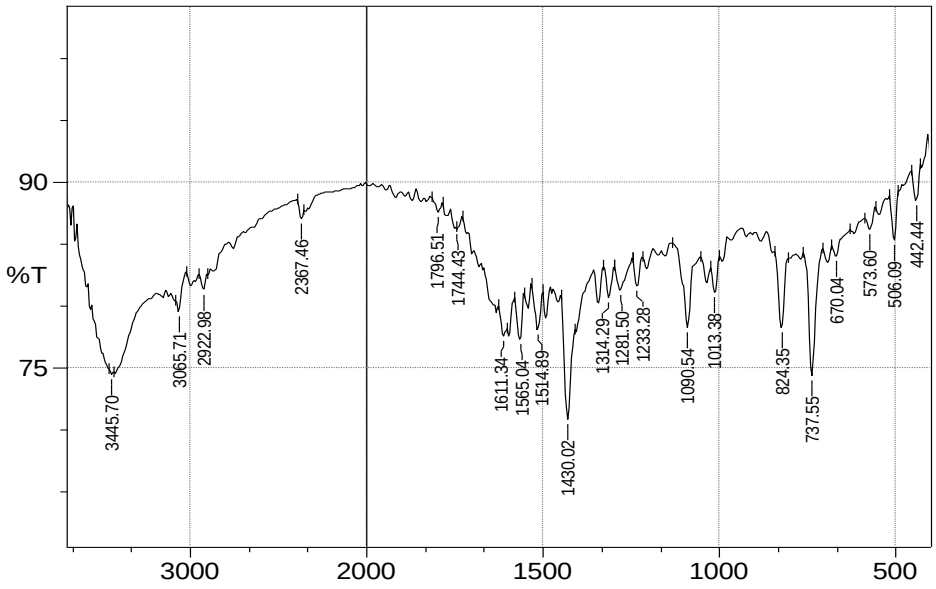


Figure 7: FT-IR spectra of compound 2

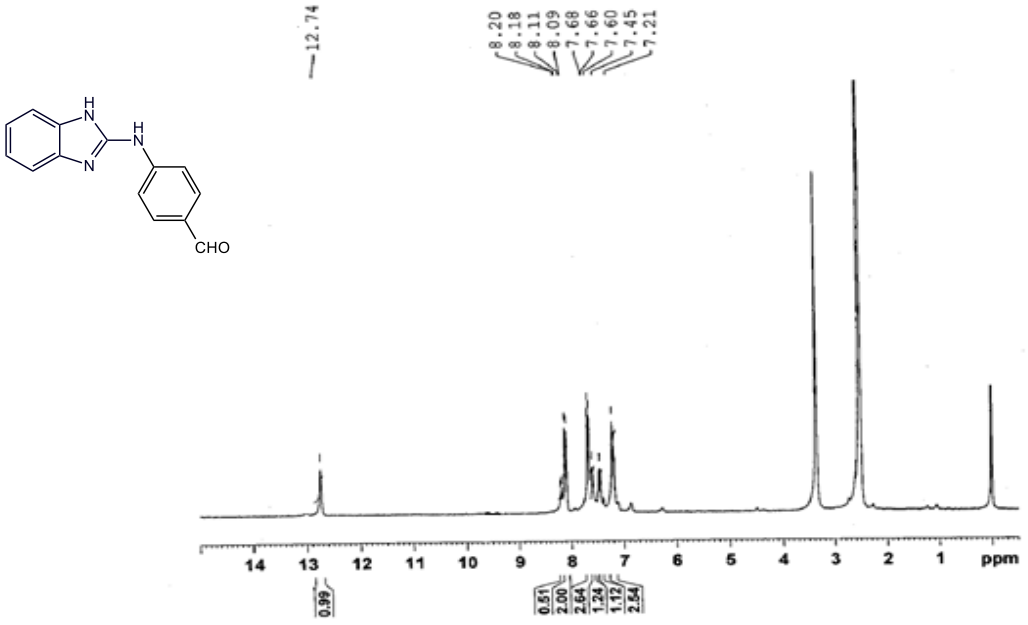


Figure 8: 1H-NMR of compound 2

4-[(1H-1,3-benzodiazol-2-yl) amino] benzaldehyde **(2).** Slightly white solid. Yield: 51%; MP: 220-222°C; R_f: 0.68 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3445 cm^{-1}(N-H str primary amine), 3064 cm^{-1} (C-H str heterocyclic ring), 2922 cm^{-1} (CH str aromatic), 1744 cm^{-1} (CHO str), 1611 cm^{-1} (C=C str aromatic), 1430 cm^{-1} (C=O str); ^{1}H NMR (400 MHz, DMSO) δ ppm 7.21(d, 2H, aromatic-H, J=7 Hz), 7.45 (d, 2H, aromatic-H, J=7 Hz), 8.09-8.20 (m, 4H, aromatic-H), 12.74 (s, 1H, aldehyde-H).

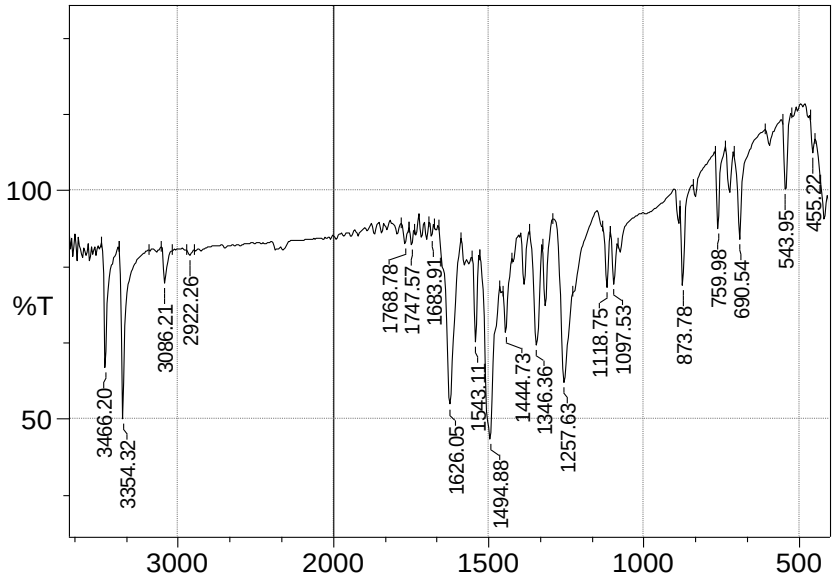


Figure 9: FT-IR spectra of compound 3

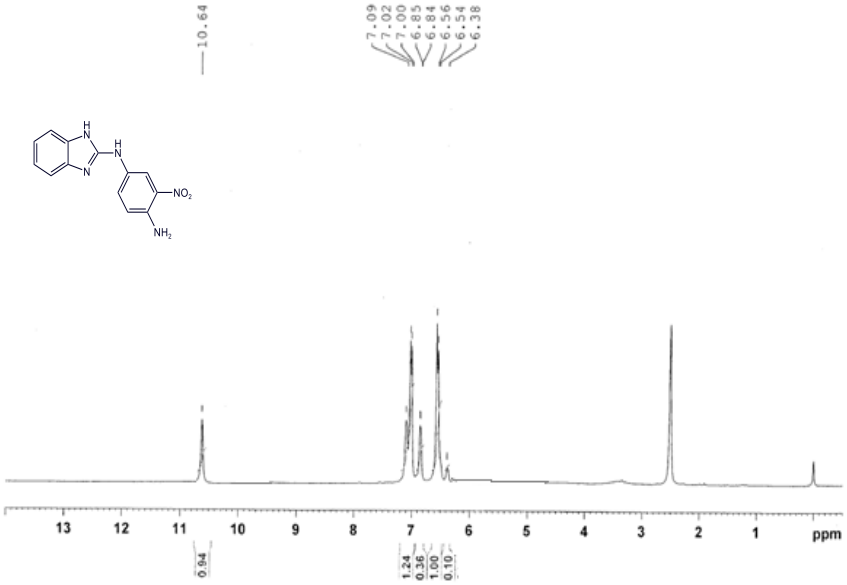


Figure 10: NMR spectra of compound 3

N1-(1H-1,3-benzodiazol-2-yl)-3-nitrobenzene-1,4-diamine **(3)**. Yield: 52%; MP: 132-134°C; R_f: 0.91; FT-IR (KBr, cm^{-1}): 3466 cm^{-1} (NH str), 3354 cm^{-1} (NH_2 str), 2922 cm^{-1} (C-H aromatic), 1626 cm^{-1} (C=C str aromatic), 1543 cm^{-1} (NO_2 Asy), 1336 cm^{-1} (NO_2 sym); ^1H NMR (400 MHz, DMSO) δ ppm 6.54-6.85 (d, 3H, nitroaniline ring, aromatic-H, J= 6 Hz), 7.00-7.09 (m, 4H, benzimidazole ring aromatic-H), 10.64 (s, 2H, amine-NH_2).

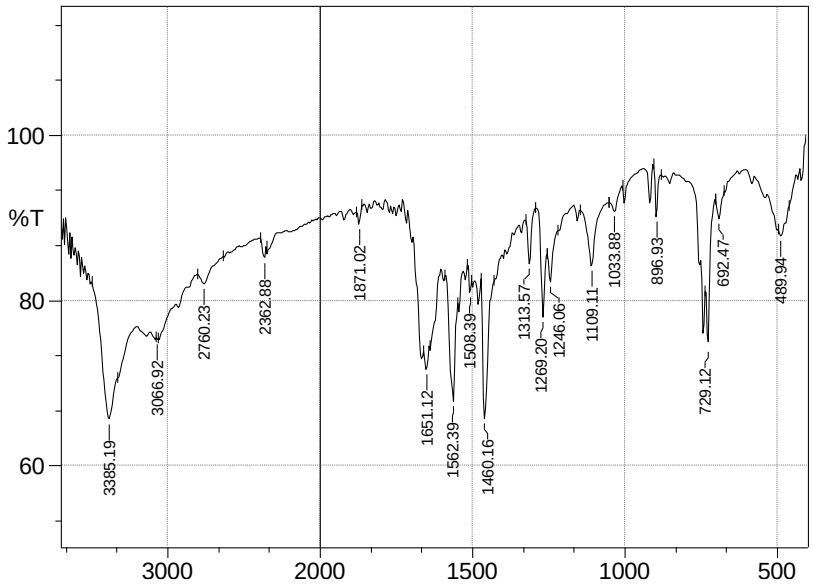


Figure 11: FT-IR spectra of compound 4

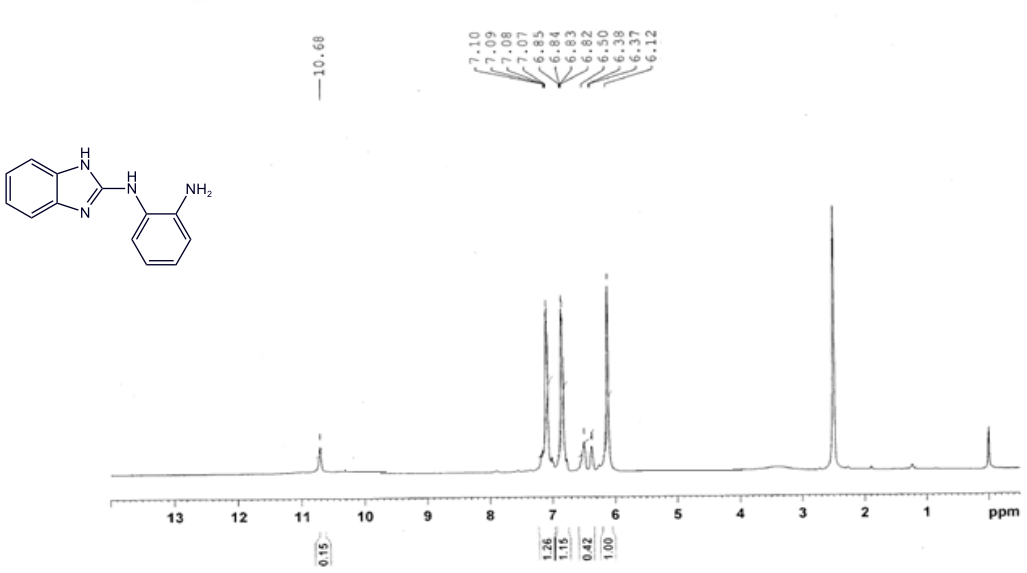


Figure 12: 1H-NMR of compound **4**

N1-(1H-1,3-benzodiazol-2-yl) benzene-1,2-diamine **(4)**.Yield: 60%; MP: 200-202℃; R_f: 0.32 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3385 cm^{-1} (NH_2 str), 3066 cm^{-1} (C-H str aromatic), 1652 cm^{-1} (C=C str aromatic); ^{1}H NMR (400 MHz, DMSO) δ ppm 6.37-6.85 (m, 4H, aniline ring, aromatic-H), 7.07-7.10 (m, 4H, benzimidazole ring aromatic-H), 10.68 (s, 2H, amine-NH_2).

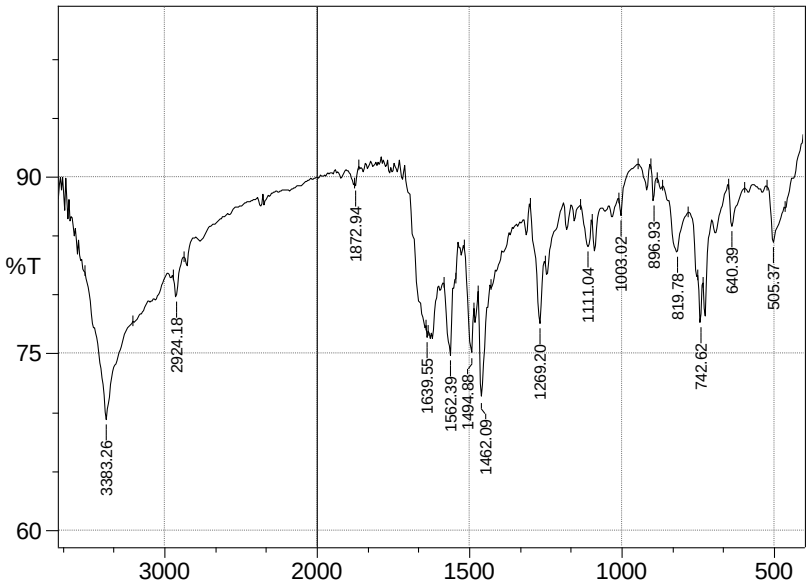


Figure 13: FT-IR spectra of compound **5**

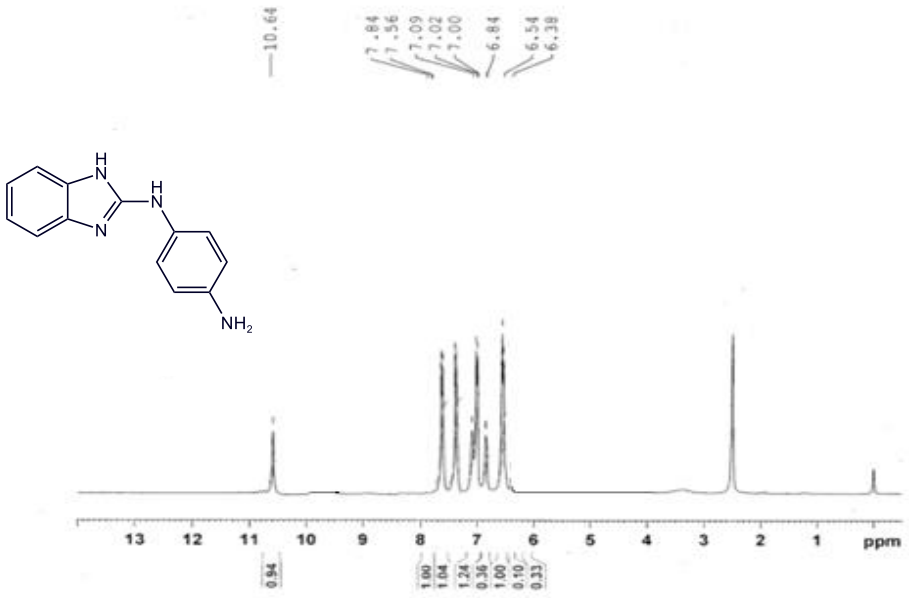


Figure 14: 1H-NMR of compound **5**

N1-(1H-1,3-benzodiazol-2-yl) benzene-1,4-diamine **(5)**. Yield: 74%; MP: 90-92°C; R_f: 0.84 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3383 cm^{-1} (NH_2 str), 2924 cm^{-1} (C-H aromatic), 1639 cm^{-1} (C=C str aromatic); ^{1}H NMR (400 MHz, DMSO) δ ppm 6.38-7.00 (m, 4H, benzimidazole ring aromatic-H), 7.02-7.84 (m, 4H, aniline ring, aromatic-H), 10.64 (s, 2H, amine-NH_2).

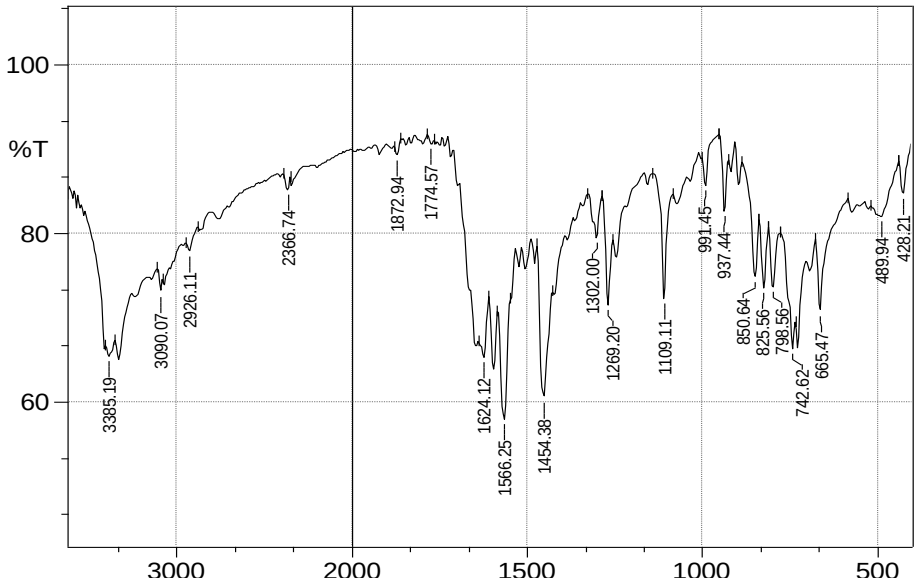


Figure 15: FT-IR spectra of compound **6**

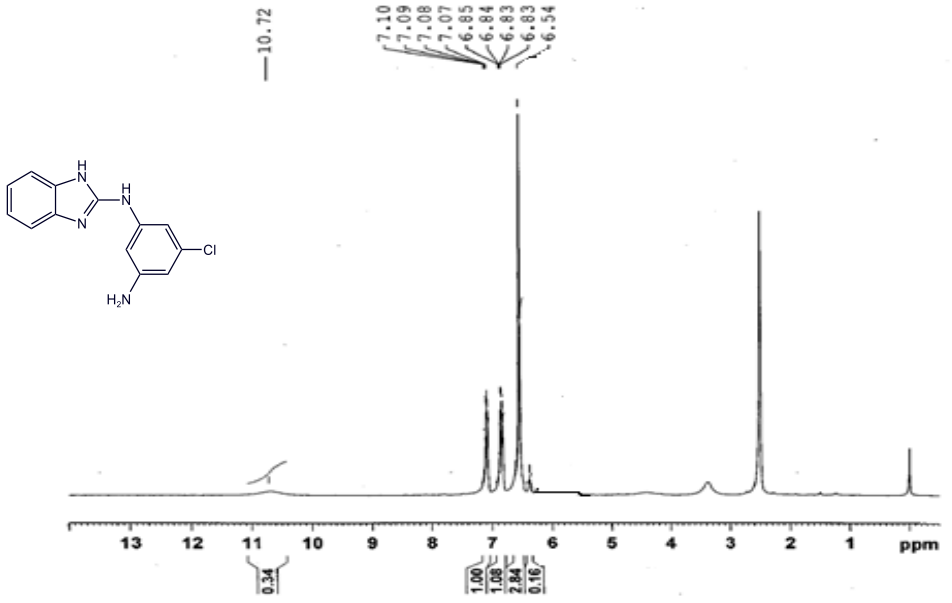


Figure 16: 1H-NMR of compound **6**

N1-(1H-1,3-benzodiazol-2-yl)-5-chlorobenzene-1,3-diamine (**6**). Yield: 58%; MP: 170-172°C; R_f: 0.74 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3385 cm^{-1} (NH_2 str), 3090 cm^{-1} (C-H str heterocyclic ring), 1872 cm^{-1}(C=C str aromatic), 1624 cm^{-1}(N=C str), 798.6 cm^{-1} (C-Cl str); ^{1}H NMR (400 MHz, DMSO) δ ppm 6.54-6.85 (m, 3H, chlorobenzene ring, aromatic-H), 7.07-7.10 (m, 4H, benzimidazole ring aromatic-H), 10.72 (s, 1H, amine-NH_2).

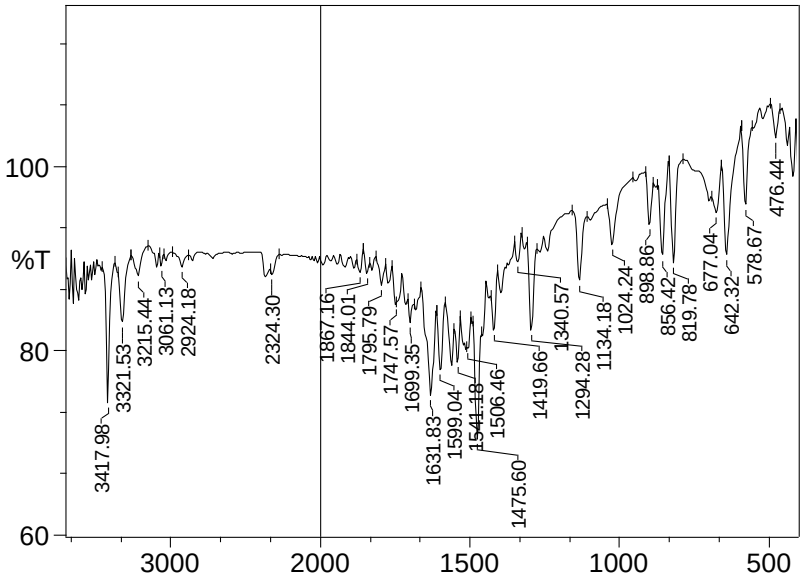


Figure 17: FT-IR spectra of compound **7**

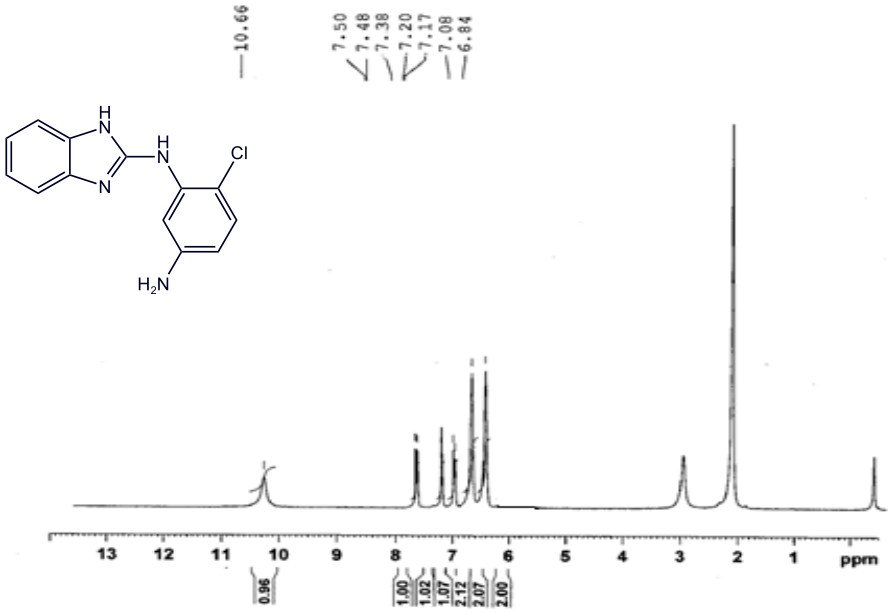


Figure 18: 1H-NMR of compound **7**

N1-(1H-1,3-benzodiazol-2-yl)-6-chlorobenzene-1,3-diamine (**7**). Yield: 51%; MP: 56-58°C; R_f: 0.50 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3417 cm^{-1} (NH_2 str), 3321 cm^{-1} (NH str), 3090 cm^{-1} (C-H str heterocyclic ring), 1872 cm^{-1}(C=C str aromatic), 1624 cm^{-1}(N=C str), 819 cm^{-1}(C-Cl str); ^{1}H NMR (400 MHz, DMSO) δ ppm 6.84-7.20 (m, 4H, benzimidazole ring aromatic-H), 7.38-7.50 (m, 3H, chlorobenzene ring, aromatic-H), 10.66 (s, 2H, amine-NH_2).

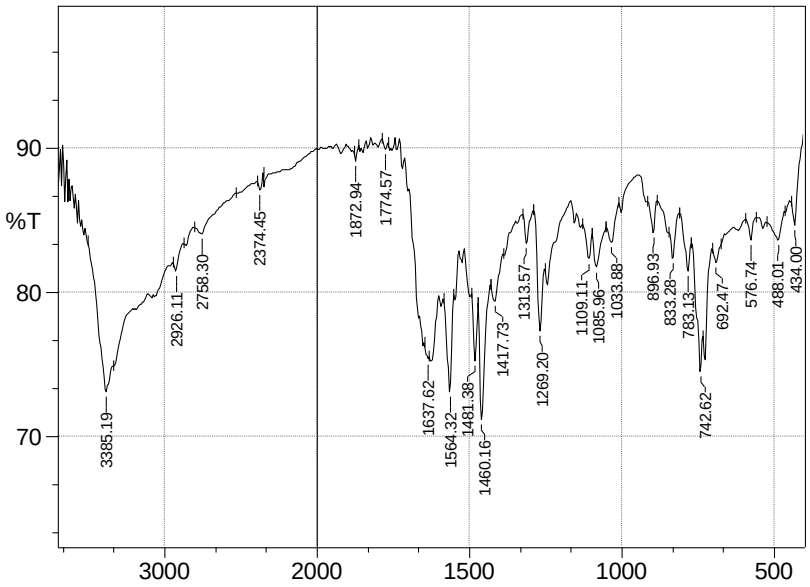


Figure 19: FT-IR spectra of compound **8**

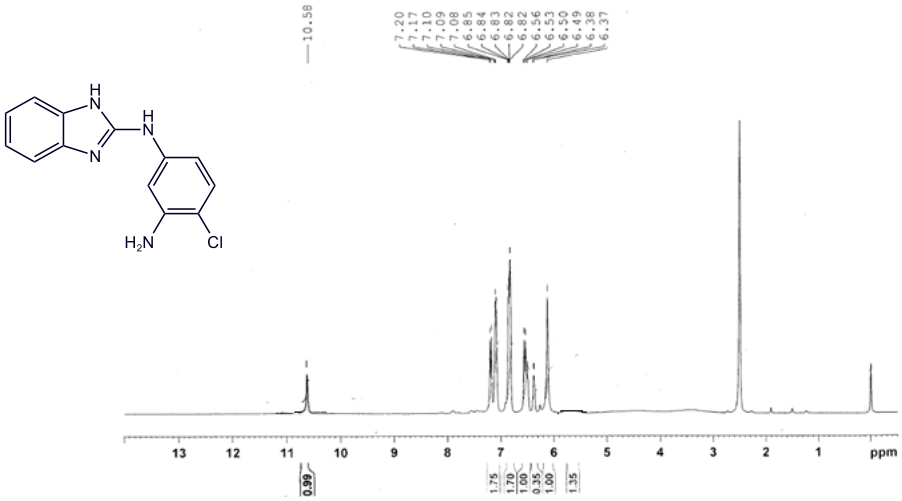


Figure 20: 1H-NMR of compound **8**

N1-(1H-1,3-benzodiazol-2-yl)-4-chlorobenzene-1,3-diamine (**8**). Yield: 72%; MP: 120-122℃; R_f: 0.83 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3385 cm^{-1} (NH_2 str), 3321 cm^{-1} (NH str), 2924 cm^{-1} (C-H aromatic), 1631 cm^{-1} (C=C str aromatic), 819 cm^{-1} (C-Cl); ^{1}H NMR (400 MHz, DMSO) δ ppm 6.53-6.85 (m, 4H, benzodiazole ring aromatic-H), 7.08-7.20 (m, 3H, chlorobenzene ring, aromatic-H), 10.58 (s, 2H, amine-NH_2).

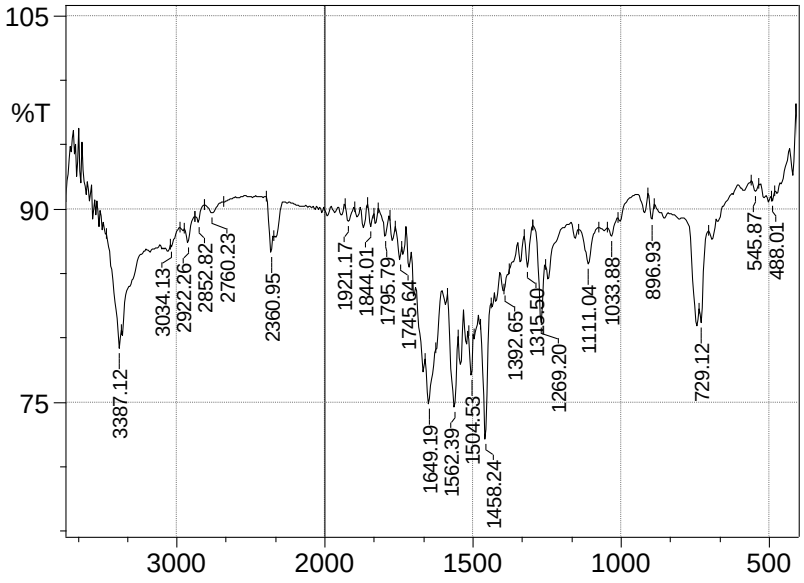


Figure 21: FT-IR spectra of compound **9**

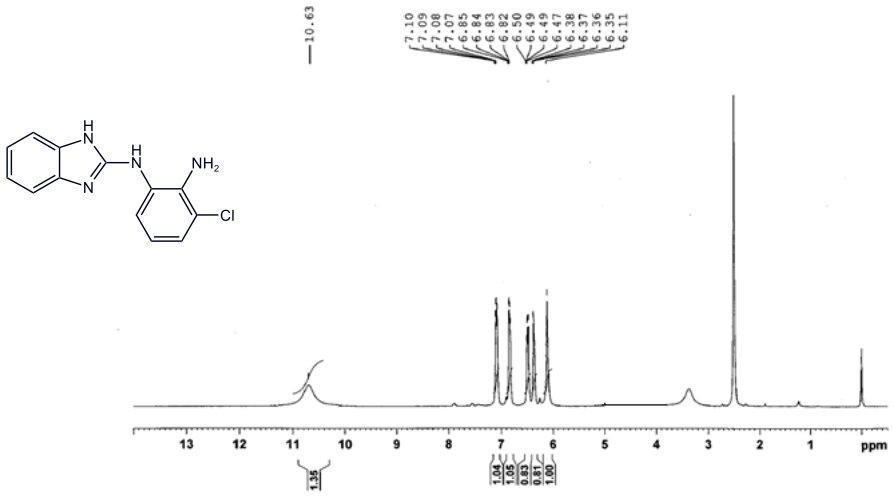


Figure 22: 1H-NMR of compound **9**

N1-(1H-1,3-benzodiazol-2-yl)-3-chlorobenzene-1,2-diamine (**9**). Yield: 56%; MP: 95-97°C; R_f: 0.75 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3387 cm^{-1} (NH_2 str), 2922 cm^{-1} (C-H aromatic), 1649 cm^{-1} (C=C str aromatic), 896 cm^{-1} (C-Cl str); ^1H NMR (400 MHz, DMSO) δ ppm 6.35-6.82 (m, 4H, benzimidazole ring aromatic-H), 7.70-7.78 (m, 3H, chloro aniline ring, aromatic-H), 10.69 (s, 2H, amine-NH_2).

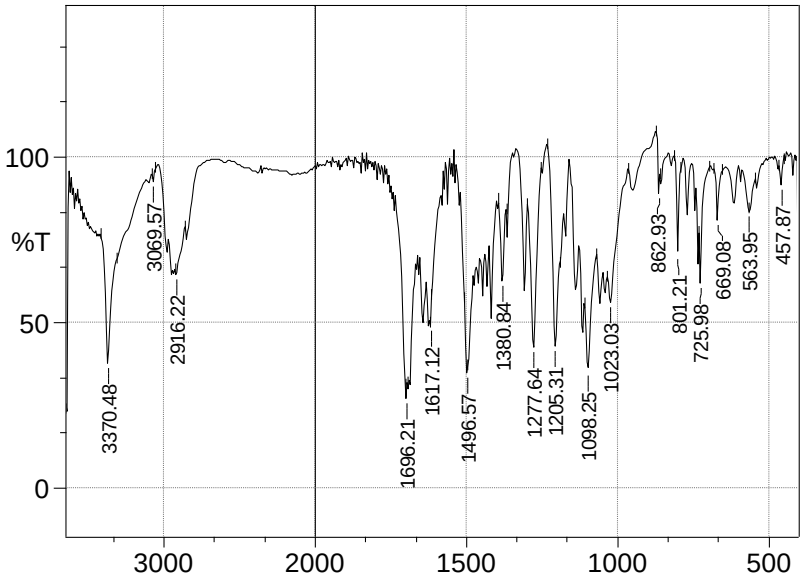


Figure 23: FT-IR spectra of compound **10**

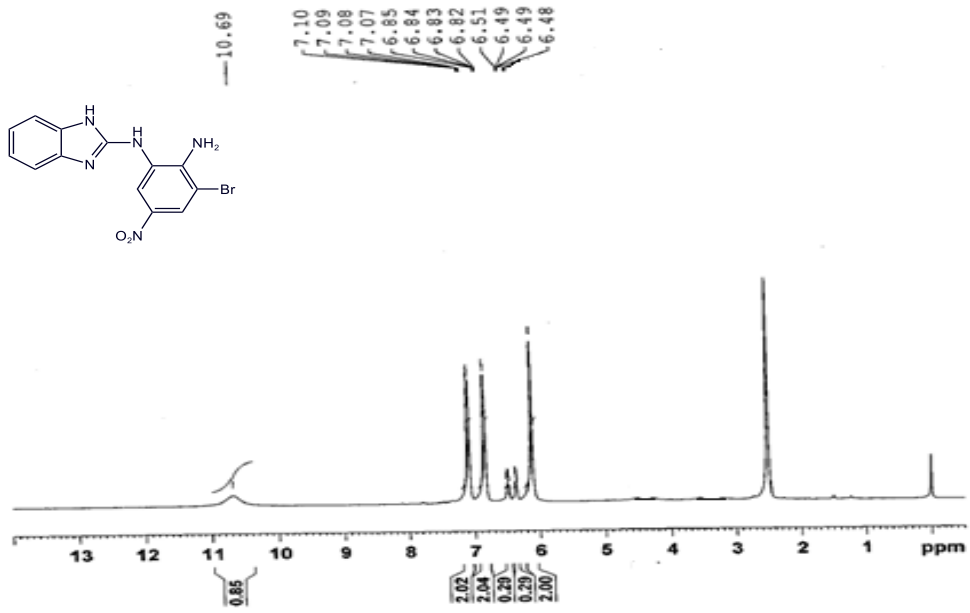


Figure 24: 1H-NMR of compound **10**

N1-(1H-1,3-benzodiazol-2-yl)-3-bromo-5-nitrobenzene-1,2-diamine (**10**). Yield: 56%; MP: 230-232℃; R_f: 0.82 (ethyl acetate: hexane. 3:1); FT-IR (KBr, cm^{-1}): 3370 cm^{-1} (NH_2 str), 3096 cm^{-1} (NH str), 2916 cm^{-1} (C-H aromatic), 1626 cm^{-1} (C=C str aromatic), 1543 cm^{-1} (NO_2 asy), 1462 cm^{-1} (NO_2 sym), 862 cm^{-1} (C-Br); ^1H NMR (400 MHz, DMSO) δ ppm 7.40-7.55 (m, 4H, benzodiazole ring aromatic-H), 7.78 (d, 2H, bromo aniline ring, aromatic-H, J=8 Hz), 10.69 (s, 2H, amine-NH_2).

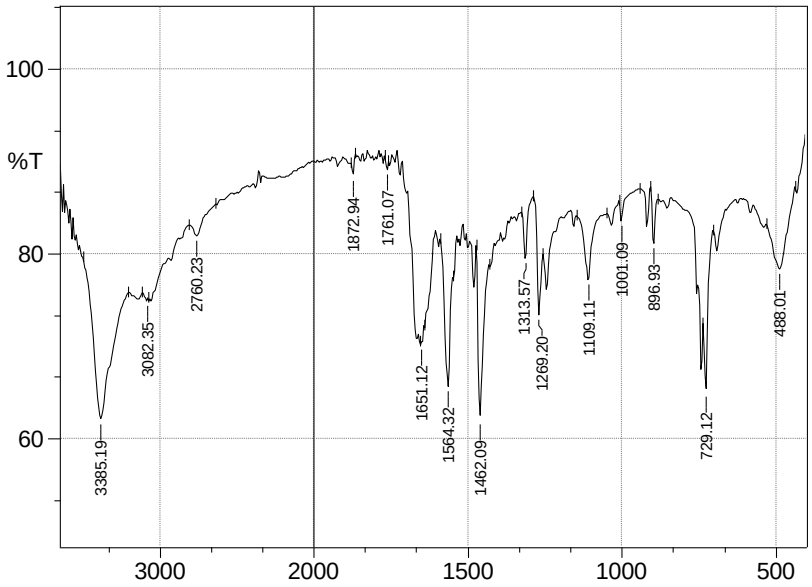


Figure 25: FT-IR spectra of compound **11**

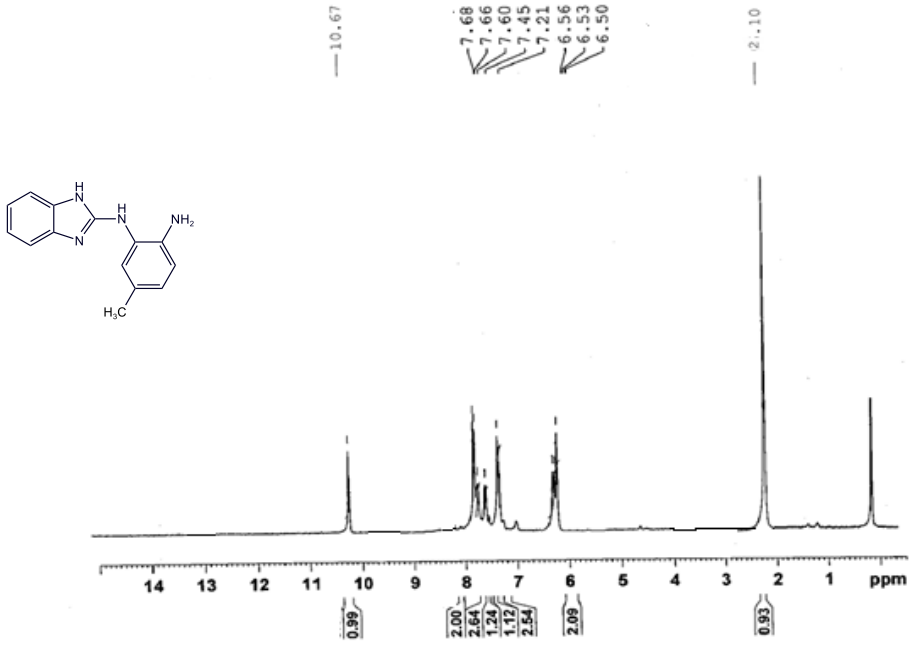


Figure 26: 1H-NMR of compound **11**

N1-(1H-1,3-benzodiazol-2-yl)-5-methylbenzene-1,2-diamine (**11**). Yield: 51%; MP: 226-228°C; R_f: 0.42 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3385 cm^{-1} (NH_2 str), 3097 (C-H str heterocyclic ring), 3082 cm^{-1} (C-H aromatic), 1651 cm^{-1} (C=C str aromatic), 1564 cm^{-1} (N=C str), 896 (C-Cl str); ^{1}H NMR (400 MHz, DMSO) δ ppm 2.10 (s, 3H, CH_3), 6.50-7.21 (m, 4H, benzimidazole ring aromatic-H), 7.45-7.68 (m, 3H, aniline ring, aromatic-H), 10.67 (s, 2H, amine-NH_2).

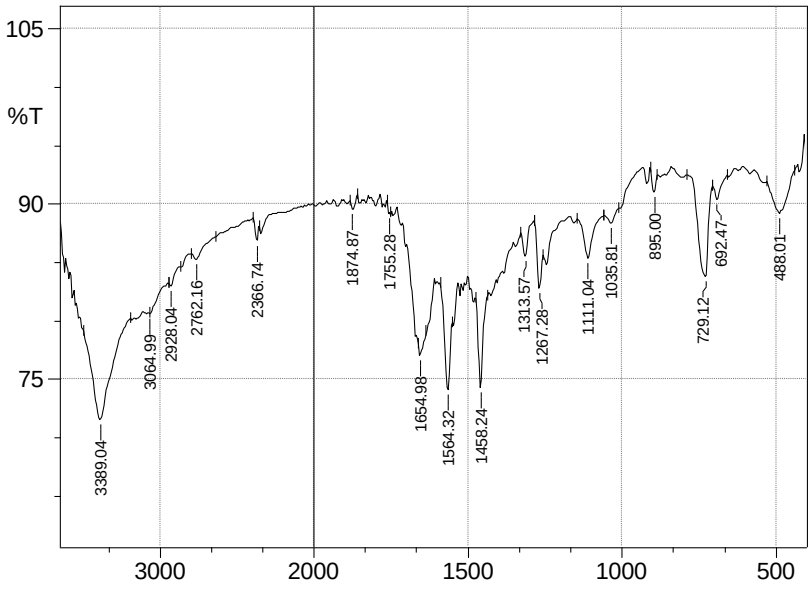


Figure 27: FT-IR spectra of compound **12**

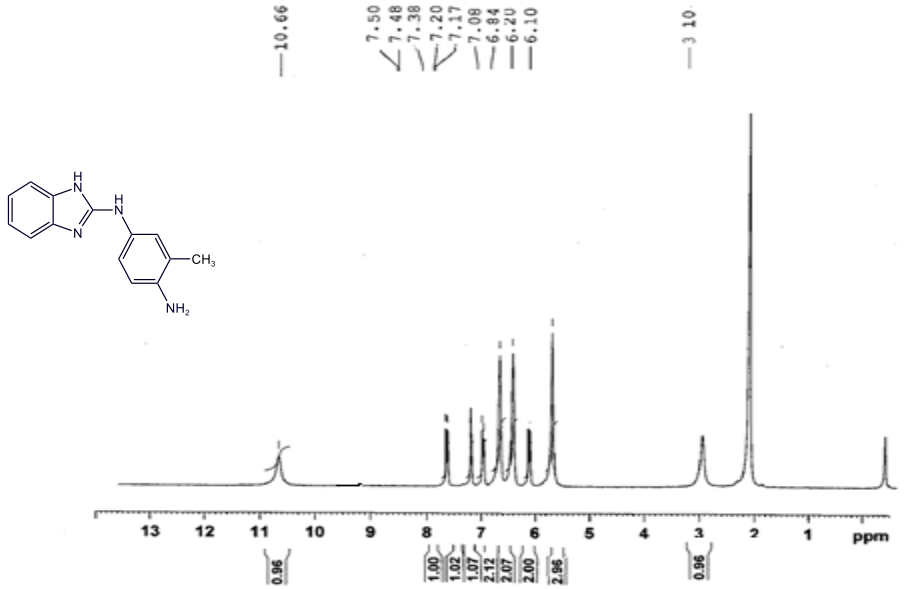


Figure 28: 1H-NMR of compound **12**

N1-(1H-1,3-benzodiazol-2-yl)-3-methylbenzene-1,4-diamine (**12**). Yield: 52%; MP: 234-236°C; R_f: 0.86 (ethyl acetate: hexane, 3:1); FT-IR (KBr, cm^{-1}): 3389 cm^{-1} (NH_2 str), 3064 (C-H str heterocyclic ring), 2928 cm^{-1} (C-H aromatic), 1654 cm^{-1} (C=C str aromatic), 1564 cm^{-1} (N=C str), 1280 cm^{-1} (C-F), 1267 cm^{-1} (C-O str); ^{1}H NMR (400 MHz, DMSO) δ ppm 3.10 (s, 3H, CH_3), 6.10-6.84 (m, 4H, benzodiazole ring aromatic-H), 7.17-7.50 (m, 3H, aniline ring, aromatic-H), 10.66 (s, 2H, amine-NH_2).