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Research Article

SYNTHESIS, SPECTROSCOPIC CHARACTERIZATION AND *IN VITRO* ANTIMICROBIAL EVALUATION OF NOVEL PYRROLO BENZIMIDAZOLE DERIVATIVES

Sanjay K Patil[1*], Sunil S Patil[1],

Sudhakar A Nirmalkar[1] and Vaishali S Nirmalkar[2]

[1]Department of Chemistry, Changu Kana Thakur Arts, Commerce & Science College, New Panvel, Maharashtra-410 206, India.
2Department of Botany, G. M. Momin Women's College, Bhiwandi-421 302, Thane, Maharashtra, India.

ABSTRACT

A series of Pyrrolo Benzimidazole derivatives were synthesized by reaction of 4/ - cyano - 3/ - oxo - 2/ - dihydro - 1*H* – pyrrolo [1,2-*a*] benzimidazole **1(a-b)** with chloroacetyl chloride formed *N*-chloroacetyl coumpounds **2(a-b)** which on further treated with thiourea affords 2-aminothiozole compounds **3(a-b)** which on treatment with methyl iodide in presence of tri-ethyl amine gave *N, N* - dimethyl-aminothiozole compounds **4(a-b)** which were treated with Hydrochloric acid formed 4-amide derivatives of pyrrolobenzimidazole **5(a-b)**. **4(a-b)** treated with sodium azide and ammonium chloride in DMF formed tetrazole compounds **6(a-b)**. All synthesized novel derivatives were characterized by Spectral and Elemental analysis. These benzimidazole derivatives were tested against fungi, Gram-positive and Gram-negative bacteria. These compounds showed remarkable antimicrobial and fungicidal activity.

Keywords: 2-aminothiazole, antimicrobial activity, fungicidal activity, pyrrolobenzimidazole.

INTRODUCTION

Benzimidazoles are biologically important molecules and they are very useful for the synthesis of pharmaceutically active compounds. 1 or 2 position substituted benzimidazoles derivatives shows wide-ranging therapeutic applications[1-7]. Aminothiazole commonly used as precursor for the synthesis of many active compounds including sulpha drugs, biocides, fungicides. 2-Aminothiazole has antibacterial activity[8] and also used as a therapeutic drug for prion diseases[9]. Amide derivatives exhibit variety of biological activities like antibacterial[10-11], antifungal[12]. Tetrazole derivatives exhibit different biological activities such as antimicrobial[13], antiviral [14], antiallergic[15] and anti- Inflammatory[16]. When aminothiazole, amides and tetrazole are conjugates with other heterocyclic compound, enhance biological activity. Hence during extensive work on synthesis of Benzimidazole analogs, substituted aminothiazole, amide and tetrazole with pyrrolobenzimidazoles were synthesized.

MATERIALS AND METHODS

The reactions were monitored by TLC using 0.25 mm E-Merck silica gel plates, which were visualized in Iodine Chamber. Melting points were taken in open capillaries and are uncorrected. ^{1}H NMR spectra was performed in DMSO-d6 on 300 MHz using TMS as an internal standard.

Synthesis of Compounds 4/-Cyano-2/-dihydro-3/-oxo-3-(2-chloroacetyl)-1*H*-pyrrolo[1,2-*a*] benzimidazole 2(a-b)

Triethyl amine (6.20g, 0.060 mole) was added to the solution of 4/-cyano-3/-oxo-2/-dihydro-1*H*-pyrrolo [1,2-*a*]benzimidazole **1(a-b)** (10.0g,

0.050 mole) in dry benzene (50 ml) and stirred for 30min at room temperature. The reaction mass was chilled at 0-5^0 C then chloroacetyl chloride was added (6.0g, 0.053 mole) under stirring below 5^0 C. The reaction mass was subsequently refluxed for 4 h on water bath. The completion of the reaction was monitored by TLC using n-hexane: ethyl acetate (7:3) as a solvent system. The solvent was removed under reduced pressure and the residue was poured into water. The solid obtained was recrystallized by methanol to get pure product 4$^{/}$-cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2-chloroacetyl)-1*H*-pyrrolo[1,2-*a*]benzimidazole **2(a-b)**.

4$^{/}$-Cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-amino-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*] benzimidazole 3(a-b)

Brown powder of 4$^{/}$-cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2-chloroacetyl)-1*H*-pyrrolo[1,2-*a*]benzimidazole **2(a-b)** (5.5g, 0.02 mole) was added in dry acetone (50 ml) and stirred for 10 min. Then thiourea (1.53 g, 0.02 mole) was added and refluxed for 8 h. The completion of the reaction was monitored by TLC using n-hexane: ethyl acetate (7:3) as solvent system. After completion of reaction excess of acetone was distilled off and the residue obtained was poured into crushed ice which was filtered, dried and recrystallized from methanol which gave 4$^{/}$-cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-amino-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*] benzimidazole 3**(a-b)**.

4$^{/}$-Cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-(dimethyl amino)-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole 4(a-b)

To the solution of 4$^{/}$-cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-amino-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*] benzimidazole 3**(a-b)** (10.0g. 0.033 mole) in DMF (10 ml) triethyl amine (4.2 g, 0.041 mole) was added at room temperature. Then methyl iodide (10.0 g, 0.070 mole) was added into the reaction mixture and stirred at room temperature. The completion of the reaction was monitored by TLC using n-hexane: ethyl acetate (5:5) as a solvent system. The reaction was accomplished within 5 h at room temperature. After accomplished reaction water was added in the reaction mass resulting into brown coloured precipitate which was separated by filtration. The crude solid was recrystallized from ethanol/water (4:1) to get pure product of 4$^{/}$-cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-(dimethylamino)-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole 4(a-b).

4$^{/}$-Carbamoyl-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-(dimethylamino)-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole 5(a-b)

4$^{/}$-cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-(dimethylamino)-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole 4(a-b) (10 g, 0.031 mole) and conc. HCl (40 ml) was immersed in the flask at 40^0 C. The reaction mixture was stirred vigorously at 40^0 C for 3 h. The progress and completion of the reaction was monitored by TLC using n-hexane: ethyl acetate (5:5) as a solvent system. After completion of reaction, reaction mass was poured onto ice-water afford 4$^{/}$-carbamoyl-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-(dimethylamino)-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole 5(a-b). The obtained solid was filtered off, washed with cold water, dried and recrystallized from ethanol.

3-(2$^{//}$-(dimethylamino)-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-2$^{/}$-dihydro-4$^{/}$-[(1$^{//}$-H(1$^{///}$2$^{///}$,3$^{///}$,4$^{///}$) tetrazol] -3$^{/}$-oxo-1*H*-pyrrolo[1,2-*a*]benzimidazole 6(a-b)

Process for preparation of tetrazoles was as per US 5744612 A Ref. [17]

Sodium azide (3.0 g, 0.046 mole) and ammonium chloride (2.50 g, 0.046 mole) was stirred at room temperature in 50 ml xylene. To this reaction mixture powder of 4$^{/}$-cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2$^{//}$-(dimethylamino)-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole 4(a-b) (10.0 g, 0.031 mole) was added at room temperature, then the reaction mixture was heated with stirring at 125 to 130°C. The progress and completion of reaction was monitored by TLC using n-hexane: ethyl acetate (5:5) as a solvent system. After completion of the reaction, the reaction mixture was cooled to 100° C. After the solvent under reduced pressure was distilled out, oily mass was obtained. To this, 50 ml water and 36 % hydrochloric acid (5.0g, 0.048 mole) were added, thus precipitate was obtained**.** The precipitate was filtered, dried and recrystallized from ethanol gave 3-(2$^{//}$-(dimethylamino)-1$^{//}$,3$^{//}$-thiazol-4$^{/}$-yl)-2$^{/}$-dihydro-4$^{/}$-[(1$^{//}$-H(1$^{///}$2$^{///}$,3$^{///}$,4$^{///}$)tetrazol]-3$^{/}$-oxo-1*H*-pyrrolo[1,2-*a*]benzimidazole 6(a-b).

Characterization of Synthesized Compounds

4$^{/}$-Cyano-2$^{/}$-dihydro-3$^{/}$-oxo-3-(2-chloroacetyl)-1*H*-pyrrolo[1,2-*a*]benzimidazole (2a)

Molecular Formula: $C_{13}H_8ClN_3O_2$, Melting Point: 201-204ºC, Yield: 65 %, Elemental Analysis % (Calculated) Found: C (57.09) 57.19, H (2.95) 3.01, N (15.35) 15.51. IR (KBr): 2996 (CH), 2245 (CN), 1747 (>C=O), 1650 (HN>C=O), 1559, 1203, 1060,760 cm^{-1}.^{1}H NMR (DMSO-*d*6): δ 3.63 (s, 2H, CH_2), δ 4.06 (s, 2H, CH_2), δ 6.64-6.90 (m, 4H, Ar-H). M^{+2}: 273.67.

4^{I}-cyano-2^{I}-dihydro-3^{I}-oxo-5-fluoro-3-(2-chloroacetyl)-1*H*-pyrrolo[1,2-*a*]benzimidazole (2b)

Molecular Formula: $C_{13}H_8ClFN_3O_2$, Melting Point: 204-208ºC, Yield: 65%, Elemental Analysis % (Calculated) Found: C (53.53) 53.45, H (2.42) 2.57, Cl ((12.16) 12.23,F (4.73) 4.77, N (14.41)14.31. IR (KBr): 2966 (CH), 2258 (CN), 1730 (>C=O), 1660 (HN>C=O), 1556, 1213, 1040,765 cm^{-1}. ^{1}H NMR (DMSO-*d*6): δ 3.65 (s, 2H, CH_2), δ 4.16 (s, 2H, CH_2), δ 6.69-6.90 (m, 3H, Ar-H). M^{+2}: 291.66.

4^{I}-cyano-2^{I}-dihydro-3^{I}-oxo-3-(2^{II}-amino-1^{II},3^{II}-thiazol-4^{I}-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole (3a)

Molecular Formula: $C_{14}H_9N_5OS$, Melting Point: 188-192ºC, Yield: 55%, Elemental Analysis % (Calculated) Found: C (56.94) 57.05, H (3.07) 3.29, N (23.71) 23.61, S (10.86) 10.65. IR (KBr): 3512 (NH_2), 3040 (CH), 2257 (CN), 1760 (>C=O), 1550, 1185, 1079 cm^{-1}. ^{1}H NMR (DMSO-d6/TMS): at δ 3.88 (s, 2H, CH_2), δ 5.22 (s, 1H, CH), δ 6.60-6.90 (m, 4H, Ar-H), δ 5.85 (s, 2H, NH_2, D_2O exchangeable). M^{+1}: 295.37.

4^{I}-cyano-2^{I}-dihydro-3^{I}-oxo-5-fluoro-3-(2^{II}-amino-1^{II},3^{II}-thiazol-4^{I}-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole (3b)

Molecular Formula: $C_{14}H_8FN_5OS$, Melting Point: 276-277ºC, Yield: 55%, Elemental Analysis % (Calculated) Found: C (53.67) 53.55, H (2.57) 2.47, N (22.35) 22.21, F (6.06) 6.15, S (10.23) 10.23. IR (KBr): 3440 (NH_2), 2980 (CH), 2235 (CN), 1737 (>C=O), 1540, 1175, 1069 cm^{-1}. ^{1}H NMR (DMSO-d6/TMS): at δ 3.93 (s, 2H, CH_2), δ 5.19 (s, 1H, CH), δ 6.70-6.80 (m, 3H, Ar-H), δ 5.65 (s, 2H, NH_2, D_2O exchangeable). M^{+1}: 313.33.

4^{I}-cyano-2^{I}-dihydro-3^{I}-oxo-3-(2^{II}-(dimethylamino)-1^{II},3^{II}-thiazol-4^{I}-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole (4a)

Molecular Formula: $C_{16}H_{15}N_5OS$, Melting Point: 193-198ºC, Yield: 55%, Elemental Analysis % (Calculated) Found: C (59.43) 59.33, H (4.02) 4.09, N (21.66) 21.51, S (9.92) 10.01. IR (KBr): 3022 (CH), 2241 (CN), 1757 (>C=O), 1556, 1185, 1071 cm^{-1}.^{1}H NMR (DMSO-d6/TMS): at δ 2.78 (s, 6H, N-CH_3), δ 3.90 (s, 2H, CH_2), δ 5.45 (s, 1H, CH), δ 6.45-6.90 (m, 4H, Ar-H). M^{+1}: 323.37.

4^{I}-cyano-2^{I}-dihydro-3^{I}-oxo-5-fluoro-3-(2^{II}-(dimethylamino)-1^{II},3^{II}-thiazol-4^{I}-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole (4b)

Molecular Formula: $C_{16}H_{15}N_5FOS$, Melting Point: 188-192ºC, Yield: 55%, Elemental Analysis % (Calculated) Found: C (56.3) 56.55, H (3.54) 3.45, N (20.52) 20.52, F (5.57) 5.62, S (9.39) 9.52. IR (KBr): 3012 (CH), 2232 (CN), 1747 (>C=O), 1545, 1188, 1062 cm^{-1}.^{1}H NMR (DMSO-d6/TMS): at δ 2.90 (s, 6H, N-CH_3), δ 3.98 (s, 2H, CH_2), δ 5.59 (s, 1H, CH), δ 6.36-7.76 (m, 3H, Ar-H). M^{+1}:341.62.

4^{I}-Carbamoyl-2^{I}-dihydro-3^{I}-oxo-3-(2^{II}-(dimethylamino)-1^{II},3^{II}-thiazol-4^{I}-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole (5a)

Molecular Formula: $C_{16}H_{15}N_5O_2S$, Melting Point: 180-184ºC, Yield: 62%, Elemental Analysis % (Calculated) Found: C (56.29) 56.01, H (4.43) 4.39, N (20.51) 20.31, S (9.39) 9.28. IR (KBr): 3446 (NH_2), 2891 (CH), 1759 (>C=O), 1640 (H_2NC=O), 1575, 1362, 1198 cm^{-1}. ^{1}H NMR (DMSO-d6/TMS): δ 3.28 (s, 3H, N-CH_3), δ 3.89 (s, 2H, CH_2), δ 4.20 (s, 2H, NH_2, D_2O exchangeable), δ 4.60 (s, 1H, CH), δ 6.65-6.95 (m, 4H, Ar-H). M^{+1}:341.39.

4^{I}-Carbamoyl-2^{I}-dihydro-3^{I}-oxo-3-(2^{II}-(dimethylamino)-1^{II},3^{II}-thiazol-4^{I}-yl)-1*H*-pyrrolo[1,2-*a*]benzimidazole (5b)

Molecular Formula: $C_{16}H_{14}N_5FO_2S$, Melting Point: 175-178ºC, Yield: 67%, Elemental Analysis % (Calculated) Found: C (53.47) 53.01, H (3.93) 4.09, F (5.29) 5.39, N (19.49) 19.31, S (9.39) 9.28. IR (KBr): 3460 (NH_2), 2972 (CH), 1745(>C=O), 1665 (H_2NC=O), 1560, 1316, 1184 cm^{-1}. ^{1}H NMR (DMSO-d6/TMS): δ 3.09 (s, 3H, N-CH_3), δ 3.89 (s, 2H, CH_2), δ 4.28 (s, 2H, NH_2, D_2O exchangeable), δ 4.75 (s, 1H, CH), δ 6.60-6.82 (m, 3H, Ar-H). M^{+1}:359.39.

3-(2^{II}-(dimethylamino)-1^{II},3^{II}-thiazol-4^{I}-yl)-2^{I}-dihydro-4^{I}-[(1^{II}-H(1^{III}2^{III},3^{III},4^{III})tetrazol]-3^{I}-oxo-1*H*-pyrrolo[1,2-*a*]benzimidazole (6a)

Molecular Formula: $C_{16}H_{14}N_8OS$, Melting Point: 210-214ºC, Yield: 56 %, Elemental Analysis % (Calculated) Found: C (52.45) 52.21, H (3.85) 3.96, N (30.58) 30.28, S (8.75) 8.68. IR (KBr): 3365 (NH), 3001 (CH), 1751 (>C=O), 1583, 1328, 1181 cm$^{1.}$ ^{1}H NMR (DMSO-d6/TMS): δ 3.21 (s, 3H, N-CH_3), δ 3.83 (s, 2H, CH_2), δ 5.19 (s, 1H, CH), δ 6.65-6.93 (m, 4H, Ar-H) and δ 8.48 (s, 1H, NH, D_2O exchangeable). M^{+1}:366.40.

3-(2^{II}-(dimethylamino)-1^{II},3^{II}-thiazol-4^{I}-yl)-6-Fluoro-2^{I}-dihydro-4^{I}-[(1^{II}-H(1^{III},2^{III},3^{III},4^{III}) tetrazol]-3^{I}-oxo-1*H*-pyrrolo[1,2-*a*]benzimidazole (6b)

Molecular Formula: $C_{16}H_{13}FN_8OS$, Melting Point: 195-198ºC, Yield: 57%, Elemental Analysis % (Calculated) Found: C (49.99) 50.01, H (3.41) 3.67, F (4.94) 5.09, N (29.15) 30.31, S (8.34)8.21. IR (KBr): 3350 (NH), 2981 (CH), 1726 (>C=O), 1561, 1323, 1156 cm^{-1}. ^{1}H NMR (DMSO-d6/TMS): δ 3.10 (s, 3H, N-CH_3), δ 3.89 (s, 2H, CH_2), δ 4.99 (s, 1H, CH), δ 6.55-

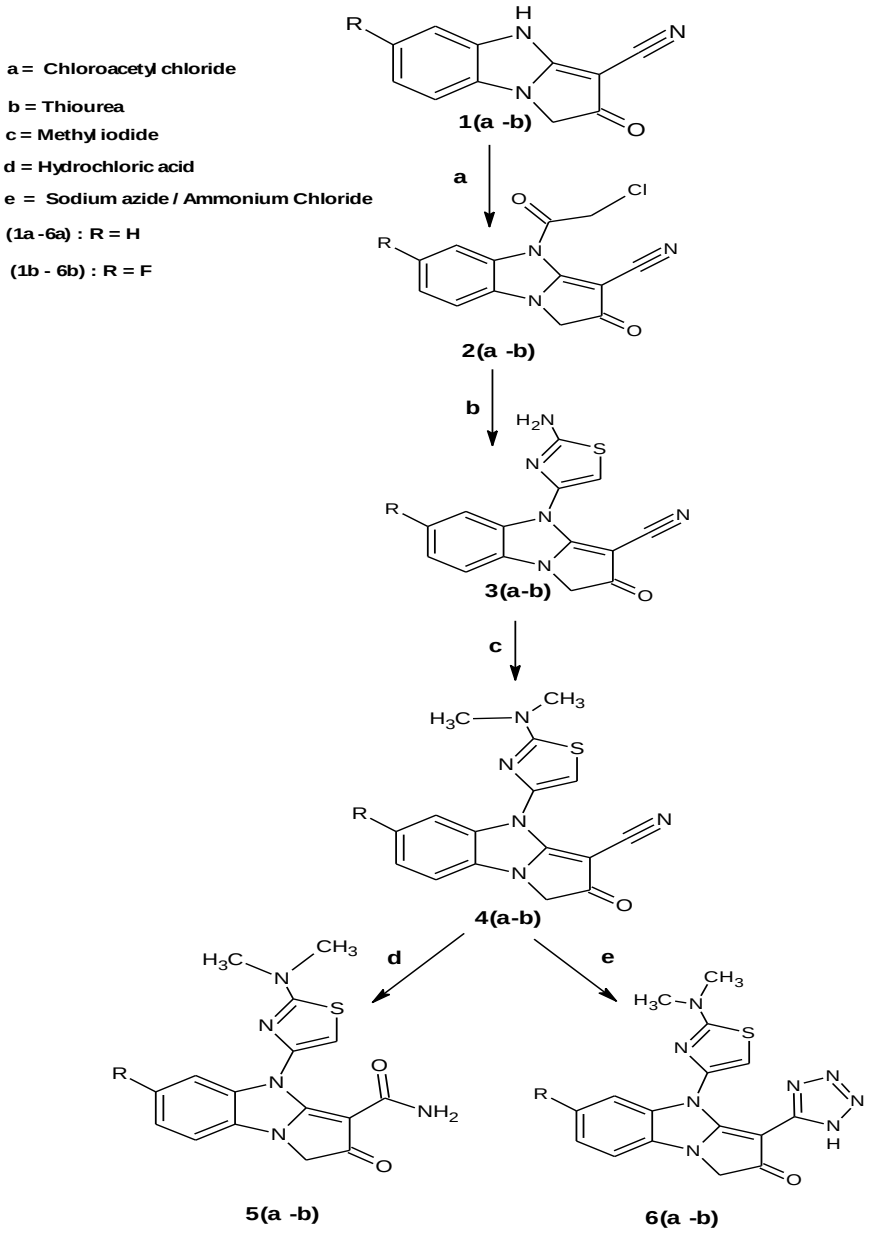
6.73 (m, 3H, Ar-H) and δ 8.32 (s, 1H, NH, D_2O exchangeable). M^{+1}:384.39.

Antibacterial activity

Antibacterial activity was evaluated by the paper disc method. The Muller-Hinton agar and 5 mm diameter paper discs of whatman paper no. 1 were used. The compounds were dissolved in DMSO. The filter paper discs were soaked in different concentrations (50 µg/ml and 100 µg/ml) of the compounds, dried and then placed in the petriplates previously seeded with the test organisms *Salmonella typhi, Escherichia coli* and *Staphylococcus aureus*. The plates were incubated for 24–30 h at 28±2°C and the inhibition zone around each disc was measured. The results are shown in Table: 1

Antifungal screening

The antifungal activity of the compounds was evaluated against *Aspergillus niger* by the paper disc method. The Sabouraud dextrose agar and 5 mm diameter paper discs of Whatman paper no.1 were used. The compounds were dissolved in DMSO. The filter paper discs were soaked in different solutions of the compounds, dried and then placed in the petriplates previously seeded with the test organisms *A. niger.* The plates were incubated for 48 h at 25±2°C and the inhibition zone around each disc was measured. The results are shown in Table: 1.



RESULTS AND DISCUSSION

In order to synthesize various pyrrolobenzimidazole derivatives, previously synthesized 4′-cyano-3′-oxo-2′-dihydro-1*H*-pyrrolo [1,2-*a*] benzimidazole 1**(a-b)** was used as an important scaffold. 1**(a-b)** reacted with chloroacetyl chloride formed *N*-acetyl chloride **2(a-b)**. IR spectra of compounds shows presence of strong band at 1747 cm^{-1} (>C=O) of amide, 1650 cm^{-1}(>C=O) of ketone and absence band at 3335 cm^{-1} of (NH). ^{1}HMR Spectra of compounds shows presence singlet's at δ 3.63 (s, 2H, CH_2), δ 4.06 (s, 2H, CH_2) and absence of singlet at δ 4.7 of NH. MS (m/z): 275.67 (M^{+2}). (Found: C, 57.19; H, 3.01; N, 15.51. $C_{13}H_8ClN_3O_2$ require C, 57.09; H, 2.95; N, 15.35). Thus the data obtained confirmed conversion of NH to N-acetyl chloride is achieved. **2(a-b)** which were treated with thiourea affords 2-aminothiozole derivatives 3**(a-b)**. IR spectra of compounds shows presence of strong band at 3512 cm^{-1}(NH_2), 2257 cm^{-1} (CN), 1714 cm^{-1}(C=O) of ketone and absence of band at 1650 cm^{-1} (HN-C=O) of amide. ^{1}H NMR spectra of compounds shows presence singlet's at δ 3.88 (s, 2H, CH_2), δ 5.22 (s, 1H, CH) and δ 5.85 (s, 2H, NH_2, D_2O exchangeable). MS (m/z): 295.37 (M^{+1}). (Found: C, 57.05; H, 3.29; N, 23.61; S, 10.65 require for $C_{14}H_9N_5OS$; C, 56.94; H, 3.07; N, 23.71; S, 10.86). Thus the data obtained confirmed conversion of N-acetyl chloride to 2-amino-1,3-thioazole is achieved. **3(a-b)** which were treated with methyl iodide in presence of triethyl amine to provide *N, N*-dimethyl aminothioazole compounds 4**(a-b).** IR spectra shows absence of strong band at 3512 cm^{-1} (NH_2) and ^{1}H NMR spectra shows singlet's at δ 2.78 (s, 6H, *N*-CH_3), δ 3.90 (s, 2H, CH_2), δ 5.45 (s,1H,-CH) and absence of δ 5.85 (s, 2H, NH_2, D_2O exchangeable). MS (m/z): 323.37 (M^{+1}). (Found: C, 59.33; H, 4.09; N, 21.51; S, 10.01 require for $C_{16}H_{15}N_5OS$: C, 59.43; H, 4.02; N, 21.66; S, 9.92). 4**(a-b)** on further reaction with Hydrochloric acid gave amide compounds **5(a-b)**. IR spectra showed band at 3446 cm^{-1} (NH_2), 1759 cm^{-1} (>C=O) of ketone and 1640 cm^{-1}(HN-C=O) of amide and absence of band at 2241 cm^{-1} (CN). ^{1}H NMR spectra showed singlet for δ 3.28 (s, 3H, N-CH_3), δ 3.89 (s, 2H, CH_2), δ 4.20 (s, 2H, NH_2, D_2O exchangeable), δ 4.60 (s, 1H, CH). MS (m/z): 341.39 (M^{+1}). (Found: C, 56.01; H, 4.39; N, 20.31; S, 9.28 and require for $C_{16}H_{15}N_5O_2S$: C, 56.29; H, 4.43; N, 20.51; S, 9.39). Thus from spectral data formation of amide compounds was confirmed. **4(a-b)** on further reaction with sodium azide and ammonium chloride in xylene gave tetrazole compounds 6**(a-b)**. IR spectra shows band at 3365 cm^{-1}(NH), 1751cm^{-1}(>C=O) of ketone and absence of band at 2241 cm^{-1} (CN). ^{1}H NMR spectra showed singlet for δ 3.21 (s, 3H, N-CH_3), δ 3.83 (s, 2H, CH_2), δ 5.19 (s, 1H, CH), δ 6.65-6.93 (m, 4H, Ar-H) and δ 8.48 (s, 1H, NH, D_2O exchangeable). MS (m/z): 366.40 (M^{+1}). (Found: C, 52.21; H, 3.96; N, 30.28; S, 8.68 require for $C_{16}H_{14}N_8OS$: C, 52.45; H, 3.85; N, 30.58; S, 8.75). Thus from spectral data formation of tetrazole compounds was confirmed.

The Inhibition zone against the bacterium *S. aureus, E. coli, S.typhi* and fungus *A. niger* due to the different substituted pyrrolobenzimidazole derivatives is shown in Table 1. Highest antimicrobial potential was observed with compounds 3b, 4b, 5b and 6b against *S. aureus.* Compounds 3a, 4a, 4b, 5a, 6b were found to be potent against *S.typhi* whereas compounds 2b, 4b, 5a, 6b exhibited inhibitory activity against *E. coli*. On the other hand compounds 2a, 2b, 3a, 3b, 5b and 6b showed highest antifungal potential against *A.niger.*

Table 1: Antibacterial activity and antifungal activity

Compounds	Zone of Inhibition (mm)							
	S.aureus		*S.typhi*		*E. coli*		*A. niger*	
	50 µg ml^{-1}	100 µg ml^{-1}	50 µg ml^{-1}	100 µg ml^{-1}	50 µg ml^{-1}	100 µg ml^{-1}	50 µg ml^{-1}	100 µg ml^{-1}
2a	11	17	12	18	13	15	16	20
2b	12	18	11	15	15	19	17	20
3a	14	18	15	20	10	15	15	21
3b	17	19	14	18	12	17	16	18
4a	15	20	15	21	14	16	12	17
4b	18	21	16	20	16	20	11	15
5a	12	18	15	19	15	20	10	16
5b	16	19	14	17	12	16	15	19
6a	14	18	12	18	13	17	11	16
6b	16	19	17	19	16	19	16	19

CONCLUSION

Spectral techniques used in the scheme, confirm the formation and synthetic route of novel pyrrolobenzimidazole derivatives. The results of antibacterial and antifungal activity depicts that synthesized derivatives exhibited significant to moderate activity. This confers that all the newly synthesized 2-aminothidiazole, *N,* *N*-dimethyl aminothidiazole, amide, tetrazole derivatives of pyrrolobenzimidazole are biologically active against the tested bacterial and fungal strains.

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