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7-Azaindole Derivatives as Potential Antibacterial Agents

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Abstract. Azaindole analogues, as antimicrobial agent, have shown significant response against a number of gram positive and gram negative bacteria. In the present work, synthesis of novel derivatives of 7- azaindole and their antibacterial and cytotoxic activities are reported.

Keywords: azaindole, antibacterial agent, cytotoxicity

Introduction

Much work has been rendered on the antimicrobial activity of azaindole derivatives (Mushtaq *et al*., 2008; Saify *et al*., 1994a; Saify, 1986, 1984) which showed significant response against a number of microorganisms (Minakala *et al*., 1992). The aza-isatogens synthesized by Hooper *et al*. (1965) were effective against gram positive organisms. Also the 2-pyridyl-6-aza-indoles showed a broad spectrum of antibacterial activity and were generally more effective than the analogoue of indoles.

Bayomi *et al*. (1985a) described the synthesis of various pyrrolo (3,2-b) pyridine-6-carboxylic acid derivatives as potential antimicrobial agents against several gram positive and gram negative organisms. The results of microbial evaluation *in vitro* of most of the compounds exhibited moderate activity. Remarkable compounds, active against *Shigella sonnei*, are 1, 4-dimethyl-3-carbomethoxy, 7-oxo-pyrrolo (3,2-b)pyridine-6-carboxylic acid and 1-methyl, 4-ethyl, 3-carbomethoxy 7-oxo-pyrrolo (3, 2-b)pyridine-6-carboxylic acid.

In their next communication, Bayomi *et al*. (1985b) reported the synthesis of a series of 1, 4-dihydro-4-oxo-pyrrolo (3, 4-b) pyridine-3-carboxylic acid as an extension of the interest in fused pyrrolopyridines as potential antimicrobial agent. Few compounds of this series were found to exhibit a relatively broad spectrum of activity.

During the last decade a considerable attention has been focused on azaindole analogues as antimicrobial agents. A series of derivatives of 7-dihydro-4-oxo-7-azaindole-5-carboxylic acid were synthesized by Toja *et al*. (1986).

One compound of this series, 4,7-dihydro-4-oxo-1,2-dimethyl-7-ethyl-7-azaindole-5-carboxylic acid, was found to be the most potent antibacterial agent.

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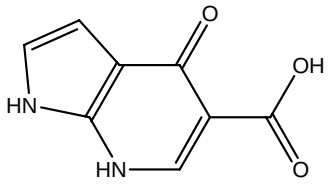
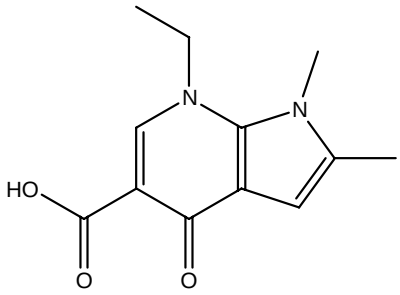


7-Dihydro-4-oxo-7-azaindole-5-carboxylic acid

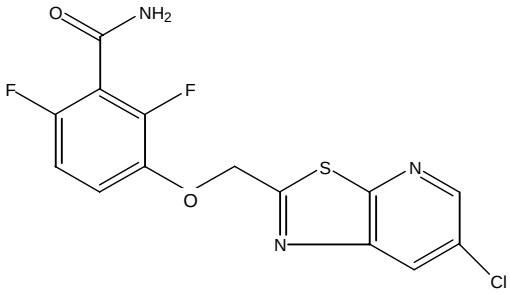


4,7-Dihydro-4-oxo-1, 2-dimethyl-7-ethyl-7-azaindole-5-carboxylic acid

Mohamed (1992) introduced some new azaindole derivatives as antimicrobial agents. These compounds had high moderate and weak inhibitory effect against the tested gram positive and gram negative bacteria. In a similar attempt, some more azaindole derivatives were prepared showing satisfactory antibacterial activity on the basis of related biological activity (Saeed *et al*., 1997, Saify *et al*., 1994b).

Drug resistance to antibiotics and related natural and synthetic drugs poses a great challenge to the chemists, in general, and the drug designers, in particular. Haydon *et al*., 2008, report the discovery of a class of small synthetic antibacterials,

PC190723, which inhibits FtsZ and prevents cell division. PC190723 has potent and selective *in vitro* bactericidal activity against staphylococci, including methicillin- and multi-drug-resistant *Staphylococcous aureus*.



PC190723

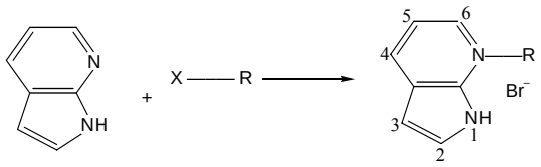
Flouro pharmaceuticals have shown significant antibacterial activity and have been drugs of choice against antibiotic-resistant strains. The flouro compounds synthesized during the course of our project have shown significant activity. Further research is in progress to find out their efficacy as potential antifungal agents.

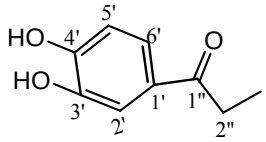
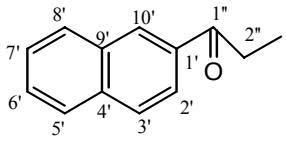
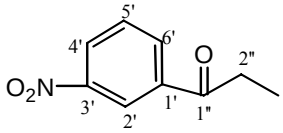
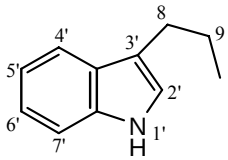
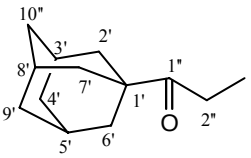
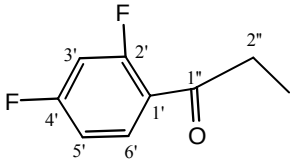
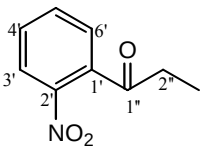
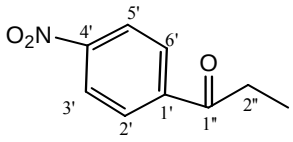
Materials and Methods

General method of synthesis. Equimolar quantities of 7-azaindole and substituted phenacyl halide and/or 2-(2-bromoethyl)-2, 5, 5-trimethyl-1, 3-dioxane were dissolved in approximately 25 ml of acetone in separate conical flasks and then mixed together in another conical flask. The reaction mixture was stirred at room temperature for 2 to 3 h. After completion of the reaction, solid precipitates were obtained. The reaction was monitored by TLC (solvent system of $CHCl_3$-MeOH in different proportions). The resultant compound was filtered and washed with acetone and/or mixture of acetone and ether to remove the unreacted starting materials. Crude precipitates were recrystallized several times from ethanol and/or the mixture of solvents to give pure crystals of the compound.

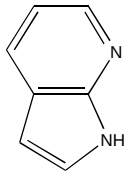
Confirmational techniques. All melting points were recorded on Gallenkamp melting point apparatus and are uncorrected. Silica gel type 60 P254 of E. Merck was used for preparing TLC plates. Spots on plates were detected by iodine using iodine tank. Ultraviolet (UV) spectra were recorded in methanol on Hitachi U-3200 spectrophotometer. Infra red (IR) spectra were measured on Shimadzu IR 460 spectrophotometer using KBr disc, mass spectra (MS) on Massen spectrometer MAT 311A Varian Bermen spectrometer and nuclear magnetic resonance (NMR) spectra, on Bruker AM-300 spectrometer at 300 MHz.

Synthesis scheme

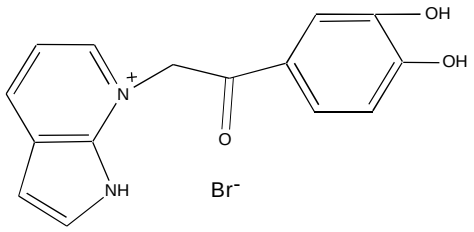


X	R	Compound no.
Br		**2**
Br		**3**
Br		**4**
Br		**5**
Br		**6**
Cl		**7**
Br		**8**
Br		**9**

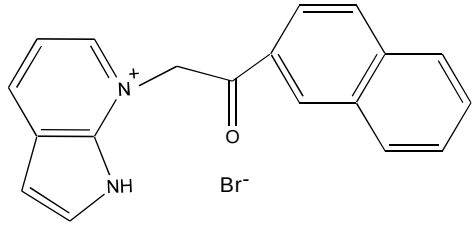
Spectral studies. ***Compound 1: 1H-prrolo[2,3-b]pyridine (7-azaindole).***



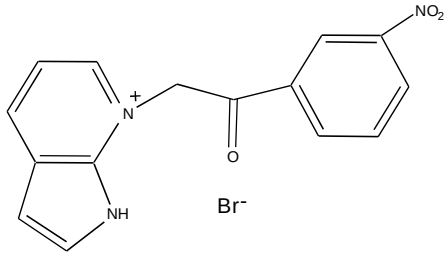
Compound 2: 1-[3-(3,4-dihydroxyphenyl) 3-oxoethyl]-7H-pyrrolo[2,3-b]pyridine-1-ium;bromide. Molecular formula: $C_{15}H_{12}N_2O_3Br$, 348.011amu; Yield: 79%; UV(MeOH) λ_{max} nm: 289, 227 and 208; IR(KBr) ν_{max} cm^{-1}: 3100, 1670, 1595 and 1290; EIMS *m/z* (relative int., %): 268 (M^+-HBr, 4), 239(14), 193(3), 165(12), 137(15), 118(100) and 109(25); ^{1}H-NMR (D_2O, 300 MHz): δ 8.72 (1H, d, *J*=7.85 Hz, H-6), 8.24 (1H, d, *J*=6.80 Hz, H-4), 7.70 (1H, dd, *J*=8.46, 2.21 Hz, H-6'), 7.67 (1H, d, *J*=3.65 Hz, H-2), 7.62 91H, dd, *J*=7.85, 6.80 Hz, H-5), 7.55 (1h, d, *J*=2.19 Hz, H-2'), 7.06 (1H, d, *J*=8.46 Hz, H-5'), 6.97 (1H, d, *J*=3.65 Hz, H-3) and 6.48 (2H, s, H-2").



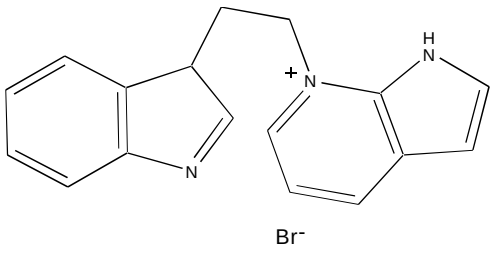
Compound 3: 1-[3-(2-naphthyl)3-oxoethyl]-7H-pyrrolo[2,3-b]pyridine-1-ium;bromide. Molecular formula: $C_{19}H_{15}N_2O$ Br, 367.23 amu; Yield: 86.2%; UV(MeOH) λ_{max} nm: 340, 293, 250, 224, 203; IR(KBr)ν_{max} cm^{-1}: 3755, 2923, 1687, 1361, 987, 823.5, 783, 545, 474.5; EIMS *m/z* (relative int, %): 286 (M^+, 7.4) 259(8.2), 258(62), 257(52), 155(15), 81(18), 77(22); ^{1}H-NMR(CD_3OD, 300 MHz): δ 8.82 (1H, dd, *J*=7.96,1.82 Hz, H-6), 8.67 (1H, d, *J*=6.12Hz, H-4), 8.16 (2H, d, *J*=7.99 Hz, H-2,8′), 8.09 (1H, d, *J*=3.93 Hz, H-2), 8.05(2H, d, *J*=7.57H,H-3′,9′), 7.73(1H,dd, *J*=7.57,4.00 Hz, H-4), 7.65 (2H,m,H-5′,8′), 7.01(1H,d, *J*=3.49 Hz, H-3), 6.65 (2H,s, H-2″).



Compound 4: 1-[3-(3-nitrophenyl)3-oxoethyl]-7H-pyrrolo[2,3-b]pyridine-1-ium;bromide. Molecular formula: $C_{15}H_{12}N_3O_3$ Br, 362.178 amu; Yield: 80%; UV(MeOH) λ_{max} nm: 299.6, 228, 200; IR(KBr)ν_{max} cm^{-1}: 3232, 2916, 1965, 1797, 1697, 1529, 1475, 1356, 1224.9, 1172.8, 1091.5, 930, 883, 799, 598, 519, 481.2; EIMS *m/z* (relative int., %): 282(M^+, 9.8), 252(100), 236(41), 206(57), 193(6.1), 150(15.6), 131(53.5), 118(13.3), 90(6.2), 77(17.1), 63(6.6); ^{1}H-NMR (CD_3OD, 300 MHz): δ 8.93 (1H, s, H-2′), 8.81 (1H, d, *J*=7.79 Hz, H-6), 8.69 (1H, d, *J*=7.71,Hz, H-2′), 8.64 (1H, d, *J*=4.73 Hz, H-4′), 8.52 (1H, d, *J*=8.85 Hz, H-4), 8.42 (1H, t, H-6′), 8.39 (1H, S, H-5′), 7.93 (1H,dd,*J*=8.02, 3.35 Hz H-5)7.77 (1H, d, *J*=3.35 Hz, H-3) 7.67(1H, d, *J*=6.5 Hz, H-6) 7.01 (1H, d, *J*=3.50 Hz, H-2),6.9(2H,s, H-2″).

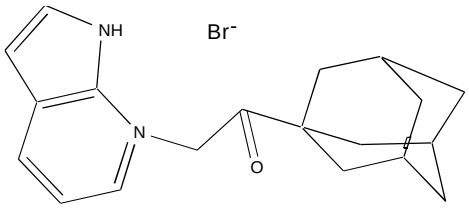


Compound 5: 1-[2-(1H-indol-3-yl) ethyl]-7H-pyrrolo[2,3-b] pyridine-1-ium;bromide. Molecular formula: $C_{17}H_{15}N_3Br$ 340.01 amu; Yield: 75%; UV(MeOH) λ_{max} nm: 200, 221, 283, 289; IR(KBr)ν_{max} cm^{-1}: 3437, 3375, 3217, 2917, 2074, 1837, 1616, 1462, 1360, 1297, 1102, 1005, 800.5, 726, 604, 543, 428.3; EIMS *m/z* (relative intensity, %): 261(M^+, 2) 260(1), 225(1), 143(100), 142(20) 115(37), 103(5), 91(12), 82(10), 63(7); ^{1}H-NMR (CD_3OD, 300 MHz): δ 8.53 (1H, d, *J*=7.74 Hz, H-6), 7.91 (1H, d, *J*=6.03 Hz, H-4), 7.74 (1H, d, *J*=3.5 Hz, H-5), 7.27 (2H, dd, *J*= 4.84,3.51 Hz, H-4',6'), 7.06(1H, s, H-5'),6.85 (1H,s, H-2'), 5.02 (1H,t,H-2), 4.83(2H,s,H-2"),3.50 (2H,s,H-1"),3.28 (1H,t,H-3).

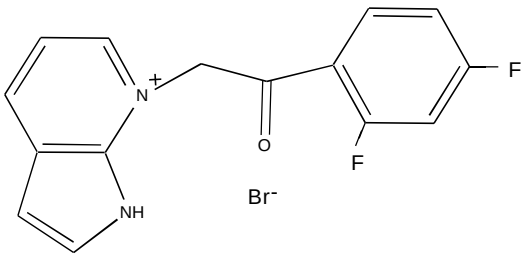


Compound 6: 1-[3-(1-adamantyl)3-oxoethyl]-7H-pyrrolo [2,3-b]pyridine-1-ium;bromide. Molecular formula: $C_{19}H_{23}N_2O$ Br, 375.30 amu; Yield: 81.5%; UV(MeOH) λ_{max} nm: 299.6, 226.0; IR(KBr)ν_{max} cm^{-1}: 3409, 2918, 2850, 2773, 1712, 1620, 1458, 1357,

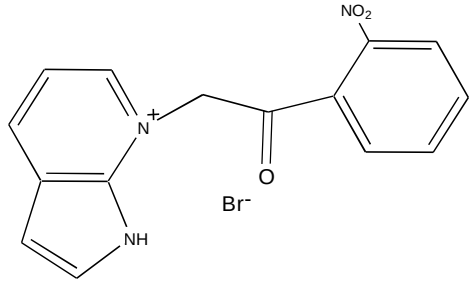
1164, 1097, 887, 779, 727, 661, 536, 476; EIMS *m/z* (relative intensity; %): 295 (M^+, 7.3), 294(35), 237(2.6), 176(3), 159(15.5), 131(100), 93(18.4), 79(27); ^{1}H-NMR(DMSO-d_6, 300 MHz): δ 8.77 (1H, d, *J*=8.68 Hz, H-6), 8.48 (1H, d, *J*=6.15 Hz, H-4), 7.95(1H,d, *J*=3.48Hz, H-2), 7.66 (1H, dd, *J*=7.8,1.5 Hz, H-5), 6.97 (1H, d, *J*=3.57, H-2), 6.06(2H,s,H-2"), 1.97 (3H,s,H-4',7',8'),1.73(3H,s , H-2',3',7',10').



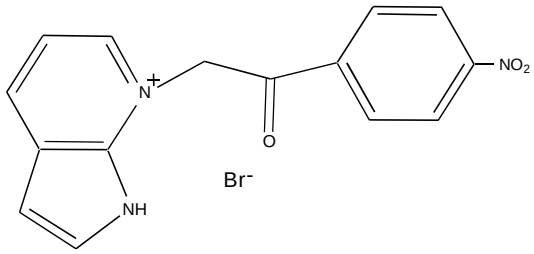
Compound 7: 1-3-[(2,4-diflorophenyl) 3-oxoethyl]-7H-pyr-rolo[2,3-b]pyridine-1-ium;bromide. Molecular formula: $C_{15}H_{10}F_2N_2O$ Cl, 352.0026 amu; Yield: 32; UV(MeOH) λ_{max} nm: 301, 276 and 198; IR(KBr)ν_{max} cm^{-1}: 3400, 2800, 1610, and 1560; EIMS *m/z* (relative int., %): 272 (M^+-HBr, 53), 235 (6), 141(100), 132 (70), 118 (12) 113 (48) and 77(45); ^{1}H-NMR (D_2O, 300 MHz): δ 8.79 (1H, dd, *J*=7.85, 1.96 Hz, H-6), 8.42 (1H, d, *J*=8.85 Hz, H-4), 8.21 (1H, dd, *J*=7.94, 5.42 Hz, H-6'), 7.96 (1H, d, *J*=3.40 Hz, H-2), 7.72 (1H, dd, *J*=8.85, 7.85 Hz, H-5), 7.41 (1H, m, H-3'), 7.32 (1H, d, *J*=3.40 (Hz, H-3), 7.21 (1H, dd, *J*=11.96, 7.94 Hz, H-5') and 6.18 (2H, s, H-2").



Compound 8: 1-[3-(2-nitrophenyl)3-oxoethyl]-7H-pyrrolo [2,3-b]pyridine-1-ium;bromide. Molecular formula: $C_{15}H_{12}N_3O_3Br$, 817.1410 amu; Yield: 48%; UV(MeOH) λ_{max} nm: 290, 252 and 202; IR(KBr)ν_{max} cm^{-1}: 3385, 2930, 1695, 1610 and 1340; EIMS *m/z* (relative int., %): 282 (M^+-Br, $C_{15}H_{12}N_3O_3$, 10), 224(30), 164(10), 144 (4), 132(10) and 118(80); ^{1}H-NMR (CD_3OD, 300 MHz): δ 9.22 (1H, dd, *J*=8.32, 1.21 Hz, H-6), 9.01 (1H, dd, *J*=6.18, 1.21 Hz, H-4) 8.96 (1H, dd, *J*=8.32, 6.18 Hz, H-5), 8.32 (1H, d, *J*=3.26 Hz, H-2), 8.32 (1H, dd, *J*=7.90, 1.68 Hz, H-6'), 8.31 (1H, ddd, *J*=8.30, 7.48, 1.68 Hz, H-4'), 7.93 91H, ddd, *J*=8.30, 7.90, 1.64 Hz, H-5'), 7.85 (1H, dd, *J*=8.30, 1.64 Hz, H-3'), 7.64 (1H, d, J=3.26 Hz, H-3) and 6.25 (2H, s, H-2").



Compound 9: 1-[(4-nitrophenyl)3-oxoethyl]-7H-pyrrolo [2,3-b]pyridine-1-ium;bromide. Molecular formula: $C_{15}H_{12}N_3O_3Br$; Yield: 61%; UV(MeOH) λ_{max} nm: 270, 248 and 201; IR(KBr)ν_{max} cm^{-1}: 3390, 2920, 1690, 1600 and 1340; EIMS *m/z* (relative int., %): 282 (M^+-Br, $C_{15}H_{12}N_3O_3$, 8), 164(4), 160(12), 132 (11), 122(18), 118(100) and 77 (23); ^{1}H-NMR (CD_3OD, 300 MHz): δ 8.81(1H, d, *J*=7.84, 1.08 Hz, H-6), 8.84 (2H, d, *J*=8.02, Hz, H-3',5') 8.26 (1H, d, *J*=8.99 Hz, H-4), 7.78 (2H, d, *J*=8.02 Hz, H-2',6'), 7.71 (1H, d, *J*=3.51 Hz, H-2), 7.68 (1H, dd, J=8.99, 7.84 Hz, H-5), 7.02 (1H, d, *J*=3.51 Hz, H-3) and 6.02 (2H, s, H-2").



Antibacterial activity. ***Method.*** Antibacterial activitiy of all compounds was studied using disc diffusion assay method of Bauer *et al*. (1996). Stock solution of test compound (20,000 µg/ml) was prepared by dissolving 20 mg of test compound in 1 ml of DMSO. Filter paper disc of about 6 mm were sterilized by autoclaving at 15lb/in^2 pressure for about 30 min. Each disc was soaked in 10 µl of the stock solution of compound extract in order to achieve a final concentration of 200 µg/disc.

Sterile petri plates were poured with about 18-20 ml of auto-claved Muller hinton agar (Mueller and Hinton, 1941) and were pre-incubated at 37 °C for 18-24 h. The test cultures were inoculated in about 4-5 ml of Mueller hinton broth, incubated overnight at 37 °C. Next day inoculated cultures were vortexed and a uniform lawn of culture was made on Mueller hinton agar plate after streaking sterile cotton swab in overnight broth culture. Plates were air dried for 10-15 min then filter

paper discs soaked in the test compound solution, were placed at different places on the plate. Plates were then incubated at 37 °C for 18-24 h. Next day, the zone of inhibition around each disc was measured in millimeter.

Cytotoxicity evaluation using 3T3 cell. *Method.* Cytotoxic activity of compounds was evaluated in 96-well flat-bottom micro plates by using standard MTT (3-[4, 5-dimethylthiazole-2-yl]-2,5-diphenyl-tetrazolium bromide) colorimetric assay. For this purpose, 3T3(mouse fibroblast) were cultured in Dulbecco's modified Eagle's medium, supplemented with 5% of foetal bovine serum (FBS), 100 IU/ml of penicillin and 100 µg/ml of streptomycin in 25 cm^3 flask and kept in 5% CO_2 incubator at 37 °C. Exponentially growing cells were harvested, counted with haemocytometer and diluted with a particular medium. Cell culture with the concentration of $1x10^5$ cells/ml was prepared and introduced (100 µl/well) into 96-well plates. After overnight incubation, medium was removed and 200 µl of fresh medium was added with different concentrations of compounds (1-100 µm). After 72 h, 50 µl MTT (2 mg/ml) was added to each well and incubated for further 4 h. Subsequently, 100 µl of DMSO was added to each well. The extent of MTT reduction to formazan within cells was calculated by measuring the absorbance at 570 nm, using a microplate ELISA reader (Spectra Max plus, molecular devices, CA, USA). The cytotoxicity was recorded as concentration causing 50% growth inhibition for 3T3 cells.

Results and Discussion

Antibacterial activity of compounds **1-9** against gram positive and gram negative organisms are presented in Table 1 and 2, respectively.

Table 1. Results of compounds **1-9** against gram positive organisms

Compound no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Staphylococcous aureus AB188	28	10	7	8	-	7	7	-	-
Staphlococcous epidermidis	-	-	9	7	-	7	-	-	-
Methicillin resistant *Staphlococcous aureus 3*	-	13	9	7	7	7	-	-	-
Micrococcous luteus	7	20	15	20	7	11	11	-	-
Micrococcous luteus ATCC 9341	-	21	-	-	-	13	7	-	-
Bacillus subtilis ATCC	9	12	11	12	15	14	10	-	-
Bacillus cereus ATCC	8	12	11	7	8	11	9	-	-
Corynebacterium diphtheriae	8	15	9	8	15	14	10	-	-
Corynebacterium hofmanii	-	-	-	-	9	14	10	-	-
Corynebacterium xerosis	8	15	8	7	7	15	-	-	-
Listeria monocytogene	7	-	9	7	-	7	-	-	-
Streptococcous feacalis	7	-	8	7	7	10	-	-	-
Microbacterium seregmotis	-	-	-	-	7	15	-	-	-

- = no activity

Table 2. Results of compounds **1-9** against grams negative organisms

Compound no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Salmonella typhi ATCC	-	10	9	9	10	7	-	-	-
Salmonella paratyphi A	7	7	9	12	-	7	-	-	-
Salmonella paratyphi B	-	17	10	11	-	-	-	-	-
Shigella dysenteriae	20	11	8	8	-	7	-	-	-
Proteus micrabilis	7	7	7	-	-	7	-	-	-
Enterobecter sp.	7	17	7	8	7	8	10	-	-
Escherichia coli ATCC	-	18	10	12	7	-	-	-	-
Escherichia coli MDR	-	9	11	12	7	-	-	-	-
Klebsiella pneumoniae	17	15	10	12	7	8	11	-	-
Pseudomonas aerugonosa	8-	7	7	7-	-	9	-	-	-

- = no activity

The parent compound **1,** 1H-pyrrolo[2,3-b]pyridine(7-azaindole) showed negligible activity except against *Staphylococcous aureus* AB 188 among gram positive strains and *Shigella dysenteriae* and *Klebsiella pneumonia* among gram negative strains.

Compound **2** is a 3,4 dihydroxy derivative of compound **1** which showed significant activity against methicillin resistant *Staphylococcous aureus 3*, *Micrococcous luteus, Micrococcous luteus* ATCC, *Bacillus cereus* ATCC among the grain positive strains while against *Salmonella paratyphi B, Enterobacter* sp., *Escherichia coli* ATCC and *Klebsiella pneumonia* among the gram negative bacteria.

Compound **3** is an acetonaphthone derivative which showed good activity against *Micrococcous luteus* among the gram positive strains but no reasonable activity against the gram negative strains.

Compound **4** is a 3 nitro acetophenone derivative and showed significant results against *Micrococcous luteus* and *Bacillus* ATCC among the gram positive strains and among the gram negative bacteria, it showed better activity against *Salmonella typhi* A, *Escherichia coli* ATCC and MDR, and *Klebsiella pneumonia* strains.

Compound **5** is a bromoethyl indole derivative of compound **1** and demonstrated better activity against gram positive strains including *Bacillus subtilis* ATCC, *Corneybacterium diphtheriae* while it was inactive against all the tested gram negative strains.

Compound **6** is an adamantyl derivative which displayed significant results against the gram positive *Micrococcous luteus* ATCC, *Bacillus subtilis* ATCC, *Corneybacterium hofmanii, Corneybacterium diphtheriae, Corneybacterium xerosis* and *Microbacterium seregmotis* while it was inactive against the gram negative strains.

Compound **7**, a diflouro-acetophenone derivative showed weak activity against both the tested strains.

Compound **8** and **9** are *ortho* and *para*-nitroacetophenone derivatives which did not display any activity against all the tested strains.

Regarding SAR, all the derivatives of 7-azaindole derivative except **3**, **5** and **6** have different functional groups at the phenyl ring. Compounds **4**, **8** and **9** are nitro derivatives; the difference is only in the position of nitro group at phenyl ring. Compound **4**, a *meta* nitro derivative, showed reasonable inhibitory activity while compounds **8** and **9** are *ortho* and *para* nitro derivatives, respectively, which were devoid of any inhibitory activity.

Hydroxyl, naphthalene containing group also enhanced the activity of parent compound **1** while bromoethyl indole and diflouro-acetophenone binding to 7-azaindole (**1**) decreased the activity against both the gram positive and the gram negative bacteria.

From the above discussion it can be concluded that binding and position of different functional groups in 7-azaindole have influence on the antibacterial activity.

References

Bauer, A.W., Kirby, W.M.M., Sherris, J.C., Turck, M. 1996. Antibiotic susceptibility testing by a standardized single disk method. *American Journal of Clinical Pathology* **45:** 493-496.

Bayomi, S.M., Price, K.E., Sowell, J.W. Sr. 1985a. Synthesis of 7-oxopyrrolo[3, 2-b]pyridine-6-carboxylic acid derivatives as potential antimicrobial agents. *Journal of Heterocyclic Chemistry* **22:** 83-88.

Bayomi, S.M., Price, K.E., Sowell, J.W., Sr. 1985b. Synthesis of 1,4-dihydro-4-oxopyrrolo[3,4-b]pyridine-3-carboxylic acid derivatives as potential antimicrobial agents. *Journal of Heterocyclic Chemistry* **22:** 729-734.

Hooper, M., Patterson, D.A., Wibberley, D.G. 1965. Preparation and antibacterial activity of isotagens and related compounds. *Journal of Pharmacy and Pharmacology* **17:** 734-741.

Haydon, D.J., Stokes, N.R., Ure, R., Galbraith, G., Bennett, J.M., Brown, D.R., Baker, J.P., Baryanin, V.V., Rice, D.W., Sedelinikova, S.E., Heal, J.R., Sheridan, J.M., Aiwale, S.T., Chauhan, P.K., Srivastava, A., Taneja, A., Collins, I., Errington, J., Czaplewski, L.G. 2008. An inhibitor of FtsZ with patent and selective anti staphylococcal activity. *Science* **321:** 1673-1675.

Mohamed, T.A. 1992. Synthesis and biological study of some pyrrolopyridine derivatives. *Journal of Chemical Technology and Biotechnology* **55:** 239-244.

Mueller, J.H., Hinton, J. 1941. A protein free medium for primary isolation of the gonococcus and meningococcus. Proceedings of Society of Experimental. *Biology and Medicine* **48:** 330-333.

Mushtaq, N., Saify, S.S., Noor, F., Takween, S., Akhter, S., Arif, M., Khan, K.M. 2008. Synthesis and pharmacological activities of 7-azaindole derivatives. *Pakistan Journal of Pharmaceutical Science* **21:** 36-39.

Minakata, S., Itoh, S., Komatsu, M., Ohshiro, Y. 1992. Functionalization of 1H-pyrrolo[2, 3-b] pyridine. *Bulletin of the Chemical Society of Japan* **65:** 2992-2997.

Saeed, S.A., Khan, A., Saify, Z.S., Haider, S.M. 1997. The Effect of substituted nicotinamide and azaindoles on lipid

peroxidation and platelet aggregation. In: *Proceeding of Second International Conference on Pharmaceutical Sciences*, Karachi, Pakistan.

Saify, Z.S., Haider, S.M., Ahmed, M., Saeed, M., Khan, A., Siddiqui, B.S. 1994a. Synthesis of some 7-azaindole derivative their cytotoxicity and bacterial activity. *Pakistan Journal of Scientific and Industrial Research* **37:** 439-441.

Saify, Z.S., Haider, S.M., Haleem, D.J. 1994b. Neurochemical studies on some 7-azaindole derivatives. *Proceedings of 1st ISBBPS Symposium on Biochemistry and Biophysics*, M. A. Haleem, H. S. A. Athar and Darakhshan J. Haleem (eds.), pp. 1-20, Department of Biochemistry, University of Karachi, Karachi, Pakistan.

Saify, Z.S. 1986. 7-azaindole derivatives as potential anti-inflammatory agents. *Pakistan Journal of Pharmacology* **2:** 43-46.

Saify, Z.S. 1984. Synthesis of some azaindole derivatives of potential biological interest; Significance of physical parameters in drug design. *Journal of Pharmacy* **2:** 99-103.

Toja, E., Kettenring, J., Gddstein, B., Trazia, G. 1986. Pyrrolopyridine analogs of nalidixic acid, II: pyrrolo [2,3-b]pyridines. *Journal of Heterocyclic Chemistry* **23:** 1561-1564.