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Synthesis and Antimicrobial Evaluation of Pyrrole Based New Heterocycles

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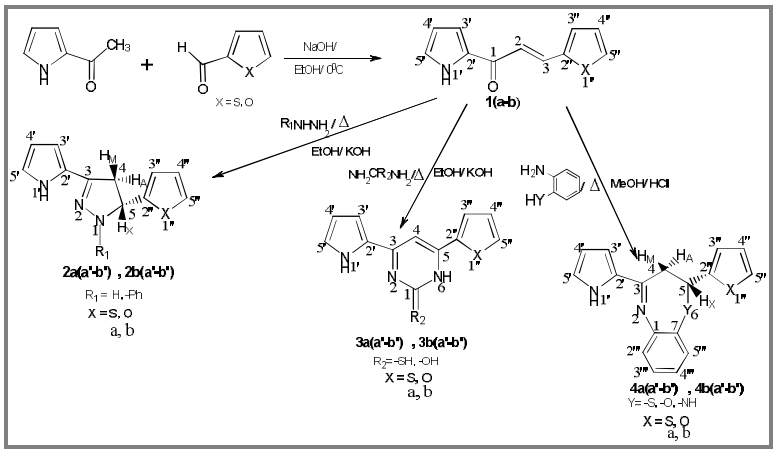
ABSTRACT

In the present research work, we have investigated the synthesis of five, six and seven membered heterocycles. These have been realized from the cyclization of the Chalcones with suitable cyclizing agents. The intermediate chalcone were obtained from the condensation reaction of acetyl pyrrole with thiophene carboxaldehyde/furfaldehyde. The antimicrobial and antioxidant properties of the newly prepared compounds evaluated and many of these products could exhibit significant antimicrobial and antioxidant behavior.

Graphical Abstract



Keywords: Pyrazolines, Pyrimidines, Benzoazepines, Antimicrobial and Antioxidant properties.

INTRODUCTION

Incorporation of nitrogen, oxygen, sulfur into an organic ring structure in place of a carbon atom gives rise to a heterocyclic compound, halogens do not form heterocyclic compounds although they may be substituents on a heterocyclic ring. Heterocyclic nitrogenous compounds and their fused analogues exist in numerous natural products, display a wide range of medicinal and biological activities. Pyrazolines are important nitrogen containing five member heterocyclic compounds and their

derivatives embedded with variety of functional groups are significant biological agents. In particular, they are used as anesthetics, analgesic, antitubercular, antitumor, immunosuppressive, antidepressant, anti-inflammatory, anticonvulsant and antiparasitic [**1-8**]. These possess a broad spectrum of tranquillizing, muscle relaxant, psychoanaleptic, antihypertensive, anti HIV, molluscicidal and cerebroprotective properties. Pyrazolines derivatives are also recognized as nitricoxide synthase (NOS) inhibitors which are useful in neurodegenerative diseases and inflammatory arthritis [**9-13**]. These are also associated with high excellent blue emission, easy accessibility, hole-transport efficiency and high quantum yields.[14-15] Pyrazolines acts as brightening reagents for synthetic fibers [**16-17**], fluorescence chemosensors in recognition of transition metal ions [**18-20**] hole-transport materials in electrophotography and organic light-emitting diodes (OLED) [**21-23**].

Pyrimidine is the colorless six membered heterocyclic containing two nitrogen atoms at position no. 1 and 3. The name of the pyrimidine was derived from the combination of two words pyridine and amidine. Pyrimidines are also known as 1,3-diazines and their fused analogues led to a large group of heterocyclic compounds. Pyrimidine is an integral part of DNA and RNA and its derivatives are associated with a wide range of biological potential i.e. analgesic, antioxidant, antiviral, anti-inflammatory and antimalarial [**24-28**]. Recently pyrimidines have attracted attention as an important class of chemotherapic agents. Alloxan is a diabetogenic agent, sulfadiazine, sulfamerazine and sulfadimidine are potent agent against urinary tract infections, these all are associated with the pyrimidine moiety [**29-30**]. Pyrimidine ring was further highlighted by the reported use of sulphonamide–trimethoprim for the treatment of opportunisticinfections in patients with AIDS and cytopathic effects of HIV [**31-32**].

The seven-membered, N-heterocyclic azepane scaffold is a biologically significant and useful building block for the synthesis of novel glycosidase inhibitors [**33-34**], anticancers [**35-36**] and DNA minor groove-binding agents [**37-38**]. Oxo-azepines and azepanols are useful epitopes in both materials and medicinal chemistry due to the unique flexibility of the seven-membered. Pyrrolobenzodiazepines (PBDs) were first found in the cell cultures of Streptomyces species. It is presumed that scientists have made use of their antibiotic properties as a form of chemical defense, for the treatment of cancer. Anthramycin and sibiromycin are PBD products and Anthramycin particularly have significant cytotoxicity against sarcomas, lymphomas breast cancers, and gastrointestinal without having significantly side effects towards red blood cells [**39-42**].

Chalcones are extensively distributed in nature and originally extracted from natural sources e.g. licochalcone A, licochalcone D, morachalcone A. These are bioactive compounds with 1,3-diarylpropane skeleton belonging to the flavonoid family. Chalcones carry out conjugated double bonds and a complete delocalized π-electron, thus possess relatively low redox potentials and have a greater probability of undergoing electron transfer reactions. The compounds bearing chalcone moiety possess various biological activities such as anti-inflammatory, analgesic, anti platelet, antimicrobial, anticancer, antiviral, anti leishmanial, immune modulatory, anti ulcerative, anti malarial, antioxidant, anti tubercular, anti hyperglycemic, inhibition of chemical mediators release, inhibition of tyrosinase and inhibition of aldose reductase activities [**43-57**]. In addition to the pharmaceutical applications of chalcones, these are also associated with application such as analytical reagent for amperometric estimation of copper [**58**], spectrophotometric study of germanium [**59**], light stabilizing agent [**60**] sweetening agent [**61**] and as synthetic reagent for the synthesis of various heterocycles of biodynamic behaviors [**62-64**]. In this study we have synthesized five, six and seven membered heterocycles from pyrrole based chalcones.

MATERIALS AND METHODS

The chemicals required in this study were taken from E. Merck, S.D. Fine Chem. Ltd., and Sigma-Aldrich. The melting points were obtained through the open capillary technique. The Infrared (IR) spectra were scanned using KBr pellets with the help of Perkin Elmer RXIFT Infrared

spectrophotometer. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$/DMSO-d_6 solvent on a 400 MHz Bruker spectrophotometer. The integrity of the compounds was checked by TLC plates coated with silica gel and vapors of iodine were used as the visualizing agent.

General procedure

Synthesis of(2E)-1-(1H-pyrrol-2-yl)-3-(thiophen-2-yl)prop-2-en-1-one 1a: A mixture of 2-acetyl pyrrole (1.09 g, 0.01 mol), 2-thiophenecarboxaldehyde (1.12 g, 0.01 mol), and sodium hydroxide (5.0 g, 0.024 mol) in ethanol (20 mL) was stirred at 0°C on ice bath for 6 h and the reaction mixture was kept in refrigerator overnight. The reaction mixture was put into acidic ice and a yellow solid was obtained which was filtered and further recrystallized from methanol:chloroform to yield a pure chalcone **1a** [66].

Synthesis of (2E)-3-(furan-2-yl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one 1b: The chalcone **1b** was synthesized from treatment of 2-acetyl pyrrole (1.09 g, 0.01 mol) with 2-furfuraldehyde (0.96 g, 0.01 mol) under the similar conditions as described for chalcone **1a**. The physical and spectral data of chalcones **1(a-b)** were found be similar as reported in the literature [67].

Synthesis of 3-(1H-pyrrol-2-yl)-5-(thiophen-2-yl)-4,5-dihydro-1H-pyrazole 2aa*:* A mixture of chalcone **1a** (2.03 g, 0.01 mol), hydrazine hydrate (0.50 g, 0.01 mol) and potassium hydroxide (as a catalyst) in dry EtOH (25.0 mL) was refluxed for 4 h in 100 ml round bottom flask. With the help of thin layer chromatography the progress and completion of reaction was noticed. The resulting solution was cooled in an ice bath to yield a crude solid and was recrystallized from a mixture of methanol and chloroform to provide pure compound **2aa'** [68].

2aa': Creamish white solid; yield: 59%; m.p. 98-100^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3299 (1-NH), 3213 (1'-NH), 3178 (aromatic C-H), 2969, 2890 (methylene CH_2), 1603 (C=N);^{1}H-NMR (400 MHz, C*D*Cl$_3$): δ 11.21 (1H, s, N***H***), 7.62 (1H, d, $J_{5'',4''}$=6.1 Hz, H-5''), 7.40 (1H, d, $J_{5',4'}$=5.7 Hz, H-5'), 7.27 (1H, t, $J_{4'',3''}$=3.8 Hz, $J_{4'',5''}$=11.4 Hz, H-4''), 7.05 (1H, d, $J_{3'',4''}$=3.2 Hz, H-3''), 6.98 (1H, d, $J_{3',4'}$=3.5 Hz, H-3'), 6.80 (1H, t, $J_{4',3'}$=3.4 Hz, $J_{4',5'}$=6.1 Hz, H-4'), 6.25 (1H, s, 1-N***H***), 6.06 (1H, dd, J_{XM}=8.4 Hz, J_{XA}=6.9 Hz, H-X), 4.01 (1H, dd, J_{MX}=9.2 Hz, J_{MA}=18.4 Hz, H-M), 3.34 (1H, dd, J_{AX}=6.3 Hz, J_{AM}=16.4 Hz, H-A); ^{13}C-NMR (100 MHz, C*D*Cl$_3$): δ 146.78 (C=N), 126.69 (C-2''), 125.90 (C-5''), 125.44 (C-3''), 124.51 (C-4'') 124.40 (C-2'), 120.35 (C-5'), 109.09 (C-3'), 108.34 (C-4'), 58.63(C-5), 42.70 (C-4); ESI-MS: m/z 240 (M+Na, 10%), 217 (M, 100%); Anal. calc. for $C_{11}H_{11}N_3S$: C, 60.80; H, 5.10; N, 19.34; Found: C, 60.59; H, 5.07; N, 19.26%.

Synthesis of 1-phenyl-3-(1H-pyrrol-2-yl)-5-(thiophen-2-yl)-4,5-dihydro-1H-pyrazole 2ab': The pyrazoline **2ab'** was synthesized on reacting chalcone **1a** (2.03 g, 0.01 mol) with phenyl hydrazine (0.11 g, 0.01 mol) under the similar conditions as described for pyrazoline **2aa'**.

2ab': Brown solid; yield: 68%; m.p.179-180^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3451 (N-H), 3104 (aromatic C-H), 2928, 2888 (methylene CH_2), 1594 (C=N);^{1}H-NMR (400 MHz, C*D*Cl$_3$): δ 11.30 (1H, s, N***H***), 7.29 (1H, d, $J_{5'',4''}$ = 4.9 Hz, H-5''), 7.15 (5H, m, H-2''', 3''', 4''', 5''', 6'''), 6.93 (1H, t, $J_{4'',5''}$=4.6 Hz, $J_{4'',3''}$=3.9 Hz, H-4''), 6.87 (1H, s, H-5'), 6.72 (1H, t, *J*=7.0, 7.0 Hz, H-4'), 6.35 (1H, s, H-3''), 6.11 (1H, d, *J*=2.5 Hz, H-3'), 5.61 (1H, dd, J_{XM}=11.3 Hz, J_{XA}=6.0 Hz, H-X), 3.81 (1H, dd, J_{MX}=11.4 Hz, J_{MA}=17.0 Hz, H-M), 3.14 (1H, dd, J_{AX}=6.0 Hz, J_{AM}=17.0 Hz, H-A); ^{13}C-NMR (100 MHz, C*D*Cl$_3$): δ 145.96 (C=N), 145.22 (C-1'''), 142.44 (C-2''), 128.46 (C-3''', 5'''), 126.66 (C-5''), 124.86 (C-3''), 124.53 (C-4''), 124.45 (C-4'''), 121.07 (C-2'), 118.37 (C-5'), 113.31 (C-2''',6'''), 110.09 (C-3'), 108.73 (C-4'), 59.06 (C-5), 43.82 (C-4); ESI-MS: m/z 316 (M+Na, 20%), 294 (M+1, 20%), 293 (M, 100%); Anal. calc. for $C_{17}H_{15}N_3S$: C, 69.59; H, 5.15; N, 14.32; Found: C, 60.59; H, 5.07; N, 19.26%.

Synthesis of 5-(furan-2-yl)-3-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole 2ba': The pyrazoline **2ba'** was synthesized on reacting chalcone **1b** (1.88 g, 0.01 mol) with hydrazine hydrate (0.50 g, 0.01 mol) under the similar conditions as described for pyrazoline **2aa'**.

2ba': Off white solid; yield: 57%; m.p. 99-101^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3304 (1-NH), 3233 (1'-NH), 3098 (aromatic C-H), 2977, 2889 (methylene CH_2), 1599 (C=N);^{1}H-NMR (400 MHz, C*D*Cl$_3$): δ 11.91 (1H, s, N***H***), 6.97 (1H, d, $J_{5'',4''}$ = 10.7 Hz, H-5''), 6.86 (2H, m,H-4', 4''), 6.78 (1H, d, $J_{5',4'}$=8.0 Hz, H-5'), 6.66 (1H, d, $J_{3'',4''}$=2.0 Hz, H-3''), 6.64 (1H, d, $J_{3',4'}$=2.1 Hz, H-3'), 5.53 (1H, s, 1-N***H***), 4.35 (1H, dd, J_{XM}=14.1 Hz, J_{XA}=3.6 Hz, H-X), 3.82 (1H, dd, J_{MX}=12.6 Hz, J_{MA}=16.8 Hz, H-M), 3.49 (1H, dd, J_{AX}=3.9 Hz, J_{AM}=17.1 Hz, H-A); ^{13}C-NMR (100 MHz, C*D*Cl$_3$): δ 146.09 (C=N), 145.73 (C-2''), 134.67 (C-5''), 128.65 (C-2'), 118.82 (C-5'), 116.80 (C-3''), 111.33 (C-4''), 110.29 (C-3', 4'), 55.31(C-5), 48.20 (C-4); ESI-MS: m/z 202 (M+1, 20%), 201 (M, 100%); Anal. calc. for $C_{11}H_{11}N_3O$: C, 65.66; H, 5.51; N, 20.88; Found: C, 65.39; H, 5.48; N, 20.79%.

Synthesis of 1-phenyl-5-(furan-2-yl)-3-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole 2bb': The pyrazoline **2bb'** was synthesized on reacting chalcone **1b** (1.88 g, 0.01 mol) with phenyl hydrazine (0.11 g, 0.01 mol) under the similar conditions as described for pyrazoline **2aa'**.

2bb': Brown solid; yield: 63%; m.p. 179-181^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3431 (N-H), 3029 (aromatic C-H), 2924, 2876 (methylene CH_2), 1602 (C=N);^{1}H-NMR (400 MHz, C*D*Cl$_3$): δ 10.66 (1H, s, N***H***), 7.22 (1H, d, $J_{5'',4''}$=7.8 Hz, H-5''), 7.15 (3H, m, H-2''', 4''', 6'''), 6.95 (1H, d, $J_{5',4'}$=7.9 Hz, H-5'), 6.81 (2H, dd, *J*=8.1, 13.8 Hz, H-4', 4''), 6.70 (2H, t, *J*=7.3, 7.2 Hz, H-3''', 5'''), 6.55 (1H, d, $J_{3'',4''}$=3.0 Hz, H-3''), 6.15 (1H, d, $J_{3',4'}$=2.4 Hz, H-3'), 5.30 (1H, dd, J_{XM}=12.0 Hz, J_{XA}=6.2 Hz, H-X), 3.80 (1H, dd, J_{MX}=12.2 Hz, J_{MA}=17.2 Hz, H-M), 2.98 (1H, dd, J_{AX}=6.2 Hz, J_{AM}=17.2 Hz, H-A); ^{13}C-NMR (100 MHz, C*D*Cl$_3$): δ 145.85 (C=N), 144.20 (C-2''), 143.67 (C-1'''), 139.10 (C-5''), 129.98 (C-2') 128.64 (C-5'), 118.36 (C-3''', 5'''), 117.55 (C-4'''), 112.88 (C-3'), 112.80 (C-4'), 111.86 (C-3''), 111.70 (C-4''), 107.98 (C-2''', 6'''), 55.51 (C-5), 42.79 (C-4); ESI-MS: m/z 278 (M+1, 10%), 277 (M, 100%); Anal. calc. for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15; Found: C, 73.33; H, 5.42; N, 15.08%.

Synthesis of 4-(1H-pyrrol-2-yl)-6-(thiophen-2-yl)pyrimidine-2(1H)-thione 3aa': A mixture of chalcone **1a** (2.03 g, 0.01 mol) with thiourea (0.76 g, 0.01 mol) under basic medium in MeOH (20.0 mL) was refluxed for 6 h taken in 100 ml round bottom flask. The progress and completion of the reaction was confirmed with the help of TLC plates. On completion a yellow solid was obtained which was further recrystallized with methanol to obtain pure compound **3aa'** [71].

3aa': Pale yellow solid; yield: 71%; m.p. 100-102^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3398 (1'-NH), 3199 (6-NH), 3041 (aromatic C-H), 2971, 2859 (methylene CH_2), 1588 (C=N), 1045 (C=S);^{1}H-NMR (400 MHz, C*D*Cl$_3$): δ 10.86 (1H, s, N***H***), 8.81 (1H, d, $J_{5'',4''}$= 8.6 Hz, H-5''), 7.91 (1H, d, $J_{3'',4'}$= 2.9 Hz, H-3''), 7.89 (1H, m, H-4''), 7.79 (1H, s, 6-N***H***), 7.64 (1H, d, $J_{5'',4''}$=6.2 Hz, H-5'), 7.45 (1H, m, H-4'), 7.19 (1H, d, $J_{3',4'}$=7.3 Hz, H-3'), 5.19 (1H, s, H-4); ^{13}C-NMR (100 MHz, C*D*Cl$_3$): δ 162.35 (C=S), 150.20 (C=N), 149.99 (C-5), 138.60 (C-2''), 136.61 (C-5''), 133.68 (C-3''), 131.22 (C-4''), 130.59 (C-2'), 128.82 (C-5'), 124.51 (C-3'), 120.87 (C-4'), 118.69 (C-4); ESI-MS: m/z 282 (M+Na, 7%), 260 (M+1, 100%); Anal. calc. for $C_{12}H_9N_3S_2$: C, 55.57; H, 3.50; N, 16.20; Found: C, 55.34; H, 3.48; N, 16.13%.

Synthesis of 4-(1H-pyrrol-2-yl)-6-(thiophen-2-yl)pyrimidin-2(1H)-one 3ab': The pyrimidine **3ab'** was prepared on reacting chalcone **1a** (2.03 g, 0.01 mol) with urea (0.60 g, 0.01 mol) under the similar conditions as described for pyrimidine **3aa'**.

3ab': Yellow solid; yield: 61%; m.p. 140-142^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3402 (1'-NH), 3182 (6-NH), 3088 (aromatic C-H), 2963, 2869 (methylene CH_2), 1660 (C=O), 1591 (C=N);^{1}H-NMR (400 MHz, C*D*Cl$_3$): δ 12.01 (1H, s, N***H***), 7.84 (1H, d, $J_{5'',4''}$= 7.4 Hz, H-5''), 7.61 (1H, d, $J_{3'',4''}$=3.4 Hz, H-

3''), 7.36 (1H, d, $J_{5',4'}$=7.4 Hz, H-5'), 7.32 (1H, t, *J*=3.5, 7.0 Hz, H-4''), 7.23 (1H, d, $J_{3',4'}$=3.0 Hz, H-3'), 7.18 (1H, s, 6-N***H***), 7.16 (1H, t, *J*=1.6, 4.7 Hz, H-4'), 5.45 (1H, s, H-4); ^{13}C-NMR (100 MHz, C*D*Cl_3): δ 177.28 (C=O), 159.60 (C=N), 139.87 (C-5), 133.55 (C-2''), 132.79 (C-5'') 129.44 (C-3''), 128.54 (C-4''), 126.36 (C-2'), 121.45 (C-5'), 117.04 (C-3', 4'), 110.20 (C-4); ESI-MS: m/z 244 (M+1, 15%), 243 (M, 100%); Anal. calc. for $C_{12}H_9N_3OS$: C, 59.24; H, 3.73; N, 17.27; Found: C, 59.00; H, 3.71; N, 17.20%.

Synthesis of 6-(furan-2-yl)-4-(1H-pyrrol-2-yl)pyrimidine-2(1H)-thione 3ba': The pyrimidine **3ba'** was prepared on reacting chalcone **1b** (1.88 g, 0.01 mol) with urea (0.76 g, 0.01 mol) under the similar conditions as described for pyrimidine **3aa'**.

3ba': Brown solid; yield: 64%; m.p. 111-113^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3408 (1'-NH), 3165 (6-NH), 3099 (aromatic C-H), 2951, 2877 (methylene CH_2), 1598 (C=N), 1038 (C=S);^{1}H-NMR (400 MHz, C*D*Cl_3): δ 11.52 (1H, s, N***H***), 7.90 (1H, d, $J_{5'',4''}$= 6.9 Hz, H-5''), 7.66 (1H, s, H-5'), 7.21 (1H, m, H-4''), 7.16 (1H, s, 6-N***H***), 6.96 (1H, d, $J_{3'',4''}$=8.0 Hz, H-3''), 6.92 (1H, t, *J*=6.2, 7.6 Hz, H-3'), 6.58 (1H, dd, *J*=1.7, 2.9 Hz, H-4'), 4.32 (1H, s, H-4); ^{13}C-NMR (100 MHz, C*D*Cl_3): δ 166.44 (C=S), 144.84 (C=N), 142.24 (C-5), 135.75 (C-2''), 132.24 (C-5''), 128.92 (C-2'), 127.12 (C-5'), 119.17 (C-3''), 116.13 (C-4''), 115.58 (C-3'), 111.47 (C-4'), 107.64 (C-4); ESI-MS: m/z 246 (M+Na, 7%), 243 (M, 10%), 199 (100%); Anal. calc. for $C_{12}H_9N_3OS$: C, 59.24; H, 3.73; N, 17.27; Found: C, 59.04; H, 3.72; N, 17.22%.

Synthesis of 6-(furan-2-yl)-4-(1H-pyrrol-2-yl)pyrimidin-2(1H)-one 3bb': The pyrimidine **3bb'** was prepared on reacting chalcone **1b** (1.88 g, 0.01 mol) with urea (0.60 g, 0.01 mol) under the similar conditions as described for pyrimidine **3aa'**.

3bb': Brown solid; yield: 53%; m.p. 154-156^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3426 (1'-NH), 3317 (6-NH), 3036 (aromatic C-H), 2946, 2893 (methylene CH_2), 1654 (C=O), 1592 (C=N);^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.88 (1H, s, N**H**), 7.34 (1H, d, $J_{5'',4''}$=1.7 Hz, H-5''), 7.31 (1H, m, H-3''), 7.22 (1H, d, $J_{5',4'}$=1.7 Hz, H-5'), 7.07 (1H, m, H-4''), 6.75 (1H, d, $J_{3',4'}$=1.7 Hz, H-3'), 6.50 (1H, m, H-4'), 5.29 (1H, s, 6-N**H**), 5.27 (1H, s, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 178.48 (C=O), 146.22 (C=N), 135.60 (C-5), 128.61 (C-2''), 128.43 (C-5''), 128.38 (C-2'), 127.79 (C-5'), 127.48 (C-3'), 127.17 (C-4'), 125.20 (C-3''), 124.86 (C-4''), 110.17 (C-4); ESI-MS: m/z 246 (M+Na, 7%), 228 (M+1, 20%), 230 (M, 100%); Anal. calc. for $C_{12}H_9N_3O_2$: C, 63.43; H, 3.99; N, 18.49; Found: C, 63.17; H, 3.97; N, 18.41%.

Synthesis of 4-(1H-pyrrol-2-yl)-2-(thiophen-2-yl)-2,3-dihydro-1,5-benzothiazepine 4aa': A mixture of chalcone **1a** (2.03 g, 0.01 mol), 2-aminothiophenol (1.25 g, 0.01 mol) and MeOH (20.0 mL) was taken in 100 ml round bottom flask and refluxed for 3 h in the presence of conc. HCl (using as a catalyst). Thin layer chromatography was used to notice the progress of the reaction. After the completion of the reaction a yellow color solid separated out this was filtered and dried. The obtained yellow solid was recrystallized from a mixture of ethanol and to provide pure compound **4aa'** [72].

4aa': Yellow solid; yield: 67%; m.p. 110-112^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3409 (N-H), 3077 (aromatic C-H), 2955, 2882 (methylene CH_2), 1600 (C=N);^{1}H-NMR (400 MHz, $CDCl_3$): δ 13.54 (1H, s, N**H**), 7.84 (1H, s, H-5''), 7.70 (1H, t, J = 7.6, 10.7 Hz, H-4''), 7.48 (4H, m, H-2''', 3''', 4''', 5'''), 7.37 (1H, d, $J_{5',4'}$= 4.9 Hz, H-5'), 7.10 (1H, d, $J_{3'',4''}$= 3.1 Hz, H-3''), 6.96 (1H, t, J= 4.7, 3.8 Hz, H-4'), 6.59 (1H, s,H-3'), 5.57 (1H, dd, J_{XM}=11.1 Hz, J_{XA}=5.6 Hz, H-X), 3.60 (1H, dd, J_{MX}=7.0 Hz, J_{MA}=10.4 Hz, H-M), 3.14 (1H, dd, J_{AX}=4.8 Hz, J_{AM}=12.8 Hz, H-A); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 161.63 (C=N), 145.90 (C-1), 139.60 (C-5'''), 135.98 (C-7), 135.57 (C-3''', 4'''), 130.88 (C-3''), 126.63 (C-4''), 129.12 (C-2'), 125.77 (C-2''), 125.33 (C-5''), 125.20 (C-5'), 124.72 (C-3'), 114.68 (C-4'), 52.86 (C-5), 37.93 (C-4); ESI-MS: m/z 333 (M+Na, 7%), 310 (M, 7%), 260 (100%); Anal. calc. for $C_{17}H_{14}N_2S_2$: C, 65.77; H, 4.55; N, 9.02; Found: C, 65.50; H, 4.53; N, 8.98%.

Synthesis of 4-(1H-pyrrol-2-yl)-2-(thiophen-2-yl)-2,3-dihydro-1,5-benzoxazepine 4ab': The oxazepine **4ab'** was synthesized on reacting chalcone **1a** (2.03 g, 0.01 mol) with 2-aminophenol (1.09 g, 0.01 mol) under the similar conditions as described for thiazepine **4aa'**.

4ab': Brown solid; yield: 56%; m.p. 137-139^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3421 (N-H), 3098 (aromatic C-H), 2978, 2892 (methylene CH_2), 1588 (C=N);^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.57 (1H, s, N**H**), 7.32 (1H, d, $J_{5'', 4''}$ = 6.3 Hz, H-5''), 7.28 (1H, t, J= 2.3, 5.6 Hz H-4'''), 7.18 (1H, d, J_o= 6.9 Hz, H-2'''), 6.98 (1H, m, H-3'), 6.88 (1H, d, $J_{5',4'}$=5.8 Hz, H-5'), 6.83 (1H, dd, $J_{4'', 3''}$=2.3 Hz, $J_{4'', 5''}$=6.9 Hz, H-4''), 6.72 (1H, d, $J_{3'', 4''}$=2.8 Hz, H-3''), 6.63 (1H, d, J_o=7.2 Hz, H-5'''), 6.49 (1H, d, $J_{3', 4'}$=6.6 Hz, H-3'), 6.12 (1H, dd, $J_{4', 3'}$=6.1Hz, $J_{4', 5'}$=6.1 Hz, H-4'), 5.76 (1H, dd, J_{XM}=10.8 Hz, J_{XA}=9.3 Hz, H-X), 3.72 (1H, dd, J_{MX}=9.6 Hz, J_{MA}=15.6 Hz, H-M), 2.98 (1H, dd, J_{AX}=8.2 Hz, J_{AM}=14.8 Hz, H-A); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 159.98 (C=N), 147.36 (C-7), 143.27 (C-2''), 130.44 (C-5''), 129.89 (C-1), 127.33 (C-4''), 126.60 (C-3''), 125.56 (C-3'''), 122.32 (C-2'), 121.40 (C-4'''), 120.51 (C-5'), 118.76 (C-2'''), 115.32 (C-5'''), 111.36 (C-3'), 109.90 (C-4'), 54.49 (C-5), 35.65 (C-4); ESI-MS: m/z 317 (M+Na, 15%), 294 (M, 100%); Anal. calc. for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52; Found: C, 69.08; H, 4.75; N, 9.48%.

Synthesis of 4-(1H-pyrrol-2-yl)-2-(thiophen-2-yl)-2,3-dihydro-1H-1,5-benzodiazepine 4ac': The diazepine **4ac'** was synthesized on reacting chalcone **1a** (2.03 g, 0.01 mol) wit orthophenylenediammine (1.08 g, 0.01 mol) under the similar conditions as described for thiazepine **4aa'**.

4ac': Dark brown solid; yield: 62%; m.p. 164-166^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3399 (N-H), 3087 (aromatic C-H), 2960, 2880 (methylene CH_2), 1597 (C=N);^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.98 (1H, s, N**H**), 7.46 (1H, d, $J_{5'', 4''}$= 6.0 Hz, H-5''), 7.19 (1H, t, J= 3.4, 6.7 Hz, H-4'''), 7.08 (1H, d, J_o=7.8 Hz, H-5'''), 6.93 (1H, d, $J_{5', 4'}$= 2.8 Hz, H-5'), 6.90 (IH, dd, $J_{4'', 5''}$=5.8 Hz, $J_{4'', 3''}$=7.8 Hz, H-4''), 6.83 (1H, d, J_o=6.9 Hz, H-2'''), 6.80 (1H, s, N**H**), 6.78 (1H, d, $J_{3'', 4''}$=7.2 Hz, H-3''), 6.67 (1H, m,H-3'''), 6.51 (1H, d, $J_{3', 4'}$=3.6 Hz, H-3'), 6.12 (1H, dd, $J_{4', 3'}$=3.9 Hz, $J_{4', 5'}$=2.9 Hz, H-4'), 5.03 (1H, dd, J_{XM}=11.8 Hz, J_{XA}=6.2 Hz, H-X), 4.01 (1H, dd, J_{MX}=12.0 Hz, J_{MA}=15.8 Hz, H-M), 3.93 (1H, dd, J_{AX}=6.8 Hz, J_{AM}=14.9 Hz, H-A); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 156.43 (C=N), 145.11 (C-7), 138.44 (C-2''), 135.91 (C-1), 131.85 (C-5'') 129.99 (C-3''), 129.28 (C-2'''), 126.40 (C-4''), 124.06 (C-4'''), 121.44 (C-2'), 120.80 (C-3'''), 119.67 (C-5'), 115.25 (C-3'), 114.88 (C-5'''), 110.26 (C-4'), 56.68 (C-5), 35.73 (C-4); ESI-MS: m/z 294 (M+1, 25%), 293 (M, 100%); Anal. calc. for $C_{17}H_{15}N_3S$: C, 69.95; H, 5.15; N, 14.32; Found: C, 69.67; H, 5.12; N, 14.26%.

Synthesis of 2-(furan-2-yl)-4-(1H-pyrrol-2-yl)-2,3-dihydro-1,5-benzothiazepine 4ba': The thiazepine **4ba'** was prepared on reacting chalcone **1b** (1.88 g, 0.01 mol) with 2-aminothiophenol (1.25 g, 0.01 mol) under the similar conditions as described for thiazepine **4aa'**.

4ba': Green solid; yield: 69%; m.p. 103-105^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3455 (N-H), 3051 (aromatic C-H), 2959, 2894 (methylene CH_2), 1597 (C=N);NMR (400 MHz, $CDCl_3$): δ 11.50 (1H, s, N**H**), 7.57 (1H, d, $J_{5'', 4''}$= 8.3 Hz, H-5''), 7.51 (1H, dd, J= 3.8, 8.1 Hz, H-4''), 7.31 (1H, d, $J_{5', 4'}$=3.3 Hz, H-5'), 7.29 (2H, m, H-3''', 4'''), 7.07 (IH, dd, J=2.0, 5.5 Hz, H-4'), 7.03 (1H, d, $J_{3'', 4''}$=2.0 Hz, H-3''), 6.72 (1H, d, $J_{3', 4'}$=4.3 Hz, H-3'), 6.67 (1H, dd, J=1.3, 8.5 Hz, H-2'''), 6.55 (1H, m,H-5'''), 5.20 (1H, dd, J_{XM}=14.3 Hz, J_{XA}=5.3 Hz, H-X), 4.47 (1H, dd, J_{MX}=14.2 Hz, J_{MA}=7.0 Hz, H-M), 4.08 (1H, dd, J_{AX}=3.6 Hz, J_{AM}=7.1 Hz, H-A); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 143.23 (C=N), 139.56 (C-1), 139.44 (C-2''), 138.79 (C-5''), 138.59 (C-7), 136.81 (C-3'''), 136.75 (C-2'), 134.83 (C-4'''), 134.73 (C-5'''), 134.67 (C-5'), 131.96 (C-3'), 129.28 (C-4', 4''), 129.23 (C-2'''), 124.84 (C-3''), 124.64 (C-5'''), 45.72 (C-5), 34.95 (C-4); ESI-MS: m/z 317 (M+Na, 10%), 295 (M+1, 5%) 294 (M, 100%); Anal. calc. for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52; Found: C, 69.08; H, 4.77; N, 9.48%.

Synthesis of 2-(furan-2-yl)-4-(1H-pyrrol-2-yl)-2,3-dihydro-1,5-benzoxazepine 4bb': The oxazepine **4bb'** was prepared on reacting chalcone **1b** (1.88 g, 0.01 mol) with 2-aminophenol (1.09 g, 0.01 mol) under the similar conditions as described for thiazepine **4aa'**.

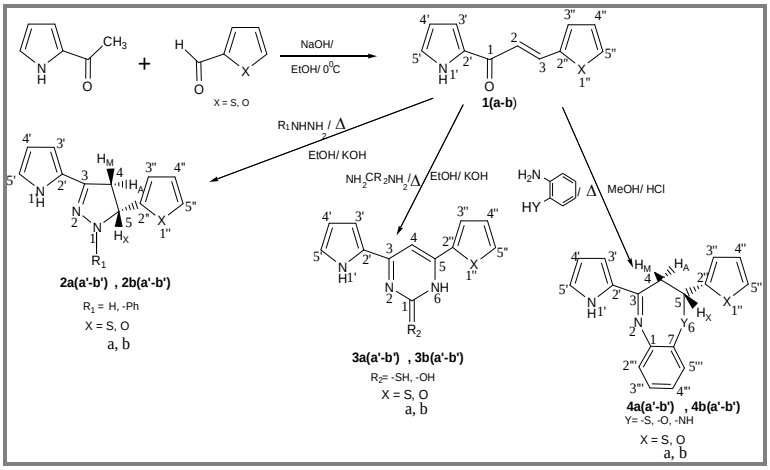
4bb': Dark green solid; yield: 61%; m.p. 103-105^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3400 (N-H), 3102 (aromatic C-H), 2979, 2871 (methylene CH_2), 1597 (C=N);^{1}H-NMR (400 MHz, $CDCl_3$): ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.83 (1H, s, N**H**), 7.21 (4H, m,H-2''', 3''', 4''', 5'''), 7.05 (2H, d, J= 7.2 Hz, H-5', 5''), 6.87 (1H, t, J= 7.6, 7.8 Hz, H-4''), 6.77 (1H, t, J=7.1, 7.8 Hz, H-4'), 6.40 (1H, d, $J_{3'', 4''}$= 7.2 Hz, H-3''), 6.04 (IH, d, $J_{3', 4'}$=7.6 Hz, H-3'), 5.13 (1H, dd, J_{XM}=12.4 Hz, J_{XA}=8.1 Hz, H-X), 3.75 (1H, dd, J_{MX}=12.3 Hz, J_{MA}=16.8 Hz, H-M), 3.06 (1H, dd, J_{AX}=7.9 Hz, J_{AM}=16.3 Hz, H-A); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 163.72 (C=N), 159.83 (C-7), 147.65 (C-1), 147.57 (C-2''), 143.16 (C-5''), 133.86 (C-4''), 130.15 (C-2'), 128.81 (C-3'''), 120.72 (C-4'''), 115.65 (C-2'''), 115.57 (C-5'''), 108.44 (C-5'), 107.38 (C-3''), 101.42 (C-3', 4'), 54.05 (C-5), 32.76 (C-4); ESI-MS: m/z 279 (M+1, 15%), 278 (M, 100%); Anal. calc. for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07; Found: C, 73.07; H, 5.05; N, 10.02%.

Synthesis of 2-(furan-2-yl)-4-(1H-pyrrol-2-yl)-2,3-dihydro-1H-1,5-benzodiazepine 4bc': The diazepine **4bc'** was prepared on reacting chalcone **1b** (1.88 g, 0.01 mol) with orthophenyl enediammine (1.08 g, 0.01 mol) under the similar conditions as described for thiazepine **4aa'**.

4bc': Brick red solid; yield: 65%; m.p. 188-190^{o}C; IR (KBr): ν_{max} (cm^{-1}): 3398 (N-H), 3088 (aromatic C-H), 2985, 2893 (methylene CH_2), 1585 (C=N);^{1}H-NMR (400 MHz, $CDCl_3$): δ 11.88 (1H, s, N**H**), 7.82 (1H, d, $J_{5'', 4''}$= 8.2 Hz, H-5''), 7.63 (1H, t, J= 6.2, 7.8 Hz, H-4'''), 7.48 (1H, d, J_o=8.8 Hz, H-5'''), 7.03 (1H, d, $J_{5', 4'}$= 6.8 Hz, H-5'), 6.98 (IH, dd, $J_{4'', 5''}$=8.8 Hz, $J_{4'', 3''}$=7.1 Hz, H-4''), 6.90 (1H, d, J_o=6.9 Hz, H-2'''), 6.85 (1H, s, 6-N**H**), 6.83 (1H, d, $J_{3'', 4''}$=3.6 Hz, H-3''), 6.76 (2H, m,H-2''', 3'''), 6.66 (1H, d, $J_{3', 4'}$=6.1 Hz, H-3'), 6.36 (1H, dd, $J_{4', 3'}$=6.9 Hz, $J_{4', 5'}$=6.3 Hz, H-4'), 5.36 (1H, dd, J_{XM}=11.2 Hz, J_{XA}=6.9 Hz, H-X), 3.95 (1H, dd, J_{MX}=11.9 Hz, J_{MA}=16.2 Hz, H-M), 3.45 (1H, dd, J_{AX}=6.2 Hz, J_{AM}=16.1 Hz, H-A); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 159.97 (C=N), 155.60 (C-7), 149.74 (C-1), 146.77 (C-2''), 141.18 (C-5''), 133.44 (C-2'''), 129.79 (C-3'), 128.40 (C-5'''), 127.19 (C-3''), 123.22 (C-4''), 118.80 (C-5'), 115.77 (C-3''', 4'''), 110.87 (C-3'), 108.19 (C-4'), 57.19 (C-5), 31.68 (C-4); ESI-MS: m/z 278 (M+1, 15%), 277 (M, 100%); Anal. calc. for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15; Found: C, 73.33; H, 5.42; N, 15.08%.

RESULTS AND DISCUSSION

Chemistry: The heterocycles **2a(a'-b')**, **2b(a'-b')**, **3a(a'-b')**, **3b(a'-b')**, **4a(a'-c')** &**4b(a'-c')** needed for the present study were synthesized from the chalcones **1(a-b)** upon reacting with various cyclizing reagents like hydrazine hydrate, phenyl hydrazine, urea, thiourea, 2-aminothiophenol, 2-aminophenol and orthophenylenediammine using the appropriate solvents. The chalcones were synthesized by reacting 2-acetylpyrrole with thiophene-2-carboxaldehyde and furfuraldehyde under the Claisen Schmidt reaction (Scheme 1).



Scheme 1. Claisen Schmidt reaction

The IR spectra of **2a(a'-b')** & **2b(a'-b')** showed a suitable absorption at because of C=N stretching vibration at 1603-1594 cm^{-1} of the dihydropyrazole moiety. Absence of C=O stretching indicates that this group took place in ring formation. In the ^{1}H-NMR spectra of pyrazolines the N-phenyl, thienyl and furfuryl ring protons appeared in the form of appropriate signals in the aromatic region from δ 7.27–6.35, 7.05-6.81 and 7.62-6.97 and pyrrole ring protons 3', 4' and 5' were found to resonate at δ 6.98–6.11, 6.86-6.72 and 7.40-6.78 respectively. Here three well defined doublet of doublet at δ 6.06-4.35, 4.01-3.80 and 3.49-2.98 could be easily represented by the heterocyclic ring protons H-X, H-M and H-A respectively. The mutual coupling values among these protons were really helpful to describe their mutual stereochemical relationship. It reflects from the coupling constants that H-X and H-M are cis to each other and H-X and H-A is trans to each other.

The carbon framework of the five member heterocycles **2(b-c)** and **2(e-f)** were also studying through their ^{13}C-NMR spectra (100MHz, DMSO-d_6). The noticeable signals were situated at δ 146.78–145.85 for carbon atom in C=N and at δ 59.06–55.31 and 48.20-42.79 for C-4 and C-5 respectively. The resulting carbon atoms were easily resonating at appropriate positions in the aromatic region.
The appearance of singlets δ 5.45-4.32 in the ^{1}H-NMR spectra of **3a(a'–b')** and **3b(a'–b')** confirmed the formation of pyrimidine rings. The noticeable N-H protons were resonating at as a singlet at δ 7.79-5.29. The two noticeable doublets placed at δ 7.90-7.34 and 7.66-7.22 could be assigned to H-5''and 5' of the thienyl/furfyryl and pyrrole ring respectively. . Other protons H-3', 4', 3'', 4'' were found observed at the suitable δ values in the aromatic region (*See experimental*).

After studying their ^{13}C-NMR spectra (100 MHz, DMSO-d_6) of the **3a(a'-b') and 3b(a'-b')** it is found that the most downfield signal was observed at δ 178.48–177.28 and 166.44-162.35 due to their direct linkage to heteroatom. The carbon atom doubly bonded to nitrogen atom (N=***C***H) in pyrimidines **3(a-d)** were noticed in the regionδ 159.60–144.84. The aromatic carbon atoms C-2', 3', 4', 5' of the pyrrole ring and C-2'', 3'', 4'', 5'' of the thienyl and furfuryl ring were very well situated at δ 138.60–111.47. The carbon atom C-4 was easily resonating at δ 118.69–107.64 which is the confirmatory signal for the pyrimidine ring formation.

In the ^{1}H-NMR spectra of **4a(a'–c')**&**4b(a'–c')** three doublet of doublet were found at δ 5.61-5.13, 4.47-3.15 and 4.10-2.98 for protons H-X, H-M and H-A which are confirmatory signal for the formation of the azepine ring. The stereochemistry of these protons H-X, H-M and H-A has been studied through their coupling constant values which suggest that H-X and H-M are vicinal to each other & H-M and H-A are trans to each other. Phenyl ring protons H-2''', 3''', 4''', 5''' appeared very well in the aromatic region at δ 7.63-6.55. Heterocyclic ring protons H-3', 5', 3'', 5'' resonated very well in the form of doublet at δ 7.84-6.04 and H-4', 4'' appeared in the form of triplet or multiplet in the suitable aromatic region (*check experimental*).

The carbon framework of the **4a(a'–c')**&**4b(a'–c')** were explained very well after studying their ^{13}C-NMR spectra (100 MHz, DMSO-d_6). The carbon atom in ***C***=N moiety in azepines was found to be situated at δ 163.72–143.23 and C-1 and C-7 carbon atoms appeared in the downfield region at δ 155.60–135.91 & 149.74–135.98 due to their direct linking to the hetero atom. Other aromatic ring carbon atoms of the thienyl/ furfuryl and pyrrole were found resonate at the appropriate δ values (*vide experimental*). The most important signal of the C-5 and C-4 noticed at δ 57.19–52.86 and 37.93–31.68 which confirmed the formation of the azepine ring.

Antimicrobial activity: The synthesized heterocycles compounds **2a(a'-b'), 2b(a'-b'), 3a(a'-b'), 3b(a'-b'), 4a(a'-c')** and **4b(a'-c')** were screened for their antimicrobial behavior against five bacterial species namely *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klubsellia pneumonia*, *Escherichia coli*, *Bacillius subtilis* and five fungal strains namely *Penicillium glabrum*, *Aspergillus niger*, *Aspergillius janus*, *Fusarium oxysporum*, *Aspergillus sclerotum* respectively. Minimum inhibitory concentrations (MICs) of the chalcones, pyrazolines, pyrimidines and benzothiazoles were

determined by using Serial dilution technique and the minimum concentration required to check the growth of bacteria and fungi was regarded as minimum inhibitory concentration (MIC) [**65**].

Amoxicillin for bacterial strain and fluconazole for fungal strain were used as the standard drug. 1 mL volume of nutrient broth and 1 ml volume of malt extract for bacterial and fungal strain was added to each tube. Different dilutions of the concerned compound at the concentration 100, 50, 25, 12.5, 6.25, 3.12, 1.56 µg mL^{-1} were tested against above said microorganisms. The observed MIC-µg mL^{-1} of the concerned heterocycles has been represented in table 1.

Table 1 shows that the prepared compounds exhibited moderate to significant antimicrobial action. The compounds **2aa'** exhibited good activity against fungal strain *Pencillium glabrum* at MIC of 6.25 µg mL^{-1}. Similarly compound **2bb'** was active (MIC of 6.25 µg mL^{-1}) against bacterial strain namely *Escherichia coli*, *Pseudomonas aeruginosa* and fungal strain namely *Penicillium glabrum*, *Aspergillus niger* respectively.

It is clearthat the pyrimidine **3aa'** showed noticeable behavior against *Klubsellia pneumonia*, *Pseudomonas aeruginosa*, and *Aspergillus niger*, *Penicillium glabrum*at the MIC of 6.25 µg mL^{-1}. Similarly pyrimidine **3ab'** was found to be active against strains namely *Escherichia coli*, *Klubsellia pneumonia*, and *Aspergillus niger*, *Fusarium oxysporum* at the same MIC value. The copmpound**3ba'** against fungal strains *Penicillium glabrum* and *Aspergillus niger* and compounds **3bb'** was most active against *Aspergillus sclerotum* and it had the MIC of 3.12 µg mL^{-1}.

The product **4aa'**possessed good activities (MIC-6.25 µg mL^{-1}) against *Escherichia coli*, *Pseudomonas aeruginosa* and *Aspergillus niger*while compound **4ab'**exhibited antibacterial action against *Klubsellia pneumonia* and *Pseudomonas aeruginosa*. The benzothiazepine **4ba'** showed MIC value of 6.25 µg mL^{-1}l against only one fungal strain *Aspergillius janus* and diazepine **4bc'** was found to be active against most of the bacterial and fungal strains namely against *Klubsellia pneumonia*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Aspergillius janus*, *Aspergillus sclerotum* respectively.

Table 1. MIC (µg mL^{-1}) data of 2a(a'-b'), 2b(a'-b'), 3a(a'-b'), 3b(a'-b'), 4a(a'-c')& 4b(a'-c')

.Compound No	Gram (-ve) Bacteria			Gram (+ve) bacteria			Fungi			*Moniaginosarum sporumrotiorum*
	E. coli	*K. Pneu*	*P. aeru*	*S. aureus*	*B. subtilis*	*P. glab*	*A. Niger*	*F. oxy*	*A. Scle*	
2aa'	25	25	25	25	25	25	25	25	12.5	12.5
2ab'	12.5	25	12.5	25	25	12.5	**6.25**	12.5	25	50
2ba'	25	25	12.5	25	25	25	12.5	25	12.5	12.5
2bb'	**6.25**	25	**6.25**	12.5	25	12.5	**6.25**	**6.25**	25	25
3aa'	25	**6.25**	**6.25**	25	25	**6.25**	**6.25**	25	12.5	12.5
3ba'	25	**6.25**	12.5	12.5	25	25	25	**6.25**	**6.25**	12.5
3ba'	25	25	12.5	25	25	25	**6.25**	**6.25**	25	12.5
3bb'	2.5	12.5	25	25	25	25	12.5	**6.25**	12.5	**3.12**
4aa'	**6.25**	12.5	**6.25**	12.5	12.5	12.5	12.5	**6.25**	12.5	12.5
4ab'	25	**6.25**	**6.25**	25	12.5	12.5	12.5	12.5	12.5	12.5
4ac'	12.5	12.5	12.5	12.5	12.5	12.5	25	25	12.5	12.5
4ba'	12.5	25	12.5	25	25	**6.25**	2.5	25	25	**6.25**
4bb'	25	25	25	25	25	12.5	12.5	25	25	12.5
4bc'	**6.25**	**6.25**	**6.25**	12.5	12.5	12.5	12.5	**6.25**	12.5	**6.25**
Amoxicillin	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**
Fluconazole	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**	**3.12**

APPLICATION

This results shows that some of the tested heterocycles exhibited the noticeable antimicrobial and antioxidant properties.

CONCLUSION

The present study describes the general, efficient protocol for the synthesis of five, six and seven membered heterocycles and antimicrobial-antioxidant behavior of these heterocycles. Some of the tested heterocycles exhibited the noticeable antimicrobial and antioxidant properties.

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