Microwave Assisted Synthesis Characterization And Microbial Evaluation of Hexahydro-2H-pyrrolo [2,3-c:5,4-c']Dipyrazole Derivatives

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Abstract

*The new series of dipyrazole derivatives **3a-e** and **4a-e** were synthesized from reaction of 1-p-tollylpyrolodine-2,5-dione and 1-p-chloropyrolodine-2,5-dione **2 a-e** with substituted benzaldehydes upon microwave irradiation in presence of neutral alumina afforded (3Z,4Z)-3,4-bis(benzylidene) -1-(4-chlorophenyl)pyrrolidine-2,5-dione **1 a-e** and (3Z,4Z)-3,4-bis(benzylidene) -1-(p-tollyl phenyl)pyrrolidine-2,5-dione **2 a-e**. This on further treatment with hydrazine hydrate in presence of neutral alumina upon irradiation in microwave furnished in to dipyrazole derivatives. The structures of synthesized compounds determined by using FT- IR and ^{1}HNMR spectral analysis and all dipyrazole derivatives screened for microbial evaluation against phathogenic micro organisms. Among all the compounds 7-(4-chlorophenyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole-3,4-diyl-diphenol **4a** exhibited promising bacterial activity against P.aeruginosa.*

Key words: p-tollylpyrolodine-2,5-dione , p-chloropyrolodine-2,5-dione , hydrazine hydrate , bis- heterocyclic chalcones , bis-pyrazoline.

Introduction

Heterocyclic compounds play very important role for society as they serve several ways in human life. These are included in life saving various pharmaceutical compounds so from several decades many researchers engaged in synthesizing different heterocyclic compounds. Still now a day's interest of research in this area is increasing because of structural diversity and tremendous applications of heterocyclic compounds. The cyclic imide [1] is important class nitrogenous compounds which have many synthetic applications in the field of pharmaceutical science. The chalcone are versatile synthons for synthesis of variety of heterocyclic compounds [2] they found to have antifungal activity [3]-[4]. The pyrazoline are well known and important five-membered heterocyclic compounds containing two nitrogen atoms. Various methods have been worked out for their synthesis because of their tremendous applications in medicine the pyrazole derivatives found to possess antibacterial activity[5] Antihelminstic activity[6], these are also used in the field of agriculture for crop protection[7], some of derivatives of pyrazole have anti-angiogenic activity[8], anti-inflammatory activity[9], antioxidant activities [10], anti proliferative activity[11], Microwave assisted synthesis of pyazole have antimicrobial activities[12], the One pot synthesis[13] provides better opportunity in the field synthesis. The pyrazoline derivatives have hypertensive activity [14], antinociceptive effect [15], as well as its immense application in field of cancer [16]. It is also act as as antimycobacterial agents[17]. Such great importance of pyrazoline molecule in various fields so here we planned to synthesize bis-pyrazole derivatives incorporated with succinamide miotey from bis hetrocyclic chalcones. By considering environmental impact of synthesis process here environmental friendly solvent free solid phase synthesis has been carried out by use microwave oven.

Experimental

Material Methods

All chemicals used in this work are of synthetic grade. The melting points were taken in to open capillaries and are uncorrected. The I.R spectra were recorded on FTIR shimazdu spectrophotometer using KBr disc method. The ^{1}H NMR spectra were recorded on Bruker mx-500 MHz in $CDCl_3$ and DMSO d_6. The chemical shift was recorded in δ unit relative to TMS as internal standard. The reaction were executed in domestic microwave oven in hours at 450 -640 watt as solid phase solvent free conditions. The reactions were monitored by thin layer chromatography by using pre-coated silica gel aluminum plates and mixture of n-hexane: ethyl acetate 6:4 proportion was used as mobile phase. The identification of spots was done by visualizing plate in U.V chamber.

General procedure for preparation of bis-heterocyclic chalcone:

The bis-hetrocyclic chalcones (**1a-e)** and (**2a-e)** was synthesized by reaction of 1 milimole of 1-p-tollylpyrolodine-2, 5-dione and 1-p-chloropyrolodine-2,5-dione with 2 milimoles of substituted benzaldehyde in presence 1.5 to 2 gm neutral Al_2O_3 under microwave assisted solvent- free condition at 600 w power for 3 to 4 min. thus colored compound was obtained and recrystalised from ethyl alcohol.

(3Z,4Z)-3,4-bis(2-hydroxybenzylidene)-1-p-tolylpyrrolidine-2,5-dione (1a) :
Yellow solid; M.P:166-168 ^{0}C; M F $C_{25}H_{19}NO_4$; M W: 397.42; Anal Cal.: C, 75.55; H, 4.82; N, 3.52; O, 16.10; Found: C, 75.15; H, 4.22; N, 3.72; O, 16.30; FTIR (KBr, cm^{-1}): 1705 (C=O), 3368 (-OH), 2937(-CH_3), 1611(C=C); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 5.1(s, 1H, -OH), 7.31-7.17(m, 6H, Ar-H and =CH).

(3Z,4Z)-3,4-bis(3-nitro benzylidene)-1-p-tolylpyrrolidine-2,5-dione (1b):
Yellow solid; M.P:198-200 ^{0}C; M F; $C_{25}H_{17}N_3O_6$; M W: 455.42; Anal Cal.: C, 65.93; H, 3.76; N, 9.23; O, 21.08; Found: C, 65.33; H, 3.21; N, 9.53; O, 21.28;FTIR (KBr, cm^{-1}): 2937(-CH_3), 1705 (C=O), 1611(C=C) 1345 (Ar-NO_2);^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 8.47-6.67(m, 6H,Ar-H and =CH)

(3Z,4Z)-3,4-bis(2-chloro benzylidene)-1-p-tolylpyrrolidine-2,5-dione (1c):
Yellow solid; M.P: 173-175 ^{0}C; M F $C_{25}H_{17}Cl_2NO_2$; M W: 434.31; Anal Cal.: C, 69.14; H, 3.95; Cl, 16.33; N, 3.23; O, 7.37; Found: C, 69.34; H, 3.86; Cl, 16.43; N, 3.63; O, 7.57; FTIR(KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 713 (C-Cl), 1611(C=C); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 7.40-7.12 (m, 6H,Ar-H and =CH).

(3Z,4Z)-3,4-bis(4-methoxy benzylidene)-1-p-tolylpyrrolidine-2,5-dione (1d):
Yellow solid; M.P:162-164 ^{0}C; M F: $C_{27}H_{23}NO_4$ M W: 425.48; Anal Cal.: C, 76.22; H, 5.45; N, 3.29; O, 15.04; Found: C, 76.42; H, 5.75; N, 3.59; O, 15.24; FTIR (KBr, cm^{-1}): 1705 (C=O)-, 2937(-CH_3), 1178 (C-O ether) 1611(C=C); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 3.7(s, 3H, -OCH_3), 8.22-6.43(m, 6H,Ar-H and =CH).

(3Z,4Z)-3,4-bis(4-methylbenzylidene)-1-p-tolylpyrrolidine-2,5-dione (1e):
Yellow solid; MP: 144-146 ^{0}C; M. F: $C_{27}H_{23}NO_2$ M W: 393.48; Anal Cal.: C, 82.42; H, 5.89; N, 3.56; O, 8.13; Found: C, 82.62; H, 5.69; N, 3.76; O, 8.43; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 1611(C=C); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 8.22-6.43(m, 6H, Ar-H and =CH).

(3Z,4Z)-3,4-bis(2-hydroxybenzylidene)-1-(4-chlorophenyl)pyrrolidine-2,5-dione (2a):
Yellow solid; M.P:116-118^{0}C; Yield: % ; M.F: $C_{24}H_{16}ClNO_4$; Mol.Wt.: 417.84 ; Anal Cal.: C, 68.99; H, 3.86; Cl, 8.48; N, 3.35; O, 15.32; Found: C, 68.79; H, 3.66; Cl, 8.78; N, 3.65; O, 15.42; FTIR (KBr, cm^{-1}): 1705 (C=O),, 3368 (-OH), 2937(-CH_3), 713 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 5.1(s, 1H, -OH), 7.31-7.17(m, 6H,Ar-H and =CH)

(3Z,4Z)-3,4-bis(3-nitro benzylidene) -1-(4-chlorophenyl)pyrrolidine-2,5-dione (2b):
Yellowish white crystals; M.P: 66-68^{0}C; M.F: $C_{24}H_{14}ClN_3O_6$, Mol. Wt.: 475.84 ; Anal Cal.: C, 60.58; H, 2.97; Cl, 7.45; N, 8.83; O, 20.17; Found: C, 60.68; H, 2.87; Cl, 7.85; N, 8.73; O, 20.37; FTIR (KBr, cm^{-1}): 1705 (C=O),), 2937(-CH_3), 1345 (Ar-NO_2) 713 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.57-7.3(m, 6H,Ar-H and =CH)

(3Z,4Z)-3,4-bis(2-chloro benzylidene) -1-(4-chlorophenyl)pyrrolidine-2,5-dione (2c):
Yellow solid; M.P: 203-206^{0}C; M.F: $C_{24}H_{14}Cl_3NO_2$, Mol. Wt.: 454.73, Anal Cal.: C, 63.39; H, 3.10; Cl, 23.39; N, 3.08; O, 7.04; Found: C, 63.59; H, 3.30; Cl, 23.59; N, 3.28; O, 7.34; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 713 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 7.40-7.12 (m, 6H,Ar-H and =CH).

(3Z,4Z)-3,4-bis(4-methoxy benzylidene) -1-(4-chlorophenyl)pyrrolidine-2,5-dione (2d):
Yellow needle shaped crystals; MP: 156-158^{0}C; M.F: $C_{26}H_{20}ClNO_4$, Mol. Wt.: 445.89, Anal Cal.: C, 70.03; H, 4.52; Cl, 7.95; N, 3.14; O, 14.35; Found: C, 70.23; H, 4.72; Cl, 7.85; N, 3.24; O, 14.65; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 1178 (C-O ether) 713 (C-Cl),^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 3.7(s, 3H, -OCH_3), 7.6-7.2(m, 6H, Ar-H and =CH).

(3Z,4Z)-3,4-bis(4-methylbenzylidene) -1-(4-chlorophenyl)pyrrolidine-2,5-dione (2e):
Pale yellow solid; MP: 133-136 ^{0}C; M.F: $C_{26}H_{20}ClNO_2$; Mol. Wt.: 413.9, Anal Cal.: C, 75.45; H, 4.87; Cl, 8.57; N, 3.38; O, 7.73; Found: C, 75.75; H, 4.97; Cl, 8.57; N, 3.48; O, 7.83; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 713 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.3 (s, 1H, CH_3), 7.6-7.2(m, 6H, Ar-H and =CH).

General procedure for synthesis of Bis-pyrazoline derivative

The 1 mole of chalcones **1a-e** and **2a-e** with two moles of hydrazine hydrate in presence of 2 grams of neutral alumina in 100 ml glass beaker and irradiated it in microwave oven at 450 watt for 2 to 3 min the resulting fused mixture of compounds **3a-e** and **4a-e** obtained recrystalised it from ethanol.

2,2'-(7-(p-tolyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole-3,4diyl) diphenol (3a):
Yellow solid; MP: 120-123 ^{0}C; M.F: $C_{25}H_{23}N_5O_2$; M W: 425.48; Anal Cal.: C, 70.57; H, 5.45; N, 16.46; O, 7.52; Found: C, 70.87; H, 5.65; N, 16.76; O, 7.82; FTIR (KBr, cm^{-1}): 3368 (-OH), 2937 (-CH_3), 3294.79 (N-H),1611(C=C); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.34 (s, 3H, -CH3); 2.22 (d, 1H, -CH Pyrazole); 3.34 (d, 1H, -CH Pyrazole); 6.9-7.7(m, 6H, Ar-H); 10.1(s, 1H, -OH); 9.0(s, 1H,-NH Pyrazole)

3,4-bis(3-nitrophenyl)-7-(p-tolyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole (3b):
Yellow solid; MP: 143-145 ^{0}C; M.F: $C_{25}H_{21}N_7O_4$; Mol. Wt.: 483.48; Anal Cal.: C, 62.11; H, 4.38; N, 20.28; O, 13.24; Found: C, 62.71; H, 4.68; N, 20.48; O, 13.74; FTIR (KBr, cm^{-1}): 2937(-CH_3), 1611(C=C),1291.49(C-NO_2),3292.49 (N-H); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.34(s, 1H, CH3), 2.50 (d,1H ,CH pyrazole), 3.34 (d, 1H , CH pyrazole), 8.94(s, 1H, NH Pyrazole), 7.2-8.4(6H, m, Ar-H)

3,4-bis(2-chlorophenyl)-7-(p-tolyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole (3c):
Yellow solid; 180-182 ^{0}C; M.F: $C_{25}H_{21}Cl_2N_5$; Mol. Wt.: 462.37; Anal Cal.: C, 64.94; H, 4.58; Cl, 15.34; N, 15.15; Found: C, 64.98; H, 4.78; Cl, 15.64; N, 15.45;FTIR (KBr, cm^{-1}): 2937(-CH_3),

1611(C=C), 3294.79 (N-H), 716 (C-Cl); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.36 (s, 1H, CH_3), 2.50 (d,1H ,CH pyrazole), 3.34 (d, 1H , CH pyrazole), 6.98-7.94 (6H, m, Ar-H),9.02 (s, 1H, NH pyrazole)

3,4-bis(4-methoxyphenyl)-7-(p-tolyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4c']dipyrazole (3d):
Yellow solid; 150-152 ^{0}C; M.F: $C_{27}H_{27}N_5O_2$; Mol. Wt.: 453.54; Anal Cal.: C, 71.50; H, 6.00; N, 15.44; O, 7.06; Found: C, 71.60; H, 6.20; N, 15.84; O, 7.36; FTIR (KBr, cm^{-1}): 3292.49 (N-H), 2937(-CH_3), 1611(C=C), 1148 (O-CH3);^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.36 (s, 1H, CH_3), 2.50 (d,1H ,CH pyrazole), 3.34 (d, 1H , CH pyrazole), 3.79 (s, 1H, -OCH_3), 6.98-7.94 (6H, m, Ar-H), 9.02 (s, 1H, NH pyrazole)

3,4,7-tri-p-tolyl-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole (3e):
Yellow solid; MP: 176-178 ^{0}C; M.F: $C_{27}H_{27}N_5$; Mol. Wt.: 421.54; Anal Cal.: C, 76.93; H, 6.46; N, 16.61; Found: C, 76.95; H, 6.66; N, 16.81; FTIR (KBr, cm^{-1}): 2937(-CH_3), 1611(C=C), 3292.89 (N-H); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.36 (s, 1H, CH_3), 2.50 (d,1H ,CH pyrazole), 3.34 (d, 1H , CH pyrazole), 6.98-7.94 (6H, m, Ar-H), 9.02 (s, 1H, NH pyrazole)

7-(4-chlorophenyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole-3,4-diyl-diphenol (4a):
Yellow solid; MP: 210-212 ^{0}C; M.F: $C_{24}H_{20}ClN_5O_2$; Mol. Wt.: 445.9; Anal Cal.: C, 64.65; H, 4.52; Cl, 7.95; N, 15.71; O, 7.18; Found: C, 64.75; H, 4.62; Cl, 7.75; N, 15.81; O, 7.38; FTIR (KBr, cm^{-1}): 3368 (-OH), 1611(C=C), 3292.89 (N-H); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm):2.51 (d,1H, CH pyrazole), 3.34(d, 1H, CH pyrazole), 9.01(s, 1H, NH), 10.1(s, 1H, OH), 8.96-7.71(m, 6H, Ar-H) 9.02 (s, 1H, OH) 10.1(s, 1H, -OH)

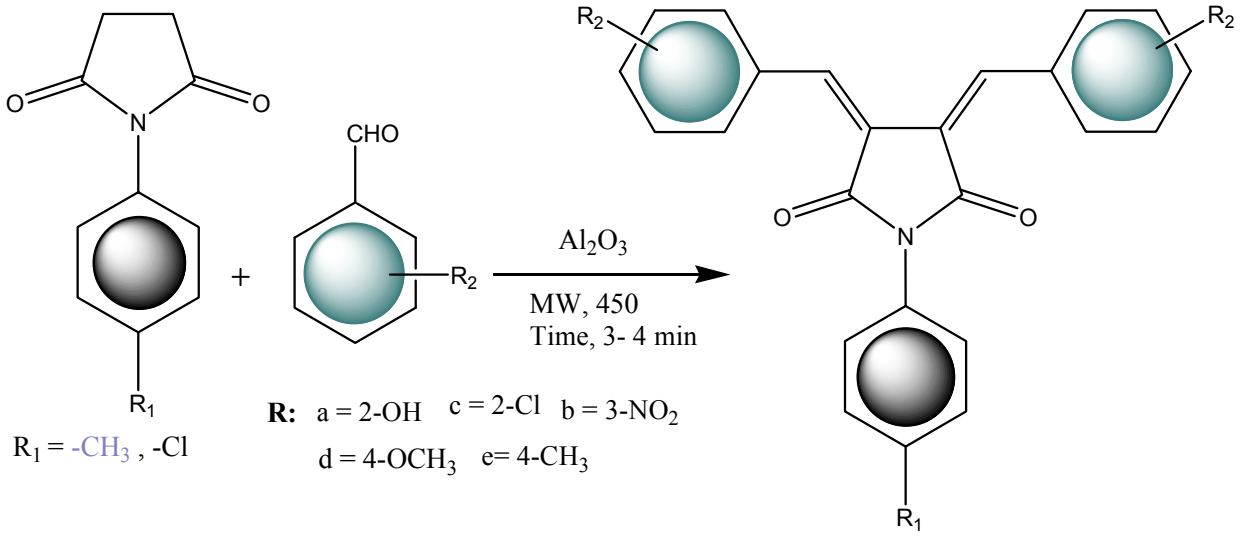
7-(4-chlorophenyl)-3,4-bis(3-nitrophenyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c'] dipyrazole (4b):
Yellow solid; 137-139 ^{0}C; M.F: $C_{24}H_{18}ClN_7O_4$; Mol. Wt.: 503.9; Anal Cal.: C, 57.21; H, 3.60; Cl, 7.04; N, 19.46; O, 12.70; Found: C, 57.41; H, 3.71; Cl, 7.24; N, 19.56; O, 12.78; FTIR (KBr, cm^{-1}): 1611(C=C), 1291.49(C-NO_2), 3292.89 (N-H); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.5(d,1H ,CH pyrazole), 3.34 (d, 1H , CH pyrazole), 8.94 (s, 1H, NH), 7.2-8.4(6H, m, Ar-H).

7-(4-chlorophenyl)-3,4-bis(2-chlorophenyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c'] dipyrazole (4c):
Yellow solid; MP: 142-144 ^{0}C; M.F: $C_{24}H_{18}C_{l3}N_5$; Mol. Wt.: 482.79; Anal Cal.: C, 59.71; H, 3.76; Cl, 22.03; N, 14.51; Found: C, 59.61; H, 3.86; Cl, 22.23; N, 14.31; FTIR (KBr, cm^{-1}): 1611(C=C), 3292.89 (N-H), 716 (C-Cl); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.36 (s, 1H, CH_3), 2.50 (d,1H ,CH pyrazole), 3.34 (d, 1H , CH pyrazole), 6.98-7.94 (6H, m, Ar-H), 9.02 (s, 1H, NH pyrazole).

7-(4-chlorophenyl)-3,4-bis(4-methoxyphenyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole (4d):
Yellow solid; MP: 157-159 ^{0}C; M.F: $C_{26}H_{24}ClN_5O_2$; Mol. Wt.: 473.95; Anal Cal.:C, 65.89; H, 5.10; Cl, 7.48; N, 14.78; O, 6.75; Found: C, 65.19; H, 5.30; Cl, 7.68; N, 14.28; O, 6.25; FTIR (KBr, cm^{-1}): 3292.49 (N-H), 1611(C=C), 1148 (O-CH3); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.50 (d,1H ,CH pyrazole), 3.34 (d, 1H , CH pyrazole), 3.79 (s, 1H, -OCH_3), 6.98-7.94 (6H, m, Ar-H), 10.1(s, 1H, OH), 9.02 (s, 1H, OH).

7-(4-chlorophenyl)-3,4-bis(4-tollylphenyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole (4e):
Greenish yellow solid; 181-183 ^{0}C; M.F: $C_{26}H_{24}ClN_5$; Mol. Wt.: 441.96; Anal Cal.: C, 70.66; H, 5.47; Cl, 8.02; N, 15.85; Found: C, 70.26; H, 5.67; Cl, 8.32; N, 15.45; FTIR (KBr, cm^{-1}): 3292.49 (N-H), 2937(-

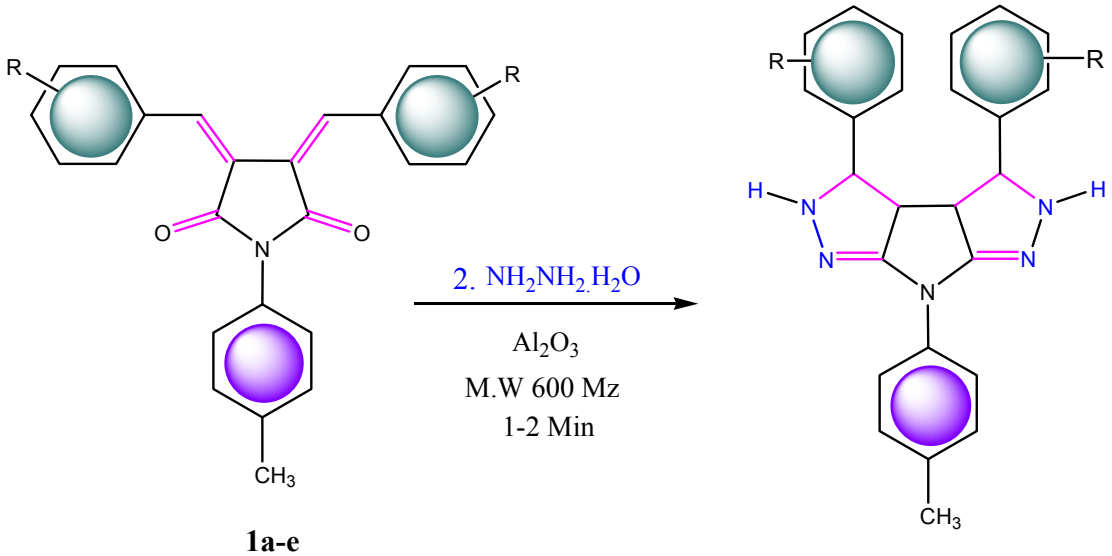
CH_3), 1611(C=C); ^{1}H NMR (500 MHz, DMSOd_6, δ ppm): 2.36 (s, 1H, CH_3), 2.50 (d,1H ,CH pyrazole), 3.34 (d, 1H , CH pyrazole), 6.98-7.94 (6H, m, Ar-H), 9.02 (s, 1H, NH pyrazole).



1a-e & 2a-e

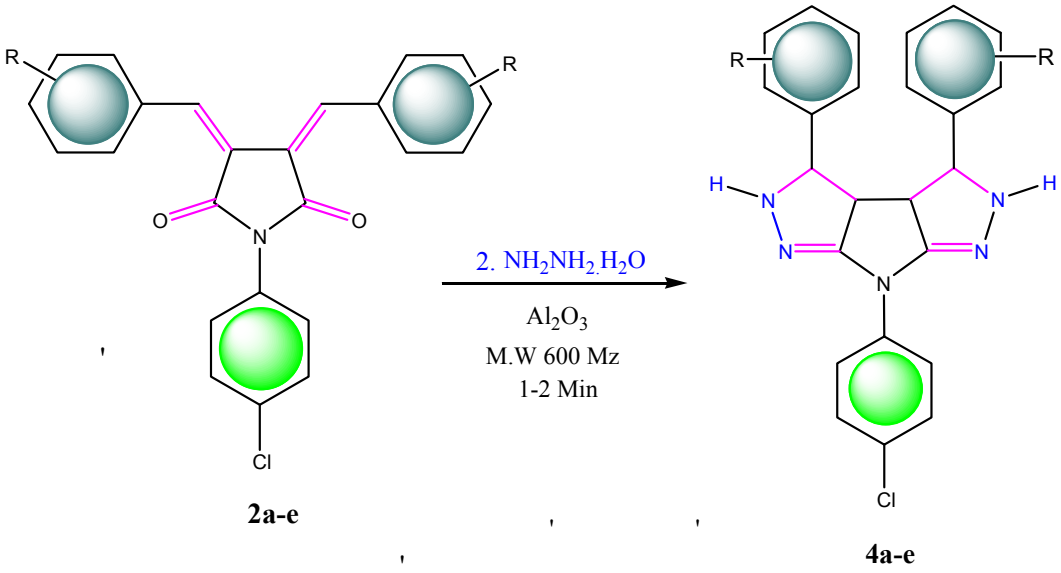
R_1 = -CH_3 , -Cl

SCHEME 1



1a-e **3a-e**

SCHEME 2



2a-e **4a-e**

SCHEME 3

Results and Discussion

Chemistry

The FT IR spectra of compounds **1a-e** and **2a-e** shows absorption band at band 1705 cm^{-1} frequency is due to presence of carbonyl group of chalcone when it is irradiated with hydroxyl amine hydrochloride in presence of neutral alumina in microwave oven it is converted in to (**3a-e**) and (**4a-e**). The carbonyl frequency is diminished it indicate formation of ring and band appear at 2225 due to C-N stretching of pyrazole. The stretching frequency appears at 3292 cm^{-1} is corresponds to presence of –NH of pyrazoline ring system. The ^1H NMR peak -CH of is obtained at 3.4 δ and 2.3 δ indicates the formation of pyrazole ring and the singlet appear at 9.2 δ is due to –NH of pyrazoline.

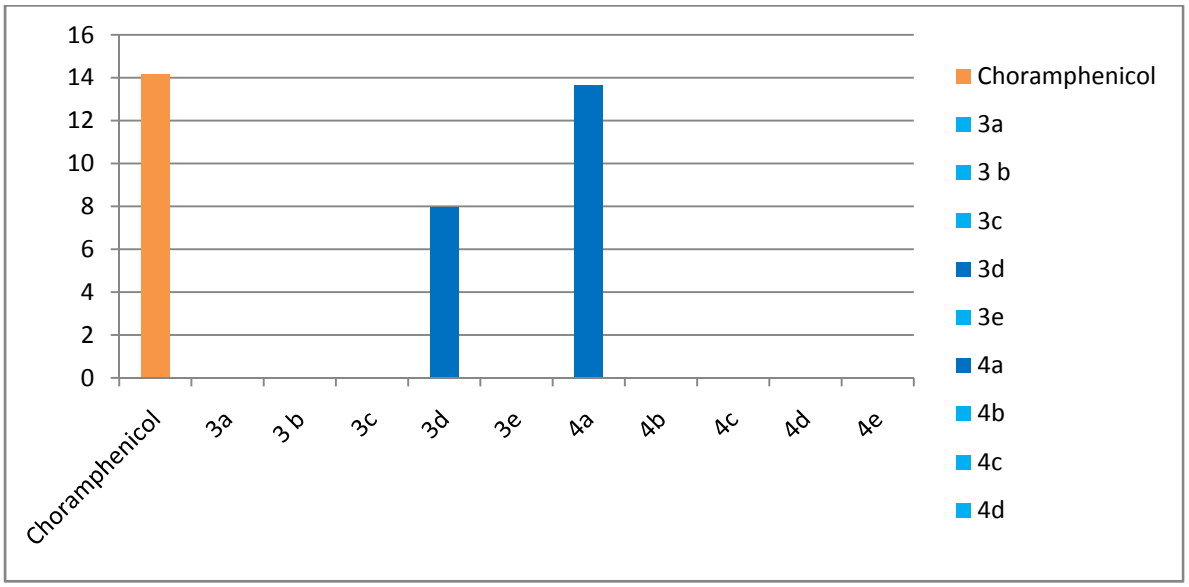
Microbial evaluation

The series of hexahydro-2H-pyrrolo [2,3-c:5,4-c']dipyrazole derivatives **(3a-e)** and **(4a-e)** were screened for antibacterial activity in vitro against Gram positive bacteria Staphylococcus auras (NCIM 2079) , Bacillus subtilies (NCIM 2250) and Gram negative bacteria pseudomonas aeruginosa (NCIM 2036), Escherichia coli (NCIM 2109). The solution of all compounds (5a-e) and (6a-e) were prepared in DMSO solvent .The assay was carried by taking 100 µgm per disc by using disc diffusion method for this purpose nutrient agar media was employed. The results were obtained in the form of zone of inhibition and noted after period of incubation (at 37^0C for 24-28 hrs).The zone of inhibition was measured in mm with help of venire caliper and compared with standard antibiotic Chloramphenicol. Similarly antifungal evaluation was also carried out in vitro against fungi Aspargillus niger (NCIM 545) and Candida albicans (NCIM 3471) in Hi-Media at conc. of 100 µgm per disc. The zone of inhibition was measured in mm and compared with standard drug Amphotericine-B. The anti-bacterial and anti-fungal results obtained are mentioned in table 1.

Table: 1. Antibacterial activity of bis-pyrazoline derivatives

Sr.no	Sample code	*S.aureus*	*B.subtilis*	*E.coli*	*P.aeruginosa*	*C.albicans*	*A.niger*
1	3a	-		-	-	-	-
2	3 b	-	-	8.64	-	-	-
3	3c	-	-	6.35	-	-	-
4	3d	-	-	7.46	7.95	-	-
5	3e	-	-	-	-	-	-
6	4a	7.57	-	-	13.65	-	-
7	4b	-	-	-	-	-	-
8	4c	-	-	-	-	-	-
9	4d	-	-	-	-	-	-
10	4e	9.27		-	-	-	-
11	Choramphenicol	32.13	28.3	27.62	14.18	NA	NA
12	Amphotericine B	NA	NA	NA	NA	17.73	10.27

The antibacterial activity of synthesized compounds compared with standard antibiotic is graphically shown in graph.1 and the zone of inhibition by -2H-pyrrolo [2,3-c:5,4-c']dipyrazole derivatives is depicted in fig.1



Graph: 1. Antibacterial activity of synthesized compounds against P.aeruginosa

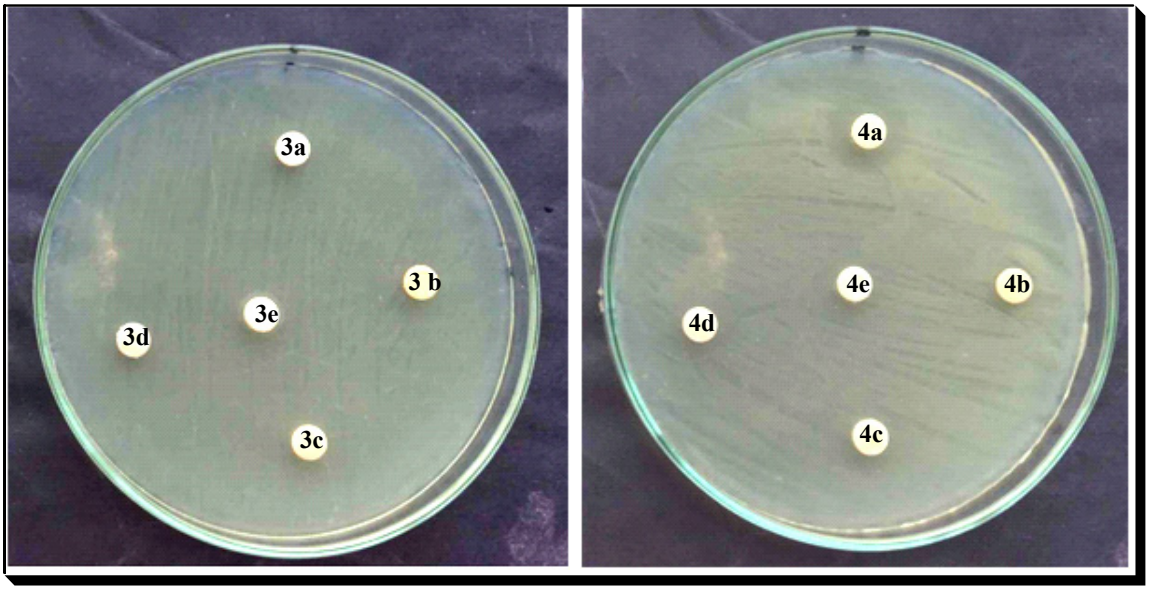


Fig: 1. It shows zone of inhibition of compound 7-(4-chlorophenyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole-3,4-diyl-diphenol (4a) in mm at 100 µgm/ml concentration against P.Aeurogenosa

Conclusion

The above study concluded that the hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole derivative are synthesized from chalcone by using microwave oven in solid phase solvent free condition with easy work up and high yield. This method provides clean and efficient synthesis of heterocyclic compounds. From microbial evaluation it is seen that the synthesized compounds have antibacterial activity against gram positive and gram negative bacterial strains. the compound 3,4-bis(4-methoxyphenyl)-7-(p-tolyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4c']dipyrazole **(3d)** shows good bacterial activity against P.Aeurogenosa and 7-(4-chlorophenyl)-3,3a,3b,4,5,7-hexahydro-2H-pyrrolo[2,3-c:5,4-c']dipyrazole-3,4-diyl-diphenol **(4a)** exhibited promising antibacterial activity against P.Aeurogenosa at 100 µgm/ml concentration. The all synthesized compounds dose not shows antifungal activity at the concentration of 100 µgm/ml.

References

[1]. Dhiware RS and Rajput SS "Synthesis and antimicrobial activity of five membered cyclic imide derivatives of mono, Di and tri substituted aromatic amine and napthyl amine" World journal of Pharmaceutical research, vol. 4, pp1650-1658, June 2015.

[2]. Patil MM Rajput SS "Succinamides: Synthesis, reaction and biological activity" International journal of pharmacy and pharmaceutical science, vol. 6, pp 8-14, November 2014 .

[3]. Rajput SS and Patole SS "Synthesis and uses of chalcone in heterocyclic Synthesis" World journal of Pharmaceutical research, vol. 4, pp1566-1591, July 2015.

[4]. Patole SS and Rajput SS Synthesis Characterization and Biological evaluation of (3z, 4z)-3,4-bis (Substituted phenyl benzylidine)-1-(4-subtituted phenyl) pyrolidine-2,5-dione, International Journal of Pharmacy and Pharmaceutical Sciences Vol. 8, pp 289-291, June 2016.

[5]. Shah PJ and Patel BP "Synthesis characterization and antibacterial activity of novel pyrazolone derivatives." Journal of University Chem Tech and Metallurgy, Vol. 47, pp 257-262, March 2012.

[6]. Patel k and Jayachandran E. "Synthesis Characterisation and antihelminstic activity peritum postuma of new oxidazol incorporated with imidazole and pyrazole". International Journal of Pharma and Bioscience, Vol. 3, pp 257-262, July 2010.
[7]. Plem SC and Muller DM. Key "intermediates: s simple and highly selective synthesis of 5-amino-1-aryl-1H-pyrazole-4-carbonitriles for application in the cop protection". Advance in chem. engineering and Sci, vol. 5 , pp 239-261, May 2015.
[8]. Christodoulou MS and Liekens S. "Novel pyrazole derivatives synthesis and evaluation of anti-angiogenic activity" Bioorganic and Medicinal Chem, Vol.18,pp 4338-4350, August2010
[9]. Nagarpu L and Gaikwad HK. "Synthesis and anti-inflammatory activity of some novel 3-phenyl-N-3-(4-phenylpiperazine-1-yl)propyl-1H-pyrazole-5-carboxamide derivatives". Bioorganic and medicinal chem Letters, Vol.21,pp 4138-4140, Jan2011
[10]. Karrouch K and Chemal L. "synthesis anti-inflammatory and antioxidant activities of some new pyrazole derivatives" Journal of pharmacy research, Vol8, pp 1171-117,Agust 2014.
[11]. Kasmogulleri R and Duran H. "Design synthesis characterization and ant proliferative activity of novel pyrazole-3-carboxyliic acid derivatives" Monaish Chem,vol.14,pp 1743-1749,June 2015.
[12]. Surendra babu MS and Rajshekhar K. "Microwave assisted synthesis characterization DFT studies and antimicrobial activities of novel pyrazole derivatives" Indian journal of advance in chemical science, vol.1, pp 52-56, Jan 2012.
[13]. Aziem AA and Abelhamid AO. "One pot synthesis of pyridine thiazollidine pyrazole and 2, 3-dihydro-1,3,4-thiadazole derivatives under solvent- free condition". International journal advance research, vol.1, pp717-728, sept 2013.
[14]. Turan ZG and Chevallet P. "Synthesis of some thiazolyl-pyrazoline derivatives and preliminary investigation of their hypertensive activity" European Journal of Medicinal Chemistry, vol.3, pp 635-541, May 2000.
[15]. Godey CM and Fighera MR "α_2-Adrenoceptor and 5-HT receptor mediate the antinociceptive effect of new pyrazoline but not of dipyrone" European Journal Pharmacology, vol.49, pp 93-97, june 2004.
[16]. Pal D and Saha S. "Importance of pyrazoline moiety in the field of cancer" International Journal of Pharmacy and Pharmaceutical Sciences, vol.4, pp, Feb 2012.
[17]. Keri RS and Chand K. "Recent progress on pyrazole scaffold-based antimycobacterial agents" Archival of Pharm Chem Life Science, vol 34,pp 299-314, August 2015