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Research Article

Synthesis and antimicrobial activity of chalcones and pyrazolines

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Abstract

Chalcones are 1,3-diphenyl-2-propene-1-one, in which two aromatic rings are linked by a three carbon α,β-unsaturated carbonyl system. They have displayed a broad spectrum of biological activities. In this view it was proposed to synthesize some novel pyrazolines from chalcones. Chalcones are prepared by treating 2-acetyl-5-bromothiophene with different aromatic compounds. These chalcones on condensation with phenyl hydrazine HCl. pyridine as a catalyst gave 3-(5-bromothiphene-2yl)-1-phenyl-1H-pyrazole derivatives. The synthesized compounds have been characterized by their melting point, TLC, IR and 1H NMR spectral data. They have been screened for their antibacterial activity against Gram positive bacteria *B.subtillis* & *B.pumilus* and Gram negative bacteria *E. coli* & *P.vulgaris* and antifungal against *A.niger* & *p.crysogenium*.

Keywords: Pyrazolines, Chalcones, 2-acetyl-5-bromothiophene, 3-(5-bromothiphene-2yl)-1-phenyl-1H-pyrazole.

1. Introduction

Pyrazolines and Chalcones were reported to possess various biological activities. In the present communication we report the synthesis of novel pyrazolines via chalcones[1-6]. Hence, chalcones are important intermediates in the synthesis of various heterocyclic ring compounds like pyrazolines, pyrimidines, isoxazolines and thiazolines etc. Therefore the present research work is viewed on the synthesis of Pyrazolines via chalcones by claisen-schmidt condensation using 3-acetylpyridine with either aromatic or heteroaromatic aldehydes in the presence of alkali [7-15]. The resulting chalcones after purification and characterization by physical and spectral methods have been successfully converted into novel substituted pyrazolines by reaction with phenyl hydrazine hydrochloride in absolute ethanol. The structures of the various synthesized compounds were assigned on the basis of elemental analyses, IR, ^{1}H NMR, and mass spectral data. These compounds were screened for their antimicrobial activity [16].

2. Materials and methods

Melting points were determined on a capillary melting point apparatus and are uncorrected. 1H NMR and 13C NMR spectra were recorded in the indicated solvent on Bruker AMX 400 MHz spectrophotometer using TMS as an internal standard. Infrared spectra were recorded in KBr on Perkin-Elmer BXF1 spectrophotometer. Microanalyses were performed on carlo Ebra 1108 element analyzer and were within the ± 0.5% of the theoretical values. Column chromatography was performed on silica gel (Merck, 100-200 mesh)[17-23].

2.1 Experimental section

General procedure for the synthesis of pyrazolines from chalcones:

Step-1: Synthesis of Chalcones:

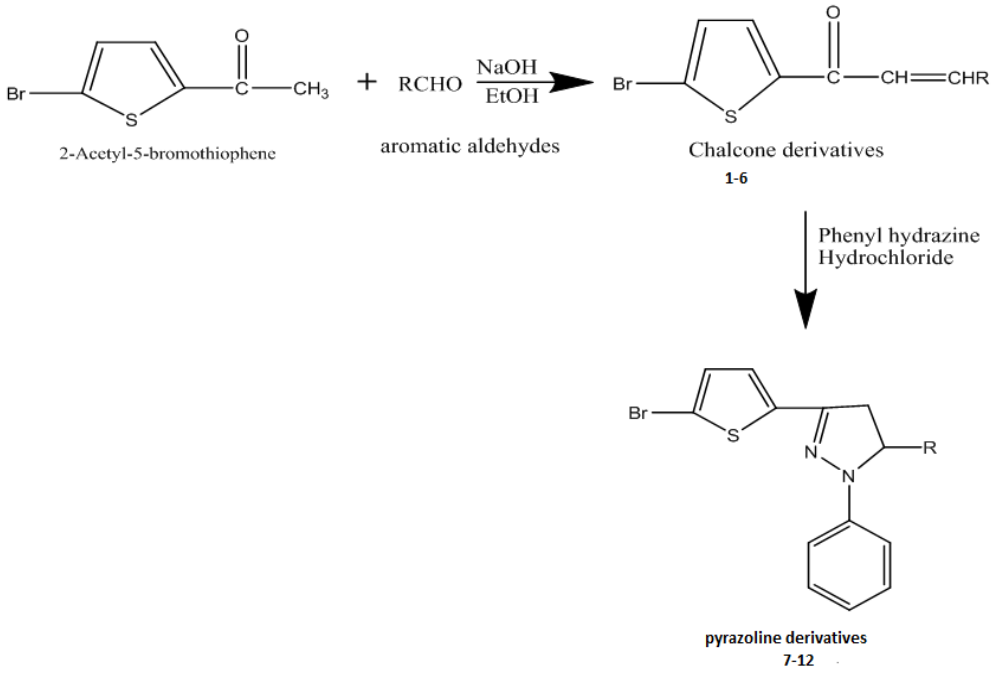
A mixture of 2-acetyl-5-bromothiophene (0.01 Mol) and benzaldehyde derivative (0.01 Mol) was stirred in ethanol (25 mL) and then aqueous solution of 10% potassium hydroxide (6mL) was added to it. The mixture

was kept overnight at room temperature. After completion of the reaction, it was poured into crushed ice and acidified with dil. HCl. The chalcone precipitated out as solid. Then it was filtered, dried and purified by column chromatography using hexane and ethylacetate mixture (90:10) as mobile phase [24,25].

Step-2: Synthesis of Pyrazolines via Chalcones:

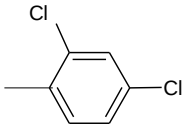
To a solution of Chalcone (0.001 Mol) and phenyl hydrazine Hcl (500 mg) in 20 mL ethanol, pyridine (0.3mL) was added as catalyst. The mixture was refluxed for 5hrs and the solvent was evaporated completely using rotary evaporator. The reaction mixture was poured in to ice water and the solid mass separated was filtered, dried and purified by column chromatography with N-hexane/EtOAC and recrystalised from chloroform to give white crystallised needles [26-28].

Reaction

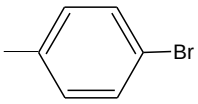


R-indicates:

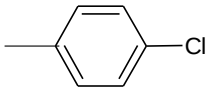
1,7) 2,4-dichloro



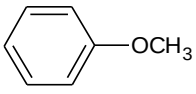
2,8) 4-bromo



3,9) 4-chloro

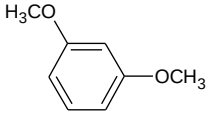


4,10) 4-Methoxy



5,11) 4-fluoro

6,12) 2,4-Dimethoxy



1-(5-bromothien-2-yl)-3-(2,4-dichlorophenyl)- prop-2-en-1- one(1)

IR- (C-Cl) 550.50, (C=C) 1648.68, (=C-H) 3105.37, (C=O) 1520, (C-Br) 672.10. [1] H-NMR 7.0 (1H,d, -CO=CH), 7.4 (2H,d, C-2''H & C-6''H), 7.5(2H,d ,C-3'''H & C- 5''H), 7.7(1H,d,C4'H), 7.8(Ar-CH-CO-,1H,d), 7.26(1H,d,C-3'H).

3-(4-bromophenyl)-1-(5-bromothien-2-yl)-prop-2-en-1-one (2)

IR=(C-H) 3442.76, (C=C) 1648.36, (C-Br) 674.48,(C=O) 1528. [1]H-NMR Alkyl 2923.517.0, (1H,d, -CO=CH), 7.4(2H,d, C-2''H & C-6''H), 7.5(2H,d ,C-3'''H & C-5''H), 7.7(1H,d,C-4'H), 7.8(Ar-CH-CO-,1H,d), 7.26(1H,d,C-3'H).

1-(5-bromothien-2-yl)-3-(4-chlorophenyl)- prop-2-en-1-one(3)

IR(C-Br) 768.99, **(**C-Cl) 487.68, (C=O) 1539.68, (C=C) 1648.69, (=C-H) 3020.27. [1] H-NMR 7.0 (1H,d, -CO=CH), 7.4 (2H,d,C-2''H & C-6''H), 7.5 (2H,d,C-3'''H&C-5'', 7.7(1H,d,C-4'H), 7.8(Ar-CH-CO-,1H,d), 7.26(1H,d,C-3'H).

1-(5-bromothien-2-yl)-3-[4-methoxy)-phenyl]prop-2-en-1- one(4)

IR (=C-H) 3020.27, (C=C) 1648.88, (C=O) 1699.02, (C-Cl) 748.99, (C-Br) 627.28. [1]H-NMR 3.85(3H,S,OCH_3), 6.9(1H,d, =CH-Ar), 7.5-8.90(9H,s).

1-(5-bromothien-2-yl)-3-(4-fluorophenyl)- prop-2-en-1-one(5)

IR **(=**C-H) 3023.43, **(**C=C) 1678.99, (O=C) 1699.98, (C-Br) 768.72, (C-F) 487. [1] H-NMR 7.0(1H,d, J=17HZ, -CO=CH), 7.4(2H,d, J=8HZ, C-2''H &C-6''H), 7.5(2H,d,J=8HZ,C-3'''H&C-5''H), 7.7(1H,d,C-4'H), 7.8(Ar-CH-CO-,1H,d), 7.26(1H,d,C-3'H).

1-(5-bromothien-2-yl)-3-(2,4-dimethoxy)- prop-2-en-1-one(6)

IR (=C-H) 2989.69,(C-Br) 616.69,(C-O) 1048.96,(C-H) 2078.87, Ester 1655.04.

[1] H-NMR 3.85(3H,S,OCH_3), 6.9(1H,d,J=17HZ,=CH-Ar), 7.5-8.90(7H,M Ar-Hz) .

1-(5-bromothien-2-yl)-3-(2,4-dichlorophenyl)-1phenyl-4,5dihydro-1H-pyrazole(7)

IR (=C-H) 3042.32,(N=C) 2224.34,(C-Cl) 558.5,(C-Br) 727.28,(C-C) 1565,(C=C) 1587.20

[1]H-NMR 2.9, (1H,dd,H_A), 3.8(1H,dd,H_B), 5.5(1H,dd,H_x), 6.9-7.9(10H) M, Ar-H.

3-(4-bromophenyl)-1-(5-bromothien-2-yl)- 1phenyl-4,5dihydro-1H-pyrazole(8)IR(=C-H) 3077.60, (N=C)2347.58, (C-Br) 656.56, (C-C) 2864.54(C=C) 1565.13 [1] H-NMR 2.9(1H,dd,H_A), 3.8(1H,dd,H_B), 5.5(1H,dd,H_x), 6.9-7.9(10H) M, Ar-H.

1-(5-bromothien-2-yl)-3-(4-chlorophenyl)- 1phenyl-4,5dihydro-1H-pyrazole(9)

IR(=C-H) 3072.60,(C-Br) 576.78,(C-N) 1014.56, (C-Cl) 757.85.(N=C)2762.82[1] H-NMR 2.9(1H,dd,H_A), 3.8(1H,dd,H_B), 5.5(1H,dd,H_x), 6.9-7.9(10H) M, Ar-H.

1-(5-bromothien-2-yl)-3-[4-methoxy phenyl]-1phenyl-4,5 dihydro-1H-pyrazole(10)

IR(=C-O) 1154.93,(=C-H) 3042.32, (N=C) 2671.30, (C-N) 2423.42, Ester 1648, [1] H-NMR 2.9(1H,dd,H_A), 3.9(1H,dd,H_B), 5.6(1H,dd,H_x), 3.7(3H,S,-OCH_3).

1-(5-bromothien-2-yl)-3-(4-fluorophenyl)- 1phenyl-4,5dihydro-1H-pyrazole(11)

IR(=C-H) 3064.58, (N=C) 2808.51,(C-F) 534.21, (C-Br) 608.20, (C-N)2838.22

[1]H-NMR 2.9(1H,dd,H_A), 3.8(1H,dd,H_B), 5.4(1H,dd,H_x), 6.9-7.9(10H) M, Ar-H.

1-(5-bromothien-2-yl)-3-(2,4-dimethoxy)-1phenyl-4,5dihydro-1H-pyrazole(12)

IR(=C-H) 3563.53, (N=C) 2934.83, (C-N) 2831.50, (C-Br) 693.44, (C-O) 1138.83, Ester 1641.42,[1] H-NMR 2.9(1H,dd,H_A), 3.8(1H,dd,H_B), 5.5(1H,dd,H_x), 3.7-3.9(6H,S,2-OCH_3), (10H,M,Ar-H).

2.2 Biological evaluation

The reported Chalcones and pyrazolines possess antibacterial and antifungal activity, so the Chalcones and pyrazolines prepared during the course of the present work were tested for antibacterial and antifungal activity [29].

A. Antibacterial Activity:

The antibacterial activity was tested by ***cup-plate method.*** The antimicrobial activity of Chalcones and Pyrazolines were tested and compared with the standard (benzylpencillin) solution at concentration of 100µg/ml. Dimethylsulfoxide (DMSO) was used as a solvent and control. The following organisms were used.

Test organisms:

Gram positive bacteria: *Bacillus pumilus* and *Bacillus subtilis*

Gram negative bacteria: *Escherichia coli and Proteus vulgaris*

B. Antifungal activity

The antifungal activity was tested by the same procedure as described in the antibacterial activity except the medium. The antifungal activity of Chalcones and Pyrazolines were tested and compared with the standard (Fluconazole) solution at concentration of 100µg/ml. The following organisms were used [30].

- *Aspergillus niger* and
- *Pencillium crysogenium*.

The results were given in table. The results showed that only some have antibacterial and antifungal activity.

3. Results and Discussion

Table 1: Antibacterial activity of Chalcones (Compounds 1- 6):

Compound code	Zone of inhibition (in mm)							
	B. subtilis		*B. pumilis*		*E. coli*		*P. vulgaris*	
	50 µl	100 µl	50 µl	100 µl	50 µl	100 µl	50 µl	100 µl
Standard	28	33	31	32	25	27	28	31
Control	-	-	-	-	-	-	-	-
1	16	16	10	17	15	19	12	17
2	15	22	16	18	15	23	12	19
3	18	18	13	18	16	18	12	18
4	17	18	15	19	18	17	12	20
5	15	18	12	18	16	19	12	21
6	20	20	12	20	18	18	14	21

Note: " No zone of inhibition"

Table 2: Antibacterial activity of Pyrazolines (Compounds 7– 12):

Compound code	Zone of inhibition (in mm)							
	B.subtilis		*B.pumilis*		*E.coli*		*P.vulgaris*	
	50 µl	100 µl	50 µl	100 µl	50 µl	100 µl	50 µl	100 µl
Standard	28	33	31	32	25	27	28	31
Control	-	-	-	-	-	-	-	-
7	16	18	13	13	14	16	13	17
8	11	19	11	12	10	13	12	18
9	10	20	12	14	11	20	12	18
10	13	20	11	13	12	17	13	17
11	12	16	12	14	13	20	12	20
12	13	20	14	13	12	20	14	21

Note: – " No zone of inhibition"

Table 3: Antifungal activity of Chalcones (compounds 1 -6):

Compound code	Zone of inhibition (in mm)			
	A.niger		*P.crysogenum*	
	50 µl	100 µl	50 µl	100 µl
Standard	24	28	22	27
Control	-	-	-	-
1	19	20	18	19
2	11	12	13	17
3	17	19	18	20
4	11	11	11	17
5	11	11	12	14
6	10	12	12	13

Note: " – " No zone of inhibition

Table 4: Antifungal activity of Pyrazolines (Compounds 7– 12):

Compound code	Zone of inhibition (in mm)			
	A. niger		*P. crysogenium*	
	50 µl	100 µl	50 µl	100 µl
Standard	24	28	22	27
Control	-	-	-	-
7	11	13	14	17
8	10	11	10	15
9	11	13	12	14
10	13	14	13	14
11	12	14	11	13
12	10	12	12	17

Note: " No zone of inhibition"

From the above results it is evident that all the synthesized compounds showed antibacterial and antifungal activities at both 50µg (0.05 ml) and 100µg (0.1 ml) dose levels but less than that of the benzylpencillin and fluconazole used as standards for antibacterial and antifungal activities respectively. Among the compounds tested, 4,5,6,9,12 were found to be more potent antibacterial compounds and 8,12 exhibited the highest and 1,3 shows moderate antifungal activity. However, in particular pyrazoline containing chlro (9) substitution at para position on phenyl ring enhanced both the antibacterial and antifungal activities. The standard drugs used were Benzylpencillin and Fluconazole for antibacterial and antifungal activity respectively.

4. Summary and conclusion

The title demonstrates "An Efficient Synthesis and ''Synthesis and antimicrobial activity of chalcones and pyrazolines'' and through the synthesis of chalcones by 2-acetyl-5-bromo- thiophene with different aldehydes. The formed chalcones were treated with phenyl hydrazine hydrochloride in presence of pyridine

The proposed compounds were synthesised successfully and characterized by Melting point, recrystallisation, ^{1}HNMR, IR, spectroscopy. All the synthesized coumpounds were subjected to antibacterial and anti-fungal activity.

The chalcones and pyrazoline derivatives evaluated for antibacterial activity and they were effective against *B.pumilis, B. subtilis,* and *E.coli, and P.vulgaris* at both the concentration levels when compared with penicillin-G as standard references.

It is interesting to note from the result of antifungal evaluation of chalcones and pyrazolines are effective against *A.niger, p.crysogenum* when compared with fluconazole as reference standard. From the above results, it is interesting to note that the challcones and pyrazolines, which are having electron releasing substituents like chlorine, fluorine, methoxyl at C-4 position of aromatic ring-B showed moderate to considerable antibacterial and antifungal activities, when compared to that of heteroaryl chalcones and pyrazolines.

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