SYNTHESIS AND BIOLOGICAL SCREENING OF DIFFERENT HETEROCYCLES DERIVED FROM 4-(PYRIDINE-2-YL)BENZALDEHYDE

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Abstract: Various chalcones derived from 4-(pyridine-2-yl)benzaldehyde were converted into biologically important heterocycles. Synthesized compounds were tested for their antifungal and antibacterial activities.

Introduction

In present years pyridine derivatives have received significant attention owing to their diverse range of biological properties viz. blood platelet disaggregation[1], anti-microbial[2-4], anthelmintic[5], anti-bacterial, anti-inflammatory[6], anti-hypertensive[7], antifungal[8].

Chalcones are the important class of natural/synthetic compounds belonging to the flavonoid family. Chalcones possess a broad spectrum of biological activities including antibacterial, anthelmintic, amoebicidal, antiulcer, antiviral, insecticidal, antiprotozoal, anticancer, cytotoxic, immunosuppressive etc[9,10].

The chemistry of chromones and its derivatives have been studied for over a century or more due to important biological activities. Activities associated with this nucleus are antimicrobial[11], agrochemical fungicides[12] etc. Some chromones are also used as beta agonist in asthma[13]. Chromones with heterocyclic nucleus at 2- or 3- position are found to be associated with promising antibacterial and antifungal properties[14].

Pyrazoles are important class of heterocyclic compounds which are associated with important applications[15,16]. The activities associated with this nucleus are antihyperglycemic[17], antibacterial[18], fungicidal[19], anticancer[20] and antiviral[21].

1,4-Benzothiazepine derivatives are of considerable interest because of their biological activities as inhibitors of HIV-1 integrase, anti-tumor, antibiotics, enzyme inhibitors, muscle relaxant, anticonvulsant, sedatives and hypnotics[22]. Some dihydrobenzothiazepines have excellent fungicidal activities[23]. Benzothiazepines are also associated with activities such as antihypertensive[24] and antibacterial[25]. Benzothiazepines have been reported as neuroleptic agents[26].

Nitrogen containing heterocyclic compounds[27] like pyrazolines have received considerable attention in recent years due to their biological activities like antiinflammatory[28], analgesic, anticonvulsant[29] etc.

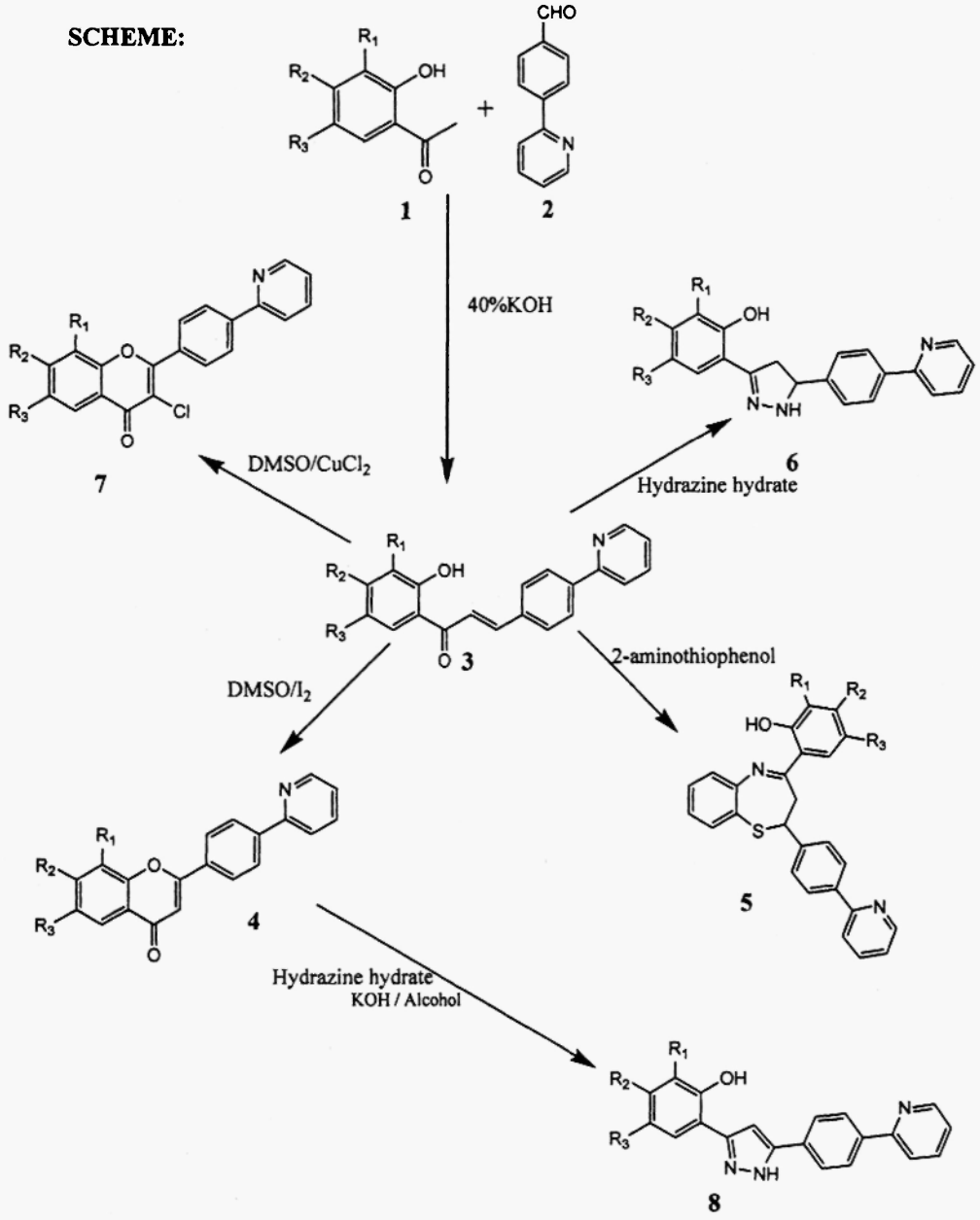
The various physiological and biological activities associated with these moieties prompted us to synthesize pyridine containing chalcones, chromones, chlorochromones, pyrazoles, pyrazolines and 1,4-benzothiazepines.

Biological activities

Antimicrobial activity: Synthesized compounds were screened for their antifungal and antibacterial activities. The invitro antimicrobial activities of the synthesized compounds were assessed against fungi and bacteria. The fungi used were *C.albicans* and *A. Fumigatus*. The bacterias used were *S. aureus*, *E. coli* and *S. faecium.* Fluconazole and Vancomycin were used as standards for comparison for antifungal and antibacterial activities respectively. The activities were determined by measuring the diameter of the inhibition zone in mm.

Among the screened compounds, most of the compounds have shown antimicrobial activities as shown in **Table-2**.

SCHEME:



Experimental

Melting points were recorded in open capillaries in liquid paraffin bath and are uncorrected. IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in KBr disc.^{1}H NMR spectra were recorded on Bruker Avance II 400 MHz NMR spectrometer in DMSO / $CDCl_3$ as a solvent and TMS as an internal standard. Peak values are shown in δ (ppm). Mass spectra were recorded on a Q-T micromass 5630 mass spectrometer. Elemental analyses were obtained on a Perkin-Elmer 2400 microanalyser.

1-(2-Hydroxyphenyl)-3-(4-(pyridin-2-yl)phenyl)prop-2-en-1-one (3a-h).

Equimolar amount of compound **1** (0.02 mole) and **2** (0.02 mole) were dissolved in 50 mL of alcohol in conical flask. To this reaction mixture 40% KOH (10ml) was added. The reaction mixture was stirred at room temperature for 24 hrs. The contents were then poured into crushed ice and neutralized with acetic acid. The yellow solid thus obtained was filtered and crystallized from alcohol to afford pure compounds **3**. The compounds synthesized by above procedure are listed in **Table-1**. Their structures have been confirmed by IR, ^{1}H NMR, mass spectra and elemental analysis.

3a: IR: 3380, 3065, 1637, 1570, 1467, 1134, 1049, cm^{-1}; ^{1}H NMR: δ 7.26-7.30 (m, 1H), 7.58-7.62 (d, 2H), 7.78-7.84 (m, 5H), 8.01- 8.05 (d, 1H), 8.10-8.12 (d, 2H), 8.72-8.74 (d, 1H), 13.39 (s, 1H); Mass: M^+ 369.

3b: IR: 3376, 3005, 1640, 1576, 1484, 1050, 977 cm^{-1}; ^{1}H NMR: δ 2.35 (s, 3H), 6.91 (s, 1H), 7.25-7.28 (q, 1H), 7.56-7.60 (d, 1H, J = 15.4 Hz), 7.75-7.77 (m, 4H), 7.86 (s,1H), 7.93-7.96 (d, 1H, J = 15.4 Hz), 8.07-8.09 (d, 2H), 8.71-8.72 (d, 1H), 12.72 (s, 1H); Mass: M^+ 349.

3h: IR: 3371, 1632, 1595, 1485 cm^{-1}; ^{1}H NMR: δ 2.30 (s, 3H), 6.84-6.88 (t, 1H), 7.25-7.38 (m, 2H), 7.70-7.74 (d, 1H, J=15.5 Hz), 7.75-7.81 (m, 5H), 7.93-7.97 (d, 1H, J=15.5 Hz), 8.07-8.09 (d, 2H), 8.71-8.73 (m, 1H), 13.15 (s, 1H); Mass: M^+ 315.

2-(4-(Pyridine-2-yl)phenyl)-4*H*-chromon-4-one (4a-h).

The compound **3** (0.001 mole) was dissolved in 15 ml DMSO. To this reaction mixture catalytic amount of I_2 was added. Contents were heated at 140°C for 1 hr and then the reaction mixture was left overnight. To the reaction mixture 100 ml of cold water was added and the separated product was filtered and washed with cold water followed by dilute sodium thiosulphate solution several times, again it was washed with cold water. The product was crystallized from alcohol to afford compounds **4**. The compounds synthesized by above procedure are listed in **Table-1**. Their structures have been confirmed by IR, ^{1}H NMR, mass spectra and elemental analysis.

4b: IR: 3039, 1640, 1583, 1513, 1049 cm^{-1}; ^{1}H NMR: δ 2.53 (s, 3H), 6.86 (s, 1H), 7.29-7.36 (m, 1H), 7.51 (s, 1H), 7.81-7.82 (q, 2H), 8.00-8.03 (q, 2H), 8.16 (s, 1H), 8.18-8.19 (t, 2H), 8.73-8.75 (d,1H); Mass: M^+ 347.

4c: IR: 3077, 1638, 1509, 1040 cm^{-1}; ^{1}H NMR: δ 6.89 (s, 1H), 7.31-8.19 (m, 6H), 8.21-8.23 (d, 2H), 8.27- 8.30 (d, 2H), 8.71- 8.73 (d, 1H); Mass: M^+ 333.

4d: IR: 3060, 1644, 1487 cm^{-1}; ^{1}H NMR: δ 2.32 (s, 3H), 7.15 (s, 1H), 7.40-8.18 (m, 6H), 8.20-8.26 (d,2H), 8.28-8.34 (d, 2H), 8.72-8.74 (d, 1H); Mass: M^+ 313.

2,3-Dihydro-2-(4-(pyridin-2-yl)phenyl)benzo[b][1,4]thiazepin-4-yl)phenol (5a-h).

Compounds **3** (0.001 mole) and 2-amino thiophenol (0.001 mole) were taken in 100 ml RBF with 15 ml ethanol. The contents were heated under refluxed for 4 hr. Then to the reaction mixture, 5 mL gl. acetic acid was added and heating was continued for further 4 hr. After completion of heating, the contents were cooled to room

temperature and poured into crushed ice. The solid thus obtained was separated by filtration. The resulting product was crystallized from alcohol to afford compounds **5.** Products obtained were identified with the help of spectral data and elemental analysis. Their characterization data is given in the **Table-1**.

5a: IR: 3300, 1578, 1488, 1066 cm^{-1}; ^1H NMR: δ 2.56 (s, 3H) 3.10-3.13 (dd,1H), 3.42-3.46 (dd,1H), 5.10-5.13 (dd,1H), 7.17 (s, 1H), 7.30-8.68 (m, 13H), 13.82 (s, 1H); Mass: M^+ 456.

5b: IR: 3250, 3049, 1585, 1493, 656 cm^{-1}; ^1H NMR: δ 2.30 (s, 3H), 3.08-3.15 (dd, 1H), 3.40-3.44 (dd, 1H), 5.09-5.13 (dd, 1H), 6.97-8.69 (m, 15H), 14.27 (s, 1H); Mass: M^+ 422.

5c: IR: 3270, 1580, 1472, 1061 cm^{-1}; ^1H NMR: δ 3.09-3.12 (dd, 1H), 3.39-3.42 (dd, 1H), 5.09-5.12 (dd, 1H), 7.28-8.72 (m, 15H), 14.01 (s, 1H); Mass: M^+ 442.

2-(4,5-Dihydro-5-(4-(pyridine-2-yl)phenyl)-1*H*-Pyrazol-3-yl)phenol (6a-h).

Compound **3** (0.001mole) was dissolved in 25 ml alcohol in 100 ml RBF. To this reaction mixture 1 ml hydrazine hydrate was added and the contents were heated under reflux for 4 hours. Then to the same reaction mixture, 2 ml gl. acetic acid was added and heating was continued for further 4 hours. After completion of reaction, the contents were cooled to room temperature and poured into crushed ice. The solid thus obtained was separated by filtration and crystallized from alcohol to get compounds **6.** Products obtained were identified with the help of spectral data and elemental analysis. Their characterization data is given in the **Table-1**.

6b: IR: 3400, 3326, 3040, 1589, 1493 cm^{-1}; ^1H NMR: δ 2.24 (s, 3H), 3.14-3.21 (dd, 1H), 3.57-3.64 (dd, 1H), 4.93-4.97 (dd, 1H), 6.2 (s, 1H), 7.70-8.70 (m, 11H), 10.83 (s, 1H); Mass: M^+ 329.

6e: IR: 3395, 3039, 1580, 1490 cm^{-1}; ^1H NMR: δ 2.31 (s, 3H), 3.12-3.17 (dd, 1H), 3.60-3.64 (dd, 1H), 4.95-4.99 (dd, 1H0, 6.27 (bs, 1H), 7.19 (s, 1H), 7.30-7.92 (m, 9H), 10.80 (s, 1H); Mass: M^+ 363.

6f: IR: 3398, 3045, 1590, 1495 cm^{-1}; ^1H NMR: δ 3.15 (dd, 1H), 3.62-3.67 (dd, 1H), 4.96-5.00 (dd, 1H), 6.25 (s, 1H), 7.20-7.89 (m, 11H), 10.82 (s, 1H); Mass: M^+ 349.

3-Chloro-2-(4-(pyridin-2-yl)phenyl)-4*H*-chromon-4-one (7a-h).

Compound **3** (0.001 mole) was dissolved in 15 ml DMSO. To this reaction mixture excess (2 gm) of $CuCl_2$ was added. The reaction mixture was heated under mild reflux for 3 hours and left overnight. Then 100 ml ice cold water was added in it. The solid thus obtained was filtered and washed with dil.HCl and again with water. The product was crystallized from acetic acid and purified by column chromatography to afford pure compounds **7**. The compounds synthesized by above procedure are listed in **Table-1**.

7b: IR: 3075, 1666, 1560, 1460, 1047 cm^{-1}; ^1H NMR: δ 7.38 to 8.11 (m, 10H); Mass: M^+ 402.

7d: IR: 3072, 1665, 1509, 1040 cm^{-1}; ^1H NMR: δ 2.35 (s, 3H), 7.36-8.10 (m, 11H); Mass: M^+ 347.

7e: IR: 3070, 1670, 1513, 1049 cm^{-1}; ^1H NMR: δ 2.38 (s, 3H), 7.12 (s, 1H), 7.38-8.32 (m, 9H); Mass: M^+ 382.

2-(5-(4-(Pyridine-2-yl)phenyl)-1*H*-pyrazol-3-yl)phenol (8a-h).

A mixture of **4** (0.001mole) and (0.002mole) of hydrazine hydrate were dissolved in 10 ml ethanol with 0.25 g KOH. The reaction mixture was then refluxed for 3 hrs. After completion of heating, the reaction mixture was cooled to room temperature and

then poured into crushed ice and neutralized with acetic acid. The resulting product was separated by filtration. The product was crystallized from ethanol and purified by column chromatography to afford pure compounds **8**. The compounds synthesized by above procedures are listed in **Table-1**. Their structures have been confirmed by IR, ^{1}H NMR, mass spectra and elemental analysis.

8b: IR: 3140, 3080, 1590, 1498 cm^{-1}; ^{1}H NMR: δ 2.28 (s, 3H), 6.98-8.23 (m, 11H), 8.78 (s, 1H), 10.40 (s 1H); Mass: M$^+$ 327.

8e: IR: 3136, 3082, 1589, 1508, 1097 cm^{-1}; ^{1}H NMR: δ 2.36 (s, 3H), 6.92 (s, 1H), 6.99 (s, 1H), 7.31-8.15 (m, 9H), 8.74 (s, 1H), 10.60 (s, 1H); Mass: M$^+$ 361.

Table-1: Characterization data of the synthesized compounds.

Compd.	R1	R2	R3	m.p. °C	Yield (%)	C Found (Calcd)	H Found (Calcd)	N Found (Calcd)
3a	Cl	H	Cl	173	68	63.91 (64.88)	3.46	3.65 (3.54)
3b	H	Me	Cl	167	67	71.68 (72.10)	4.55	3.95 (4.61)
3c	H	Me	H	139	65	78.79 (79.98)	5.40	4.41 (5.43)
3d	H	H	Me	132	64	78.99 (79.97)	5.35	4.40 (5.43)
3e	H	H	Cl	125	66	71.05 (71.54)	4.15	4.13 (4.20)
3f	H	H	H	118	61	79.02 (79.73)	4.95	4.60 (5.02)
3g	H	H	F	138	60	74.21 (75.23)	4.05	4.32 (4.42)
3h	Me	H	H	127	58	78.97 (79.98)	5.35	4.40 (5.43)
3i	Me	H	Me	166	55	79.28 (80.22)	5.74	4.20 (5.81)
4a	Cl	H	Cl	206	52	64.23 (65.24)	2.95	3.75 (3.01)

4b		H	Me	Cl	266	57	74.50	4.00
	3.97						(75.52)	
	(4.06) (4.03)							
4c		H	H	Cl	252	58	71.06	3.55
	4.16						(71.97)	
	(3.62) (4.25)							
4d		H	H	Me	176	55	79.48	4.75
	4.42						(80.49)	
	(4.82) (4.47)							
4e		H	Me	H	171	52	79.08	4.70
	4.40						(80.49)	
	(4.82) (4.47)							
4f		Me	H	Me	159	49	79.79	5.00
	4.08						(80.71)	
	(5.23) (4.28)							
4g		H	H	H	224	55	79.23	4.30
	4.61						(80.25)	
	(4.38) (4.68)							
4h		H	H	F	178	57	74.95	4.75
	4.15						(75.66)	
	(4.84) (4.20)							
5a		H	Me	Cl	222	69	69.90	4.55
	6.01						(70.96)	
	(4.63) (6.13)							
5b		H	H	Me	173	65	75.71	5.20
	6.55						(76.75)	
	(5.25) (6.63)							
5c		H	H	Cl	221	69	69.01	4.25
	6.25						(70.50)	
	(4.32) (.32)							
5d		Cl	H	Cl	190	71	64.49	3.75
	5.82						(65.41)	
	(3.80) (5.87)							
5e		H	H	H	205	63	75.42	4.90
	6.82						(76.44)	
	(4.93) (6.86)							
5f		H	H	F	197	64	73.18	4.45
	6.55						(73.22)	
	(4.49) (6.57)							
5g		Me	H	H	203	59	75.79	5.20
	6.58						(76.75)	
	(5.25) (6.63)							

6a			H	Me	H	173	53	76.50	5.75
	12.70							(76.57)	
	(5.81)	(12.76)							
6b			H	H	Me	143	54	76.49	5.73
	12.60							(76.57)	
	(5.81)	(12.76)							
6c			H	H	F	166	50	71.01	4.77
	12.49							(76.06)	
	(4.84)	(12.60)							
6d			Me	H	H	178	51	76.51	5.75
	12.66							(76.57)	
	(5.81)	(12.76)							
6e			H	Me	Cl	165	55	68.34	4.90
	11.48							(69.32)	
	(4.99)	(11.55)							
6f			H	H	Cl	169	57	76.00	5.35
	13.25							(76.17	
	(5.43)	(13.52)							
6g			Cl	H	Cl	171	59	62.20	3.89
	10.88							(62.51)	
	(3.93)	(10.94)							
7a			H	H	H	164	49	71.89	3.55
	4.03							(71.97)	
	(3.62)	(4.20)							
7b			Cl	H	Cl	203	52	58.95	2.35
	3.40							(59.66)	
	(2.50)	(3.48)							
7c			H	H	F	218	50	68.17	3.06
	3.76							(68.29)	
	(3.15)	(3.98)							
7d			H	H	Me	205	52	72.23	3.83
	3.80							(72.52)	
	(4.06)	(4.03)							
7e			H	Me	Cl	158	51	64.88	3.41
	3.55							(65.99)	
	(3.43)	(3.66)							
7f			H	H	Cl	147	50	65.62	2.86
	3.68							(65.24)	
	(3.03)	(3.80)							
7g			Me	H	H	141	48	71.93	3.84
	3.90							(72.52)	
	(4.06)	(4.03)							
7h			Me	H	Me	204	49	72.69	4.33
	3.78							(73.02)	
	(4.46)	(3.87)							

8a			H	H	Cl	232	66	68.68 3.93
	11.89							
								(69.070
	(4.06)	(12.08)						
8b			H	H	Me	209	62	76.72 5.10
	12.50							
								(77.04)
	(5.23)	(12.83)						
8c			Cl	H	Cl	328	70	62.28 3.08
	10.05							
								(62.84)
	(3.43)	(10.99)						
8d			Me	H	Me	227	64	76.42 5.40
	11.79							
								(77.40)
	(5.61)	(12.31)						
8e			H	Me	Cl	246	66	68.70 4.18
	11.33							
								(69.71)
	(4.46)	(11.61)						

Table-2: Antimicrobial activities of synthesized compounds. (Dilution: 100 μg/ml.)

Compd.	Conc. (μg/ml.)	Zone of inhibition (mm) C.albicans	A.fumigatus	S.aureus	E.coli	S.faecium
3a	100	12	08	08	06	10
3b	100	14	12	10h	12	12
3c	100	10h	06h	12	09	08
3e	100	12h	06	08	10	08
3f	100	10	04	12	13	12
3g	100	12	06h	08	08	12
3i	100	10h	04h	06	08	06
4a	100	10	04	06	08	-
4b	100	08	05h	08h	08	06
4c	100	10	06h	06	05h	06h
4e	100	08h	06h	04	07	08
4f	100	10	06h	08	09	08
4g	100	14	08	08h	10	12
4h	100	08h	04	09	08h	06h
5a	100	14	08	12	10	10
5b	100	12	06	10h	09	10

5c	100	16h	07	10	12
12					
5d	100	18	07	10h	12
10					
5e	100	16	08	12	10
12					
5f	100	12	07	10	08
12					
5g	100	16	08	14	10
12					
6b	100	10h	04	08	10
08					
6c	100	12h	08	10	08
12					
6d	100	12	04	12	12
10					
6e	100	10h	04h	10	08
12					
6f	100	10	06	12	08
12					
6g	100	12	04	10	10
12					
8a	100	10	06	09	07h
-					
8c	100	10	04	06	08
07h					
8d	100	12	06h	08	07
07					
8e	100	12	04h	07	08
08h					
Fluconazole	10	24h	10vh	NA	NA
NA					
Vancomycin	20	NA	NA	15	15
14					

NA: Not Applicable, h: hazy, vh: very hazzy.

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References:

1. S. K.Nandeeshaiah & S. Y. Ambedkar: *Indian J.Chem.* **37B**, 995 (1998).
2. J. M. Parmar etal: *Indian J. Chem.* **38B**, 995 (1998).
3. J. K. Joshi & M. T. Chabria: *Indian J. Heterocycl. Chem.***15**, 391 (2006).
4. K. M. Basavaraja, V. M. Patil & Agasimundin: *Indian J. Heterocycl. Chem.***15**, 318 (2006).
5. K. M. Mahadevan, B. Padmashali & V. P. Vaidya: *Indian J. Heterocycl. Chem.***11**, 15 (2001).
6. K. M. Basavaraja, V. M. Patil & Y. S. Agasimundin: *Indian J. Heterocycl. Chem.***15**, 1 (2005).
7. K. S. Atwal, G. C. Rovnyak, B. C. O'Reilly & J. Schwartz: *J. Org. Chem.* **54**, 5898 (1989).

8. M. N. Ghosh: *Fundamentals of Experimental Pharmacology,* **Ed. II**, 153 (1984).
9. M. Chen, S. B. Christensen, J. Blom, E. Lemmich, L. Nadelmann, K. Fich, T. G. Theander, A. Kharazmi: *Antimicrob Agents,* **37,** 2550 (1993).
10. M. Chen, T. G. Theander, S. B. Christensen, L. Hviid, L. Zhai, A. Kharazmi: *Antimicrob. Agents Chemother*, **38**,1470 (1994).
11. R. Gasparova, M.Lacova, H. M. El-Shaaer & Z. Olderova: *Farmaco,* **52**(4), 251 (1997).
12. J. A. Macritchie, M. J. O' Mahony & S. D. Lindell: *Pct. Int. appl. WO*, **9827080 A1**, 33 (25 Jun 1998).
13. S. Valente, M. De Rosa, C. G. Maria, N. Barbarito, G. Fumagalli, A. Carlucci, B. Zerillo & G. Ciappi: *Int. J. Immunopathl. Pharmacol.***10(2),** Suppl. 45 (1997).
14. B. K. Karale, V. P. Chavan, A. S. Mane, R. V. Hangarge, C. H. Gill & M. S. Shingare: *Korean J. Med. Chem.* **10(2),** 84 (2000).
15. G. Varounis, Y. Fiamagos & G. Pilidid: *Adv. Heterocycl. Chem.* **80**, 73 (2001).
16. B. Stanovnikand & J. Svete: *"Pyrazoles" in "Science of Synthesis, Houben-Weyl Methods of Organic Transformation"*, Vol.12, Georg Thieme Verlag, Stuttgart, **15**, 225 (2002).
17. A. Sharon, R. Pratap, P. Tiwari, A. Srivastava, P. R. Maulik & V. J. Ram: *Bioorganic & Medicinal Chem Letters*, **15(8)**, 2115 (2005).
18. M. R. Maurya, V. V. Parhate & P. R. Rajput: *Asian J..Chem.***15(3)(4)**, 1843 (2003).
19. M. Kidwai, R. Sharma & P. Misra: *Indian J. Chem.* **41B(2)**, 427 (2002).
20. S. D.Bhardwaj & V. S. Jolly: *Orient. J. Chem.* **12(2),** 185 (1996).
21. V. K. Pandey, D. Misra & A. Shukla: *Indian Drugs*, **31(11)**, 532 (1994).
22. (a) N. Neamati, J. A. Turpin, A. Orr, W. G. Rice, Y. Pommier, A. Garofalo, A. Brizzi, G. Campiani, I. Fiorini & V. J. Nacci: *Med. Chem.* **42**, 3334 (1999). (b) A. Garafelo, G. Balconi, M. Botta, F. Corelli, M. Incalci, G. Fabrizi, D. Lamba & V. Nacci: *Eur. J. Med.Chem.* **28**, 213 (1993). (c) G. L. Grunewald, V. H. Dahanukar, P. Ching & K. R. Criscione: *J. Med. Chem.* **39,** 3539 (1996). (d) H. Toshiyuki, I. Takirio & Hisao: JP7272107, (1972) (*Chem. Abstr.* **77,** 140187f, 1972).
23. Pravin K. Singh, Vishal Srivastava, J. Singh & Siddiqui: *Indian J. Chem.* **44B**,2178 (2005).
24. H. Inoue, M. Konda, T. Hashiyama, H. Oskuka, A. Watanbe, K. Okamura, M. Takida, T. Date, T. Narita, S. Murata, A. Odwara, H. Sasaki &T. Nagao: *Chem. Pharm. Bull.* **45(6),** 1008 (1997).
25. S. V. Agarkar & V. M. Gurav: *Indian J. Heterocycl. Chem.* **13**, 273 (2004).
26. K. Bajaj, V. K. Srivastava & A. Kumar: *Indian J. Chem.* **42B**, 1149 (2003).
27. H. B. Oza, D. G. Joshi & H. H. Parikh: *Heterocycl. Comm.* **3**, 3 (1997).
28. A. Kumar, R. S. Verma & B. P. Jagu: *J. Indian Chem. Soc.* **67**, 920 (1990).
29. S. Tripathi, B. R. Pandey: *Indian J. Pharmacol.* **24**, 155 (1980).

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