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## Convenient Synthesis of Some 3, 5-Arylated-2-Pyrazolines Carrying 4-Methylthiophenyl Moiety and Evaluation of Their Antimicrobial Activity

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**Abstract:** 4-Methylthiobenzaldehyde reacts with various substituted acetophenones under aldol conditions to afford  $\alpha$ ,  $\beta$ -unsaturated ketones (chalcones) which undergo facile and clean cyclization with hydrazines RNHNH<sub>2</sub> (R = H, Ph) to give 3, 5-arylated-2-pyrazolines in quantitative yields. The structures of the newly synthesized compounds have been confirmed on the basis of elemental analysis, IR, <sup>1</sup>H NMR and mass spectral studies. All the newly synthesized compounds were tested for their antimicrobial activity against a variety of microorganisms.

**Key words:** 4-Methylthiobenzaldehyde, chalcones, pyrazolines, antimicrobial

### Introduction

Various substituted pyrazolines and their derivatives are important biological agents and a significant amount of research activity has been directed towards this class of compounds. In particular, they are used as antitumour, antibacterial, antifungal, antiamebic and insecticidal agents (Roelof Van *et al.*, 1979; Taylor and Patel, 1992; Holla *et al.*, 2000; Azarifar and Shaebanzadeh, 2002; Asha *et al.*, 2006). Various pyrazolines were synthesized and reported for their hypotensive, anti-inflammatory, antidepressant, antiarthritic and analgesic activities (Satyanarayana and Rao, 1995; Gulhan *et al.*, 2000; Ekta *et al.*, 2001; Erhan *et al.*, 2001). Moreover, pyrazolines have played a crucial part in the development of heterocyclic chemistry and have been extensively used as important synthons in organic synthesis (Klimova *et al.*, 1999; Padmavathi *et al.*, 1999). A classical synthesis of these compounds involves the base catalysed reaction of aromatic ketones and aldehydes to give  $\alpha$ ,  $\beta$ -unsaturated ketones (chalcones), which undergo a subsequent cyclization reaction with hydrazines affording 2-pyrazolines. As a continuation of our present study to explore potent biologically active pyrazoline containing molecules (Holla *et al.*, 2006a, b), we have synthesized some new 1-Acetyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles and 1-Phenyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles and screened them for their antimicrobial activities.

### Materials and Methods

The melting points were determined by an open capillary method and are uncorrected. IR spectra in KBr ( $\nu_{\text{max}}$  in  $\text{cm}^{-1}$ ) were recorded on a Shimadzu-FTIR Infrared spectrophotometer. <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> on a Bruker AMX-400 (400 MHz) spectrometer using TMS as an internal standard. FABMS spectra were recorded on a JEOL SX 102/DA-6000 Mass spectrometer using argon/xenon (6 kv, 10 mA) as the FAB gas. The purity of the compounds was confirmed by thin layer chromatography using Merck silica gel 60 F<sub>254</sub> coated aluminium plates.

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Table 1: Characterization data of chalcones (3a-j)

Compound No.	R	Molecular formula	M.P (°C)	Yield (%)	Elemental analysis found (Calc.)		
					C	H	N
3a	H	C <sub>16</sub> H <sub>14</sub> OS	82-84	84	75.52 (75.56)	5.52 (5.55)	--
3b	Cl	C <sub>16</sub> H <sub>13</sub> ClOS	142-44	80	75.81 (75.86)	5.12 (5.17)	--
3c	OCH <sub>3</sub>	C <sub>17</sub> H <sub>16</sub> O <sub>2</sub> S	106-08	82	71.81 (71.80)	5.66 (5.67)	--
3d	NO <sub>2</sub>	C <sub>16</sub> H <sub>12</sub> NO <sub>2</sub> S	134-36	78	64.17 (64.20)	4.39 (4.38)	4.65 (4.68)
3e	CH <sub>3</sub>	C <sub>17</sub> H <sub>16</sub> OS	96-98	86	76.04 (76.08)	6.03 (6.01)	--
3f	Br	C <sub>16</sub> H <sub>13</sub> BrOS	156-58	79	57.65 (57.67)	3.95 (3.93)	--
3g	F	C <sub>16</sub> H <sub>13</sub> FOS	100-02	81	70.52 (70.56)	4.80 (4.81)	--
3h	2,4-Dichloro	C <sub>16</sub> H <sub>12</sub> Cl <sub>2</sub> OS	110-12	76	59.41 (59.45)	3.71 (3.74)	--
3i	2,4-Dichloro-5-Fluoro	C <sub>16</sub> H <sub>11</sub> FC <sub>2</sub> OS	106-08	74	56.30 (56.32)	3.21 (3.25)	--
3j	C(CH <sub>3</sub> ) <sub>3</sub>	C <sub>20</sub> H <sub>22</sub> OS	88-90	85	77.39 (77.38)	7.12 (7.14)	--

*General Procedure for the Synthesis of 1-Aryl-3-(4-methylthiophenyl)-2-propen-1-ones (3a-j)*

To a mixture of 4-methylthiobenzaldehyde (0.01 mol) and substituted acetophenones (0.01 mol) in ethanol, a solution of potassium hydroxide (5%, 5 mL) was added slowly with stirring. The resulting mixture was stirred at room temperature for 24 h. The precipitated solid was filtered, washed with water, dried and recrystallized from ethanol. The characterization data of these compounds are given in the Table 1.

*3b. 1-(4-Chlorophenyl)-3-(4-methylthiophenyl)-2-propen-1-one*

IR (KBr,  $\nu$  in  $\text{cm}^{-1}$ ): 3027, 2911 (Ar-H), 1654 (C=O), 1589 (C=C), 742 (C-Cl), <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 2.52 (s, 3H, SCH<sub>3</sub>), 7.26 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.44 (d, 1H, J = 15.64 Hz, olefinic CH), 7.48 (d, 2H, J = 8.56 Hz, 4-chlorophenyl), 7.56 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.77 (d, 1H, J = 15.64 Hz, olefinic CH), 7.96 (d, 2H, J = 8.56 Hz, 4-chlorophenyl), FABMS (m/z, %): 289(M<sup>+</sup>, 80), 217(100), 199(45), 181(50), 139(30), 109(70), 91(90).

*3d. 1-(4-Nitrophenyl)-3-(4-methylthiophenyl)-2-propen-1-one*

IR (KBr,  $\nu$  in  $\text{cm}^{-1}$ ): 3029, 2917 (Ar-H), 1660 (C=O), 1581 (C=C), 1521, 1344 (asym. and sym. NO<sub>2</sub>), <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 2.53 (s, 3H, SCH<sub>3</sub>), 7.27 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.43 (d, 1H, J = 15.64 Hz, olefinic CH), 7.57 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.81 (d, 1H, J = 15.64 Hz, olefinic CH), 8.13 (d, 2H, J = 8.76 Hz, 4-nitrophenyl), 8.35 (d, 2H, J = 8.76 Hz, 4-nitrophenyl), FABMS (m/z, %): 300(M<sup>+</sup>+1, 50), 299(M<sup>+</sup>, 40), 289(30), 166(40), 154(100), 136(60), 107(25), 89(10).

*3e. 1-(4-Methylphenyl)-3-(4-methylthiophenyl)-2-propen-1-one*

IR (KBr,  $\nu$  in  $\text{cm}^{-1}$ ): 3025, 2911 (Ar-H), 1658 (C=O), 1586 (C=C), <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 2.43 (s, 3H, CH<sub>3</sub>), 2.52 (s, 3H, SCH<sub>3</sub>), 7.26 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.30 (d, 2H, J = 8.16 Hz, 4-methylphenyl), 7.49 (d, 1H, J = 15.64 Hz, olefinic CH), 7.56 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.76 (d, 1H, J = 15.64 Hz, olefinic CH), 7.76 (d, 2H, J = 8.16 Hz, 4-methylphenyl).

*3f. 1-(4-Bromophenyl)-3-(4-methylthiophenyl)-2-propen-1-one*

IR (KBr,  $\nu$  in  $\text{cm}^{-1}$ ): 3029, 2911 (Ar-H), 1652 (C=O), 1585 (C=C), 665 (C-Br), <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 2.52 (s, 3H, SCH<sub>3</sub>), 7.26 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.43 (d, 1H, J = 15.64 Hz, olefinic CH), 7.55 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.64 (d, 2H, J = 8.48 Hz, 4-bromophenyl), 7.77 (d, 1H, J = 15.64 Hz, olefinic CH), 7.88 (d, 2H, J = 8.48 Hz, 4-bromophenyl).

Table 2: Characterization data of pyrazolines (4a-h) and (5a-h)

Compound No.	R	Molecular formula	M.P (°C)	Yield (%)	Elemental analysis found (Calc.)		
					C	H	N
4a	H	C <sub>18</sub> H <sub>18</sub> N <sub>2</sub> OS	136-38	72	69.61 (69.65)	5.83 (5.84)	9.04 (9.02)
4b	Cl	C <sub>18</sub> H <sub>17</sub> ClN <sub>2</sub> OS	128-30	78	62.65 (62.69)	4.96 (4.97)	8.10 (8.12)
4c	OCH <sub>3</sub>	C <sub>19</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub> S	94-96	72	67.00 (67.03)	5.93 (5.92)	8.19 (8.23)
4d	NO <sub>2</sub>	C <sub>18</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> S	100-02	76	60.81 (60.83)	4.83 (4.82)	11.83 (11.82)
4e	CH <sub>3</sub>	C <sub>19</sub> H <sub>20</sub> N <sub>2</sub> OS	114-16	70	70.31 (70.34)	6.20 (6.21)	8.62 (8.63)
4f	Br	C <sub>18</sub> H <sub>17</sub> BrN <sub>2</sub> OS	122-24	79	55.50 (55.53)	4.42 (4.40)	7.17 (7.20)
4g	F	C <sub>18</sub> H <sub>17</sub> FN <sub>2</sub> OS	146-48	75	65.80 (65.83)	5.19 (5.22)	8.51 (8.53)
4h	2,4-Dichloro	C <sub>18</sub> H <sub>16</sub> Cl <sub>2</sub> N <sub>2</sub> OS	86-88	80	57.01 (57.00)	4.21 (4.25)	7.36 (7.39)
5a	H	C <sub>22</sub> H <sub>20</sub> N <sub>2</sub> S	108-10	68	76.73 (76.71)	5.86 (5.85)	8.10 (8.13)
5b	Cl	C <sub>22</sub> H <sub>19</sub> ClN <sub>2</sub> S	158-60	72	69.71 (69.74)	5.01 (5.05)	7.38 (7.39)
5c	OCH <sub>3</sub>	C <sub>23</sub> H <sub>22</sub> N <sub>2</sub> OS	122-24	70	73.76 (73.77)	5.93 (5.92)	7.45 (7.48)
5d	NO <sub>2</sub>	C <sub>22</sub> H <sub>19</sub> N <sub>3</sub> O <sub>2</sub> S	124-26	74	67.83 (67.85)	4.90 (4.92)	10.76 (10.79)
5e	CH <sub>3</sub>	C <sub>23</sub> H <sub>22</sub> N <sub>2</sub> S	136-38	69	77.08 (77.06)	6.16 (6.19)	7.82 (7.81)
5f	Br	C <sub>22</sub> H <sub>19</sub> BrN <sub>2</sub> S	172-74	72	62.42 (62.41)	4.50 (4.52)	6.59 (6.62)
5g	F	C <sub>22</sub> H <sub>19</sub> FN <sub>2</sub> S	132-34	73	72.91 (72.90)	5.24 (5.28)	7.70 (7.73)
5h	2,4-Dichloro	C <sub>22</sub> H <sub>18</sub> Cl <sub>2</sub> N <sub>2</sub> S	78-80	76	63.93 (63.92)	4.35 (4.39)	6.75 (6.78)

*General Procedure for the Synthesis of 1-Acetyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles (4a-h)*

A mixture of 3 (0.01 mol) and a molar equivalent of hydrazine hydrate (99%) in glacial acetic acid (15 mL) was heated under reflux for 6-8 h. The resulting reaction mixture was poured into crushed ice with vigorous stirring. The solid obtained was filtered at the pump, washed with water, dried and recrystallized from ethanol to afford the pyrazolines. The characterization data of these compounds are given in the Table 2.

*4b. 1-Acetyl-3-(4-chlorophenyl)-5-(4-methylthiophenyl)-4,5-dihydropyrazole*

IR (KBr, cm<sup>-1</sup>): 3030, 2919 (Ar-H), 1664 (C=O), 1594 (C=C), 754 (C-Cl), <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.40 (s, 3H, COCH<sub>3</sub>), 2.44 (s, 3H, SCH<sub>3</sub>), 3.12 (dd, 1H, J = 17.64 Hz, 4.68 Hz, pyrazoline CH<sub>2</sub>), 3.72 (dd, 1H, J = 17.64 Hz, 11.88 Hz, pyrazoline CH<sub>2</sub>), 5.56 (dd, 1H, J = 11.88 Hz, 4.68 Hz, pyrazoline CH), 7.14 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.20 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.39 (d, 2H, J = 8.56 Hz, 4-chlorophenyl), 7.66 (d, 2H, J = 8.56 Hz, 4-chlorophenyl), FABMS (m/z, %): 345(M<sup>+</sup>+1, 100), 344(M<sup>+</sup>, 30), 302(20), 207(15), 181(20), 179(55), 154(10), 136(10).

*4d. 1-Acetyl-3-(4-nitrophenyl)-5-(4-methylthiophenyl)-4,5-dihydropyrazole*

IR (KBr, cm<sup>-1</sup>): 3091, 2913 (Ar-H), 1673 (C=O), 1596 (C=C), 1515, 1344 (asym. and sym. NO<sub>2</sub>), <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.40 (s, 3H, COCH<sub>3</sub>), 2.44 (s, 3H, SCH<sub>3</sub>), 3.12 (dd, 1H, J = 17.64 Hz, 4.68 Hz, pyrazoline CH<sub>2</sub>), 3.72 (dd, 1H, J = 17.64 Hz, 11.88 Hz, pyrazoline CH<sub>2</sub>), 5.56 (dd, 1H, J = 11.88 Hz, 4.68 Hz, pyrazoline CH), 7.14 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.20 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 8.04 (d, 2H, J = 8.76 Hz, 4-nitrophenyl), 7.08 (d, 2H, J = 8.76 Hz, 4-nitrophenyl), FABMS (m/z, %): 356(M<sup>+</sup>+1, 30), 355(M<sup>+</sup>, 30), 222(25), 190(20), 154(25), 136(20), 91(15), 89(10).

*4g. 1-Acetyl-3-(4-fluorophenyl)-5-(4-methylthiophenyl)-4,5-dihydropyrazole*

IR (KBr, cm<sup>-1</sup>): 3083, 2919 (Ar-H), 1664 (C=O), 1604 (C=C), 1114 (C-F), <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.40 (s, 3H, COCH<sub>3</sub>), 2.44 (s, 3H, SCH<sub>3</sub>), 3.12 (dd, 1H, J = 17.64 Hz, 4.64 Hz, pyrazoline CH<sub>2</sub>), 3.72 (dd, 1H, J = 17.64 Hz, 11.84 Hz, pyrazoline CH<sub>2</sub>), 5.55 (dd, 1H, J = 11.84 Hz, 4.64 Hz, pyrazoline CH), 7.10 (d, 2H, J = 8.64 Hz, 4-fluorophenyl), 7.14 (d, 2H, J = 8.36 Hz,

4-methylthiophenyl), 7.20 (d, 2H, J = 8.36 Hz, 4-methylthiophenyl), 7.74-7.71 (m, 2H, J = 8.80 Hz, 6.72 Hz, 3.28 Hz, 4-fluorophenyl), FABMS (m/z, %): 329(M<sup>+</sup>+1, 100), 328(M<sup>+</sup>, 20), 285(30), 270(5), 207(10), 163(60), 150(5), 137(5), 122(5).

*General Procedure for the Synthesis of 1-Phenyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles (5a-h)*

A mixture of 3 (0.01 mol) and a molar equivalent of phenyl hydrazine in glacial acetic acid (15 mL) was heated under reflux for 6-8 h. The resulting reaction mixture was poured into crushed ice with vigorous stirring. The solid obtained was filtered at the pump, washed with water, dried and recrystallized from ethanol to afford the pyrazolines. The characterization data of these compounds are given in the Table 2.

*5b. 1-Phenyl-3-(4-chlorophenyl)-5-(4-methylthiophenyl)-4,5-dihydropyrazole*

IR (KBr, cm<sup>-1</sup>): 3045, 2913 (Ar-H), 1596 (C=C), 748 (C-Cl), <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.45 (s, 3H, SCH<sub>3</sub>), 3.08 (dd, 1H, J = 17.00 Hz, 7.20 Hz, pyrazoline CH<sub>2</sub>), 3.81 (dd, 1H, J = 17.00 Hz, 12.36 Hz, pyrazoline CH<sub>2</sub>), 5.25 (dd, 1H, J = 12.36 Hz, 7.20 Hz, pyrazoline CH), 7.85-6.77 (m, 9H, Ar-H), FABMS (m/z, %): 379(M<sup>+</sup>+1, 50), 378(M<sup>+</sup>, 100), 307(10), 289(5), 255(5), 154(40), 136(30).

*5f. 1-Phenyl-3-(4-bromophenyl)-5-(4-methylthiophenyl)-4,5-dihydropyrazole*

IR (KBr, cm<sup>-1</sup>): 3025, 2919 (Ar-H), 1596 (C=C), 692 (C-Br), <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.45 (s, 3H, SCH<sub>3</sub>), 3.08 (dd, 1H, J = 17.00 Hz, 7.20 Hz, pyrazoline CH<sub>2</sub>), 3.80 (dd, 1H, J = 17.00 Hz, 12.36 Hz, pyrazoline CH<sub>2</sub>), 5.25 (dd, 1H, J = 12.36 Hz, 7.20 Hz, pyrazoline CH), 7.79-6.77 (m, 9H, Ar-H), FABMS (m/z, %): 424(M<sup>+</sup>+1, 45), 423(M<sup>+</sup>, 20), 422(45), 307(25), 289(20), 242(10), 165(10), 154(100), 136(70), 107(20).

*5g. 1-Phenyl-3-(4-fluorophenyl)-5-(4-methylthiophenyl)-4,5-dihydropyrazole*

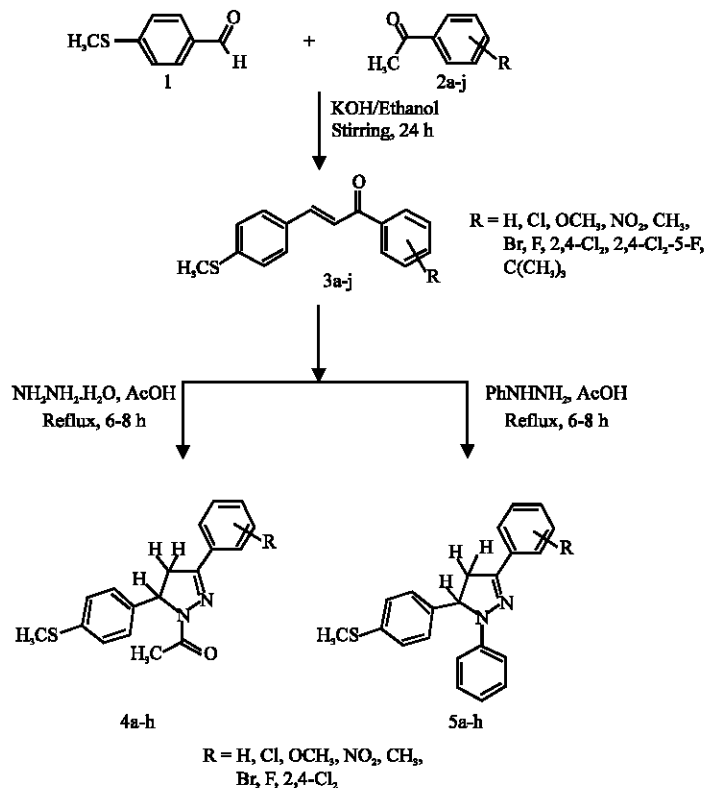
IR (KBr, cm<sup>-1</sup>): 3035, 2919 (Ar-H), 1592 (C=C), 1105 (C-F), <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.45 (s, 3H, SCH<sub>3</sub>), 3.08 (dd, 1H, J = 17.00 Hz, 7.28 Hz, pyrazoline CH<sub>2</sub>), 3.81 (dd, 1H, J = 17.00 Hz, 12.32 Hz, pyrazoline CH<sub>2</sub>), 5.24 (dd, 1H, J = 12.32 Hz, 7.28 Hz, pyrazoline CH), 7.89-6.74 (m, 9H, Ar-H), FABMS (m/z, %): 363(M<sup>+</sup>+1, 60), 362(M<sup>+</sup>, 100), 361(40), 276(10), 248(10), 239(20), 160(5).

## Results and Discussion

As a result of present studies related to the development of new heterocyclic compounds, we herein report an easy access to 3, 5-Arylated-2-pyrazolines in good yields. We report in this study some aldol condensation reactions between 4-methylthiobenzaldehyde and various substituted acetophenones in the presence of potassium hydroxide/ethanol affording intermediate 1-Aryl-3-(4-methylthiophenyl)-2-propen-1-ones (3a-j), which undergo a rapid cyclization with hydrazine and phenyl hydrazine to afford two series of novel pyrazolines namely 1-Acetyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles (4a-h) and 1-Phenyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles (5a-h), respectively (Scheme 1). The structures of the newly synthesized compounds were well confirmed by recording IR, <sup>1</sup>H NMR mass spectra and elemental analysis. All the compounds were isolated in good yields after recrystallization from ethanol. Few selected compounds were characterized by IR, <sup>1</sup>H NMR and mass spectral analysis. Characterization data are given in the respective tables and the spectral data are given in the experimental section.

### *Antibacterial Activity*

We investigated the newly synthesized 1-Acetyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles (4a-h) and 1-Phenyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles (5a-h)



Scheme 1:

Table 3: Antibacterial activity of compounds (4a-h) and (5a-h) at the conc.  $10 \mu\text{g mL}^{-1}$  (Disc diffusion method)

Compound No.	<i>S. aureus</i>	<i>P. aeruginosa</i>	<i>K. pneumoniae</i>	<i>E. coli</i>
4a	19 (12.5)	24 (6)	20 (6)	17 (12.5)
4b	20 (12.5)	24 (6)	19 (6)	18 (12.5)
4c	18 (12.5)	25 (6)	10 (12.5)	10 (25)
4d	19 (12.5)	23 (6)	19 (6)	12 (25)
4e	20 (12.5)	24 (6)	19 (6)	10 (25)
4f	18 (12.5)	23 (6)	18 (6)	10 (25)
4g	19 (12.5)	25 (6)	18 (6)	15 (25)
4h	18 (12.5)	24 (6)	18 (6)	10 (25)
5a	10 (25)	23 (6)	10 (12.5)	17 (12.5)
5b	20 (12.5)	24 (6)	10 (12.5)	10 (25)
5c	10 (25)	10 (12.5)	10 (12.5)	10 (25)
5d	12 (25)	10 (12.5)	10 (12.5)	12 (25)
5e	10 (25)	10 (12.5)	10 (12.5)	10 (25)
5f	10 (25)	12 (12.5)	12 (12.5)	18 (12.5)
5g	12 (25)	10 (12.5)	12 (12.5)	17 (12.5)
5h	18 (12.5)	10 (12.5)	12 (12.5)	12 (25)
Ciprofloxacin	19 (12.5)	25 (6)	20 (6)	18 (12.5)

(Values in the bracket indicates MIC)

for their antibacterial activity against *Escherichia coli* (ATTC-25922), *Staphylococcus aureus* (ATTC-25923), *Pseudomonas aeruginosa* (ATTC-27853) and *Klebsiella pneumoniae* (recultured) bacterial stains by disc diffusion method (Cruickshank *et al.*, 1975; Arthington *et al.*, 2000). Ciprofloxacin was used as a standard drug. Solvent and growth controls were kept and the zone of inhibition in mm and Minimum Inhibitory Concentration (MIC) was noted. The results of such studies are given in Table 3. It can be seen that most of the compounds are moderately active against all the bacterial

Table 4: Antifungal activity of compounds (4a-h) and (5a-h) at conc. 10-100 µg mL<sup>-1</sup> (Serial plate dilution method)

Compound No.	<i>A. fumigatus</i>	<i>A. flavus</i>	<i>C. albicans</i>	<i>P. marneffei</i>
4a	10 (12.5)	10 (25)	10 (12.5)	10 (12.5)
4b	10 (12.5)	10 (25)	10 (12.5)	10 (12.5)
4c	12 (12.5)	10 (25)	12 (12.5)	12 (12.5)
4d	10 (12.5)	10 (25)	12 (12.5)	10 (12.5)
4e	10 (12.5)	11 (25)	12 (12.5)	10 (12.5)
4f	10 (12.5)	10 (25)	10 (12.5)	12 (12.5)
4g	15 (12.5)	14 (25)	16 (12.5)	15 (12.5)
4h	12 (12.5)	12 (25)	10 (12.5)	10 (12.5)
5a	21 (6)	18 (12.5)	20 (6)	20 (6)
5b	10 (12.5)	10 (25)	10 (12.5)	10 (12.5)
5c	11 (12.5)	12 (25)	10 (12.5)	11 (12.5)
5d	12 (12.5)	12 (25)	12 (12.5)	12 (12.5)
5e	10 (12.5)	12 (25)	10 (12.5)	10 (12.5)
5f	16 (12.5)	14 (25)	16 (6)	16 (6)
5g	12 (12.5)	10 (25)	10 (12.5)	10 (12.5)
5h	10 (12.5)	10 (25)	12 (12.5)	12 (12.5)
Ciclopiroxolamine	22 (6)	18 (12.5)	20 (6)	20 (6)

(Values in the bracket indicates MIC)

strains. The compounds 4a, 1-Acetyl-3-phenyl-5-(4-methylthiophenyl)-4,5-dihydropyrazole and 4b, 1-Acetyl-3-(4-chlorophenyl)-5-(4-methylthiophenyl)-4,5-dihydropyrazole have exhibited maximum activity.

#### *Antifungal Studies*

Newly synthesized compounds 1-Acetyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles (4a-h) and 1-Phenyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles (5a-h) were screened for their antifungal activity against *Aspergillus flavus* (NCIM No.524), *Aspergillus fumigatus* (NCIM No.902), *Candida albicans* (NCIM No.3100) and *Penicillium marneffei* (recultured) in DMSO by serial plate dilution method (Cruickshank *et al.*, 1975; Arthington *et al.*, 2000). Antifungal activity was determined by measuring the diameter of the inhibition zone. The results of such studies are given in Table 4. Activity of each compound was compared with Ciclopiroxolamine as standard drug. The study reveals that most of the compounds possess less inhibition against the fungal strains. The compound 5a, 1,3-Diphenyl-5-(4-methylthiophenyl)-4,5-dihydropyrazole exhibited highest inhibition.

#### **Conclusions**

Novel 1-Acetyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles and 1-Phenyl-3-aryl-5-(4-methylthiophenyl)-4,5-dihydropyrazoles were prepared and screened for their antibacterial and antifungal activities. The compounds 4a, 1-Acetyl-3-phenyl-5-(4-methylthiophenyl)-4,5-dihydropyrazole and 4b, 1-Acetyl-3-(4-chlorophenyl)-5-(4-methylthiophenyl)-4,5-dihydropyrazole exhibited maximum antibacterial activity and the compound 5a, 1,3-Diphenyl-5-(4-methylthiophenyl)-4,5-dihydropyrazole exhibited maximum antifungal activity. The compounds 4a, 4b and 5a can be recommended for further studies.

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