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Synthesis and antimicrobial activity of 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines

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ABSTRACT

A convenient and solventless synthesis of 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines is reported. The procedure does not involve the use of any additional reagent/catalyst, produces no waste, and represents a green synthetic protocol. The structures of newly synthesized compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR, mass and elemental analyses. All the seven compounds were evaluated for in vitro antibacterial activity against Gram-positive Bacillus subtilis, Staphylococcus aureus, Gram-negative Escherichia coli and in vitro antifungal activity against Candida albicans and Aspergillus niger.

Keywords: 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines, pyrazole aldehyde, antibacterial activity**,** antifungal activity.

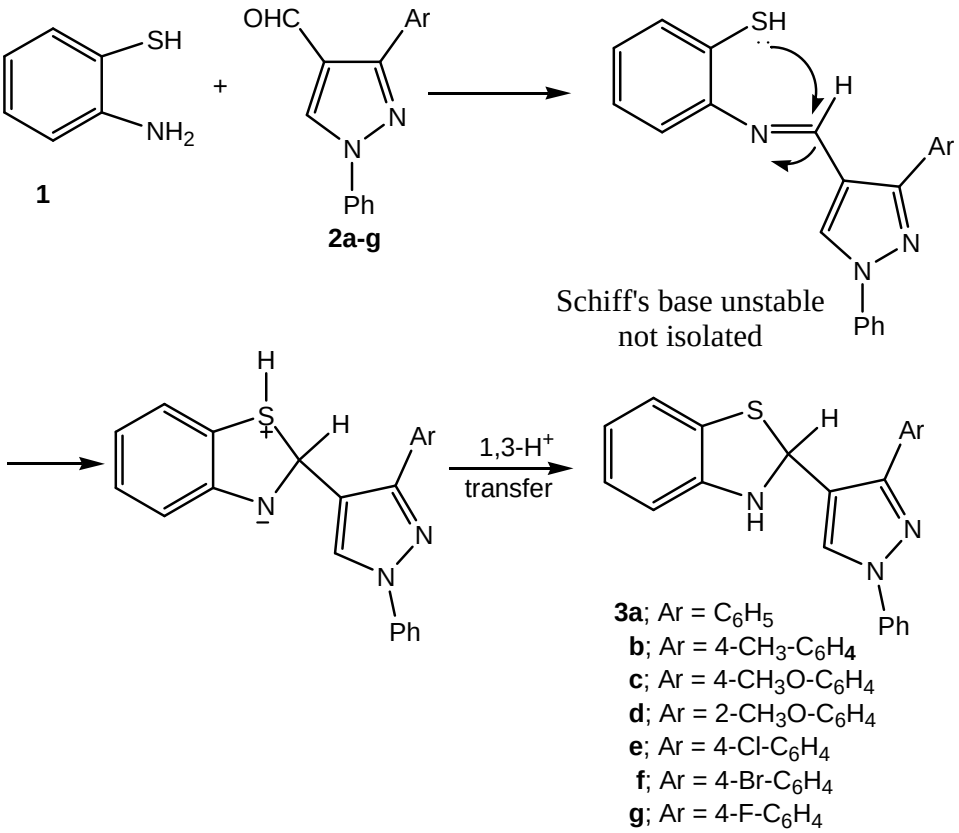
INTRODUCTION

Benzothiazolines are very important group of heterocyclic compounds that have many applications in both pharmaceutical and industrial research. They are widely used in bioorganic and medicinal chemistry with applications in drug discovery [1-3]. They have also found potent utility as fluorescent probe for the identification of superoxide anion radicals and the determination of superoxide dismutase activity in scallion genus foods [4]. On the other hand, the substituted pyrazole ring also exhibits a broad spectrum of biological activities such as antidiabetic [5], antimicrobial [6-9] and herbicidal [10-11]. Led by these observations, the synthesis of some new 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines **(3a-g)** [12] was undertaken with a view to evaluate their antibacterial and antifungal activities.

MATERIALS AND METHODS

Melting points were uncorrected and determined in open capillaries. FTIR spectra were obtained as KBr pellets with a Perkin Elmer Spectrum RX1 instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 MHz and 100 MHz NMR Spectrometer, respectively, in $CDCl_3$ with TMS as an internal standard. Elemental analyses were carried out on Perkin Elmer 2400. Analytical TLC was performed on precoated plastic sheets of silica gel G/UV-254 of 0.2 mm thickness (Macherey-Nagel, Germany).

General Procedure for the synthesis of 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines (3a-g): Equimolar quantities of 2-aminothiophenol (**1**) (4.0 mmol, 0.50 g) and the appropriate pyrazole aldehydes (**2a-g**) (4.0 mmol) were heated together for 5-10 min at 50-60˚C, the reaction mixture was cooled and triturated with hexane, and the solid was collected and recrystallized with methanol. All the benzothiazolines were obtained as pale yellow or white crystalline solids and were characterized by elemental analysis and spectroscopic techniques. Pyrazole aldehydes (**2a-g**) used in this reaction were synthesized according to literature method [13].



Scheme 1: Synthesis of 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines (3a-g)

Antimicrobial Activity

The *in vitro* antibacterial and antifungal activity of 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines (**3a-g**) were carried out against the bacteria *Bacillus subtilis*, *Staphylococcus aureus* and *Escherichia coli* and fungi *Candida albicans* and *Aspergillus niger* using serial

dilution technique [14] in double strength nutrient broth-I.P. and Sabouraud dextrose broth-I.P. as a medium. The conventional bactericide Tetracycline, Chloramphenicol, Kanamycin, Cefazoline sodium, Cefotaxime and fungicide Cycloheximide, Carbendazim and Fluconazole were used as standards for comparing the activity of compounds.

Antibacterial assay

2-[1-Phenyl-3-arylpyrazol-4-yl]benzothiazolines (**3a-g**) were dissolved in DMSO to give a concentration of 100 µg/mL (stock solution) which was serially diluted in tubes containing 1 mL of sterile double strength nutrient broth-I.P. to get a concentration of 100 to 3.12 µg/mL and then inoculated with 100 µL of suspension of respective organisms in sterile saline (*B. subtilis*, *S. aureus* and *E. coli*). The inoculated tubes were incubated at 37±1°C for 24 h and minimum inhibitory concentrations (MIC) were determined.

Antifungal assay

The antifungal activity of activity of 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines (**3a-g**) against the fungal species *C. albicans* and *A. niger* was determined by serial dilution method similar to antibacterial assay using Sabouraud dextrose broth-I.P. following the incubation condition of 37±1°C for a period of 36 h for *C. albicans* and 25±1°C for a period of 7 days for *A. niger*.

Table 1: The in vitro antimicrobial activity of 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines (3a-g) (MIC in µg/ml)

3a-g	Bacteria			Fungi	
	B. subtilis	*S. aureus*	*E. coli*	*C. albicans*	*A. niger*
3a	12.5	6.25	12.5	6.25	25
3b	12.5	3.12	25	12.5	12.5
3c	6.25	12.5	12.5	12.5	6.25
3d	6.25	6.25	12.5	6.25	25
3e	3.12	6.25	12.5	3.12	12.5
3f	12.5	12.5	50	25	25
3g	6.25	6.25	25	12.5	25

Characterization and spectral data of 3a-g:

2-(1,3-Diphenyl-1-H-pyrazol-4-yl)benzothiazoline (3a): White solid; mp 130˚C; R_f = 0.43 (AcOEt/petroleum ether 10%). IR (KBr, cm^{-1}): 3350, 3051, 2916, 1598, 1580, 1543, 1503, 1459, 1447, 1396, 1351, 1223, 1121, 1064, 1012, 956, 744. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.33 (bs, 1H, NH), 6.51 (s, 1H, C_2-H), 6.64-6.66 (dd, 1H, J = 7.68 & 0.60 Hz, C_4-H), 6.76-6.80 (dt, 1H, J = 7.52 & 1.04 Hz, C_6-H), 6.92-6.96 (dt, 1H, J = 7.68 & 1.20 Hz, C_5-H), 7.06-7.08 (dd, 1H, J = 7.56 & 0.96 Hz, C_7-H), 7.23-7.29 (m, 1H, $C_{4'}$-H), 7.35-7.50 (m, 5H, $C_{3''}$-H, $C_{4''}$-H, $C_{5''}$-H, $C_{3'}$-H & $C_{5'}$-H), 7.70-7.80 (m, 4H, $C_{2'}$-H, $C_{6'}$-H, $C_{2''}$-H & $C_{6''}$-H), 8.28 (s, 1H, pyrazolyl-H). ^{13}C NMR (100 MHz, $CDCl_3$): 150.75 (C_3-pyrazole), 146.08 (C_{4a}), 139.75 (C_1'), 132.45 (C_1''), 129.47 (C_3' & C_5'), 128.83 (C_3'' & C_5''), 128.46 (C_4''), 128.13 (C_2'' & C_6''), 127.70 (C_4'), 127.26 (C_4-

pyrazole), 126.76 (C_7), 125.69 (C_5-pyrazole), 122.29 (C_{7a}), 122.01 (C_6), 121.29 (C_5), 119.05 (C_2' & C_6'), 110.72 (C_4), 62.53 (C_2). Anal. calcd. for $C_{22}H_{17}N_3S$: C, 74.34; H, 4.82; N, 11.82; S, 9.02%. Found: C, 74.00; H, 4.23; N, 11.99; S, 8.58%. ESI-MS $[M+H]^+$ = 356.26, calcd for $C_{22}H_{17}N_3S$ = 355.11.

2-(1-Phenyl-3-p-tolyl-1-H-pyrazol-4-yl)benzothiazoline (3b): White solid; mp 134˚C; R_f = 0.42 (petroleum ether/AcOEt %). IR (KBr, cm^{-1}): 3310, 3143, 3066, 2920, 2859, 1596, 1581, 1541, 1500, 1469, 1455, 1408, 1363, 1333, 1221, 1058, 960, 826, 735. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 3H, CH_3), 4.39 (bs, 1H, NH), 6.54 (s, 1H, C_2-H), 6.67-6.69 (m, C_4-H), 6.77-6.81 (dt, 1H, J = 7.52 & 1.02 Hz, C_6-H), 6.93-6.97 (dt, 1H, J = 7.60 & 1.16 Hz, C_5-H), 7.08-7.10 (dd, 1H, J = 7.92 & 0.80 Hz, C_7-H), 7.25-7.29 (m, 3H, $C_{4'}$-H, $C_{3''}$-H & $C_{5''}$-H), 7.41-7.45 (m, 2H, $C_{3'}$-H & $C_{5'}$-H), 7.60-7.62 (d, 2H, J = 8.04 Hz, $C_{2''}$-H & $C_{6''}$-H), 7.71-7.73 (m, 2H, $C_{2'}$-H & $C_{6'}$-H), 8.29 (s, 1H, pyrazolyl-H). ^{13}C NMR (100 MHz, $CDCl_3$): 150.79 (C_3-pyrazole), 146.02 (C_{4a}), 139.85 (C_1'), 139.05 (C_4''), 129.54 (C_3'' & C_5''), 129.45 (C_3' & C_5'), 129.38 (C_2'' & C_6''), 129.16 (C_1''), 127.98 (C_4'), 127.17 (C_4-pyrazole), 126.61 (C_7), 125.58 (C_5-pyrazole), 122.50 (C_{7a}), 121.97 (C_6), 121.27 (C_5), 119.06 (C_2' & C_6'), 110.70 (C_4), 62.45 (C_2), 21.28 (C_4''-CH_3). Anal. calcd. for $C_{23}H_{19}N_3S$: C, 74.77; H, 5.18; N, 11.37; S, 8.68%. Found: C, 74.24; H, 5.35; N, 11.03; S, 8.36%. HRMS m/z = 370.25 [M+H], calcd for $C_{23}H_{19}N_3S$ = 369.13.

2-[3-(4-Methoxy-phenyl)-1-phenyl-1H-pyrazol-4-yl]benzothiazoline (3c): White solid; mp 113-114˚C; R_f = 0.30 (AcOEt/petroleum ether 10%). IR (KBr, cm^{-1}): 3307, 3141, 3050, 3003, 2931, 2871, 2837, 1611, 1595, 1583, 1540, 1528, 1503, 1471, 1455, 1244, 1174, 1060, 840, 735. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H, OCH_3), 4.35 (bs, 1H, NH), 6.48 (s, 1H, C_2-H), 6.64-6.66 (dd, 1H, J = 7.72 & 0.64 Hz, C_4-H), 6.76-6.80 (dt, 1H, J = 7.56 & 1.04 Hz, C_6-H), 6.91-6.95 (dt, 1H, J = 7.60 & 1.20 Hz, C_5-H), 6.96-6.99 (m, 2H, $C_{3''}$-H & $C_{5''}$-H), 7.06-7.08 (dd, 1H, J = 7.56 & 1.04 Hz, C_7-H), 7.23-7.27 (m, 1H, $C_{4'}$-H), 7.39-7.43 (m, 2H, $C_{3'}$-H & $C_{5'}$-H), 7.62-7.66 (m, 2H, $C_{2''}$-H & $C_{6''}$-H), 7.68-7.70 (m, 2H, $C_{2'}$-H & $C_{6'}$-H), 8.24 (s, 1H, pyrazolyl-H). ^{13}C NMR (100 MHz, $CDCl_3$): 159.81 (C_4''), 150.60 (C_3-pyrazole), 146.08 (C_{4a}), 139.81 (C_1'), 129.44 (C_2'' & C_6''), 129.37 (C_3' & C_5'), 127.54 (C_4'), 127.38 (C_4-pyrazole), 126.62 (C_7), 125.64 (C_5-pyrazole), 124.98 (C_1''), 122.02 (C_{7a}), 121.83 (C_6), 121.32 (C_5), 119.01 (C_2' & C_6'), 114.23 (C_3'' & C_5''), 110.76 (C_4), 62.63 (C_2), 55.37 (C_4''-OCH_3). Anal. calcd. for $C_{23}H_{19}N_3OS$: C, 71.66; H, 4.97; N, 10.90; S, 8.32%. Found: C, 71.28; H, 4.49; N, 11.18; S, 8.09%. ESI-MS $[M+H]^+$ = 386.24 [M+H], calcd for $C_{23}H_{19}N_3OS$ = 385.12.

2-[3-(2-Methoxy-phenyl)-1-phenyl-1H-pyrazol-4-yl]benzothiazoline (3d): Pale yellow solid; mp 128-130˚C; R_f = 0.38 (AcOEt/petroleum ether 10%). IR (KBr, cm^{-1}): 3320, 3130, 3050, 2925, 1594, 1580, 1547, 1505, 1475, 1450, 1400, 1360, 1323, 1220, 1060, 950, 830, 738. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H, OCH_3), 4.51 (bs, 1H, NH), 6.17 (s, 1H, C_2-H), 6.55-6.57 (m, 1H, C_4-H), 6.70-6.74 (dt, 1H, J = 7.60 & 0.92 Hz, C_6-H), 6.87-6.91 (dt, 1H, J = 7.60 & 1.12 Hz, C_5-H), 6.96-6.98 (d, 1H, J = 8.28 Hz, $C_{3''}$-H), 7.03-7.07 (m, 2H, C_7-H & $C_{5''}$-H), 7.21-7.25 (m, 1H, $C_{4'}$-H), 7.34-7.40 (m, 3H, $C_{4''}$-H, $C_{3'}$-H & $C_{5'}$-H), 7.50-7.52 (dd, 1H, J = 7.48 & 1.68 Hz, $C_{6''}$-H), 7.66-7.68 (m, 2H, $C_{2'}$-H & $C_{6'}$-H), 8.20 (s, 1H, pyrazolyl-H). ^{13}C NMR (100 MHz, $CDCl_3$): 159.64 (C_3-pyrazole), 158.00 (C_2''), 146.10 (C_{4a}), 139.84 (C_1'), 131.72 (C_4''), 130.78 (C_6''), 129.40 (C_3' & C_5'), 127.20 (C_4-pyrazole), 127.00 (C_4'), 126.60 (C_7), 125.54 (C_5-pyrazole), 122.12 (C_{7a}), 121.18 (C_1''), 121.80 (C_6), 121.30 (C_5), 120.75 (C_5''), 119.11 (C_2' & C_6'), 111.02 (C_3''), 110.73 (C_4), 62.44 (C_2), 55.30 (C_2''-OCH_3). Anal. calcd. for $C_{23}H_{19}N_3OS$: C,

71.66; H, 4.97; N, 10.90; S, 8.32%. Found: C, 71.30; H, 5.10; N, 10.78; S, 8.49%. ESI-MS $[M+H]^+$ = 386.22, calcd for $C_{23}H_{19}N_3OS$ = 385.12.

2-[3-(4-Chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]benzothiazoline (3e): White solid; mp 124-125˚C; R_f = 0.36 (AcOEt/petroleum ether 10%). IR (KBr, cm^{-1}): 3322, 3051, 2923, 1599, 1575, 1558, 1541, 1503, 1466, 1409, 1396, 1211, 1093, 1062, 1007, 831, 743. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.35 (bs, 1H, NH), 6.50 (s, 1H, C_2-H), 6.68-6.70 (dd, 1H, J = 7.32 & 0.62 Hz, C_4-H), 6.79-6.83 (dt, 1H, J = 7.52 & 1.00 Hz, C_6-H), 6.94-6.98 (dt, 1H, J = 7.60 & 1.20 Hz, C_5-H), 7.08-7.10 (dd, 1H, J = 7.60 & 0.96 Hz, C_7-H), 7.27-7.31 (m, 1H, $C_{4'}$-H), 7.40-7.49 (m, 4H, $C_{3''}$-H, $C_{5''}$-H, $C_{3'}$-H & $C_{5'}$-H), 7.66-7.73 (m, 4H, $C_{2'}$-H, $C_{6'}$-H, $C_{2''}$-H & $C_{6''}$-H), 8.28 (s, 1H, pyrazolyl-H). ^{13}C NMR (100 MHz, $CDCl_3$): 149.78 (C_3-pyrazole), 146.16 (C_{4a}), 139.89 (C_1'), 135.03 (C_4''), 131.12 (C_3' & C_5'), 131.10 (C_3'' & C_5''), 130.67 (C_1''), 128.85 (C_2'' & C_6''), 127.75 (C_4-pyrazole), 127.71 (C_4'), 126.52 (C_7), 125.88 (C_5-pyrazole), 122.37 (C_{7a}), 122.20 (C_6), 121.74 (C_5), 119.56 (C_2' & C_6'), 111.21 (C_4), 62.59 (C_2). Anal. calcd. for $C_{22}H_{16}ClN_3S$: C, 67.77; H, 4.14; N, 10.78; S, 8.22%. Found: C, 67.40; H, 4.31; N, 10.93; S, 8.08%. ESI-MS $[M+H]^+$ = 390.21, calcd for $C_{22}H_{16}ClN_3S$ = 389.08.

2-[3-(4-Bromo-phenyl)-1-phenyl-1H-pyrazol-4-yl]benzothiazoline (3f): White solid; mp 195-196˚C; R_f = 0.40 (AcOEt/petroleum ether 10%). IR (KBr, cm^{-1}): 3293, 3111, 3050, 2924, 1597, 1576, 1533, 1505, 1473, 1398, 1360, 1308, 1277, 1200, 1117, 1065, 831, 738. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.29 (bs, 1H, NH), 6.49 (s, 1H, C_2-H), 6.68-6.70 (m, 1H, C_4-H), 6.79-6.83 (m, 1H, C_6-H), 6.94-6.98 (m, 1H, C_5-H), 7.08-7.10 (m, 1H, C_7-H), 7.24-7.31 (m, 1H, $C_{4'}$-H), 7.36-7.46 (m, 2H, $C_{3'}$-H & $C_{5'}$-H), 7.56-7.71 (m, 6H, $C_{2'}$-H, $C_{6'}$-H, $C_{2''}$-H, $C_{3''}$-H, $C_{5''}$-H & $C_{6''}$-H), 8.28 (s, 1H, pyrazolyl-H). ^{13}C NMR (100 MHz, $CDCl_3$): 149.61 (C_3-pyrazole), 145.95 (C_{4a}), 139.64 (C_1'), 132.08 (C_2'' & C_6''), 131.91 (C_1''), 129.63 (C_3'' & C_5''), 129.50 (C_3' & C_5'), 127.96 (C_4-pyrazole), 127.88 (C_4'), 126.93 (C_7), 125.73 (C_5-pyrazole), 122.65 (C_{7a}), 122.13 (C_4''), 122.04 (C_6), 121.57 (C_5), 119.11 (C_2' & C_6'), 111.04 (C_4), 62.41 (C_2). Anal. calcd. for $C_{22}H_{16}BrN_3S$: C, 60.83; H, 3.71; N, 9.67; S, 7.38%. Found: C, 60.96; H, 3.58; N, 9.791; S, 7.49%. ESI-MS $[M+H]^+$ = 434.17, calcd for $C_{22}H_{16}BrN_3S$ = 433.02.

2-[3-(4-Fluoro-phenyl)-1-phenyl-1H-pyrazol-4-yl]benzothiazoline (3g): White solid; mp 129˚C; R_f = 0.33 (AcOEt/petroleum ether 10%). IR (KBr, cm^{-1}): 3310, 3045, 3305, 1603, 1570, 1500, 1475, 1357, 1268, 1110, 836, 740. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.29 (bs, 1H, NH), 6.48 (s, 1H, C_2-H), 6.67-6.69 (d, 1H, J = 7.64 Hz, C_4-H), 6.78-6.82 (dt, 1H, J = 7.60 & 0.88 Hz, C_6-H), 6.93-6.97 (dt, 1H, J = 7.64 & 1.00 Hz, C_5-H), 7.07-7.09 (dd, 1H, J = 7.60 & 0.64 Hz, C_7-H), 7.11-7.18 (m, 2H, $C_{3''}$-H & $C_{5''}$-H), 7.26-7.30 (m, 1H, $C_{4'}$-H), 7.36-7.45 (m, 2H, $C_{3'}$-H & $C_{5'}$-H), 7.68-7.71 (m, 4H, $C_{2'}$-H, $C_{6'}$-H, $C_{2''}$-H & $C_{6''}$-H), 8.27 (s, 1H, pyrazolyl-H). ^{13}C NMR (100 MHz, $CDCl_3$): 162.01 & 164.46 (C_4''), 149.88 (C_3-pyrazole), 146.20 (C_{4a}), 139.70 (C_1'), 131.44 (C_3' & C_5'), 131.26 (C_2'' & C_6''), 128.02 (C_1''), 127.84 (C_4-pyrazole), 127.72 (C_4'), 126.60 (C_7), 125.90 (C_5-pyrazole), 122.80 (C_{7a}),122.20 (C_6), 121.46 (C_5), 119.22 (C_2' & C_6'), 115.04 (C_3'' & C_5''), 110.98 (C_4), 62.75 (C_2). Anal. calcd. for $C_{22}H_{16}FN_3S$: C, 70.76; H, 4.32; N, 11.25; S, 8.59%. Found: C, 70.90; H, 4.20; N, 11.37; S, 8.72%. ESI-MS $[M+H]^+$ = 374.24, calcd for $C_{22}H_{16}FN_3S$ = 373.10.

RESULT AND DISCUSSION

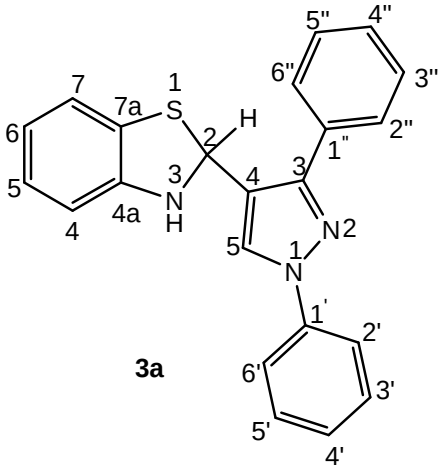
It is expected that the reaction of 2-aminothiophenol with aldehydes lead to the corresponding Schiff's bases, however, the actual products are 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines. The formation of thiazoline form may involve the attack of nonbonding electron pair of the sulfur atom on the highly electrophilic carbon centre of the internal imine followed by a 1,3-proton transfer (Scheme 1). The structures of all the newly synthesized 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines **(3a-g)** were confirmed by their spectral (IR, ^{1}H NMR, ^{13}C NMR and mass) data.

IR spectra

In the IR spectra of benzothiazolines, the NH stretching modes were observed at 3300-3350 cm^{-1}. The absence of absorption bands at 2500-2600 and 1600-1650 cm^{-1} due to ν (SH) and ν (C=N) modes, respectively, indicated benzothiazoline rather than Schiff's base structure. The bands at 3028-3040 and 2916-2938 cm^{-1} were assigned to aromatic and aliphatic C-H stretching modes, respectively. The peaks at about 1594-1611, 1570-1588, 1498-1511 and 1449-1475 cm^{-1} were due to aromatic ring skeleton (C=C) in plane vibrations.

^{1}H NMR SPECTRA

The system of numbering adopted for NMR spectral characterization is shown below for **3a** (Figure 1).



3a

Figure 1

The ^{1}H NMR data also supported the benzothiazoline rather than Schiff's base structure. The ^{1}H NMR spectra of **3a-g** showed the presence of two singlets in the range δ 4.29-4.51 and 6.17-6.54, which were assigned to the NH and C_2-H proton, respectively. There was no proton signal in the range δ 8.30-8.80 indicating the absence of CH=N proton. However, in the ^{1}HNMR spectra of **3a-g**, a singlet at δ 8.20-8.29 was observed due to the pyrazole proton.In the ^{1}H NMR spectra of 2-[3-(4-methoxy-phenyl)-1-phenylpyrazol-4-yl]benzothiazoline (**3a**), the four aromatic protons of benzothiazoline moiety i.e. C_4-H, C_5-H, C_6-H and C_7-H resonated as dd (doublet of doublet), dt (doublet of triplet), dt and dd at δ 6.64-6.66, 6.92-6.96, 6.76-6.80 and 7.06-7.08, respectively. The signals of C_4-H and C_7-H appeared as doublet of doublet due to *ortho* and *meta* coupling with C_5-H and C_6-H. C_5-H proton appeared as a doublet of triplet due to *ortho* coupling with C_4-H and C_6-H and *meta* coupling with C_7-H. A similar pattern of doublet of triplet was shown by

C_6-H due to *ortho* and *meta* coupling with neighboring protons. Three multiplets at δ 7.70-7.80, 7.35-7.50 and 7.23-7.29 were respectively due to C_2'-H, C_6'-H, C_2''-H & C_6''-H; C_3''-H, C_4''-H, C_5''-H, C_3'-H & C_5'-H and C_4'-H of two phenyl rings present at 1- and 3-positions of pyrazole ring.

^{13}C NMR SPECTRA

In the ^{13}C NMR spectra of **3a-g** the signals due to C_2, C_{4a}, C_4, C_5, C_6, C_7 and C_{7a} of benzothiazoline moiety were in the range δ 62.41-62.75, 145.95-146.20, 110.70-110.98, 121.27-121.74, 121.80-122.20, 126.52-126.93 and 122.02-122.80, respectively. The C_3, C_4 and C_5 of pyrazole ring were in the range δ 149.61-159.64, 127.17-127.96 and 125.54-125.90, respectively. In the spectra of **3b**, **3c** and **3d** the signals due to C_4''-CH_3, C_4''-OCH_3 and C_2''-OCH_3 were at δ 21.28, 55.37 and 55.30, respectively.

Antimicrobial Activity

2-[1-Phenyl-3-arylpyrazol-4-yl]benzothiazolines **(3a-g)** were evaluated for *in vitro* antibacterial activity against Gram-positive *Bacillus subtilis*, *Staphylococcus aureus*, Gram-negative *Escherichia coli* and *in vitro* antifungal activity against *Candida albicans* and *Aspergillus niger*. Minimum Inhibitory Concentrations (MIC) were determined by means of two fold serial dilution technique and are presented in Table 1. The MIC of standard drugs for antibacterial activity (Tetracycline, Chloramphenicol, Kanamycin, Cefazoline sodium and Cefotaxime) and antifungal activity (Cycloheximide, Carbendazim and Fluconazole) were found to be < 3.12 μg/mL.

It is evident from the data that the compounds are more toxic towards Gram (+) strains as compared to Gram (-) strains which may be attributed to the fact that the cell walls of Gram (-) strains have more antigenic properties due to the presence of an outer lipid membrane of lipopolysaccharides. The nature of R group attached to the phenyl ring has pronounced effect on the activity. Compounds having chloro substituted phenyl group shows better activity against most of the tested micro-organisms. Conventional fungicide and bactericide showed inhibition at concentration < 3.12 μg/mL. No compound show better inhibitory action than the conventional fungicide and bactericide. The compound **3e** has toxicity near to the conventional bactericide against *B. subtilis* and near to the conventional fungicide against *C. albicans*.

CONCLUSION

In conclusion, 2-[1-phenyl-3-arylpyrazol-4-yl]benzothiazolines **(3a-g)** were synthesized by the solventless condensation of 2-aminothiophenol and pyrazole aldehydes. All the newly synthesized compounds were evaluated for their antibacterial and antifungal activities. The compound **3e** have displayed good antibacterial and antifungal activities.

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