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SYNTHESIS AND BIOLOGICAL SCREENING OF SOME PYRAZOLINES

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A simple and efficient method is described for the synthesis of 4-(3-(benzo [*b*] thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)-1-phenyl-3-aryl-1*H*-pyrazoles **4** from (*E*)-1-(benzo [*b*] thiophen-2-yl)-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl) prop-2-en-1-ones **3** in presence of hydrazine hydrate.

Pyrazolines and their derivatives are reported to possess antiprotocolytic[1], antibacterial, antifungal[2] and antiviral[3] activities. Many substituted pyrazolines are known to possess acaricidal[4] activities and are used in the treatment of cerebral edema[5]. 1-Phenyl-2-pyrazolines are found to be useful as antioxidants[6]. They have also found to be effective as bleaching agents, luminescents and fluorescents and important intermediates in dye industry.

Like other heterocyclic compounds, pyrazoles also exhibit a wide range of biological activities[7] like antioxidant, antiinvassive, antiviral, antipyretics, antiinflammatory, antidepressant, blood pressure lowering etc. Pyrazoles are also used as agrochemicals[8,9], dyestuffs[10] and in sunscreen materials[11] etc.

Sulphur containing compounds play an important role in biological processes. Biotin is a vitamin which contains tetrahydrothiophene nucleus in its structure.

Chalcones are versatile synthones and can be converted into large number of heterocyclic compounds having pharmacological and biological importance.

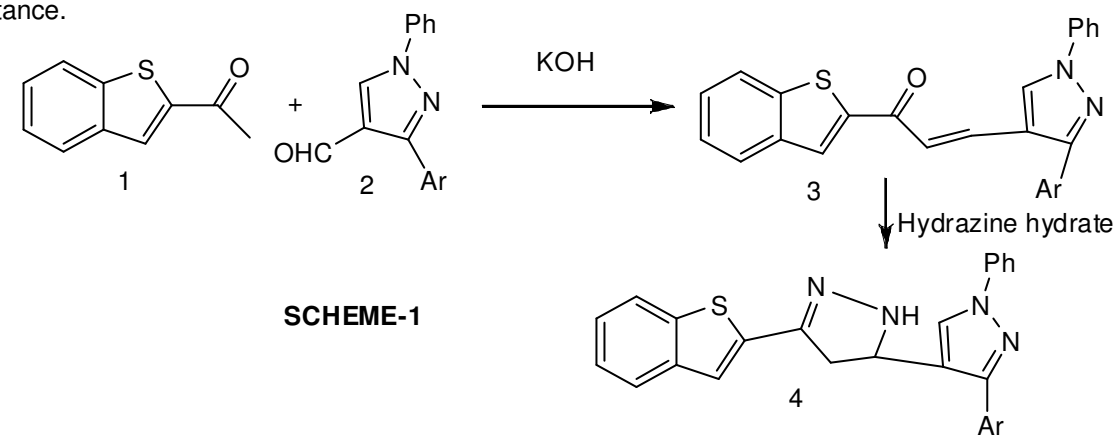
Activities associated with benzothiophenes, pyrazoles, chalcones and pyrazolines prompted us to synthesize some chalcones and pyrazolines containing benzothiophene nucleus.

In present investigation 4-formyl pyrazoles **2** were condensed with 1-(benzo [*b*] thiphen-2-yl) ethanone **1** in presence of KOH in ethanol to get (*E*)-1-(benzo [*b*] thiophene-2-yl)-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl) prop-2-en-1-ones **3**. Compounds **3** were treated with hydrazine hydrate to obtain 4-(3-(benzo [*b*] thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)-1-phenyl-3-aryl-1*H*-pyrazoles **4**.

Antimicrobial activity

The antimicrobial activity of some compounds was assessed against 24 hr culture of some selected bacteria and fungi. The bacteria used were *Escherichia coli* and *Staphylococcus aureus*; the fungi used were *Candida albicans* and *Aspergillus fumigatus*.

The antimicrobial activity was performed by agar well diffusion method at 100 and 1000μg/ml conc in



SCHEME-1

Table-1
Characterization data of the synthesized compounds

Compd	Ar	M.P. (^{0}C)	Yield (%)
3a	Phenyl	185	50
3b	4-methylphenyl	188	20
3c	4-chlorophenyl	187	70
3d	4-bromophenyl	192	80
3e	2-thienyl	162	15
4a	Phenyl	187	10
4b	4-methylphenyl	190	40
4c	4-chlorophenyl	190	40
4d	4-bromophenyl	198	35
4e	2-thienyl	168	10

DMSO. Nutrient agar and potato dextrose agar were used to culture the bacteria and fungi respectively.

Amphotericin B and Vancomycin were used as standards for comparison of antifungal and antibacterial activities respectively. The activity has been reported by measuring the diameter of the zone of inhibition. All the screened compounds were found inactive against these organisms.

Experimental

All the recorded melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on a Perkin-Elmer FTIR spectrophotometer in KBr disc. ^{1}H NMR spectra were recorded on a Varian 300 MHz spectrophotometer in DMSO as a solvent and TMS as an internal standard; Peak values are shown in δ ppm. Mass spectra were obtained on a Finnigan mass spectrometer.

(*E*)-1-(Benzo [*b*] thiophen-2-yl)-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl) prop-2-en-1-ones 3

1-(Benzo [*b*] thiophen-2-yl) ethanone **1** (0.005 mol) and 4-formyl pyrazole **2** (0.005 mol) were taken in 100 ml RBF with 25 ml ethanol. To this reaction 2g of KOH was added and resulting reaction mixture was stirred at room temp for 24 hr. Then contents were poured over crushed ice and acidified with conc. HCl, solid thus obtained was separated by filtration and crystallized from proper solvent to get compounds **3**.

3b : IR (KBr): 3062 (Ar-H), 1719 (C=O), 1637 (C=N) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.41 (s, 3H, Ar-CH_3), 7.38-8.52 (m, 16H, aromatic and olefinic protons), 9.43 (s, 1H, pyrazole proton). Mass [M$^+$] 421.

4-(3-(Benzo [*b*] thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)-1-phenyl-3-aryl-1*H*-pyrazoles 4

Compound **3** (0.003 mol) was taken in 100 ml RBF with 15 ml dioxan. To this reaction mixture 1 ml hydrazine hydrate was added and the contents were heated under refluxed for 4 hr. Then, to the reaction mixture 2 ml gl acetic acid was added and heating was continued for further 2 hr. After complete heating contents were cooled to room temp and poured over crushed ice. The solid thus obtained was separated by filtration and crystallized from ethanol to get compounds **4**.

4b : IR (KBr): 3327 (N-H), 3076 (Ar-H), 1635 (C=N); ^{1}H NMR ($CDCl_3$): 2.36 (s, 3H, Ar-CH_3), 3.07 (dd, 1H, pyrazoline proton), 3.57 (dd, 1H, pyrazoline proton), 5.04 (dd, 1H, pyrazoline proton), 7.29-7.90 (m, 15H, aromatic and olefinic protons), 8.60 (s, 1H, pyrazole proton). Mass : [M$^+$] 435.

Characterization data of **3** & **4** are given in Table-1.

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