Int. J. Chem. Sci.: 7(4), 2009, 2572-2576

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW 2-PYRAZOLINE DERIVATIVES

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ABSTRACT

Some new pyrazoline derivatives were synthesized by reacting chalcones of 2-acetyl thiophene with phenyl hydrazine hydrochloride in the presence of alcohol. The synthesized compounds were identified by spectral data and screened for antimicrobial activity. Some of these compounds showed moderate to considerable antimicrobial activity.

Key words: Synthesis, Pyrazolines, Antimicrobial activity.

INTRODUCTION

Compounds with pyrazoline structures are known to possess antimicrobial[1-3], anti-inflammatory[4], antidepressant[5,6], anti-tubercular[7] activities. In the present study, some new pyrazoline derivatives **(1 to 5)** have been synthesized by the reaction of chalcones of 2-acetyl thiophene and phenyl hydrazine hydrochloride. The structures of the various synthesized compounds are assigned on the basis of elemental analysis, IR and ^{1}H NMR spectral data. These compounds were also screened for their antimicrobial activity.

EXPERIMENTAL

Melting points were determined on a capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded in the indicated solvent on Bruker WM 400 MHz spectrometer with TMS as internal standard. Infrared spectra were recorded in KBr on Perkin-Elmer AC-1 spectrophotometer. Microanalyses were performed on Carlo Erba EA-1108 element analyzer and were within the ± 0.5% of the theoretical values. Column chromatography was performed on silica gel (Merck, 60-120 mesh).

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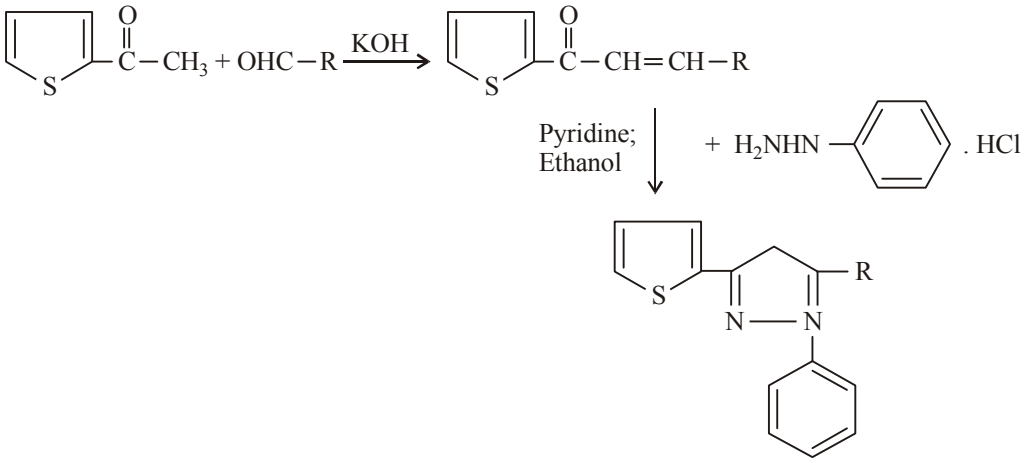
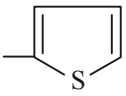
General procedure for the preparation of 2-pyrazolines (1-5)

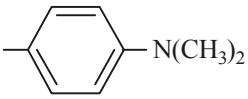
A chalcone of 2-acetyl thiophene (0.001 mol) dissolved in 20 mL of ethanol and phenyl hydrazine hydrochloride (500 mg) was added to it. To this mixture, 0.3 mL of pyridine was added drop wise at room temperature. After that, the mixture was refluxed for 5-6 hours and the solvent was evaporated completely. The reaction mixture was poured into ice-cold water and the solid mass that separated out was filtered, dried and purified by column chromatography with ethyl acetate/ hexane and recrystalized from chloroform.

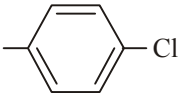


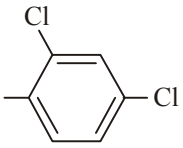
(1-5)

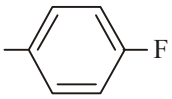
where R =

(1) 

(2) 

(3) 

(4) 

(5) 

Scheme 1: Synthesis of some new 2-pyrazoline derivatives

Table 1: Physical data of compounds (1-5)

Compound	M. F.	M.P (°C)	Yield (%)	Elemental analyses (%)					
				C		H		N	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
(1)	$C_{17}H_{12}N_2S_2$	210	71	66.23	66.12	3.89	3.81	9.09	9.06
(2)	$C_{21}H_{19}N_3S$	137	74	72.07	71.86	5.80	5.61	12.61	12.54
(3)	$C_{19}H_{13}N_2SCl$	239	74	67.65	67.64	3.8	3.74	8.30	8.28
(4)	$C_{19}H_{12}N_2SCl_2$	246	73	60.96	60.81	3.2	3.04	7.48	7.42
(5)	$C_{19}H_{13}N_2SF$	227	68	71.47	71.42	4.07	4.04	8.77	8.74

Table 2: Spectral data of the compounds (1-5)

Compd.	IR (KBr, cm^{-1})	^1H NMR ($CDCl_3$, ppm)
(1)	1594 (C=N), 1112 (C–N), 706 (C–S).	3.25 (1H, dd, HA), 3.80 (1H, dd, H B), 5.50 1H, dd, H X), 6.80 – 7.50 (11H, Ar-H).
(2)	1520 (C=N), 1080 (C–N), 690 (C–S).	3.10 (6H, S, $N(CH_3)_2$), 3.21 (1H, dd, HA), 3.80 (1H, dd, HB), 5.50 (1H, dd, HX), 6.70-8.10 (12H, Ar–H).
(3)	1595 (C=N), 1097 (C–N), 689 (C–S), 822 (C–Cl).	3.18 (1H, dd, HA), 3.85 (1H, dd, HB), 5.30 (1H, dd, HX), 6.40-7.90 (12H, Ar–H).
(4)	1645 (C=N), 1350 (C–N), 716 (C–S), 855 (C–Cl).	3.05 (1H, dd, HA), 3.91 (1H, dd, HB), 5.6 (1H, dd, HX), 6.70–7.60 (11H, Ar–H).
(5)	1640 (C=N), 1352 (C–N), 680 (C–S), 8.70 (C–F).	3.18 (1H, dd, HA), 3.88 (1H, dd, HB), 5.28 (1H, dd, HX), 6.80 – 7.45 (12H, Ar–H).

Antimicrobial activity

Cup plate method[8,9] using Mueller-Hinton agar medium was employed to study the preliminary antibacterial activity of **(1-5)** against *B. pumilis, B. substilis, E. coli* and *P. vulgaris*. The agar medium was purchased from Hi Media Laboratories Ltd., Mumbai, India. Preparation of nutrient broth, subculture, base layer medium, agar medium and peptone water was done as per the standard procedure. Each test compound (5 mg) was dissolved in 5 mL of dimethyl sulfoxide (1000 μg/mL). Volumes of 0.05 mL and 0.1 mL of each compound were used for testing.

The cups each of 9 mm diameter were made by scooping out medium with a sterilized cork borer in a petri dish, which was streaked with the organisms. The solutions of each test compound (0.05 and 0.1 mL) were added separately in the cups and petri dishes and were subsequently incubated. Sparfloxacin was used as standard reference drug (200 μg/mL) and dimethyl sulphoxide as a control, which did not reveal any inhibition. Zone of inhibition produced by each compound was measured in mm and the results are presented in Table 3.

Table 3: Antibacterial activity of the compounds (1-5)

Compd.	**Zone of inhibition (in mm)**							
	B. substilis		***B. pumilis***		***E. coli***		***P. vulgaris***	
	0.05mL	**0.1mL**	**0.05mL**	**0.1mL**	**0.05mL**	**0.1mL**	**0.05mL**	**0.1mL**
Standard	22	25	26	28	19	24	24	26
Control	-	-	-	-	-	-	-	-
1	08	12	09	12	07	10	09	13
2	11	13	12	14	11	09	13	11
3	13	17	10	15	13	16	10	16
4	14	20	12	18	12	15	11	17
5	15	21	14	18	14	18	12	18

Control : Dimethyl sulfoxide; Standard : sparfloxacin

RESULTS AND DISCUSSION

Antibacterial activity

The screening results revealed that the compounds **1** and **2** showed significant antibacterial activity at both 0.05 mL abd 0.1 mL concentration levels, when compared with standard drug sparfloxacin and other compounds **3, 4** and **5** showed moderate activity.

ACKNOWLEDGEMENTS

We are thankful to the Head, Sophisticated Instrumentation Facility, Indian Institute of Sciences, Bangalore for ^{1}H NMR spectra and to Sipra Laboratories, Hyderabad for IR spectra.

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Accepted : 22.08.2009