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Synthesis of Some New N-Thio Carbamoyl-3-Methyl-4[2′-{4′-*p*-subst./unsubst.)-phenyl}thiazolyl hydrazono]-2-Pyrazolin-5-one with Possible Antibacterial Activity

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Several new N-thio carbamoyl-3-methyl-4-[2′-{4′-*p*-subst./unsubst.)-phenyl}thiazolyl hydrazono]-2-pyrazolin-5-one (II) have been prepared by reaction of ethyl-2-(2′-aryl hydrazono)-3-oxo-butyrate (I) with thiosemicarbazide in ethylacetoacetate All these synthesized pyrazolines have been screened against a few micro-organisms for antibacterial activity. Compounds were characterised by infrared and NMR spectra.

Key Words: Synthesis, Substituted, Unsubstituted, Pyrazolin-5-one, Antibacterial activity

INTRODUCTION

The chemistry and wide range of pharmaceutical properties of 2-pyrazolin-5-one derivatives have been cited in literature[1].

Pyrazoline derivatives have been studied extensively because of their ready accessibility, diverse chemical reactivity and broad spectrum of biological activities. They are found to possess antimicrobial, antifungal, insecticidal, anti-implantation, antiarrhythmic, antiinflammatory, abortifacient and anti-protelytic activity[2, 3].

Various pyrazole and pyazolone derivatives have been reported to exhibit antibacterial[4–6], fungicidal[6–8], CNS active[9] and acaricidal[10, 11] properties. In view of potential biological activities[12] of aryl pyrazoles, it was thought worth while to synthesize some new pyrazolin-5-one[13], as possible antibacterial activity.

EXPERIMENTAL

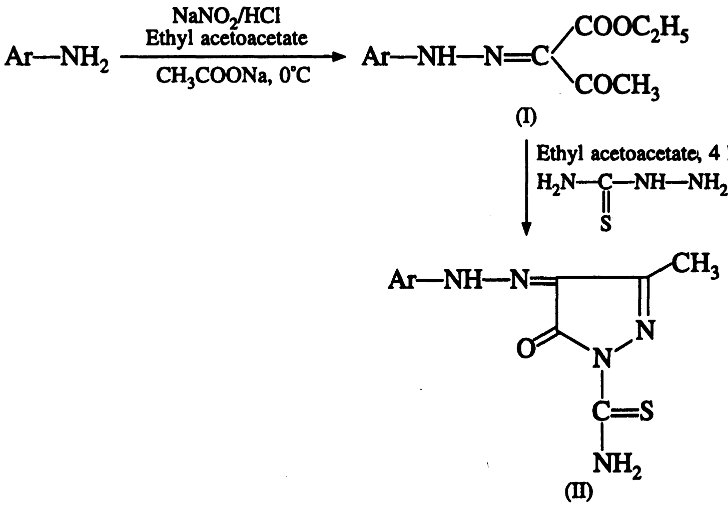
Preparation of ethyl-2-[2′-(subst./unsubst. aryl hydrazono)-3-oxo-butyrate(I)

To the 2-amino-4-(*p*-subst./unsubst.)phenyl thiazole dissolved in a mixture of HCl (8 mL) and water (6 mL) and cooled to 0°C in an ice bath, a cold aqueous solution of $NaNO_2$ (0.03 mol) was added. The diazonium salt solution was filtered into a cooled solution of ethyl acetoacetate (0.01 mol) and sodium acetate (0.122 mol) in ethanol (50 mL); the resulting solid was washed with water and crystallized from EtOH/MeOH.

Preparation of N-thio carbamoyl-3-methyl-4-[2′-{4′-*p*-subst./unsubst. phenyl}thiazolyl hydrazono]-2-pyrazolin-5-one(II)

To the compound (I) (0.002 mol) dissolved in ethylacetoacetate (20 mL), a solution of thiosemicarbazide (0.002 mol) in ethylacetoacetate (25 mL) was added and the mixture was refluxed for 4 h; it was then cooled and allowed to stand overnight; the resulting solid was dried and crystallized from EtOH/MeOH.

Compound **2**, Amino-4-{*p*-subst./unsubst.} phenyl thiazoles was prepared by the reported method[14].



Infrared spectra of compounds were recorded in solid state using KBr pellet method. The spectra were recorded on Perkin-Elmer FT-IR spectrophotometer (Model RX-1). The PMR spectra of compounds were recorded in DMSO-d_6 solvent at room temperature using TMS as reference compound. The spectra were recorded on Perkin-Elmer Model-32 NMR spectrometer at 300 MHz at CDRI Lucknow.

The antibacterial activities of synthesized compounds and standard drugs were checked against *E. coli, Lactobacillus* using filter paper disc method[15] at 500 ppm concentration using 5 mm filter paper disc.

RESULTS AND DISCUSSION

Characteristics of compound (II) and results of antibacterial activity are given in Table-1. The main absorption bands (cm^{-1}) observed in IR spectra are described as follows:

3445 ν(—NH), 1690 ν(C=O), ν(—NH—N=C), 1110 ν(C=S), 1530 and 1245 ν(C—N), 690 cm^{-1} ν(C—S—C). The position of signals in NMR spectra can be assigned to different types of protons as follows:

δ 9.3 (1H, s, NHN=C), δ 3.6 (2H, s, CS—NH_2), δ 2.52 (3H, s, —CH_3), δ7.2–8.3 (5H, m, ArH), δ 6.2–6.8 (1H, s, —CH).

TABLE-1
DATA SHOWING CHARACTERISTICS OF NEWLY SYNTHESIZED PYRAZOLIN-5-ONE AND THEIR ANTIBACTERIAL ACTIVITY

Compd. No.	Nature of Ar	m.f.	Yield (%)	m.p. (°C)	% N and S		Antibacterial activity: diameter of zone of inhibition (in mm.)	
					Calculated	Found	*E.Coli*	*L. bacillus*
IIa	2-Amino-4-phenyl thiazole	$C_{14}H_{12}N_6OS_2$	39	204	N 24.41 S 18.60	24.37 18.56	+6	+7
IIb	2-Amino-4-(*p*-chloro)phenyl thiazole	$C_{14}H_{11}N_6OS_2Cl$	29	223	N 22.19 S 16.90	21.14 16.84	+10	+9
IIc	2-Amino-4-(*p*-fluoro)phenyl thiazole	$C_{14}H_{11}N_6OS_2F$	32	217	N 23.20 S 17.67	23.16 17.62	+7	—
IId	2-Amino-4-(*p*-nitro)phenyl thiazole	$C_{14}H_{11}N_7O_3S_2$	37	232	N 25.19 S 16.45	25.14 16.40	—	+8
IIe	2-Amino-4-(*p*-methoxy)phenyl thiazole	$C_{14}H_{14}N_6O_2S_2$	30	210	N 22.45 S 17.11	22.40 17.06	+8	+10
IIf	2-Amino-4-(*p*-hydroxy)phenyl thiazole	$C_{14}H_{12}N_6O_2S_2$	31	201	N 23.33 S 17.77	23.29 17.71	+9	+9

Diameters of zones of inhibition (in mm) of standard drug streptomycin against *E. coli* and lactobacillus were found to be 13 and 11 respectively.

As compared to standard streptomycin prazolin-5-one has been found to possess significant activity against the two organisms.

Compounds **IIb, IIf** showed maximum inhibition and compounds **IIc, IId** showed moderate activity against *E. coli.*

Compounds **IIb, IIe, IIf** showed maximum inhibition and compounds **IIa, IIb** showed moderate activity against *Lactobacillus.* Other compounds showed poor activity.

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