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SYNTHESIS, CHARACTERIZATION, ANTIMICROBIAL AND ANTIFUNGAL ACTIVITIES OF SOME NEW 1*E*-1-{3-ETHOXY-1-(2,4-DINITROPHENYL/PHENYL)-5-OXO-1*H*-PYRAZOL-4-(5*H*)-YLIDENE}-4-(SUBSTITUTED PHENYL)THIOSEMICARBAZIDE

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Abstract
In the present study, various new 1*E*-1-{3-ethoxy-1-(2,4-dinitrophenyl/phenyl)-5-oxo-1*H*-pyrazol-4-(5*H*)-ylidene}-4-(substituted phenyl)thiosemicarbazide were synthesized and their antimicrobial and antifungal activities were evaluated. All the synthesized compounds were characterized by the combination of elemental analysis and standard spectroscopic methods. They were screened for antibacterial activity against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli* and *Streptomyces griveus*as well as screened for antifungal activity against *Fusarium oxysporium,* and *Penicillium funiculosum.*

Key words: Pyrazole, thiosemicarbazide, antibacterial, antifungal activity

Introduction

Pyrazoles are novel class of heterocyclic compounds possessing wide variety of applications in the agrochemical and pharmaceutical industries e.g. derivatives of pyrazole are found to show good antibacterial,[1] anti-inflammatory,[2] antipyretic,[3] antioxidant[4]and antimicrobial[5] activities. In continuation of our work on heterocyclic compounds,[6-11] we have synthesized some new pyrazole derivatives.

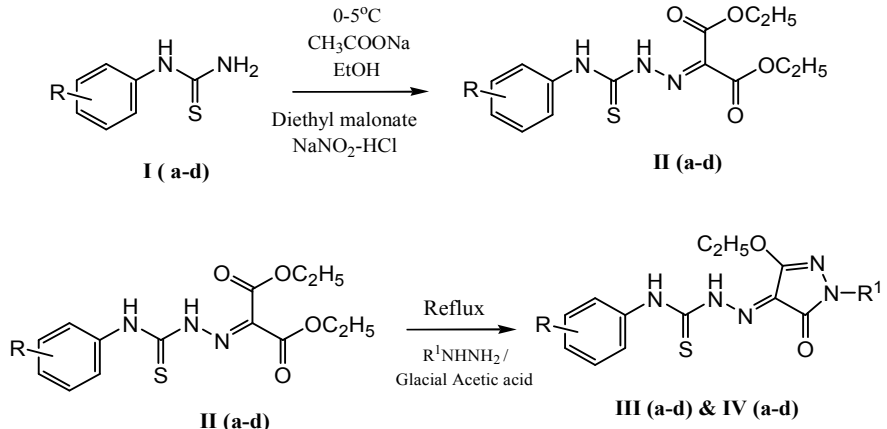
Result and Discussion

Formation of compounds **II** were confirmed by IR spectra in which these compounds show presence of peaks at 1645 cm^{-1} (>C=O) of ester group. Peaks at 3380, 1550, 1060, 1348 and 1250 cm^{-1}show the presence of>NH, C=N, >CS, $–NO_2$ and –N=O groups respectively. ^{1}H NMR showed peak at δ 7.0 ppm for –NHCSNH-, δ 3.6 ppm for $–\mathbf{CH_2}CH_3$, 1.3 for $\mathbf{-CH_3}$, δ 10 ppm for NHN=C, H bonded, δ 2.5 ppm for $–OCH_2$, δ 6.5-7.4 ppm for aromatic protons.
Compounds **III** were confirmed by IR spectra in which these compounds show>C=O at 1652 cm^{-1} and 1320 cm^{-1}at $–NO_2$. ^{1}H NMR shows peak at δ 2.4 ppm for $=C–CH_3$, δ 6.7-7.0 for aromatic proton (9H), δ 9.1 ppm for (–NH=C), δ 6.8 ppm for -NHCS.

Compounds **IV** were confirmed by IR spectra in which these compounds shows peaks for >C=O at 1650 $cm^{-1}$and 1310 $cm^{-1}$for $–NO_2$. ^1H NMR shows peak at δ 1.1 ppm for $-CH_3$, δ 7.2-7.3 ppm for aromatic protons and δ 9.0 ppm for (–NHN=C), δ 6.6 ppm for -NHCS.

Experimental

Purity of all the newly synthesized compounds was checked on silica gel G plates using iodine vapour as the detecting agent. Melting points were determined in open capillary tubes using Gallen Kamp melting point apparatus and are uncorrected. IR spectra were recorded on a SHIMADZU-8400 FT-IR spectrophotometer in KBr pellets. ^1H NMR spectra (chemical shift in δ ppm) were recorded on JEOL RESONANCE spectrometer (400 MHz) using $CDCl_3$ as a solvent. Chemical shifts being expressed in δ ppm downfield from TMS as an internal standard.



R = 3-NO_2, 4-NO_2, 2-Cl, 2,5-diCl, R^1 = -C_6H_5, 2,4-di$NO_2C_6H_4$

Scheme - 1

Diethyl-2-{4-(substituted phenyl)thiosemicarbazido)malonate (II)

Substituted-phenylthiourea (0.01 mol) was dissolved in a mixture of HCl (8 ml) and water (6 ml) then cooled to 0°C in an ice bath and a cold aqueous solution of $NaNO_2$ (0.02 mol) was added. The diazonium salt was filtered directly into a cold solution of diethyl malonate (0.01 mol) and CH_3COONa (0.1 mol) in ethanol (50 ml) and the resulting solid was washed with water and then crystallized from ethanol to give compound **II**.

1*E*-1-{3-ethoxy-1-phenyl-5-oxo-1*H*-pyrazol-4-(5*H*)-ylidene}-4-(substituted phenyl)thiosemi-carbazide (III) and 1*E*-1-{3-ethoxy-1-(2,4-dinitrophenyl)-5-oxo-1*H*-pyrazol-4-(5*H*)-ylidene}-4-(substituted phenyl)thiosemicarbazide (IV)

Compound **II** (0.004 mol) was dissolved in glacial acetic acid (40 ml), a solution of phenyl hydrazine/dinitrophenylhydrazine(0.004mol) in glacial acetic acid was added to compound II solution and the mixture was refluxed for 4 hrs. and then cooled and allowed to stand overnight. The resulting solid was dried and then crystallized from ethanol to give the title compounds **III** and **IV** respectively.

Table 1: Physical and Analytical Data of the Compounds

Compounds	R	R^1	Mol. Formula	M. P (°C)	Yield %	Elemental Analysis % found/ (calcd.) N	S
IIa	3-NO_2	-	$C_{14}H_{16}N_4O_6S$	106	82	15.18 (15.21)	8.66 (8.70)
IIb	4-NO_2	-	$C_{14}H_{16}N_4O_6S$	262	83	15.27	8.65

						(15.21)	(8.70)
IIc	2-Cl	-	$C_{14}H_{16}N_3O_4SCl$	120	81	11.70 (11.74)	8.91 (8.96)
IId	2,5-diCl	-	$C_{14}H_{15}N_3O_4SCl_2$	104	85	10.67 (10.71)	8.13 (8.17)
IIIa	3-NO_2	-C_6H_5	$C_{18}H_{16}N_6O_4S$	140	55	20.32 (20.38)	7.73 (7.77)
IIIb	4-NO_2	-C_6H_5	$C_{18}H_{16}N_6O_4S$	128	60	20.33 (20.38)	7.73 (7.77)
IIIc	2-Cl	-C_6H_5	$C_{18}H_{16}N_5O_2SCl$	132	58	17.39 (17.43)	7.91 (7.98)
IIId	2,5-diCl	-C_6H_5	$C_{18}H_{15}N_5O_2SCl_2$	110	63	15.97 (16.05)	7.30 (7.35)
IVa	3-NO_2	2,4-di$NO_2C_6H_4$	$C_{18}H_{14}N_8O_8S$	216	51	22.28 (22.30)	6.32 (6.38)
IVb	4-NO_2	2,4-di$NO_2C_6H_4$	$C_{18}H_{14}N_8O_8S$	222	50	22.27 (22.30)	6.35 (6.38)
IVc	2-Cl	2,4-di$NO_2C_6H_4$	$C_{18}H_{14}N_7O_6SCl$	156	56	19.84 (19.93)	6.46 (6.52)
IVd	2,5-diCl	2,4-di$NO_2C_6H_4$	$C_{18}H_{13}N_7O_6SCl_2$	206	54	18.59 (18.63)	6.02 (6.09)

Antimicrobial activity

The investigation of antibacterial screening data revealed that all the compounds (IIIa-d &IVa-d) showed moderate to significant bacterial inhibition. Compounds IIIc & IVd are more potent than Streptomycin (standard) against *E. coil*and *S. griveus* bacterial gram-ve strains respectively. Compounds IIId & IVd are more potent than Streptomycin (standard) against *B. subtilis* and *S. aureus* bacterial gram+ve strains respectively. Compounds IIIc and IVc exhibited better activity against *S. griveus;* IIId showed better activity against *E. coil;* IIIb, IIIc, IVc & IVd and IIIb, IIId & IVa exhibited better activity against *B. subtilis* and *S. aureus*respectively.

Antifungal activity

The investigation of antifungal screening data revealed good to moderate activity against tests fungi respectively, *P. funiculosum* and *F. oxysporium* as compared to Ketoconzole as standard.

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