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SYNTHESIS OF SOME NEW 1-BENZOTHIAZOLYL/PHENYL-4-(SUBSTITUTED PHENYLTHIOUREIDO) HYDRAZONO-3-METHYL-2-PYRAZOLIN-5-ONES AND THEIR ANTIFUNGAL ACTIVITY

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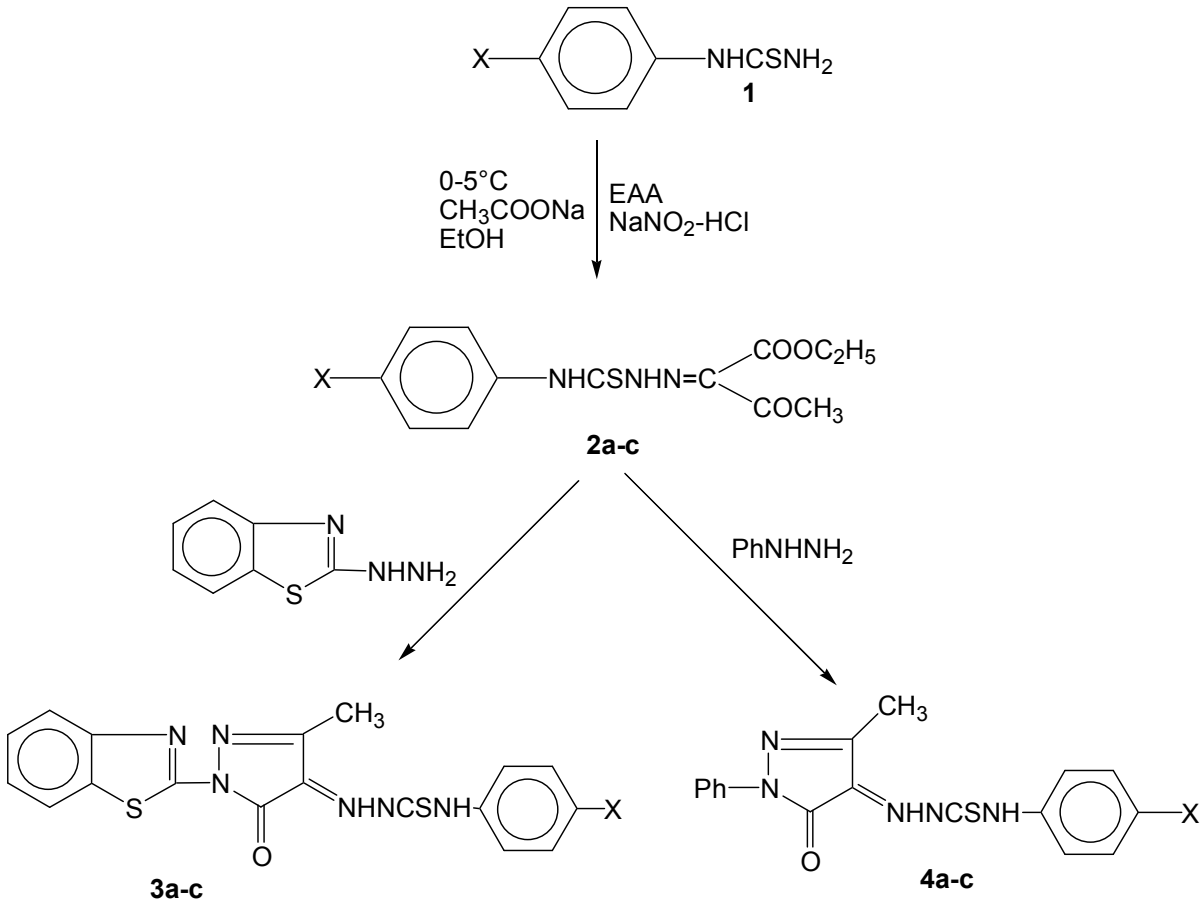
Abstract: Reaction of diazonium salt of substituted phenylthiourea with ethylacetoacetate in the presence of sodium acetate and ethanol gave 1-ethyl-2-(substituted phenyl thioureido) hydrazono-3-oxobutyrate which on reaction with 2-hydrazinobenzothiazole and phenyl hydrazine in acetic acid yielded 1-benzothiazolyl/phenyl 4-(substituted phenyl thioureido) hydrazono-3-methyl-2-pyrazolin-5-ones. The structure of all the new synthesized compounds have been confirmed by spectral and analytical data and compounds have been screened for their antifungal activities.

Introduction

Pyrazolones show anti-inflammatory,[1] antipyretic,[2] anticancer[3] activities and benzothiazoles[4] also associated with antitumor,[5] antimicrobial[6] etc. activities compounds having hydrazono group show antifungal and antidiabetic activities in rats.[7] Keeping in view the importance of above nuclei and in continuation of our work on heterocyclic compounds.[8] We have synthesized some new 2-pyrazolin-5-ones.

Experimental

Melting points were determined in open capillaries and are uncorrected. The IR spectra (KBr) were recorded on Perkin-Elmer 577 spectrophotometer. ^{1}H NMR were recorded on DRX-300 spectrometer using DMSO-d_6 + $CDCl_3$ as a solvent. Chemical shifts being expressed in δ ppm downfield from TMS. Purity of compounds were checked by TLC on silica gel plate.



a; X = F; b, X = Cl; C, X = Br

Scheme 1

Ethyl-2-(substituted phenyl thioureido) hydrazono-3-oxobutyrate (2)

4-Halosubstituted-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 cold aqueous solution of sodium nitrite (0.03 mol) was added. The diazonium salt was filtered directly into a cold solution of acetoacetic ester (0.01 mol) and sodium acetate (0.122 mol) in ethanol (50 ml) and the resulting solid was washed with water and then crystallized from ethanol to give **2**.

1-Benzothiazolyl-4-substituted phenyl thioureido hydrazono-3-methyl-2-pyrazolin-5-ones (3)

To compound **2** (0.002 mol) dissolved in glc. acetic acid (20 mol) solution of 2-hydrazino benzothiazole (0.002 mol) in glc. acetic acid was added and the mixture was refluxed for 4 hr and then cooled and allowed to stand overnight. The resulting solid was dried and then crystallized from ethanol to give **3.**

1-Phenyl (4-substituted phenyl thioureido) hydrazono-3-methyl-2-pyrazolin-5-ones (4)

To compound **2** (0.002 mol) dissolved in gl. acetic acid (20 ml) a solution of phenyl hydrazine (0.002 mol) in glc. acetic acid was added and the mixture was refluxed for 4 hr and

then cooled and allowed to stand overnight. The resulting solid was dried and then crystallized from ethanol to give **4**.

Result and Discussion

Formation of compounds **2** were confirmed by IR spectra in which it show presence of peaks at 1700 and 1660 cm^{-1} (>C=O) of ester and acetyl group respectively. Peak at 3150, 1600 and 1115 cm^{-1} shows presence of >NH, C=N and >CS respectively, ^1H NMR showed peak at δ 5.2 ppm for >NHCSNH<, δ 4.2 ppm for $-\mathbf{CH_2}CH_3$, 1.8 for $>CH_2\mathbf{CH_3}$ δ 13 ppm for NHN=C, H bonded, δ 2.25 ppm for $>COCH_3$, δ 6.7-7.8 ppm for aromatic protons and further the mass spectrum shows M^+ at m/z 279 **(2a)**.

Compounds **3** show disappearance of peak due to ester and cyclization occurs by the reaction of hydrazinobenzothiazole. In IR spectrum >C=O appeared at 1750 cm^{-1} for cyclic ketone. It show peak at 1580 cm^{-1} for C=N of benzothiazolyl ring. ^1H NMR shows peak at δ 2.5 ppm for $>CH_3$, δ 6.8-7.5 ppm for aromatic protons (8H) and δ 10.2 ppm for (–NH=C), δ 5.6 ppm for >NHCS. Further mass spectrum show M^+ at m/z 380 **(3a)**.

Compounds **4** also shown disappearance of peak of ester due to cyclization with phenylhydrazine. IR spectrum shows C=O at 1760 cm^{-1}. ^1H NMR shows peak at δ 2.7 ppm for $=C-CH_3$, δ 6.5-7.2 for aromatic proton (9H), δ 10.4 ppm for (–NH=C) δ, 5.4 ppm for >NHCS–. Further mass spectrum shows M^+ at m/z 323 **(4a)**.

Antifungal activity

All the synthesized compounds **2a-c**, **3a-c** and **4a-c** were screened for their antifungal activities against two pathogens *F. oxysporum* and *S. rolfsii* by radial growth method using food poison technique at two concentrations 500 and 1000 ppm compounds showed good to moderate activity.

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Table 1: Physical and analytical data of the compounds

Compounds	M.P. (°C)	Yield %	Mol. Formula	Elemental Analysis				Mass M^+ = M/e
				N%		S%		
				Found	Calc.	Found	Calc.	
2a	104	75	$C_{13}H_{14}N_3O_3F$	15.08	15.05	-	-	279
2b	94	72	$C_{13}H_{14}N_3O_3Cl$	14.25	14.21	-	-	295.5
2c	102	73	$C_{13}H_{14}N_3O_3Br$	12.32	12.35	-	-	340
3a	164	86	$C_{18}H_{13}N_6OSF$	22.14	22.10	8.38	8.42	380
3b	162	80	$C_{18}H_{13}N_6OSCl$	21.15	21.18	8.11	8.07	396.5
3c	169	84	$C_{18}H_{13}N_6OSBr$	19.08	19.04	7.29	7.25	441
4a	196	69	$C_{17}H_{14}N_5OF$	21.70	21.67	-	-	323
4b	220	71	$C_{17}H_{14}N_5OCl$	20.65	20.61	-	-	339.5
4c	201	75	$C_{17}H_{14}N_5OBr$	18.26	18.22	-	-	384

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