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SYNTHESIS OF SOME NEW 1-SUBSTITUTED 3-TRIFLUROMETHYL-5-PHENYL-4-(SUBSTITUTED PHENYL AZO) PYRAZOLES AS ANTIFUNGAL AGENTS

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Abstract
Some new fluorine containing azo pyrazoles have been synthesized by the condensation of hydrazono derivatives (obtained by the reaction of 1, 3-diketone with diazonium salts) in the presence of sodium acetate, with substituted hydrazines to give 1-substituted-3-trifluoromethyl-5-phenyl-4-(substituted phenyl azo) pyrazoles. The structure of these compounds are confirmed on the basis of elemental analysis and spectral studies.

Keywords: Azopyrazoles, hydrazono derivatives, substituted 3-trifluoromethyl azo pyrazoles

Introduction

Pyrazole nucleus is of great interest, due to its potent anti-inflammatory activity[1]. Fluorine containing pyrazoles and their salts are useful as cancerostatics, antineoplastics and antibacterials[2]. Pyrazoles having azo group have been found to exhibit a wide range of biological activities[3] like antibacterial, CNS depressant, antitumor, potent local anaesthetics, etc. Azopyrazoles are also used as azo dyes[4]. Keeping in view the importance of biological activities associated with the pyrazoles[5, 6], we have synthesized some new fluorine containing azo derivatives of pyrazoles.

The synthesis[7] involves the reaction of diazonium salts (formed by the diazotization of fluorinated aniline in HCl and sodium nitrite) with fluorinated 1, 3-diketone (1-phenyl-4, 4, 4-trifluorobutane-1, 3-dione) in presence of sodium acetate and ethanol to give 2-(substituted phenyl) hydrazono-1-phenyl-4, 4, 4-trifluorobutane- 1, 3-dione (II) which on reaction with hydrazine derivatives (substituted phenyl hydrazine/phenyl semicarbazide) in acetic acid yielded 1-substituted-3-trifluoromethyl-5-phenyl-4-(substituted phenyl azo) pyrazoles III (scheme-1).

ANTIFUNGAL ACTIVITY

All new fluorinated compounds were screened for their antifungal activity against Alternaria alternata, Aspergillus niger and Macrophomina using agar diffusion technique at 100 μg/ml, 500 μg/ml and 1000 μg/ml concentration.

Result showed that these compounds give 25-35 % inhibition at 100 μg/ml, 35-48 % at 500 μg/ml and 50-71 % inhibition at 1000 μg/ml concentration.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected IR spectra (cm^{-1}) were recorded on a Perkin Elmer 337 spectrophotometer in KBr pellets. ^{1}HNMR spectra were recorded on GEOL (model AL-300) spectrophotometer using TMS as an internal standard (chemical shifts are recorded in δ scale). In ^{19}FNMR spectra TFA was taken as an external standard and chemical shifts are recorded in δ ppm. Purity of the compounds was checked by TLC on silica gel plate. Physical and analytical data of the compounds are presented in Table-I.

2-Chloro/ Methyl phenyl hydrazono-1-phenyl-4, 4, 4-trifluorobutane-1, 3-dione II:

2-Chloro/ methyl aniline (0.02 mole) was dissolved in a mixture of concentrated HCl and water (20 ml, 1:1) then cooled to 0^{o}C and a cold aqueous solution of sodium nitrite (0.02 mole, 1.3 g in 10 ml water) was added to it slowly maintaining the temperature between 0-2^{o}C. The cold diazotized solution was added drop wise to a cooled mixture of 1-phenyl- 4, 4, 4-trifluorobutane-1, 3-dione (0.02 mole, 4.3 g) and sodium acetate (10 g) in 20 ml of 50 % ethanol. The stirring was continued for 1 hr and the crystals separated were filtered, washed with water, dried and crystallized from ethanol to yield II, m.p., 146/ 170 ^{o}C, yield 80/ 82 %.

1-Substituted-3-trifluoromethyl-5-phenyl-4-(substituted phenyl azo) pyrazoles (III):

Hydrazono-1-phenyl-4,4,4-trifluorobutan-1,3-dione (0.01 mole) and substituted hydrazines (0.01 mole) were dissolved in glacial acetic acid (20 ml) and heated to reflux for 5-6 hrs on a water bath then allowed to cool overnight. The separated solid was crystallized from ethanol. All fluorinated Azopyrazoles (IIIa-j) were prepared in a similar manner. The physical and analytical data are given in Table I.

Results and Discussion

IR spectra of 2-(phenyl substituted) hydrazono-1-phenyl-4,4,4-trifluorobutane-1,3-dione shows significant characteristic absorption bands in the region of ν_{max} 3030 (NH, H-bonded); 1620 (> C=O); 1490 (–N =C<); 750 – 800 (C_6H_5); 1150–1250 (–C–CF_3); 700 (–C–Cl) cm^{-1}. IR spectra of phenyl pyrazoles shows significant characteristic absorption bands in the region of ν_{max} 1610–1620 (>C=O); 1640–1730 (>C=C and >C=N); 1540 (-N=N-) 1030–1060 (>C=S); 740–750 (C_6H_5); 1200–1250 (–C–CF_3) cm^{-1}.

^{1}HNMR spectra were recorded on GEOL (Model-AL-300) spectrometer using tetramethylsilane as an internal standard. The chemical shifts are reported in ppm. ^{1}HNMR spectra of 2-(phenyl substituted) hydrazono-1-phenyl-4,4,4-trifluorobutane- 1,3-dione show significant characteristic signals at **δ** 2.20 (s, 3H, -CH_3), aromatic protons at **δ** 7.2-7.8 ppm. ^{1}HNMR spectra of 1-allylthiocarbomoyl-5-phenyl-3-trifluoromethyl-4-(2- methylphenylazo) pyrazole showed characteristic signals at **δ** 9.8 (s, 1H, >NH); 7.2-7.8 (m, 9H, aromatic); 5.7 (s, 1H, =CH); 4.75 (s, 2H, =CH_2) and 2.4 (s, 2H, CH_2NH) ppm.

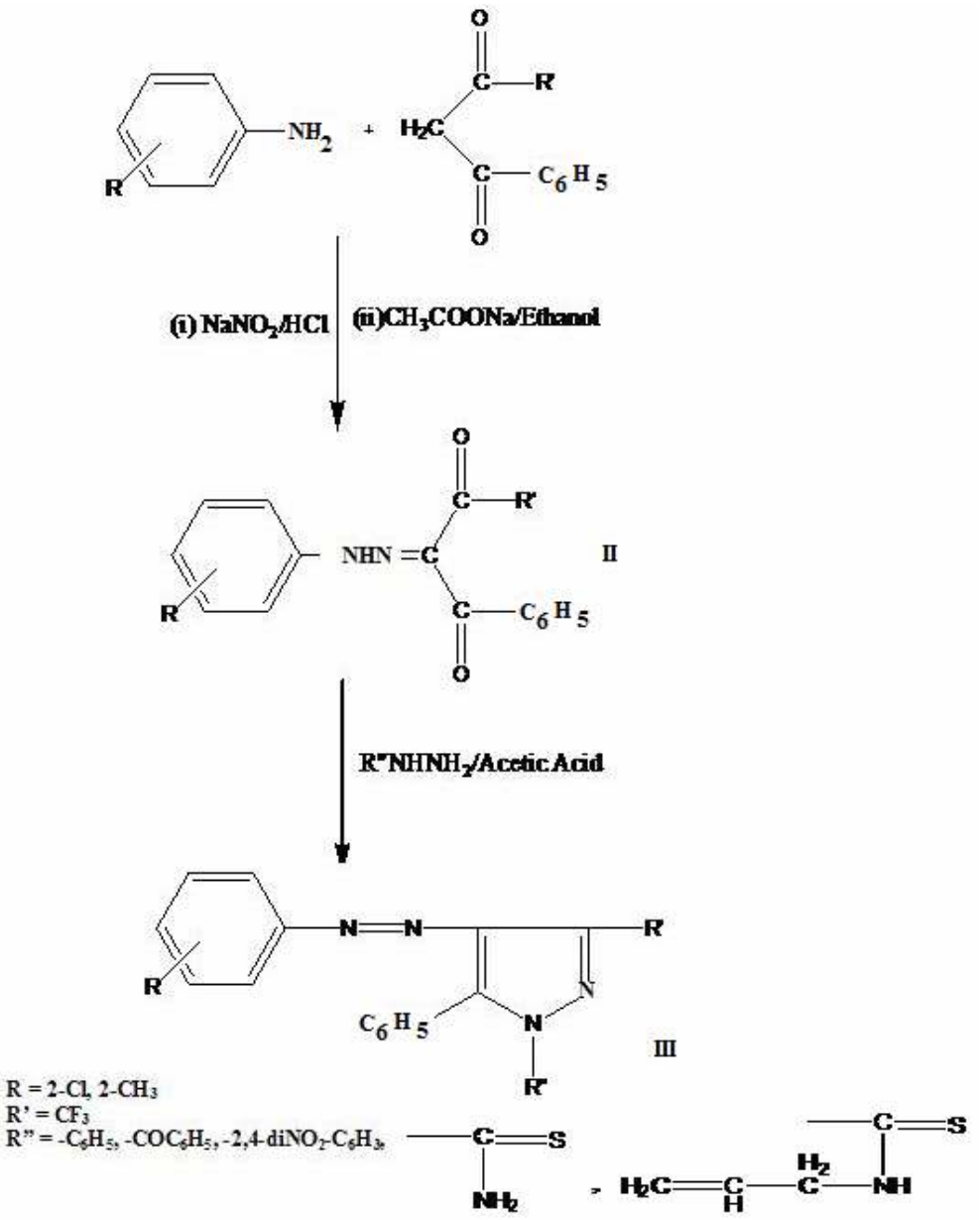
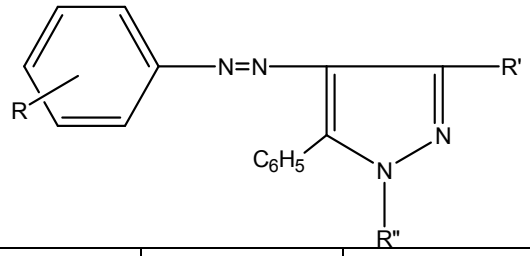
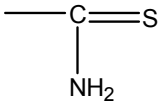
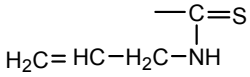
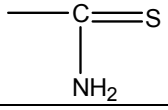
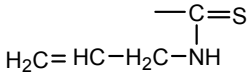

(i) NaNO2/HCl
(ii)CH3COONa/Ethanol
II
R"NHNH2/Acetic Acid
III
R = 2-Cl, 2-CH3
R' = CF3
R" = -C6H5, -COC6H5, -2,4-diNO2-C6H3,

Table I
Physical and Analytical Data of 1-Substituted-3-trifluoromethyl-5-phenyl-4-(Substituted-phenylazo) pyrazoles



Compound No.	R	R′	R″	Molecular Formula	M.P's (^oC)	Yield (%)	Element Analysis Found (Calculated)	
							N	S
IIIa	2-Cl	CF_3	$-C_6H_5$	$C_{22}H_{14}N_4ClF_3$	150	50	13.10 (13.13)	-
IIIb	2-Cl	CF_3	$-COC_6H_5$	$C_{23}H_{14}N_4ClOF_3$	190	60	12.30 (12.32)	-
IIIc	2-Cl	CF_3	2, 4-diNO_2-C_6H_3	$C_{22}H_{12}N_6ClO_4F_3$	145	55	16.24 (16.26)	-
IIId	2-Cl	CF_3		$C_{17}H_{11}N_5ClSF_3$	110	66	17.05 (17.09)	7.79 (7.81)
IIIe	2-Cl	CF_3		$C_{20}H_{15}N_5ClSF_3$	115	58	15.55 (15.57)	7.09 (7.11)
IIIf	2-CH_3	CF_3	$-C_6H_5$	$C_{23}H_{17}N_4F_3$	160	70	13.76 (13.79)	-
IIIg	2-CH_3	CF_3	$-COC_6H_5$	$C_{24}H_{17}N_4OF_3$	198	40	12.88 (12.90)	-
IIIh	2-CH_3	CF_3	-2, 4-diNO_2-C_6H_3	$C_{23}H_{15}N_6O_4F_3$	145	45	16.90 (16.93)	-
IIIi	2-CH_3	CF_3		$C_{18}H_{14}N_5SF_3$	115	60	17.97 (17.99)	8.19 (8.22)
IIIj	2-CH_3	CF_3		$C_{21}H_{18}N_5SF_3$	120	40	16.29 (16.31)	7.42 (7.45)

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