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Synthesis and Antibacterial Activity of Some Fluorine Containing 2-Pyrazolines

M.D. DESAI and K.K. DESAI*
Department of Chemistry, South Gujarat University, Surat-395 007, India

Several new 1-carboxamido-3-[2′-hydroxy-4′-(*p*-trifluoromethyl phenoxy) phen-1′-yl]-5-substituted aryl-2-pyrazolines **(II)** have been prepared by reaction of 1-[2′-hydroxy-4′-(*p*-trifluoromethyl phenoxy)-phen-1′-yl]-3-substituted aryl 2-propen-1-ones **(I)** with semicarbazide hydrochloride in ethanol. Few of these compounds are characterised by IR and NMR spectra. All these synthesized pyrazolines have been screened against a few microorganisms for antibacterial activity.

Key Words: Synthesis, Antibacterial activity, 2-Pyrazolines.

INTRODUCTION

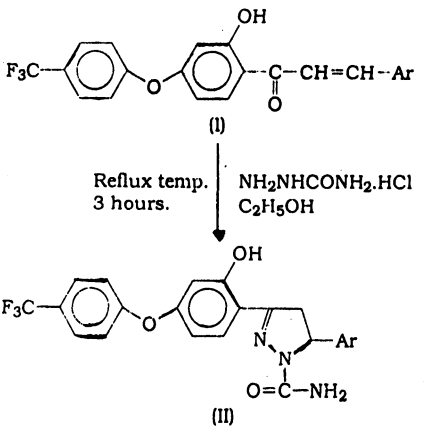
Pyrazolines are di-hydro pyrazoles. Pyrazoline derivatives have been studied extensively because of their ready accessibility, diverse chemical reactivity and broad spectrum of biological activity. They are found to possess antimicrobial, antifungal, insecticidal, antiimplantation, antiarrhythmic, antiinflammatory, abortifacient and antiproteolytic activity[1,2].

The most common procedure for the synthesis of pyrazoline is the reaction of aliphatic or aromatic hydrazine with α,β-unsaturated carbonyl compounds. (chalcones)[3]. Literature survey reveals that several workers have synthesized. pyrazolines by addition reactions of hydrazine[4], phenyl hydrazine[5] and 2,4-dinitro phenylhydrazines[6] with chalcones. However, synthesis of pyrazoline from chalcone using semicarbazide[7] has been less studied. Further, several workers have synthesized some carboxamido substituted pyrazolines[8–10] and showed their biological importance, but fluorinated compounds which find an important place in manufacture of drug have not been tried much. It may be expected that an introduction of fluroine atom or —CF_3 group into an organic molecule frequently provides compounds of pharmacological interest as compared to their non-fluorinated analogues[11, 12].

Prompted by varied biological activity of fluorinated compounds and carboxamido substituted pyrazolines, it was thought interesting to synthesize a new series of fluorine containing 1-carboxamido-2-pyrazolines and to screen them as antibacterial agents.

EXPERIMENTAL

Preparation of 1-carboxamido-3-[2'-hydroxy-4'-(p-trifluoromethyl phenoxy) phen-1'-yl]-5-substituted aryl-2-pyrazoline: A mixture of chalcone (0.01 mol) and semicarbazide-hydrochloride (0.01 mol) in ethanol (30 mL) was refluxed on water bath at 70-80°C for 4 h. It was then cooled and poured into ice water. The product thus separated was filtered, washed with water, dried and crystallised from ethanol.



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 gram positive bacteria *B. Subtilis* and *S. aureus* and gram negative bacteria *E. coli* and *S. typhi* using Agar-cup method.

RESULTS AND DISCUSION

Characteristics of compounds **(II)** and result of antibacterial activity are given in Table-1.

The main absorption bands (cm^{-1}) observed in IR spectra are as follows: 3450–3420 ν(O—H)), 1600–1590 ν(C=N)), 1675–1665 ν(C=O)), 1175–1170 ν(C—F)), 3275–3250 cm^{-1} ν(N—H).

The position of signals in NMR spectra can be assigned to different types of protons as follows: δ = 9.49 (proton of —OH), δ = 3.10 (proton of —CH_2 of pyrazoline ring), δ = 5.12 (protons of CH of pyrazoline ring), δ = 5.43 (protons of —$CONH_2$ group), δ = 6.11 to 7. 30 (aromatic protons).

Diameter of zone of inhibition (in mm) of standard drug ampicillin against *B. subtilis* and *S. aureus* (gram positive) and *E. coli* and *S. typhi* (gram negative)

TABLE-1
DATA SHOWING CHARACTERISTICS OF FLUORINE CONTAINING 2-PYRAZOLINES(II) AND THEIR ANTIBACTERIAL ACTIVITY

Comp. No.	Ar	R	m.w.	Yield (%)	m.p. (°C)	%N		Antibacterial activity Diameter of zone of inhibition (in mm)			
								Gram positive		Gram negative	
						Found	Calculated	*B. subtilis*	*S.aureus*	*E.coli*	*S. typhi*
IIa	—C_6H_5	$C_{23}H_{18}N_3O_3F_3$	441	70	198	9.14	9.52	8	9	7	5
IIb	-4-Cl—C_6H_4	$C_{23}H_{17}N_3O_3ClF_3$	475.5	75	206	8.71	8.83	14	11	12	15
IIc	-2-Cl—C_6H_4	$C_{23}H_{17}N_3O_3ClF_3$	447.5	70	200	8.69	8.83	7	5	6	8
IId	2,4-$(Cl)_2$—C_6H_3	$C_{23}H_{16}N_3O_3Cl_2F_3$	510	75	209	8.18	8.23	17	18	19	18
IIe	-4-F—C_6H_4	$C_{23}H_{17}N_3O_3F_4$	459	77	202	9.08	9.15	8	9	17	19
IIf	-4-(OCH_3)—C_6H_4	$C_{24}H_{20}N_3O_4F_3$	471	74	188	8.80	8.91	9	7	8	10
IIg	-2-(OCH_3)—C_6H_4	$C_{24}H_{20}N_3O_4F_3$	471	78	172	8.88	8.91	6	9	8	6
IIh	-3,4-$(OCH_3)_2$—C_6H_3	$C_{25}H_{22}N_3O_5F_3$	501	80	215	8.24	8.38	–	9	–	6
IIi	-3,4,5-$(OCH_3)_3$—C_6H_2	$C_{26}H_{24}N_3O_6F_3$	531	80	178	7.84	7.90	7	5	8	10
IIj	-4-$\{N(CH_3)_2\}Cl$—C_6H_4	$C_{25}H_{23}N_4O_3F_3$	484	78	190	11.52	11.57	11	13	15	12
IIk	—C_4H_3O-(2-furyl)	$C_{21}H_{16}N_3O_4F_3$	431	72	192	9.62	9.74	19	17	16	17

were found to be 24, 22, 17 and 16 respectively, while tetracycline gave 18, 17, 21 and 22 respectively under identical conditions.

As compared to standards ampicillin and tetracycline, pyrazolines have been found to posses significant activity against all the four organisms.

Compounds **IId** and **IIk** containing 2,4-dichlorophenyl and 2-furyl substituent respectively showed good activity against all four organisms. Compound **IIe** containing *p*-fluoro-phenyl substituent showed better activity only against both gram bacteria *viz. E. coli* and *S. typhi*. Compounds **IIb** and **IIj** containing *p*-chloro-phenyl and *p*-N,N-dimethylamino phenyl substituent respectively showed moderate activity. Compound **IIh** containing 3,4-dimethoxy phenyl substituent remained inactive against *B. subtilis* and *E. coli*. All other compounds showed poor activity.

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