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Synthesis, Characterization and Antimicrobial Activity of Some New Pyrazoline Derivatives of 3-Aryl-2-Isobutanoyl-N-Phenyl-Acrylamide

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ABSTRACT

Some new 5-Aryl-3-isopropyl-4-[N-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazoles.The pyrazoline derivatives of Type (1a-j) have been synthesized by the reaction of 3-Aryl-2-isobutanoyl-N-phenyl-acrylamide with hydrazine hydrate. All the prepared compounds were characterized by their spectral (I.R., N.M.R., Mass) data and screened for their antimicrobial activities.

Keywords : 3-Aryl-2-isobutanoyl-N-phenyl-acrylamide, Pyrazoles, Antimicrobial Activities.

I. INTRODUCTION

Pyrazoles and their reduced forms pyrazolines are well known nitrogen containing five membered heterocyclic compounds which possess widespread chemical and pharmacological applications[1-3] such as analgesic, antipyretic and antirheumatic.[4,5] These derivatives are also well known for their pronounced anti-inflammatory properties[6,7] and are used as potent antidiabetic agents.[8,9] In addition, the pharmacological and antitumor activities of many compounds containing pyrazoline rings have been reviewed.[10-12] Pyrazolines can be synthesized from α,β-unsaturated carbonyl compounds and hydrazines. They are reported to be potential extractants and powerful drugs.[13] The chemistry of pyrazoline was reviewed by Jorbe in 1967, which have been studied extensively for their biodynamic behaviour[14] and industrial applications.[15]

This inspired us to synthesize 5-Aryl-3-isopropyl-4-[N-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazoles.The pyrazoline derivatives of Type **(1a-j)**. The structure of synthesized compounds were assigned based on Elemental analysis , I.R. ^{1}H-NMR and Mass spectral data. The antimicrobial activity was assayed by using the cup-plate agar diffusion method [16] by measuring the zone of inhibition in mm. All the compounds were screened *in vitro* for their antimicrobial activities[17] at 40 µg concentration. Standard drugs like Amoxicillin, Benzoylpenicillin, Ciprofloxacin, Erythromycin and Griseofulvin were used for comparison purpose (Table-1).

II. RESULTS AND DISCUSSION

5-Aryl-3-isopropyl-4-[N-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazoles.The pyrazoline derivatives of Type **(1a-j)** have been synthesized by the reaction of 3-Aryl-2-isobutanoyl-N-phenyl-acrylamide with hydrazine hydrate. (scheme-1).

The formulas of the selected compounds were confirmed by the elemental analysis and their structures were determined by IR ,^{1} H-NMR , and mass spectral data.

ANTIMICROBIAL ACTIVITY:

All the compounds were found to possess moderate to good activity against Gram positive and Gram negative strains and fungi.

EXPERIMENTAL SECTION:

Melting points were taken in open capillary tubes are uncorrected. IR spectra (cm^{-1}) were recorded on Shimadzu-435-IR Spectrophotometer and , ^{1}H-NMR spectra on Bruker spectrometer(300MHz) using TMS as an internal standard, chemical shift in δ ppm.

General procedure for the preparation of 2-Isobutanoyl-3-phenyl-N-phenyl-acrylamide:

The mixture of toluene, 4-Methyl-3-oxo-N-phenyl-pentanamide(2.05 gm, 0.01 mol), benzaldehyde (1.06 gm, 0.01 mol), morpholine and acetic acid was heated to the reflux temperature for 14-16 hrs. Water was removed from the reaction mixture by Dean and Stark. The mixture was cooled at room temperature. Washed the reaction mass with sodiumbisulphite solution and finally washed with distilled water. Distilled out solvent and collect the product, purified in hexane. Yield 80%, MP. 144oC, Anal. Calcd. for $C_{19}H_{18}NO_2$ Calcd: C, 77.79; H, 6.53; N, 4.77%, Found: C, 77.07; H, 6.11; N, 4.09%.

General procedure for the preparation of 3-Isopropyl-5-phenyl-4-[N-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazole (1a-j) :

A mixture of 2-Isobutanoyl-3-phenyl-N-phenyl-acrylamide(2.93gm 0.01mol) and hydrazine hydrate (0.5gm, 0.01 mol) in methanol was refluxed for 4 hrs. Cool and pour the reaction mixture into the crushed ice, filter the material, dry it and purified in isopropyl alcohol. Yield 56% M.P.. 169-171^{o}C Anal. Calcd. for $C_{19}H_{21}N_3O$ Calcd: C, 74.24; H, 6.89; N, 13.67 %, Found: C, 74.21; H, 6.88; N, 13.64%. Similarly, other 5-Aryl-3-isopropyl-4-[N-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazoles were prepared. The physical data are recorded in Table No.1.

3-Isopropyl-5-phenyl-4-[N-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazole:

Yield 56%, m.p. 169-171^{o}C; IR(KBr) : ν 2968,1448 (Alkane,-CH_3), 1387(–$C(CH_3)_2$), 3036 (Ar, =C-H Str.) , 1602 (C=C str.) , 1176 (Aromatic, C-H i.p.), 3332 pyrazoline (-NH-), 1271 (C-N Str.), 1544 (C=N) , Carboxamide 1654 (C=O), 3296 (N-H str.)cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 1.06-1.10 (dd, 6H, -CH-$(CH_3)_2$, 2.42-2.50 (m, 1H-$(CH_3)_2$-CH), 4.07-4.15(d, 1H, pyrz-H) , 4.96-5.054 (d,1H, pyrz-H), 7.03-7.61, (overlapped, 10H, Ar-H) , 10.27 (s, 1H, N-H). Mass m/z 307 . M.F.: $C_{19}H_{21}N_3O$.

Table-1

Characterization data of the compounds (1a-j) :

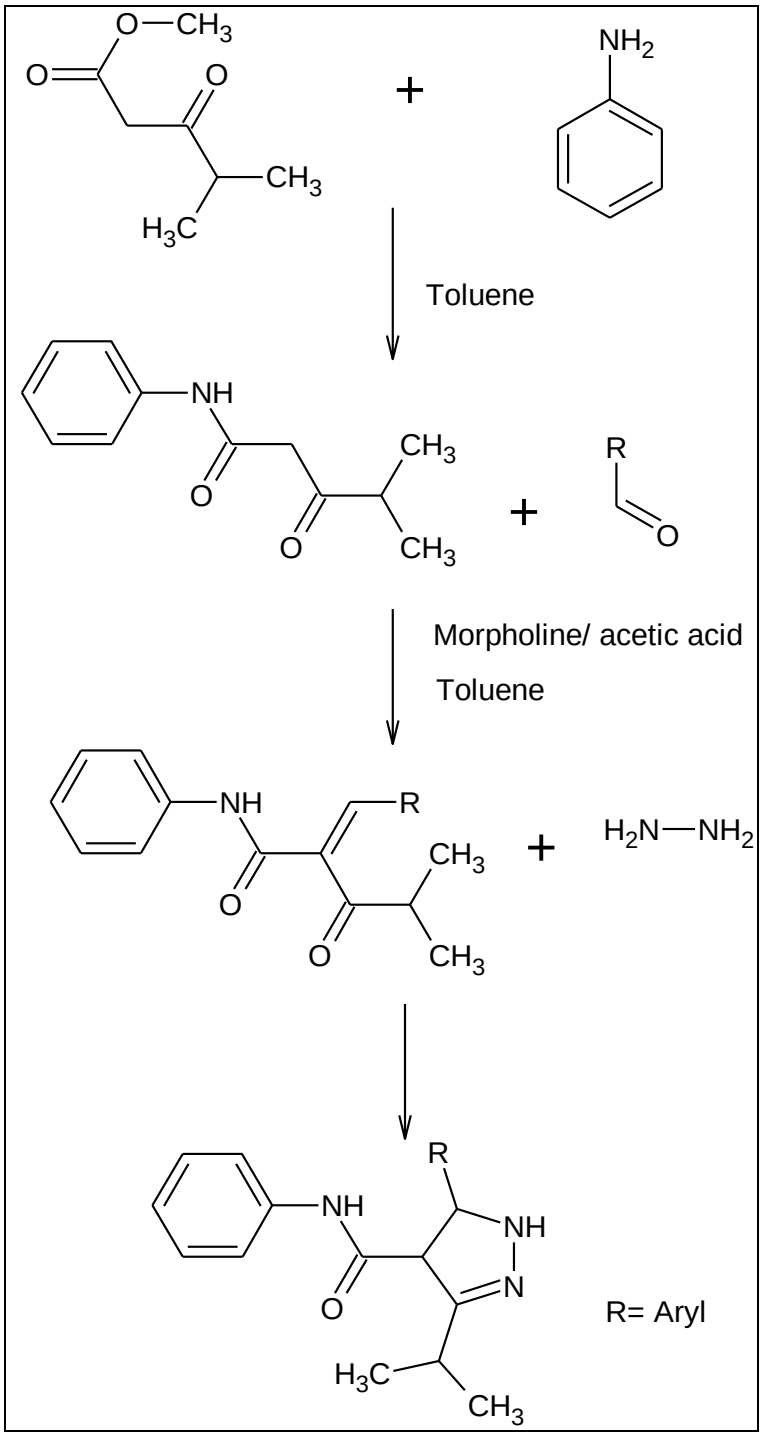
compd no.	R	Molecular formula	Mole.Wt.	M.P. (^{0}C)	Nitrogen %	
					Calcd	Found
1a	-C_6H_5	$C_{19}H_{21}N_3O$	307	169	13.67	13.64
1b	-2-Cl-C_6H_4	$C_{19}H_{20}N_3OCl$	341.5	199	12.29	12.22
1c	-3-Cl-C_6H_4	$C_{19}H_{20}N_3OCl$	341.5	175	12.29	12.30
1d	-4-Cl-C_6H_4	$C_{19}H_{20}N_3OCl$	341.5	163	12.91	12.89
1e	-2-OH- C_6H_4	$C_{20}H_{23}N_3O_3$	353	210	11.89	11.83
1f	-3-OH- C_6H_4	$C_{19}H_{21}N_3O_2$	323	190	12.99	13.00

1g	-4-CH_3- C_6H_4	$C_{20}H_{23}N_3O$	321	185	13.07	13.01
1h	-4- OCH_3- C_6H_4	$C_{20}H_{23}N_3O_2$	337	193	12.45	12.42
1i	-2-NO_2- C_6H_4	$C_{19}H_{20}N_4O_3$	352	207	15.90	15.88
1j	-3-NO_2- C_6H_4	$C_{19}H_{20}N_4O_3$	352	219	15.90	15.85

Table-2

compd no.	Antibacterial activity (zone of inhibition in mm)				Antifungal activity
	B.mega	B.subtillis	A. aero genes	E.coli	A.awamori
1a	15	14	17	16	13
1b	15	13	16	12	11
1c	15	16	24	23	17
1d	14	26	16	13	9
1e	13	14	15	17	13
1f	12	11	14	15	26
1g	11	9	12	13	17
1h	16	10	11	17	18
1i	21	14	13	14	18
1j	14	17	15	14	16
Amoxicillin	25	25	20	22	0
Benzyl penicillin	18	19	21	21	0
Ciprofloxacin	20	15	22	16	0
Griseofulvin	0	0	0	0	26

Scheme-1:



III. CONCLUSION

The present study leads to a convenient synthetic method for the synthesis of new compounds. Which show significant antibacterial and antifungal activity. Further investigation with appropriate structural modification of the above compounds may result in therapeutically useful products.

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