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Synthesis and Biological Evaluation of Some New Acetyl Pyrazoline Derivatives of 3-Aryl-2-Isobutanoyl-N-Phenyl-Acrylamide

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ABSTRACT

The broad spectrums of pharmacological properties have been demonstrated by the pyrazole nucleus. Some new 1-Acetyl-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 in glacial acetic acid. 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, Acetyl pyrazoles, Antimicrobial activities.

I. INTRODUCTION

Pyrazoles are well known five membered heterocyclic compounds and several procedures for its synthesis have been extensively studied. In fact, certain N-substituted pyrazoles are used as analgesic, anti-inflammatory, antipyretic, agrochemicals whereas some others are being studied for their medicinal interest. The synthesis and therapeutically studies of pyrazolones and their derivatives were undertaken by several groups of workers[1] Pyrazolone derivatives exhibit broad spectrum of therapeutic activities. The several biological activities associated with pyrazolone have been described as under antitumor[2], antiulcer[3] , antibacterial[4] , anticancer[5], neurotonsin receptor antagonist[6] , lipoxygenase inhibitor [7], parasitical[8], antiinflammatory[9], antitubercular[10], antidiabetic[11-12], immunosuppressive[13], leukotriene inhibitors[14], cardiac disorder [15], coagulation factor[16], antiinfective[17], organ transplantation[18], antibiotics[19].

This inspired us to synthesize 1-Acetyl-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 [20] by measuring the zone of inhibition in mm. All the compounds were screened in vitro for their antimicrobial activities[21] against varieties of bacterial strains at 40 µg concentration. Standard drugs like Amoxicillin, Benzoylpenicillin, Ciprofloxacin, Erythromycin and Griseofulvin were used for comparison purpose (Table-1).

II. RESULTS AND DISCUSSION

1-Acetyl-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 in glacial acetic acid.

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.

ANTIBACTERIAL ACTIVITY:

It has been observed from the microbiological data that all compounds **(1a-j)** were found to be mild to moderately active against Gram positive and Gram negative bacterial strains.. All the compounds were found to possess moderate to good activity against Gram positive and Gram negative strains and antifungal activity.

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, 0.01mol), 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 1-Acetyl-5-aryl-3-isopropyl-4-[n-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazoles (1a-l) :

A mixture of 2-Isobutanoyl-3-phenyl-N-phenyl-acrylamide(2.93gm 0.01mol) in glacial acetic acid (25 ml) and hydrazine hydrate (0.5gm, 0.01 mol) was heated on water bath at 70°C for 8 hrs. Cool the reaction mixture and poured into the crushed ice. Filtered the product and washed with water, dried and recrystalized in isopropyl alcohol. Yield 41% M.P. 220-222°C Anal. Calcd. for $C_{21}H_{23}N_3O_2$ Calcd: C, 72.18; H, 6.63; N, 12.03 %, Found: C, 72.16; H, 6.61; N, 12.00%.Similarly, other 1-Acetyl-5-aryl-3-isopropyl-4-[N-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazoles were prepared. The physical data are recorded in Table No.1

1-Acetyl-5-aryl-3-isopropyl-4-[n-phenyl-aminocarbonyl]-4,5-dihydro-1H-pyrazoles:

Yield 41 %, m.p. 220-222 °C; IR(KBr) : ν Alkane (CH_3)2971, C-H str.(asym.), 2887 C-H str.(sym.), 1440, C-H def.(asym.), 1380, C-H def. –C(CH_3)$_2$. 1387(–C(CH_3)$_2$), 3087 (Ar, =C-H Str.) , 1606 (C=C str.) , 1170 (Aromatic, C-H i.p.), 3274 pyrazoline (N-H), 1271 (C-N Str.), 1549 (C=N) , Carboxamide 1635 (C=O), 1240 (C-N str.)cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 1.18-1.12 (dd, 6H, -CH-(CH_3)$_2$, 2.50-2.66 (m, 1H, -(CH_3)$_2$-CH), 3.99-4.01 (d, 1H, pyrz-H) , 5.44-5.46 (d, 1H, pyrz-H), 7.10-7.61, (overlapped, 10H, Ar-H) , 10.42 (s, 1H, N-H). Mass m/z 349 . M.F.: $C_{21}H_{23}N_3O_2$.

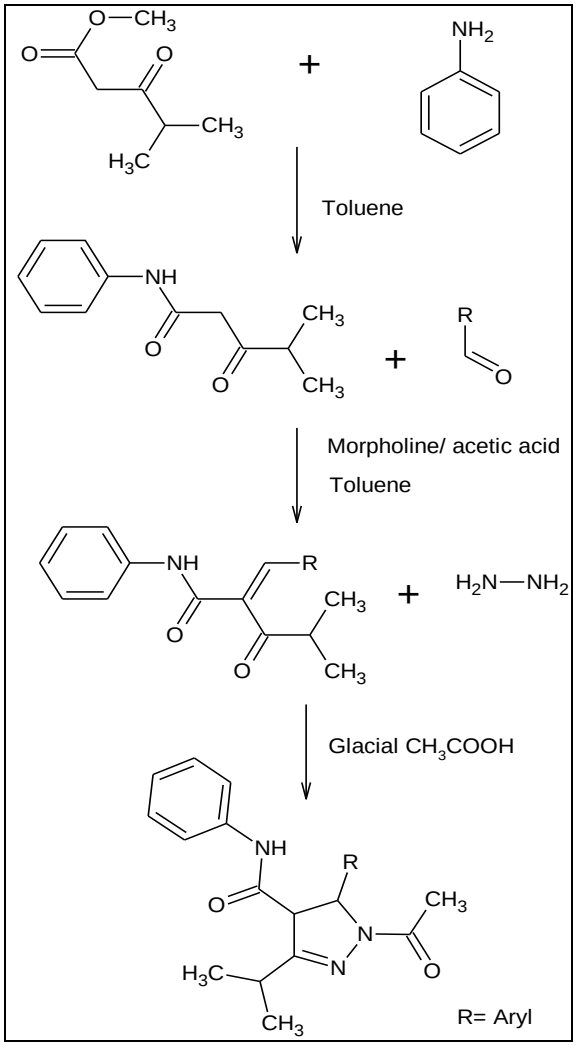
Table 1

Characterization data of the compounds (1a-l) :						
compd no.	R	Molecular formula	Mole.Wt.	M.P. (^{0}C)	Nitrogen %	
					Calcd	Found
1a	-C_6H_5	$C_{21}H_{23}N_3O_2$	349	220	12.03	12.00
1b	-4-Cl-C_6H_4-	$C_{21}H_{22}N_3O_2Cl$	383.5	229	10.95	10.92
1c	-3-Cl-C_6H_4-	$C_{21}H_{22}N_3O_2Cl$	383.5	236	10.95	10.93
1d	-2-Cl-C_6H_4-	$C_{21}H_{22}N_3O_2Cl$	383.5	239	11.44	11.41
1e	- 2-OH-C_6H_4-	$C_{21}H_{23}N_3O_3$	365	222	11.50	11.51
1f	-3-OH-C_6H_4-	$C_{21}H_{23}N_3O_3$	365	219	10.63	10.61
1g	-4-CH_3- C_6H_4	$C_{22}H_{25}N_3O_2$	363	232	11.56	11.51
1h	-4- OCH_3- C_6H_4	$C_{22}H_{25}N_3O_3$	379	229	11.07	11.01
1i	-2-NO_2- C_6H_4	$C_{21}H_{22}N_4O_4$	394	243	14.20	14.18
1j	-3-NO_2- C_6H_4	$C_{21}H_{22}N_4O_4$	394	212	14.20	14.17

Table 2

compd no.	Antibacterial activity (zone of inhibition in mm)				Antifungal activity
	B.mega	B.subtillis	A.aerogenes	E.coli	A.awamori
1a	13	12	7	9	13
1b	12	14	12	8	16
1c	14	15	10	11	14
1d	14	12	11	9	18
1e	8	11	12	14	13
1f	7	10	11	10	11
1g	17	14	15	16	16
1h	18	12	19	14	18
1i	11	13	10	7	15
1j	15	14	14	12	19
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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