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Synthesis and Biological Evaluation of some Novel Dihydropyridine Derivatives of 3-ARYL-2-ISOBUTANOYL-N-PHENYL-ACRYLAMIDE Analogue

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Abstract: ***From study of DHP compounds, it is found that both the ester groups present at 3 and 5 position play an important role in cardiovascular activity, removal of these groups may led to reduction of the activity. This conclusion has open up new scope for structural modifications at these positions. Very wide range of literature regarding the structure, synthesis, stereochemistry and hydrogen transfer mechanism of dihydropyridine is available. Some new Methyl-4-aryl-6-isopropyl-2-methyl-5-[n-phenyl-aminocarbonyl]-1,4-dihydropyridine-3-carboxylates.The Dihydropyridine derivatives of Type (1a-l) have been synthesized by the condensation of 3-Aryl-2-isobutanoyl-N-phenyl-acrylamide and Methyl-3-aminocrotonate. All the prepared compounds were characterized by their spectral (I.R., N.M.R., Mass) data and screened for their antimicrobial activities.***

Key words: 3-Aryl-2-isobutanoyl-N-phenyl-acrylamide, Methyl-3-aminocrotonate, Dihydropyridines, Antimicrobial activities.

I. INTRODUCTION

1,4-Dihydropyridines are now established as heterocycles having tremendous applications and still further scope for its pronounced drug activity like calcium channel antagonism and antihypertensive action. Since then tremendous study have been carried out on new synthesis & pharmacological activity of DHP. Some drugs currently used in market are nimodipine[1], nicardipine[2], isradipine[3], nitrendipine[4], flordipine[5].1,4- DHPs possess different pharmacological activities such as myocardial infarction[6] , stable[7] and unstable angina[8] , vasodilator[9], coronary vasodilator and cardiopathic[10], antiarrhythmic[11], antiulcer[12], antiinflammatory[13], subarachnoid hemorrhage[14], ischemic brain damage[15] , atherosclerosis[16], heart failure[17], calcium channel antagonism[18], antitumor[19], antimayocardiac ischemic[20], PAF antagonist[21], adenosine A3 receptor antagonist[22], antituberculer agents[23].

This inspired us to synthesize Methyl-4-aryl-6-isopropyl-2-methyl-5-[n-phenyl-aminocarbonyl]-1,4-dihydropyridine-3-carboxylates. The DHP derivatives of type (1a-l). 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 [24] by measuring the zone of inhibition in mm. All the compounds were screened in vitro for their antimicrobial activities[25] against varieties of bacterial strains such Staphylococcus aureus, Bacillus subtilis, Aerogenes and P. aeruginosa and fungi Aspergillus niger at 40 µg concentration. Standard drugs like Amoxicillin, Benzoylpenicillin, Ciprofloxacin, Erythromycin and Griseofulvin were used for comparison purpose (Table-1).

II. RESULTS AND DISCUSSION

Some new Methyl-4-aryl-6-isopropyl-2-methyl-5-[n-phenyl-aminocarbonyl]-1,4-dihydropyridine-3-carboxylates**.**

The Dihydropyridine derivatives of type (1a-l) have been synthesized by the condensation of 3-Aryl-2-isobutanoyl-N-phenyl-acrylamide and Methyl-3-aminocrotonate. 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.

A. Antibacterial Activity

It has been observed from the microbiological data that all compounds (1a-l), were found to be mild to moderately active against Gram positive and Gram negative bacterial strains. The screening data indicated that among pyrazoline derivatives, tested compounds 1k, 1d and possesses very good against S.aureus. However, the compounds 1d, 1k displayed comparable activity against B.subtilis. The compounds 1f, 1l, showed greater degree of antibacterial activity against Aerogenes. However, the compounds 1b, 1l, showed mildly active against P. aeruginosa. All the compounds were found to possess moderate to good activity against Gram positive and Gram negative strains.

B. Antifungal Activity

The antifungal data revealed that compounds were least toxic to the fungal strain. However mild activity was shown by the compounds against A.niger. The antibacterial activity was compared with standard drug viz. and antifungal activity was compared with standard drug viz. Griseofulvin. The screening data indicated that among pyrazoline derivatives, tested compounds 1e, 1l showed maximum activity against A.niger. All other compounds exhibit mild to moderate antifungal activity against A.niger.

III. 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.

A. General Procedure For The Preparation Of (a) 4-Methyl-3-oxo-N-Phenyl-Pentanamide

Take the mixture of Methyl-4-methyl-3-oxo-pentanoate (1.44 gm, 0.01 mol) and aniline (0.93 gm, 0.01 mol) in toluene, containing few drops of ethylene diamine. The solution was refluxed for 12 hrs. collect methanol using dean & stark. The resulting reaction mass was washed with dilute HCl and finaly with water. Separated toluene was layer was distilled out under vacuum. Yield 71%, m. p. 32oC, Anal.Calcd. for $C_{12}H_{15}NO_2$ Calcd: C, 70.22; H, 7.37; N, 6.82%, Found: C, 70.71; H, 7.36; N, 6.81%.

B. General Procedure For The Preparation Of (b) 3- Aryl-2-Isobutanoyl-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%.

C. General Procedure For The Preparation Of Methyl-6-Isopropyl-2-Methyl-4-Phenyl-5-[N-Phenylaminocarbonyl]-1,4 Dihydropyridine-3-Carboxylate :

A mixture of 2-Isobutanoyl-3-phenyl-N-phenyl-acrylamide(2.93gm 0.01mol)and Methyl-3-aminocrotonate (1.15gm,0.01mol) in methanol was refluxed in water bath for 18hrs. Cool down reaction mixture at room tempreture and stand by 24 hrs.The resulting solid mass was filtered and washed with methanol. Recrystallized the production methanol. Yield 50% m.p.191-193^{o}C Anal.Calcd. for C24H26N2O3 Calcd: C, 73.82; H, 6.71; N, 7.17 %, Found: C, 73.78; H, 6.76; N, 7.16 %. Similarly, other Methyl-4-aryl-6-isopropyl-2-methyl-5-[N-phenylaminocarbonyl]-1,4-dihydropyridine-3-carboxylates were prepared. The physical data are recorded in Table No. 1.

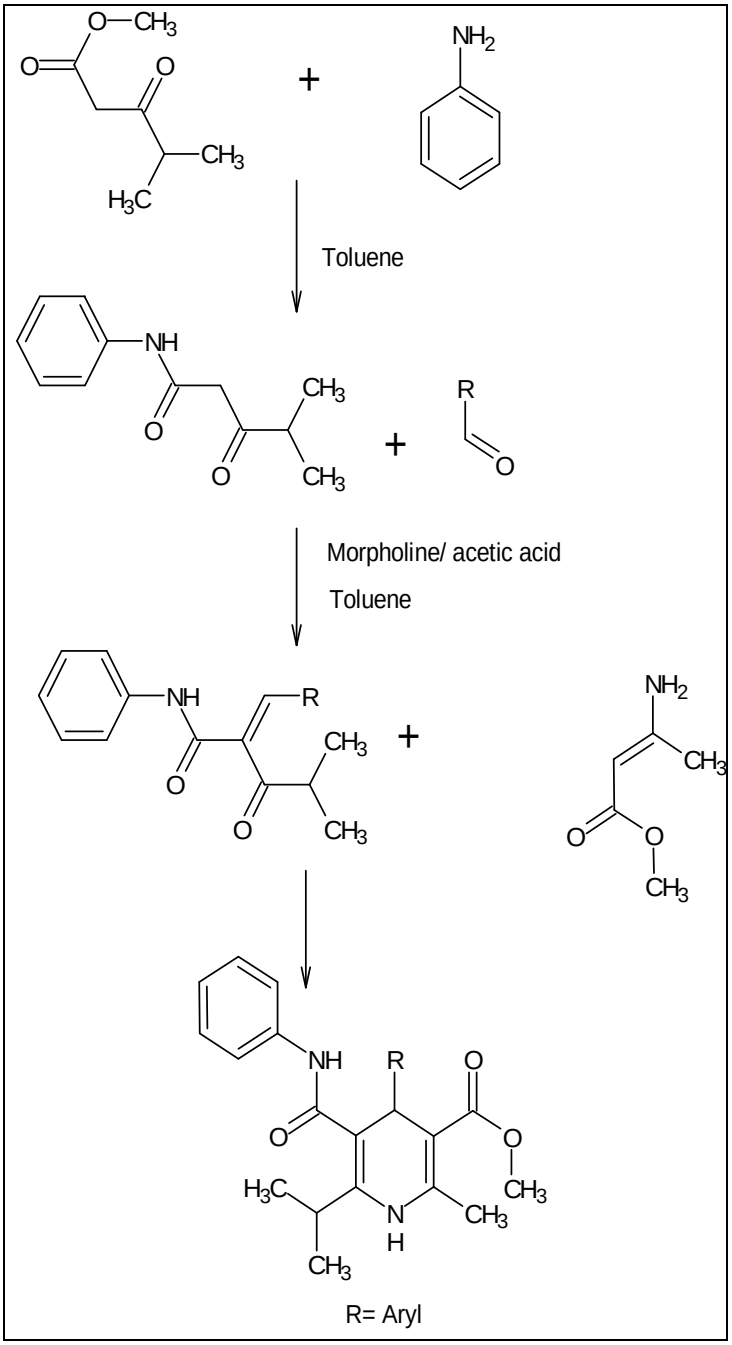
Table-1

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	$C_{24}H_{26}N_2O_3$	390	191	7.17	7.16
1b	-4-Cl-C_6H_4	$C_{24}H_{25}N_2O_3Cl$	424.5	229	6.59	6.57
1c	-2-Cl-C_6H_4	$C_{24}H_{25}N_2O_3Cl$	424.5	241	6.59	6.58
1d	-4-F-C_6H_4	$C_{24}H_{25}N_2O_3F$	408	204	6.86	6.85
1e	4-OH-3-OCH_3-C_6H_3	$C_{25}H_{28}N_2O_5$	436	210	6.45	6.43
1f	-2-OH- C_6H_4	$C_{24}H_{26}N_2O_4$	406	231	6.89	6.87
1g	-4-CH_3- C_6H_4	$C_{25}H_{28}N_2O_3$	404	212	6.93	6.89
1h	-4- OCH_3- C_6H_4	$C_{25}H_{28}N_2O_4$	420	235	6.66	6.64
1i	3-4-$(OCH_3)_2$-C_6H_3	$C_{26}H_{30}N_2O_5$	450	224	6.22	6.21
1j	-4-NO_2- C_6H_4	$C_{24}H_{25}N_3O_5$	435	245	9.65	9.64
1k	-3-NO_2- C_6H_4	$C_{24}H_{25}N_3O_5$	435	255	9.65	9.63
1l	-3-O-C_6H_5- C_6H_4	$C_{30}H_{30}N_2O_4$	482	200	5.81	5.80

Table-2

compd no.	Antibacterial activity (zone of inhibition in mm)				Antifungal activity
	S.aureus	B.subtillis	Aero genes	P. aeruginosa	A.niger
1a	10	8	11	7	18
1b	14	12	16	17	16
1c	12	16	14	15	17
1d	16	21	12	11	15
1e	13	11	10	11	18
1f	12	9	18	14	16
1g	13	10	8	11	18
1h	10	13	12	14	17
1i	10	14	13	15	16
1j	10	11	14	14	17
1k	22	16	14	15	18
1l	14	15	18	16	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



IV. 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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REFERENCES

[1] Towart R. & Kazda S.; Brit. J. Pharm. Col., 67, 409 (1979).

[2] Murakami M.; BE 811324 (1974); US 3985758 (1976).

[3] Neumann P.; EP 0150 (1979); Chem. Abstr. 92, 94404 (1980).

[4] Mayer H. et al.; Arzneim Forsch, 31, 407 (1981). DE 2117571 (1972); US 379934 (1974)

[5] Huang F. C., Lin G. J. & Jones H.; EP Appl. 109, 049 (1984)

[6] Myocardial Infarction Study Group. Secondary prevention of ischemic heart disease:long term controlled lidoflazine study. Acta Cardiol. 34 (Suppl. 24), 7-46 (1979).

[7] Mueller H. S. & Chahine R. A.; Am. J. Med., 71, 645-657 (1981).

[8] E., Muller J., Goldberg S., McAlpin R., Rubenfire M., Tabatznik B.;Engl.J. Med.,302, 1269-1273 (1980).

[9] Wehinger W. E., Horst M., Andres K. & Yoshiharu.;Cham.Abstr., 107, 217482 (1987).

[10] Hachiro, S., Kunizo, H., Tadao, S., Hideyuki, A.& Yoshihsru, D.;Eur. Patent 197,488 (1986).; Japan Patent 68,649 (1985).Cham.Abstr.,106, 328559 (1987).

[11] Masakatu H., Kenichi K., Yasuhiko S., Masakazu H., Osamu K. & Hiroyoshi H.; Japan Patent 235 909, (1985); Cham.Abstr. 107, 134209 (1987).

[12] Marco F., Andrea Z., Carmelo G. & Germini M.; Cham.Abstr.,. 109, 190259 (1988).

[13] Johnson R. C., Taylor D. J., Hann Kenneth V. & Sheng S.;U.S. Patent 4,758,669 (1988); Cham.Abstr.,. 109, 149366, (1988).

[14] Buchbeit J. M. & Tremoulet M.;Neurosurg., 23, 154-167 (1988).

[15] Gelmere H. J. & Henneric N.; Stroke, 21 (IV), 81-84 (1990).

[16] Di Bona G. F., Epstein M., Mann J. & Nordlander M.;Kidney Znt.,41 (Suppl. 36) (1991).

[17] Reicher-Reiss H. & Baruch E.; Drugs, 42(3), 343-364 (1991).

[18] Alker D., Arrowsmith J. E., Cambell S. E. & Cross P. E.; Eur. J. Med. Chem., 26 (9), 907 (1991).

[19] Zidermane A., Duburs G. & Zilbere A.; Cham.Abstr., 75, 47266, 9 (1991).

[20] Yan Z. M., Dong Y. M. & Xuebao Y.;Eur.Patent 220, 653, (1987); Japan Patent 253,909, (1985).Cham.Abstr., 116, 173968, (1992).

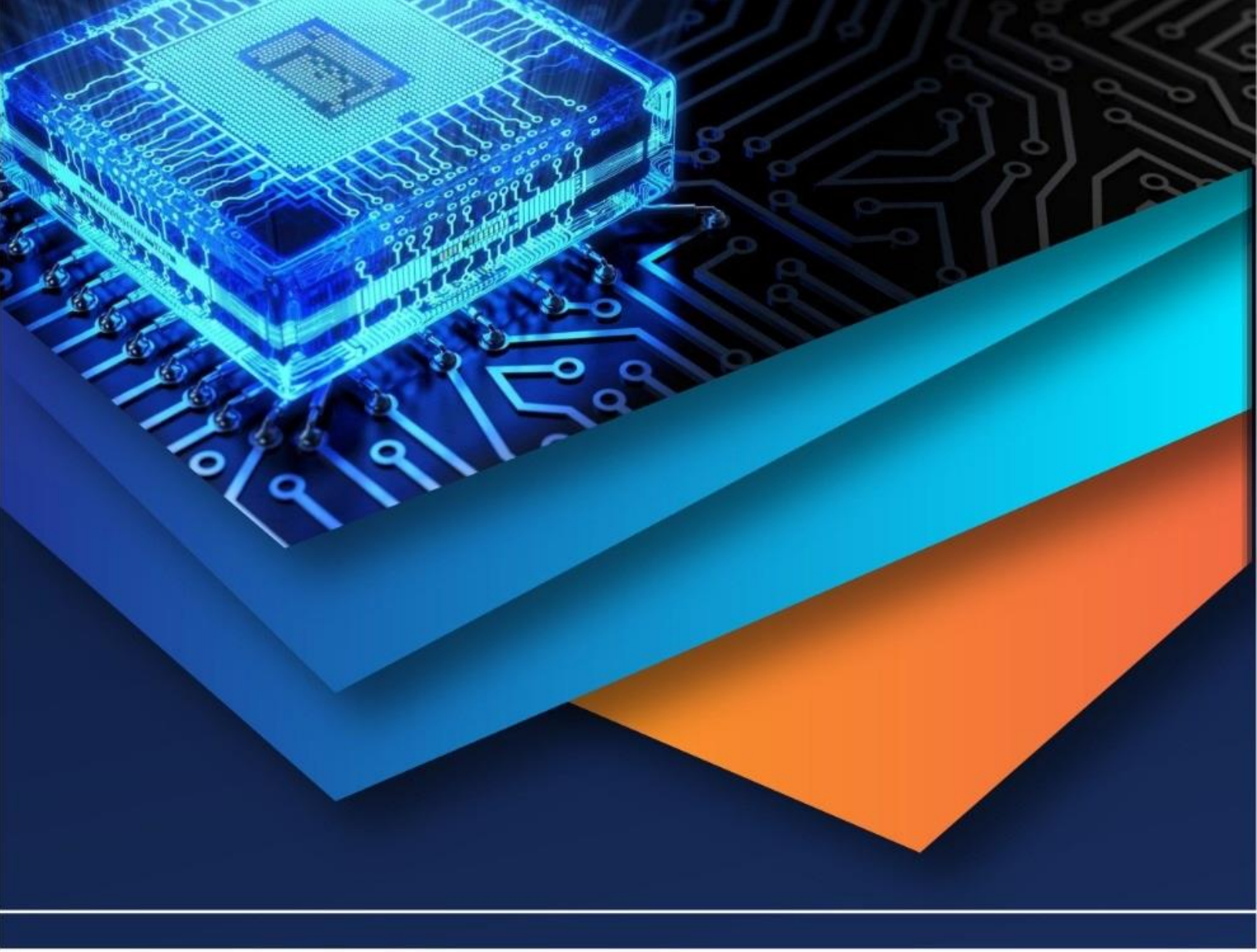
[21] Cooper K., Fray M. J., Parry M. J., Richardson K. & Steele J., J. Med. Chem. 35, 3115- 3129, (1992).

[22] Van Rhee A. M., Jiang J. L., Melman N., Olah M. E., Stiles G. L.;J. Med. Chem., 39, 2980-2989, (1996).

[23] Gevariya Harsukh, Desai Bhavik, Vora Vipul And Anamik Shah; Hetero cyclic communication, 7(5), 481, (2002).

[24] A. L. Barry; The antimicrobial susceptibility test: Principle and practices, edited by llluslea & Febiger , (Philadelphia), USA, 180; Biol. Abstr., 1977, 64, 25183

[25] Panda J. Srinivas S. V., Rao M. E.; J. Indian Chem. Soc., 79(9), 770-1 (2002); Chem. Abstr., 138, 153499n (2003).



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