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Synthesis and Biological Screening of N-(4-(6-Amino-5-cyano-4-aryl-pyridin-2-yl) phenyl) cyclopropane Carboxamide

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Abstract: ***Cyanopyridine derivatives shows good biological and therapeutic activities and exhibit wide range of applications in the field of pharmaceutical and agriculture. Cyanopyridine derivatives like some new N-(4-(6-Amino-5-cyano-4-aryl-pyridin-2-yl)phenyl)cyclopropane carboxamide of type (2a-l) have been prepared by the condensation of such new chalcone derivatives N-(4-(3-Aryl- acryloyl)phenyl)cyclopropane carboxamide of type (1a-l) with Malononitrile in presence of Ammonium acetate. All the prepared compounds were characterized by their spectral (I.R., [1]H NMR. & Mass) data and screened for their antimicrobial activities.***

Keywords: Cyanopyridines, Chalcones, Malononitrile, Antimicrobial activities.

I. INTRODUCTION

Pyridine, nucleus has been extensively explored for their applications in the field of medicine, agriculture and industrial field. Most of pyridine derivatives are synthesized by manipulation of pyridine and its simple homologues in a manner similar to chemistry of the benzenoid chemistry. However the simple pyridine compounds are prepared by the cyclization of aliphatic raw materials. Cyanopyridine derivatives have involved considerable attention in view of their great therapeutic significance such as anticonvulsant, antiHIV, antiepileptic and antihypertensive agents.

The structure of synthesized compounds were assigned based on Elemental analysis, I.R. [1]H-NMR and Mass spectral data. The antimicrobial [6] activity was analyzed by using the cup-plate agar diffusion method [13] by measuring the zone of inhibition in mm. All the synthesized compounds have been evaluated for their antibacterial activity towards Gram positive bacterial strains such as *B.subtilis* and *S.aureus* whereas *E.coli* and *P.seudomonas, were* Gram negative bacterial strains and antifungal activity towards *A.niger* at a concentration of 40 µg and synthesized compounds has been compared with standard drugs.

Standard drugs like Ampicillin, Chloramphenicol, Norfloxacin, and Griseofulvin were used for comparison purpose (Table-1).

II. EXPERIMENTAL SECTION

Melting Points were taken in open capillary tubes are uncorrected. IR spectra (cm-1) were recorded on SHIMADZU FTIR 8400 Spectrophotometer ; Frequency range : 4000-400 cm-1 (KBr disc) and , 1H-NMR Spectra on Bruker Spectrometer (400MHz) using TMS as an internal standard, chemical shift in δ ppm.

A. General procedure for the preparation of N-(4-(3-(4-methoxyphenyl)acryloyl)phenyl) cyclopropane carboxamide (1a-l) :

A mixture of N-(4-acetylphenyl)cyclopropane carboxamide 0.5 gm(0.01 mol) with 4-methoxy benzaldehydes 0.33 gm/0.29 ml (0.01 mol) using Claisen-Schmidt condensation method in presence of 40% NaOH using methanol as a solvent at room temperature under stirring for 8 hours. Reaction was monitored by TLC. Reaction mass was poured into chilled water. Product was filtered and dried. It was recrystallized from ethanol. Yield 81.25%, M.P.162-164^{0}C, Elemental Analysis Calculated for $C_{20}H_{19}NO_3$ Requires: C-74.75%; H-5.96; N-4.36%; O-14.94%, Found: C-74.70%; H-5.93; N-4.31%; O-14.91%,

B. N-(4-(3-(4-methoxyphenyl)acryloyl)phenyl)cyclopropane carboxamide (1a-l) :

Yield 81.25%, M.P.162-164^{0}C; IR(KBr) : ν Alkane C-H str. (asym.) 2938, C-H def.(asym.) 1417, , C-H o.o.p.(def) 1352, Aromatic C-Hstr. 3040 ,C=C str.1598,1511, Amine C-N str. 1294 ,N-H str. 3241, Ether C-O-C str. 1256, Ketone C=O str. 1658, Vinyl CH=CH str. 3040, cm-1; 1H-NMR ($CDCl_3$) : δ 0.80-1.51, (m,5H, Cyclopropane) ,3.748 (s, 3H,-OCH_3), 7.19 & 7.37 (d-d, 2H, CH=CH) , 6.85-7.86 (m,8 H, Ar-H), 10.48(s, 1H, 2^{0}Amide), Mass m/z 322.5 (M+); .M.F.: $C_{20}H_{19}NO_3$

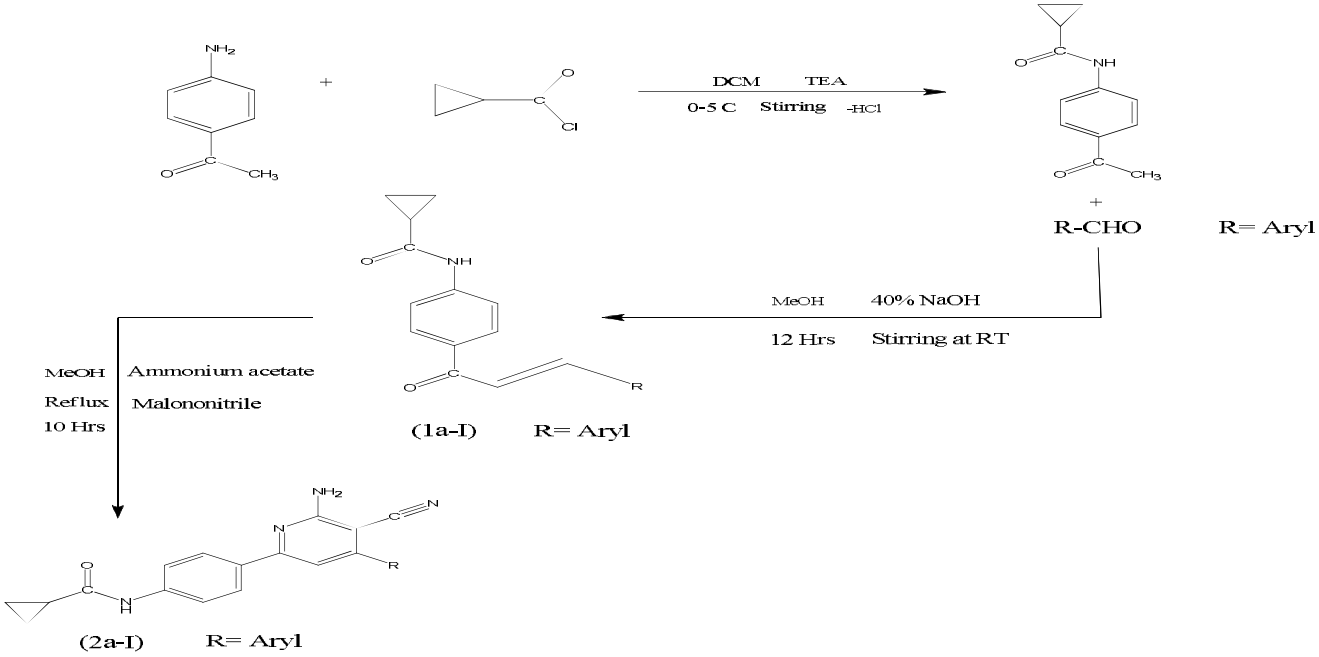
C. General procedure for the preparation of N-(4-(6-Amino-5-cyano-4-(4-methoxypenyl)pyridin-2-yl)phenyl)cyclopropane carboxamide (2a-l) :

A mixture of N-(4-(3-(4-methoxyphenyl)acryloyl)phenyl)cyclopropane carboxamide 0.5 gm (0.01mol), malononitrile 0.10 gm (0.01 mol) and ammonium acetate 0.96 gm (0.08 mol) dissolved in methanol was refluxed for 10 hrs. The reaction mixture was poured into crushed ice and kept overnight. Solid separated was filtered and recrystallized from ethanol. Yield, 69%, M.P. 178-180^{o}C.Elemental Analysis Calculated for $C_{23}H_{20}N_4O_2$; Requires : C-71.86%, H-5.24%, N-14.57 %, O-8.32% Found : C-71.80%, H-5.20, N-14.53%, O-8.30%

D. N-(4-(6-Amino-5-cyano-4-(4-methoxypenyl)pyridin-2-yl)phenyl)cyclopropane carboxamide (2a-l) :

Yield, 69%, M.P. 178-180^{o}C; IR(KBr) : Alkane C-H str. (asym.) 2922, C-H def.(asym.) 1467, Aromatic C=C str. 1586, C-H o.o.p.(def) 829, Ether C-O-C str. 1246,Pyridine C=N str. 1590, Amine NH str. 3345,Nitrile str. 2212, Pyridine C-N str. 1030 , cm-1; 1H-NMR (DMSO) : δ 0.82-1.83, (m,5H, Cyclopropane), 3.843 (s, 3H,-OCH_3), 10.59 (s,2H, -NH_2),10.43(s, 1H, 2^{0}Amide), 6.92-8.10 (m,9 H, Ar-H).Mass m/z 384 . M.F.: $C_{23}H_{20}N_4O_2$

III. REACTION SCHEME



IV. ANTIMICROBIAL ACTIVITY

It has been observed from the microbiological data that all compounds (2a-l) were found to be mild to moderately active against Gram positive and Gram negative bacterial strains. However the maximum activity was observed in compounds (2a), (2b), (2e) & (2i) against S.aureus. The significant activity was observed in compounds (2b) & (2e) against B. subtilis. The maximum activity was

displayed by the compounds (2e), (2f) & (2j) against E.coli. The compounds (2b), and (2c) were comparatively more effective against P.seudomonas.

The antifungal data revealed that compounds were least toxic to the fungal strain. However mild activity was shown by the compounds (2e) & (2h) against A.niger. The antibacterial activity was compared with standard drug viz. Ampicillin, Chloramphenicol, Norfloxacin and antifungal activity was compared with standard drug viz. Griseofulvin. (Table-2)

TABLE-1

Characterization data of the compounds (2a-l) :

Compound No.	R	Molecular Formula	Molecular Weight	M.P. (^{0}C)	Nitrogen %	
					Found	Calcd
2a	-C_6H_5	$C_{22}H_{18}N_4O$	354.40	166-170	15.78	15.81
2b	4-OCH_3-C_6H_4-	$C_{23}H_{20}N_4O_2$	384.43	178-180	14.53	14.57
2c	-4-N $(CH_3)_2C_6H_4$	$C_{24}H_{23}N_5O$	397.47	202-204	17.60	17.62
2d	-C_4H_3O	$C_{20}H_{16}N_4O_2$	344.37	164-166	16.28	16.27
2e	-2-Cl-C_6H_4-	$C_{22}H_{17}ClN_4O$	388.85	208-210	14.38	14.41
2f	-4-F-C_6H_4-	$C_{22}H_{17}FN_4O$	372.39	203-205	15.00	15.04
2g	-4-OH-C_6H_4-	$C_{22}H_{18}N_4O_2$	370.40	175-177	15.11	15.13
2h	-4-OH-3-OCH_3-C_6H_3-	$C_{23}H_{20}N_4O_3$	400.43	196-198	13.95	13.99
2i	-2-OH-C_6H_4-	$C_{22}H_{18}N_4O_2$	370.40	182-184	15.10	15.13
2j	-2-NO_2-C_6H_4-	$C_{22}H_{17}N_5O_3$	399.13	174-176	17.50	17.53
2k	-4-Cl-C_6H_4-	$C_{22}H_{17}ClN_4O$	388.85	208-210	14.37	14.41

TABLE-2

Antimicrobial Activity: (Zone of inhibition in mm) :

Compound No.	E. coli	B.subtilis	Pseudomonas	S. aureus	A . Niger
2a	7	0	1	4	0
2b	0	4	19	8	0
2c	4	0	6	0	0
2d	0	2	3	2	0
2e	11	6	2	4	6
2f	11	0	3	0	0
2g	0	1	0	3	0
2h	7	1	0	0	2
2i	8	1	1	4	0
2j	13	0	3	0	0
2k	0	0	0	0	0
Ampicillin	15	7	20	10	0
Chloramphenicol	14	8	21	9	0
Norfloxacin	12	8	19	10	0
Griseofulvin	0	0	0	0	8

V. RESULTS AND DISCUSSION

Cyanopyridine derivatives have involved considerable attention in view of their great therapeutic significance. Cyanopyridine derivatives like some new N-(4-(6-Amino-5-cyano-4-aryl-pyridin-2-yl)phenyl)cyclopropane carboxamide of type (2a-l) have been

prepared by the condensation of N-(4-(3-Aryl- acryloyl)phenyl)cyclopropane carboxamide of type (1a-l) with Malononitrile in presence of Ammonium acetate.

The formulas of the selected compounds were confirmed by the elemental analysis and their structures were determined by IR, 1H-NMR, and Mass Spectral data.

VI. CONCLUSION

The present study leads to a convenient synthetic method for the synthesis of new molecules. These were characterized by I.R., NMR, Mass Spectrometry studies and Elemental analyses. The compounds were obtained in good yield in basic conditions which show significant antibacterial and antifungal activity further investigation with appropriate structural modification of the above compounds may result in therapeutically useful products.

VII. ACKNOWLEDGMENT

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REFERENCES

[1] Jagdish V. Dodia; World J. of Pharma. Research;Vol 7,Issue 05, 917-923; (Jan 2018).

[2] V. R. Dangar, J. V. Dodia, V. R. Shah; Vol 5, Issue XI, Inter. J. for Research in Applied Sc. and Engg. Tech.(IJRASET),Vol 5, Issue XI, (Nov 2017).

[3] V. R. Dangar, K. N. Borkhataria, V. R. Shah; Inter. J. of Pharma Sc. and Research (IJPSR),Vol 5 No. 02, (Feb 2014).

[4] Sayed G. H., Kassab R. R.; Bull. Fac. Pharm., (1998); Chem. Abstr., 131, 15727p (1999).

[5] Yoshida H., Omori K., Yasuyuki Y. , Kensaku F.; Jpn. Kokai Tokkyo Koh JP, 10, 120, 677; Chem. Abstr., 129, 16062q, (1998).

[6] Parikh A. R., Sorathia S. D., Patel V. B.; Indian J. of Chem. 36B, Sept. 97, 822 (1997).

[7] D. D. Erol, N. Yulung and A. Turk; Eur. J. Med. Chem, 1994; 29(11): 893-7; Chem. Abstr, 1995; 122: 13650a.

[8] P. Fey, H. K Rudolf, H. Walter and K Thomas; Eur. Pat. Appl. Ep. 62, 3611, (Cl. C07D 401/14); Chem. Abstr, 1995; 122: 55897r.

[9] M. R. Pavia, C. P. Taylor, F. M. Hershenson and S.J. Lobbestael; J. Med. Chem., 30, 1210, (1987).

[10] N. Latif, N. Mishry and N. S. Girgis; Indian J. Chem., 20 (B), 147-149, (1981).

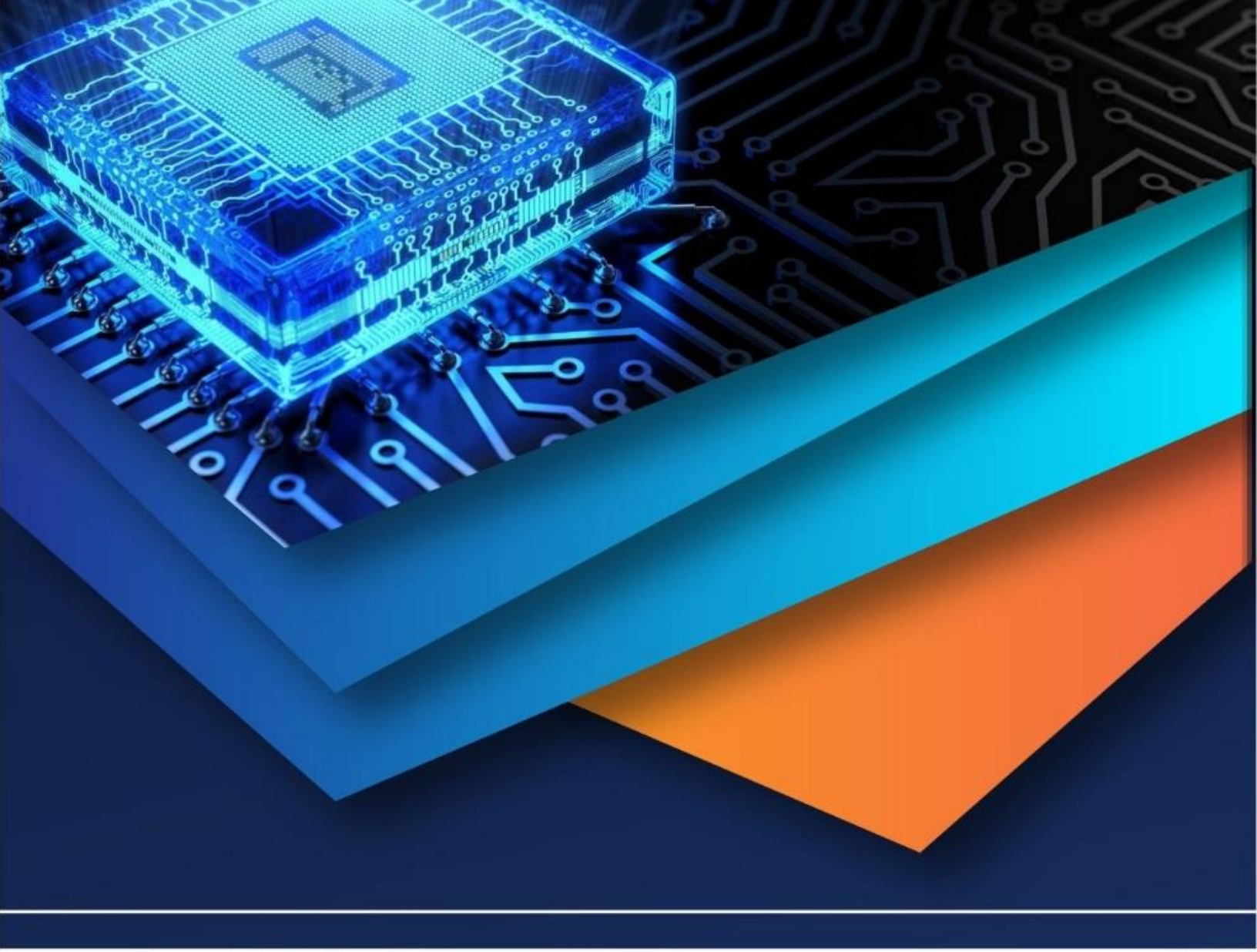
[11] Baldwin J. J. ,Scriabine A., Ponticeello G. S. , Engelhardt E. L. and Sweeti C. S;

[12] J. Heterocycl. Chem., 17(3), 425 (1980); Chem. Abstr., 93, 186222x ,(1980).

[13] Baldwin J. J., Scriabine A., Ludden C. T.and Morgan G.; Experientia, 35(3), 653 (1979); Chem. Abstr., 91,83212y, (1979).

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

[15] Barton, John E D, Freeman Peter F. M.; Ger. Offen, 2 029, 079 (Cl. AOIN007d), 21 Jan. 1971, Brit. Appl. 12 June (1969); Chem. Abstr.,74, 99891d (1971).



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