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Synthesis and Biological Evaluation of Some New CYANOPYRIDINE Derivatives of IMIDAZO [1,2-*A*]PYRIDINE Nucleus

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Abstract: Like other heterocyclic compounds, pyridines with different functional groups exhibit wide range of applications in the field of pharmaceutical and agriculture. Cyanopyridine derivatives like some new 2-Amino-6-aryl-4-[6-methyl-2-(4-methylphenyl)imidazo[1,2-a]pyridin-3-yl]nicotinonitriles derivatives of type (2a-l) have been prepared by the cyclocondensation of 1-Aryl-3-[6-methyl-2-(4-methylphenyl)imidazo [1,2-a] pyridin-3-yl]prop-2-ene-1-ones derivatives of type (1a-l) with malononitrile in presence of ammonium acetate. All the prepared compounds were characterized by their spectral (I.R., N.M.R., Mass) data and screened for their antimicrobial activities.

Keywords: Chalcones, cyanopyridines , antimicrobial activities.

I. INTRODUCTION

Cyanopyridine have attracted considerable attention as they appeared of interest to possess antibacterial1, antihistamic2, fungicidal & insecticidal3, antihypertensive4-6 analgesic7 and anti-inflammatory8, anticancer9 activities. However the simple pyridine compounds are prepared10-11 by the cyclization of aliphatic raw materials. In our continuation work in the chemistry of pyridine nucleus, we have undertaken the synthesis of imidazo[1,2-a]pyridine derivatives.

The structure of synthesized compounds were assigned based on Elemental analysis , I.R. 1H-NMR and Mass spectral data. The antimicrobial12 activity was assayed by using the cup-plate agar diffusion method 13 by measuring the zone of inhibition in mm. All the compounds were screened in vitro for their antimicrobial activities26 against varieties of bacterial strains such Staphylococcus aureus, Bacillus subtilis, Escherichia coli, P. aeruginosa and fungi Aspergillus niger at 40 µg concentration. Standard drugs like Ampicillin, Benzyl penicillin, Ciprofloxacin, Erythromycin 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 , ^{1}H-NMR spectra on Bruker spectrometer (200MHz) using TMS as an internal standard, chemical shift in δ ppm.

A. General procedure for the preparation of 1-Aryl-3-[6-methyl-2-(4-methylphenyl)imidazo [1,2-*a*] pyridin-3-yl]prop-2-ene-1-ones *(1a-l)*

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6-Methyl-2-(4-methylphenyl)imidazo[1,2-*a*]pyridine-3-carbaldehyde 2.5g (0.01mol) was dissolved in 25 ml methanol at room temperature. P-Methoxy acetophenone 1.40g (0.01mol) and 0.2 ml 40% sodium hydroxide solution was added. Stirred the content at room temperature for 24 hrs then filtered it and washed with chilled methanol. Yield 76 %, m. p. 200 oC, Elemental Analysis Calcd for C25H22N2O2 Requires: C-78.51%, H-5.80%, N-7.32%, Found : C-78.40%, H-5.72%, O-7.35%.

B. 1-Aryl-3-[6-methyl-2-(4-methylphenyl)imidazo [1,2-a] pyridin-3-yl]prop-2-ene-1-ones (1a-l)

Yield 76 %, m.p. 200^{0}C; IR(KBr) : ν Alkane C-H str. (asym.) 2966, -CH_3 C-H str. (sym.)2876, C-H def.(asym.) 1453 , C-H def. (sym.) 1352, C=C str. 1503, C-H o.o.p.(def) 1352, Aromatic C-Hstr. 3061, Amine NH str. 3372 , Ether C-O-C str. 1206, Pyridine C=C str. 1503 , C=N str. 1610 , un satd.C=O str. 1682, Imidazo[1,2-a] C=N str. 1610, pyridine C-N str. 1110 , vinyl C=C str. 1536, cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 2.41 & 2.43, (s,6H, Ar-CH_3) , 3.85 (s, 3H,-OCH_3), 7.40 & 8.10 (d-d, 2H, CH=CH) , 6.91-8.25 (m,13 H, Ar-H) , .Mass m/z 382 .M.F.:$C_{25}H_{22}N_2O_2$.

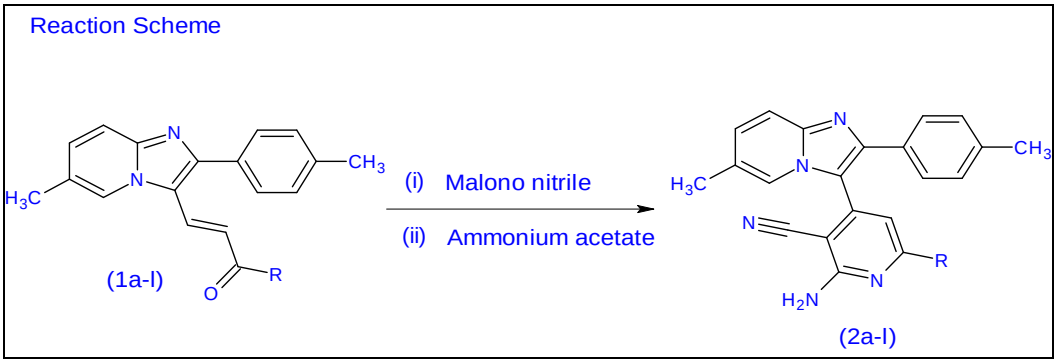
C. General procedure for the preparation of 2-Amino-6-aryl-4-[6-methyl-2-(4-methylphenyl)imidazo[1,2-a]pyridin-3-yl]nicotinonitriles (2a-l)

A mixture of 1-(4-Methoxyphenyl)-3-[6-methyl-2-(4-methylphenyl)imidazo [1,2-*a*] pyridin-3-yl]prop-2-ene-1-one 3.82gm (0.01mol), malononitrile 0.66 gm (0.01 mol) and ammonium acetate 6.16gm (0.08 mol) dissolved in methanol was refluxed for 12 hrs. The reaction mixture was poured into crushed ice and kept overnight. Solid separated was filtered and recrystallized from ethanol. Yield, 68%, m.p. 245^{o}C. Elemental Analysis Calculated for C28H23N5O ; Requires : C-75.49%, H-5.20%, N-15.72 %; Found : C-75.41%, H-5.15, N-15.73%. Similarly, other 2-Amino-6-aryl-4-[6-methyl-2-(4-methylphenyl)imidazo[1,2-*a*]pyridin-3-yl]nicotinonitriles were synthesized.

D. 2-Amino-6-aryl-4-[6-methyl-2-(4-methylphenyl)imidazo[1,2-a]pyridin-3-yl]nicotinonitriles (2a-l) :

Yield 68 %, m.p. 245 ^{0}C; IR(KBr) : Alkane C-H str. (asym.) 2917, -CH_3 C-H str. (sym.)2857, C-H def.(asym.) 1453 , C-H def. (sym.) 1323, C=C str. 1513, C-H o.o.p.(def) 800, Aromatic C-Hstr. 3061, Amine NH str. 3372 , Ether C-O-C str. 1206, Pyridine C=C str. 1513 , C=N str. 1590 , amine NH str. 3372, Imidazo[1,2-a] C=N str. 1556, pyridine C=N str. 1590 ,Nitrile str. 2257, pyridine C-N str. 1039 , cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 2.31 & 2.34, (s,6H, Ar-CH_3) , 3.91 (s, 3H,-OCH_3), 3.91 (s, 2H, -NH_2) , 6.92 (s, 1H, pyr.) 7.12-8.16 (m,16 H, Ar-H).Mass m/z 445 . M.F.: C28H23N5O.

Scheme-1



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Table-1

Characterization data of the compounds (2a-l)						
compd no.	R	Molecular Formula	Mole.Wt.	M.P. (^{0}C)	Nitrogen %	
					Found	Calcd
2a	-C_6H_5	$C_{27}H_{21}N_5$	415	158	16.81	16.86
2b	-4-Cl-C_6H_4	$C_{27}H_{20}CIN_5$	449.5	240	15.59	15.57
2c	-2,4-(Cl_2)- C_6H_3	$C_{27}H_{19}CI_2N_5$	484	dec.200	14.54	14.46
2d	-4-NO_2- C_6H_4	$C_{27}H_{20}N_6O_2$	460	144	18.31	18.25
2e	-4-OCH_3- C_6H_4	$C_{28}H_{23}N_5O$	445	245	15.79	15.72
2f	-4-CH_3- C_6H_4	$C_{28}H_{23}N_5$	429	189	16.27	16.31
2g	-4-OH-3-OCH_3 - C_6H_4	$C_{28}H_{23}N_5O_2$	461	226	15.27	15.17
2h	-4-Br-C_6H_4	$C_{27}H_{20}BrN_5$	494	196	14.12	14.17
2i	-2-OH- C_6H_4	$C_{27}H_{21}N_5O$	431	190	16.28	16.23
2j	-4-OH- C_6H_4	$C_{27}H_{21}N_5O$	431	145	16.31	16.23
2k	-4-NH_2-C_6H_4	$C_{27}H_{22}N_6$	430	230	19.47	19.52
2l	-2-C_4H_3S-	$C_{25}H_{19}N_5S$	421	110	16.54	16.61

E. Antibacterial activity

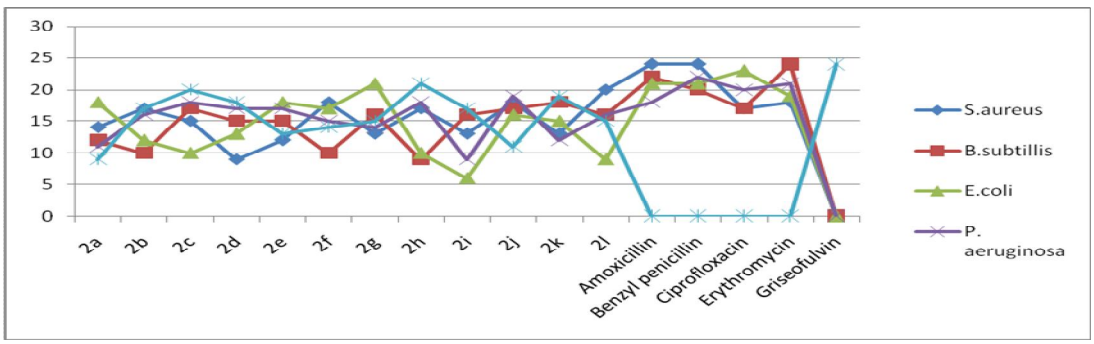
It has been observed from the microbiological data that all compounds (2a-l) were found to be mild to moderately active against Gram positive and Gram negative bacterial strains. How ever the maximum activity was observed in compounds (2j), (2l) against S.aureus. The significant activity was observed in compounds (2j), (2k) against B. subtilis. The maximum activity was displayed by the compounds (2a), (2g), against E.coli. The compounds (2h), and (2j) were comparatively more effective against P. aeruginosa.

F. Antifungal activity

The antifungal data revealed that compounds were least toxic to the fungal strain. However mild activity was shown by the compounds (2c), (2h) against *A.niger*.

The antibacterial activity was compared with standard drug viz. Ampicillin, Benzyl penicillin, Ciprofloxacin, Erythromycin and antifungal activity was compared with standard drug viz. Griseofulvin.

Table-2 Antimicrobial activity : (zone of inhibition in mm) :



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III. RESULTS AND DISCUSSION

Cyanopyridines play a vital role owing to their range of biological and physiological activities. In the light of these biological activities and variety of industrial applications, some new 2-Amino-6-aryl-4-[6-methyl-2-(4-methylphenyl)imidazo[1,2-*a*]pyridin-3-yl] nicotinonitriles derivatives of type (2a-l) have been prepared by the cyclocondensation of 1-Aryl-3-[6-methyl-2-(4-methylphenyl)imidazo [1,2-*a*] pyridin-3-yl]prop-2-ene-1-ones 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 ,^{1} H-NMR , and mass spectral data.

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.

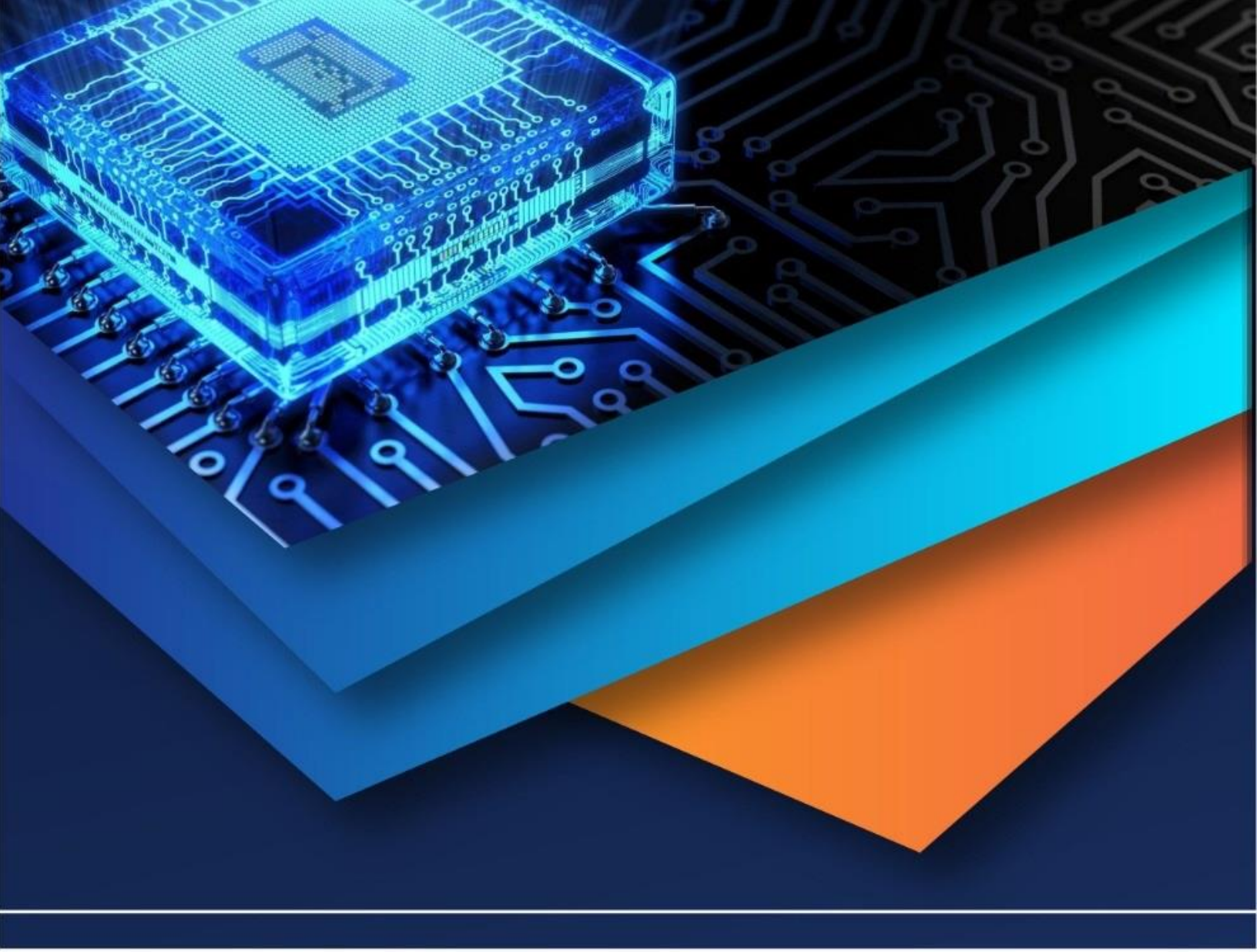
V. ACKNOWLEDGMENT

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