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Synthesis, Characterisation and Antimicrobial activity of E-N-(5-Chloro-2 Isopropyl benzylidene) aryl amine

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Abstract: **In strive to develop compounds with pharmacological significance, a new series of Schiff bases have been synthesized by the condensation of 5-Chloro- Isopropyl Benzaldehyde with primary amines. Isopropyl Benzaldehyde is enormously used in traditional medicines to treat variety of diseases. The chemical characterizations of the synthesized compounds were carried out by Infrared, 1H NMR, Mass spectral techniques and elemental analysis. The resulting benzamine Schiff bases were evaluated for antimicrobial study against various strains of gram positive and gram negative bacteria. Antimicrobial study has been done by Agar diffusion method using Ciprofloxacin and fluconazole as standard.**

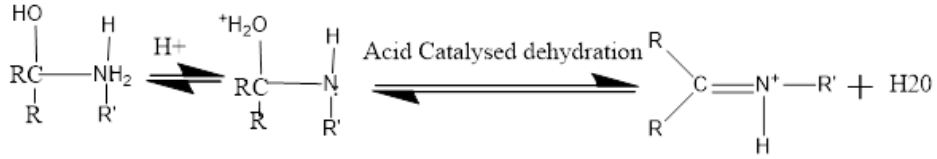
Index Terms: **Antimicrobial activity, 5- Chloro Isopropyl Benzaldehyde, Gram positive strain, Gram negative strain, Schiff Bases**

I. INTRODUCTION

Schiff Bases forms the significant class of bioactive compounds containing azomethine (-CH=N-) group and frequently used as an appreciable therapeutic agent (Dina et al., 2017; Mandewale et al ,2018). Due to the presence of lone pair of electron on nitrogen atom of imine group, it used to show considerable chemical & biological significance (Brodowska et al., 2014). Schiff base are formed by the condensation of primary amine with aromatic or aliphatic aldehyde, the reaction involves the nucleophilic attack of nitrogen atom present in primary amine on carbonyl carbon which produces hydroxyl group, which further on removal of water molecule gives azomethine group (Scheme I).

Hydrogen ion catalyses the nucleophillic attack of lone pair of electron from nitrogen of amine group to the carbon atom present in carbonyl group. Schiff bases shows a wide spectrum of application in biological activities viz. antifungal, antiviral, antibacterial, antimalarial, anti-inflammatory, anticancer, antitumor, antitubercular, antioxidant, apart from its medicinal importance they are widely used as intermediates in the synthesis of various drug molecule (Wenling et al., 2013) polymers, industrial field (Kumar et al, 2009). In recent years scaffolds of new molecules get its recognition in pharmaceutical field. Therapeutic properties cuminaldehyde containing drugs p-cymene (antifungal, antimicrobial), Limonene (anticancer), Eugenol (Flavouring agent) foster us to synthesize new series of therapeutic agent apart from non- medical properties (Abdelgaleil et al, 2009; Sung-Woong, 2013).

Isopropyl Benzaldehyde provides an ample range of biomedical properties viz. antifungal (Kedia et al., 2014), antibacterial (Hajlaoui et al., 2010), antiviral (Zheljazkov et al., 2014), antioxidant (Nitoda et al., 2017), anticarcinogenic (Bi .X., 2017), antidiabetic (Bhosale et al., 2012) anti-inflammatory (Tommy et al., 2014; Ferreira. et al., 2009) and other significant applications (Dhandapani , 2002; Nostro et al., 2005; Vador et al., 2012) thus become a probable potential moiety to consider for the synthesis. It is an oxidizable aldehyde monoterpene



Scheme I.

forms a major constituent of essential oil (Rihawy et al., 2014).

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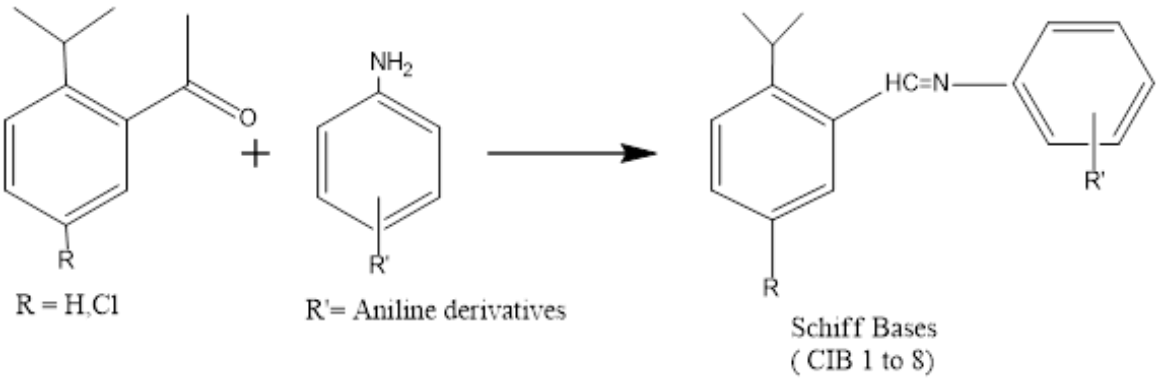
Due to its emerging properties we have now focused our attention towards it. Schiff bases of Isopropyl Benzaldehyde forms the extension of the study. In present work, we reported the synthesis, spectral characterization of Benzamine Schiff bases along with biological assay of the synthesized compounds.

II. Experimental

The melting point of all the synthesized were determined by Buchi melting point apparatus and uncorrected. All the chemicals used in experiment were purchased from Loba chemicals, SD Fine and Merck. The purity of the compound was checked by silica gel coated aluminum plates (Merck). Structures of the synthesized compounds were confirmed by spectral techniques. IR Spectra were recorded using KBr pellets on a Bruker FTIR Spectrophotometer, the peaks were found in the range 4000cm-1 -600 cm-1. 1-H NMR were measured using Tetra methyl Silane (TMS) as internal standard , on Bruker 400 NMR spectrophotometer Thermo scientific analyser was used for elemental analysis. Synthetic pathway for the reaction is depicted in Scheme II.

III. Result and Discussion

The chemical structure of the synthesized compounds were confirmed by spectral chracterisation with FT-IR, 1H-NMR, MS and elements analysis. NMR spectral studies confirms the presence of Azomethine (-N=CH-) proton whose singlet will appear at δ 8.40-8.48 and also a sharp singlet depicted at δ 10.88-11.72 which is due to–CONH- proton . In the mass spectrum , m/z values of the synthesized compounds shows relevance with the molecular formula of the compound .IR spectra showed absorption band at 3200-3500cm^{-1} ,1560-1580 cm^{-1},2259-2258cm^{-1} due to C=N,NH and C=O stretching vibration respectively. Physiochemical data of the synthesized compounds are listed in Table. I. The compounds were screened for their biological potential using Well diffusion assay against gram positive gram negative and fungi stain. Compound 2b and 2c show effectiveness against both gram positive & gram negative bacteria with maximum MIC value while compounds 2a , 2d and 2f having moderate activity with MIC value ranges between 11-13 mm. Considering Antifungal properties of synthesized compounds 2d shows appreciable results as compared to other compound which have moderate activity.



Scheme II. Route of synthesis is depicted in the scheme

Physiochemical properties and antimicrobial evaluations of the synthesized compounds are given in Table I & II respectively.

Structure of the molecule confirms with spectral interpretation of the compounds.

A. General Procedure for the synthesis of Schiff Base (E-N-(5-Chloro-2 isopropyl benzylidene aryl amine)

To the dry RBF, Aniline (2mmol) and ethanol 25 ml are taken , acidified the solution with acetic acid then add 5-chloro-2-(methyl ethyl benzaldehyde) (2mmol) to it. The reaction mass was refluxed for 1-2 hours at room temperature .Further the content was cooled at 0°C for overnight . The product were filtered and recrystallized with ethanol. The compound was dried in oven (M.P. 65°C, yield -89.65%.

A. Anti- microbial Activity

The synthesized compound (2a -2h) tested for their antimicrobial potential using Agar well diffusion method. DMF is used as solvent (negative control) did not show inhibition against microbes. Ciprofloxacin & Flucnazole were used as standard. Compounds were screened against gram positive and gram negative bacteria and fungi at 100 µg/ml concentration. The strain shows the activity of the compounds depicted in Table II.

Table I. Physio Chemical & Spectral Characterization of Synthesized compounds

Compound	Ar-	Molecular Formula	Elemental Analysis Calc./Found			Spectral Interpretation
			C %	H%	N%	
2a.	**E-N-(5-Chloro-2 isopropyl benzylidene) aryl amine**	$C_{16}H_{15}NCl$	74.56 (74.66)	5.86 (5.76)	5.436 (5.55)	IR(cm^{-1}, KBr) : 3074 (Aromatic C-H str.), 2972, 2819, (C-H str), 1572 (C-C str),1669 (C=N str), 1346 (C-N str),1479(C-C ring stretch). 1H-NMR (400MHz, DMSO-*d*), 8.16 (N=CH), 7.0-8.08 (Ar H), MS: m/z- 257.5 (M+).
2b.	**E-N-(5-Chloro-2 isopropyl benzylidene) Fluoro amine**	$C_{16}H_{14}$ NF Cl	52.45 (53.20)	5.100 (5.2)	5.100 (5.300)	IR(cm^{-1}, KBr) : 1502(C-C ring stretch 3120 (Ar. C-H str.),2951 (C-H str), 1592 (C-C str),1643 (C=N str), 1308 (C-N str),). 1H-NMR (400MHz, DMSO-*d*), 8.52 (s, 1H,N=CH), 7.8-8.8 (Ar H), 7.9-8.25(s, Ar), MS: m/z- 274.5 (M+).
2c.	**E-N-(5-Chloro-2 isopropyl benzylidene) 2-Nitro 4-Chloro amine**	$C_{16}H_{15}N_2O_2Cl_2$	56.80 (56.91)	4.43 (4.49)	8.28 (8.31)	IR(cm^{-1}, KBr) : 1689 (C=N str), 3102(Aromatic C-H str.), 2862, 2951 (C-H str), 1572 (C-C str), 1328 (C-N str),1H-NMR (400MHz, DMSO-*d*), 8.23 (s, 1H,N=CH), 7.0-8.08 (s, 3H, Ar), 7.0-8.28(s, 5H, Ar), MS: m/z- 338 (M+).
2d.	**E-N-(5-Chloro-2 isopropyl benzylidene) (4-o-methoxy) amine**	$C_{17}H_9NOCl$	73.24 (73.28)	3.23 (3.26)	5.026 (5.030)	IR(cm^{-1}, KBr) : 1120 (C-O) ,2990 (Aromatic C-H str.), 2922, 2931 (C-H str), 1513 (C-C str),1645 (C=N str), 1354 (C-N str),1478(C-C ring stretch). 1H-NMR (400MHz, DMSO-*d*), 8.32 (s, 1H,N=CH), 7.0-8.18 (s, 3H, Ar), 7.0-8.08(s, 5H, Ar), MS: m/z- 278.5 (M+).
2e.	**E-N-(5-Chloro-2 isopropyl benzylidene) (2-Bromo) amine**	C_{16} H_{18} NBr Cl	56.57 (56.67)	5.30 (5.38)	4.12 (4.16)	IR(cm^{-1}, KBr) : 3020 (Ar. C-H str.), 1627 (C=N str), 2912, 2909, 2940 (C-H str), 1522 (C-C str), 1328 (C-N str),1416(C-C ring stretch). 1H-NMR (400MHz, DMSO-*d*), 8.32 (s, 1H,), 7.10-8.28 (s, 3H,), 7.0-8.08(s, 5H, Ar), MS: m/z- 339.5 (M+).
2f.	**E-N-(5-Chloro-2 isopropyl benzylidene) (Benzene 1,2 diamine)(**	$C_{16}H1_8ClN_2$	70.20 (70.28)	6.58 (6.67)	9.76 (9.31)	IR(cm^{-1}, KBr) : 3210 (NH str.),2990(Aromatic C-H str.), 2912, 2809, 2811 (C-H str), 1678 ,1652 (C=N str), 1298 (C-N str),1426(C-C ring stretch). 1H-NMR (400MHz, DMSO-*d*), 8.00 (s, 1H,N=CH), 7.0-8.00 (s, 3H, Ar), MS: m/z- 273.5(M+).
2g.	**E-N-(5-Chloro-2 isopropyl benzylidene)(2-oic acid)amine**	C_{17} $H_{17}NClO_2$	67.43 (67.50)	5.619 (5.51)	4.62 (4.50)	IR(cm^{-1}, KBr) : 3031 (Aromatic C-H str.), 3611 (-OH broad),2972, 2811 2800 (C-H str), 1532 ,1650 (C=N str), 1338 (C-N str),1470(C-C ring stretch). 1H-NMR (400MHz, DMSO-*d*), 8.00 (s, 1H,N=CH), 7.0-8.18 (s, 3H, Ar), 7.5(s, 5H, Ar), MS: m/z- 302.5(M+).
2h.	**E-N-(5-Chloro-2 isopropyl benzylidene) Napthyl amine**	C_{20} $H_{19}NCl$	77.79 (77.91)	6.158 (6.231)	4.53 (4.510)	IR(cm^{-1}, KBr) : 3020 (Aromatic C-H str.), 2902, 2819, (C-H str), 1502 (C-C str),1670 (C=N str), 1311 (C-N str),1402(C-C ring stretch). 1H-NMR (400MHz, DMSO-*d*), 8.02 (s, 1H,N=CH), 7.0-8.0 (s, 3H, Ar), 7.0-8.02(m, 8H, Ar), MS: m/z- 308.5(M+).

Table II. Anti-Microbial Activity of E-N-(5-Chloro-2 isopropyl benzylidene) aryl amine

Compound	Zone of Inhibition				
	E.Coli	P.Aeruginosa	B.Subtilis	S.Aureus	C.Albicans
2 a	11	9	10	9	9
2 b	9	8	8	8	10
2 c	18	18	19	20	9
2 d	20	19	21	20	18
2 e	12	11	10	12	11
2 f	11	12	13	12	9
2 g	9	11	9	10	8
2 h	10	12	11	10	8
Ciprofloxin	28	24	25	23	-
Fluconazole	-	-	-	-	28

CONCLUSION

Schiff bases are prepared from the condensation of substituted aniline and 5-Chloro –Isopropyl Benzaldehyde in faintly acidic condition. The structure of the compounds were confirmed by spectral techniques IR, 1H-NMR, Mass. Biological Screening of the synthesized compounds were done by agar well diffusion method. The compounds 2c & 2d shows excellent activity, while other compounds have moderate activity.

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