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Der Pharma Chemica, 2014, 6(1):262-266
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis of substituted schiff's bases and their antimicrobial activity

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ABSTRACT

The chloro , nitro and methyl substituted benzaldehyde condensed with aniline and nitro aniline in ethanol medium in presence of conc.H_2SO_4 isolate schiff's bases. The structures of these compounds have been characterized by spectral analysis (NMR & IR). These compounds were tested for antimicrobial activity against bacteria such as E.coli, S.typhi, S.aureus, P.vulgaris and P.paratyphi are found to have remarkable activity.

Key words: Schiff's bases, synthesis, antimicrobial activity

INTRODUCTION

From literature survey it has been established that the chloro, nitro, methyl substituted benzaldehyde have medicinal, biological, pharmacological, industrial and agricultural values but very less work has been carried out on the derivatives of substituted benzaldehyde groups. The number of schiff's bases have been reported for their bactericidal[1-3] ,fungicidal[1-2] ,antipyretic[2], antitumor[4] , antitubercular and anticancer activity.

Synthesis and antimicrobial activity of new schiff bases containing coumarin moiety and their spectral characterization by V.S.V.Satanarayana et al [5]. Kadu et al [6] studied on synthesis and antimicrobial activity of schiff bases. antimicrobial agents reduce or completely block the growth and multiplication of bacteria and are helpful in the treatment of various infectious diseases like meningitis, maleria, tuberculosis, pneumonia, AIDS and so forth. The compounds with the structure of -C=N-(azomethine group) are known as schiff bases, which are usually synthesized from the condensation of primary amines and active carbonyl groups. Schiff bases derived from aromatic amines and aromatic aldehydes have a wide variety of applications in many fields, for example biological, inorganic, and analytical chemistry.[7-10] in addition, schiff bases and heterocyclic ring are important class of compounds in medicinal and pharmaceutical field.[11-14] Perumal Panneerselvam etal studied on synthesis, analgesic, anti-inflammatory and antimicrobial activities of some novel schiff's bases of 5-subsituted isatin.[15] synthesis of novel 4-thiazolidinone derivatives incorporated with benzothiaazole and it's antimicrobial activity studied by sambhaji P.vartale et al.[16] shubhangi G.Patil et al studied on synthesis, characterization and anti-microbial activity of 6-Bromo-4-(substituted phenyl) iminoflavone[17]. Present work deals with the study of antimicrobial activity of chloro, nitro, methyl substituted schiff bases synthesized against pathogenic bacteria.

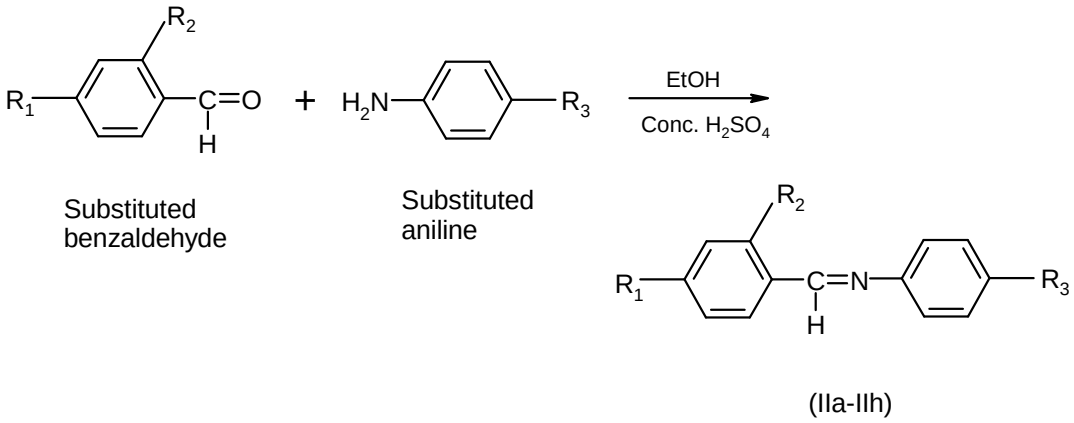
MATERIALS AND METHODS

The melting points were determined in open capillary tube and are uncorrected; purity of compounds was checked by TLC silica gel-G plates. IR spectra was recorded in KBr pellets . 1 H NMR spectra were recorded in CDCL3 on Bruker AC 300 F NMR spectrophotometer at 300MHZ using TMS as internal reference. Antimicrobial activity of the compounds was tested by agar disc diffusion method. [18].

RESULTS AND DISCUSSION

The structures of all synthesized compounds (scheme-I) viz, 4-Nitrophenylidine-4'-aniline(IIa), 4-Nitrophenylidine-4'-nitroaniline(IIb), 4-cholorophenylidine-4'aniline(IIc), 4-chlorophenylidene-4'nitroaniline(IId), 4-methoxyphenylidene-4'aniline(IIe), 4-methoxyphenylidene-4'nitroaniline(IIf), 2, 4-dimethylphenylidene-4'-aniline(IIg), 2, 4-dimethylphenylidene-4'-nitroaniline(IIh) have been confirmed by analytical data (Table-1) and chemical properties.

REACTION SCHEME:-



(IIa-IIh)

(SCHEME-I)

Similarly other schiff's bases IIb to IIh were synthesized from 4-substituted phenylidine – 4 - substituted aniline with substituted aniline. (Scheme –I)

SPECTRAL DATA:-

IIa: -IR (KBr) ν max cm-1:- 1683.74(-C=N stretching), 1343.63(C-No2 stretching), 3075.38(-Ar-H stretching), 2886.04(-Ar-CH stretching); 1H NMR: [δ CDCl3]: 6.8-7.05(m,C-H),8.216-8.610(m.Ar-H)

IIc: -IR (KBr) ν max cm-1:-3061.76(-Ar-H stretching),2873.54(-Ar-CH stretching), 1700.37(-C=N stretching),875.12(C-Cl stretching); 1H NMR: [δ CDCl3]: 6.6762-6.7556(m,Ar-CH),7.1360-7.8515(m,Ar-H)

IId: -IR (KBr) ν max cm-1:- 3074.26(-Ar-H stretching),2933.36(-Ar-H stretching),1688.95(-C=N stretching),1252.29(-OCH3 stretching); 1H NMR **[δ CDCl3]**: 7.8-8.5(m,Ar-CH),6.93-7.2182(m,C-H), 3.8245(S,-CH3O)

IIf: -IR (KBr) ν max cm-1:-3081.59(-Ar-H stretching), 2916.97(-Ar-CH stretching),1587.54(-C=N stretching) 1H NMR [δ CDCl3]: 2.1718-3.8937(m,-CH3),6.6062-8.84240(m,-Ar-H),4.3877(s,-Ar-CH)

PHYSICAL DATA OF COMPOUNDS

Table -1

Comp. No.	Molecular Formula	Mol. Weight	Colour	m.p. (°C)	Yield (%)	R_f value
IIa	$C_{13}H_{10}N_2O_2$	226	Brown	65	90	0.76
IIb	$C_{13}H_9N_3O_4$	271	Yellow	190	89	0.82
IIc	$C_{13}H_9N_2Cl$	214	Green	50	91	0.68
IId	$C_{13}H_9O_2N_2Cl$	260	Yellow	143	87	0.72
IIe	$C_{14}H_{13}ON$	211	Cream	60	92	0.79
IIf	$C_{14}H_{13}O_2N_2$	257	Greenish Yellow	98	91	0.84
IIg	$C_{15}H_{15}N$	209	Brown	40	80	0.74
IIh	$C_{15}H_{14}N_2O_2$	254	Greenish Yellow	115	92	0.75

ANTIMICROBIAL ACTIVITY:-

The present compounds were tested against pathogenic bacteria for their antimicrobial activity by agar disc diffusion method. The minimum inhibitory concentration (MIC) were measured by serial dilution method.[19,20].The organism tested were E.Coli, S.typhi, S.paratyphi, P.vulgaris, and S.aureus.

Disc Diffusion Method:-
The disc diffusion method is also known as kirby-bauer disc diffusion method. In this method, every time fresh sterile nutrient agar medium was prepared. The proceedings were carried out aseptically. All the glassware and apparatus required were sterilized.

In each sterile petridish, 15-20 ml molten medium was added.

It was allowed to solidify at room temperature. A sterile cotton swab was dipped into 24 hrs fresh diluted culture of organism under study and the inoculum was spread evenly over the entire surface of petriplate by swabbing in three directions. Then 6 mm discs of sterlized Whatmann filter paper No. 42 was moistened thoroughly with the same concentration of each of the compound and with the standard drug solution also. The moist discs were placed on the surface of inoculated plate. They were allowed to diffuse in the media and then the plates were incubated at 37°C for 24 hrs. The diameter of inhibition zone was observed and measured with the help of ruler [21].

Serial Dilution Method: - The following procedure was followed in serial dilution method to determine the MIC of various compounds.

Nutrient broth was prepared by dissolving 13 gms of dehydrated medium in 1 litre of distilled water. The pH of the medium was adjusted to 7.4. The 5 ml of the medium was distributed in each test tube. All the test tubes were sterilized at 121°C for 20 min. The 0.01 M solution of the test compounds were prepared in 1,4-dioxane solvent. Various amounts of the above stock solution was aseptically added to the various nutrient broth test tubes (viz. 0.5, 1.0, 1.2, 1.4, 1.6, 1.8, ... 5.8, 6.0 ml). Fresh culture of the test bacterium was inoculated in each test tube (0.2 ml culture). All the test tubes were incubated at 37°C for 24 hrs. Uninoculated test tube was kept as a control in which nutrient broth and 5 ml of the solvent was taken. After 24 hrs of incubation, all the test tubes were observed for MIC against test bacterium.

Table – 1 MIC values of Schiff's bases in µg/ml

Sr. No.	Compd. No.	*E. coli*	*S. typhi*	*S. paratyphi*	*P. vulgaris*	*S. aureus*
1.	IIa	1400	700	800	840	860
2.	IIb	800	600	650	650	700
3.	IIc	1650	1000	1080	1100	1040
4.	IId	1000	980	980	1040	1000
5.	IIe	2200	2900	1850	1800	1800
6.	IIf	1550	1400	1460	1480	1450
7.	IIg	1000	1000	1060	1100	1140
8.	IIh	1200	1280	1400	1450	1500

From the Table-1, it is clear that (IIa) ranges from 700-1400 □g/ml, the MIC values of (IIb) ranges from 600-800 □g/ml. The Schiff base is active because of nitro group.

The MIC value of (IIc) ranges from 1000-1650 □g/ml, the MIC value of (IId) ranges from 980-1040 □g/ml. The Schiff base (IIc) and (IId) are good inhibitory active due to the presence of one chloro and one nitro group in their structure respectively.

In short nitro group and chloro group are electron withdrawing groups. The nitro group is more electron withdrawing than chloro group, so that the compounds having such groups in their structure have more inhibiting active.

The MIC value of (IIe) ranges from 1800-2900 µg/ml, the MIC value of (IIf) ranges from 1400-1550 □g/ml, (IIf) is more active as compared to (IIe). (IIe) is less reactive because of the presence of methyl substituent in its structure; -CH_3 group is electron donating group.

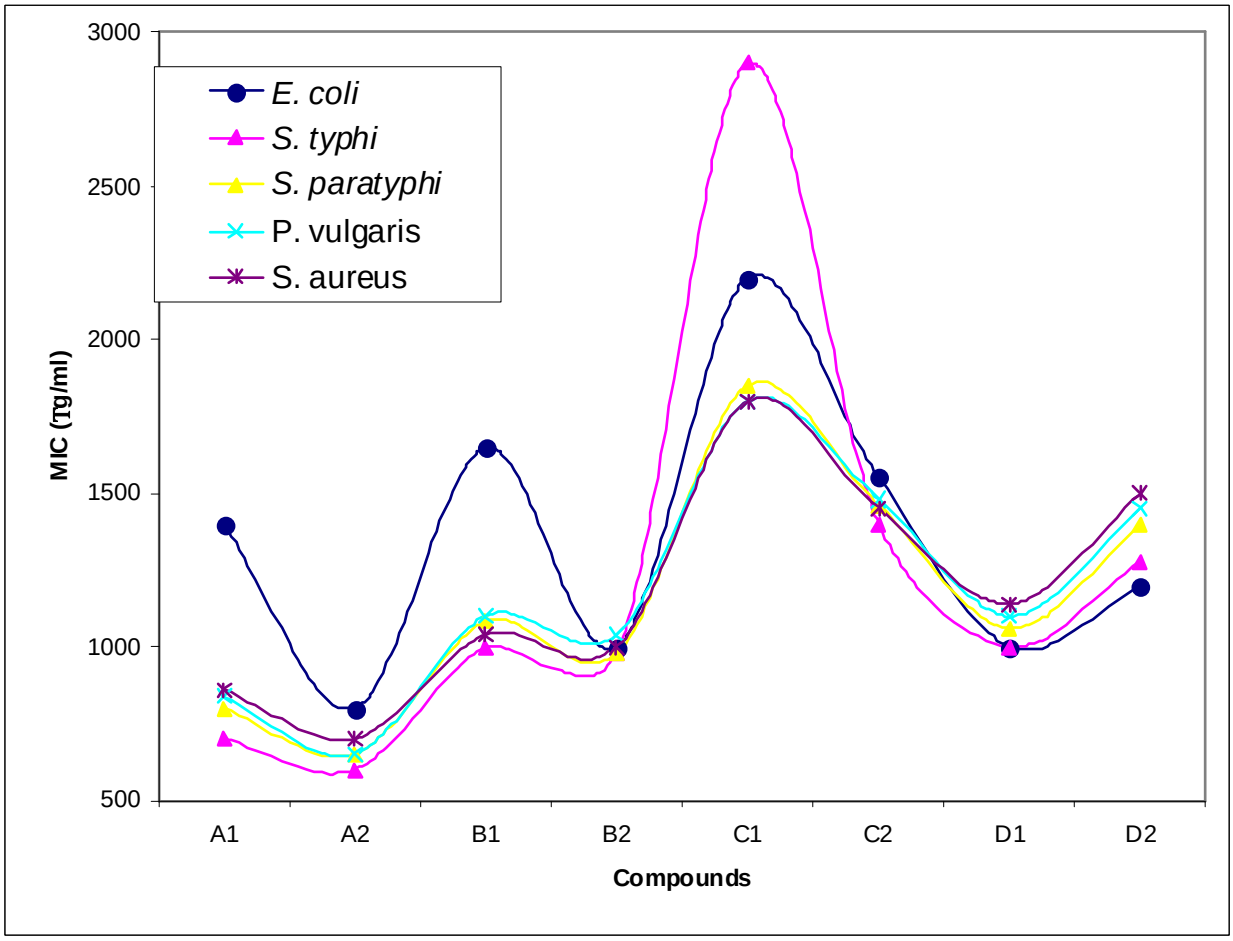
The MIC value of (IIg) ranges from 1000-1140 µg/ml, the MIC value of (IIh) ranges from 1200-1500 □g/ml.

From the result it has been observed that the presence of nitro group increases the activity and increase in activity is also related to the number of nitro groups. However, if chloro group is introduced in the structure, the increase in activity is more.

The order was found to be NO_2, NO_2 > NO_2Cl > NO_2.

Also the presence of methyl group decrease the activity. As number of methyl group increases the decrease in activity is more. This may be due to the electron withdrawing nature of $-NO_2$ group and electron donating nature of $-CH_3$ group. Thus, the relationship between the structure and activity of the compounds are established.

MIC Values of Schiff bases in µg/ml



Acknowledgements
The authors are very much thankful to Dr. S. B. Lohiya , Principal , Brijlal Biyani Science College, Amravati, for providing me laboratory facilities to carry out this work.

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