ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Synthesis of Schiff bases of N- based methylene derivatives

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Manuscript Info

Manuscript History:

Received: 11 January 2014
Final Accepted: 23 February 2014
Published Online: March 2014

Key words:
Aldehyde,44'-Methylenebis 2-methyl aniline, catalyst, Schiff bases.

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Abstract

A simple and efficient method has been developed for the synthesis of some Schiff bases via the reaction of aromatic aldehydes with 44'-Methylenebis 2-methyl aniline by using catalytic amount of glacial acetic acid in an organic solvent at room temperature. Some advantages of this protocol are its very good yields, use of available catalysts, simple workup procedure, and short reaction times

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INTRODUCTION

Schiff bases are widely used for synthetic purposes both by organic and inorganic chemists (Nagpal and Singh 2004). Schiff bases derived from aromatic amines and aromatic aldehydes are also a very important class of organic compounds because of their applications in many fields including biological, inorganic, and analytical chemistry (Ramla et al., 2007; Kazimierzcuk and Shugar, 1989; Ottana et al 2005; Mohamed et al 2006 Yildiz-Oren et al 2004) . Azomethine group (-C=N-)-containing compounds, typically known as Schiff's bases, have been synthesized via condensation of primary amines with active carbonyls. It is well established that the biological activity of hydrazone compounds is associated with the presence of the active (-CO-NHN=C-) pharmacophore and these compounds form a significant category of compounds in medicinaland pharmaceutical chemistry with several biological applications that include antitumoral (Walsh et al 1996), antifungal, antibacterial (Singh et al. 2006; Ahluwalia et al. 1983; Sengupta and Srivastava 1989), antimicrobial (Karthikeyan et al 2006) and anthelmintic uses (Sharma et al 2008).Schiff bases form an important group of compounds in synthetic chemistry due to their useful physical and chemical

properties and large number of reactions they undergo. Schiff bases are also used widely in pharmaceutical industry and have interesting pharmacological activities (Husain et al 1979). The study of Schiff base has been fast developing because they possess excellent characteristics such as structural similarities with natural biological substances, relatively simple preparation procedures and the synthetic flexibility that enables design of suitable structural properties. Studies on new classes of chemotherapeutic Schiff bases are now attracting the attention of biochemists (K.Kiranmai et al 2010). Schiff's bases have the potentials to be used in different areas such as electrochemistry, bioinorganic, catalysis, metallic deactivators, separation processes and environmental chemistry (Shemirani et al 2004).

MATERIALS AND METHODS

Experimental

Melting points of the synthesized compounds were determined by open capillary and are uncorrected. The purity of the compounds was checked using precoated TLC plates(MERCK, 60F) using Ethylacetate: Toluene (3:7) solvent system.

The developed chromatographic plates were visualized under UV at 254nm. IR spectra were recorded using KBr on Shimadzu FTIR model 8400 spectrophotometer, ^{1}H NMR spectra in DMSO on a BRUKER FT-NMR instrument using TMS as internal standard.

General procedure for the synthesis of44' Methylene bis 2- methyl anline:
O-Toluidine (10.7 g, 0.1 mol) was dissolved in water (125 ml) and 36.5% hydrochloric acid (25 ml) at 50 °C. The reaction mixture was then reacted with 3% aqueous formaldehyde (35 ml) solution at 60 °C with stirring for 1 hr and neutralized with 10% sodium hydroxide solution. The white precipitates obtained were filtered, washed with hot water, dried and recrystallized from acetic acid. Yield 80%, m.p. 146°C-148°C.

General procedure for the synthesis of Schiff bases of44' Methylene bis 2- methyl anline (Ma-Mj).
The Schiff base was prepared by reaction of one mole of 44' Methylene bis 2-methyl aniline and two moles substituted aromatic aldehydes. Each reactant was dissolved in a minimum amount of methanol, then mixed together and followed by addition of 1 ml glacial acetic acid. The solution was refluxed for 12 hr then cools to room temperature and poured into ice cold water. The solid product was collected through filtration and then dried using drying oven at 75 ºC. The product was redissolved in methanol for recrystallization and then dried to give a product.

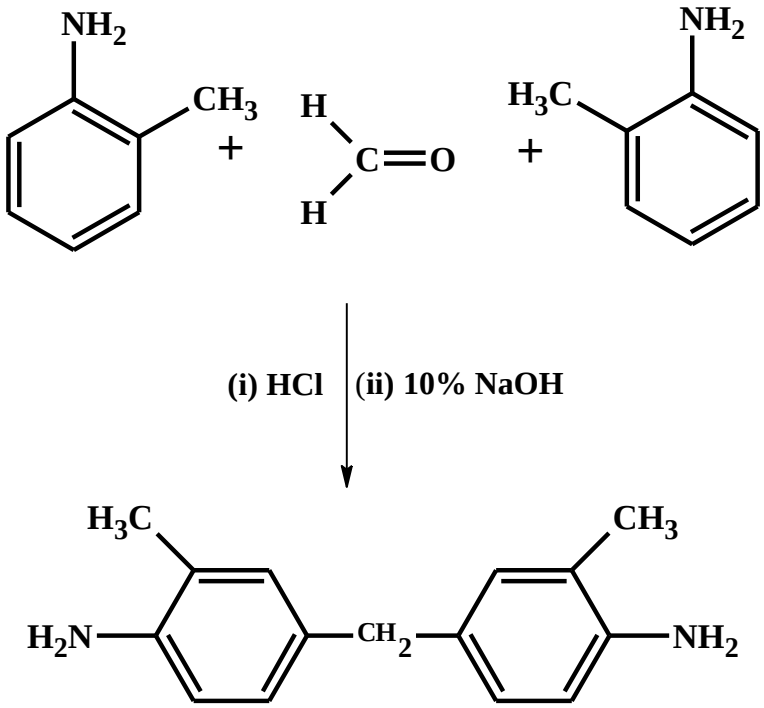
44' Methylenebis(*N*-(2-hydroxy benzylidine)-2-methyl aniline) (Ma):
IR (KBr cm-1): 1616.03 (HC=N), 2918.13(-CH_2), 3420.54(Phenolic -OH).
^{1}H-NMR (DMSO δ ppm): 8.8 (1H, S,HC=N), 7.0-7.6 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S, -CH_2) 5.3 (-OH).
44' Methylenebis(*N*-(2-chloro benzylidine)-2-methyl aniline) (Mb):
IR (KBr cm-1): 1577.82 (HC=N), 2836.0 (-CH_2), 720.0(C-ClArstr).
^{1}H-NMR (DMSO δ ppm): 8.8 (1H, S,HC=N), 7.4-7.7 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S,-CH_2).
44' Methylenebis(*N*-(4-chloro benzylidine)-2-methyl aniline) (Mc):
IR (KBr cm-1): 1575.86 (HC=N), 2824.0 (-CH_2), 698.0(C-ClArstr).
^{1}H-NMR (DMSO δ ppm): 8.6 (1H, S,HC=N), 7.5-7.8 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S, -CH_2).
44' Methylenebis(*N*-(2-nitro benzylidine)-2-methyl aniline) (Md):
IR (KBr cm-1): 1577.82 (HC=N), 2844.0 (-CH_2), 1554.0(-NO_2)
^{1}H-NMR (DMSO δ ppm): 8.8 (1H, S,HC=N), 7.5-8.1 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S,-CH_2).
44' Methylenebis(*N*-(4-methyl benzylidine) 2-methyl aniline) (Me):
IR (KBr cm-1): 1580.86 (HC=N), 2817.0 (-CH_2).1258.0(C-CH_3Arstr)
^{1}H-NMR (DMSO δ ppm): 8.6 (1H, S,HC=N), 7.5-8.1 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S, -CH_2).
44' Methylenebis(*N*- (4-hydroxy benzylidine)-2-methyl aniline) (Mf):
IR (KBr cm-1): 1614.47 (HC=N), 2819.0 (-CH_2), 3428.09(Phenolic-OH)
^{1}H-NMR (DMSO δ ppm): 8.6 (1H, S,HC=N), 7.5-8.1 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S, -CH_2).
44' Methylenebis(*N*-(4-methoxy benzylidine)-2-methyl aniline) (Mg):
IR (KBr cm-1): 1572 (HC=N), 2822.0 (-CH_2),1232.0(C-OCH_3Arstr)
^{1}H-NMR (DMSO δ ppm): 8.6 (1H, S,HC=N), 7.0-7.8 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S, -CH_2)3.83 (-OCH_3).
44' Methylenebis(*N*-(2-bromo benzylidine)-2-methyl aniline) (Mh):
IR (KBr cm-1): 1629.38 (HC=N), 2838.0 (-CH_2), 648.0(C-BrArstr).
^{1}H-NMR (DMSO δ ppm): 8.8 (1H, S,HC=N), 7.4-7.7 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S, -CH_2).
44' Methylenebis(*N*-(2-fluoro benzylidine)-2-methyl aniline) (Mi):
IR (KBr cm-1): 1621.33 (HC=N), 2914.14 (-CH_2),1068.0 (C-FArstr).
^{1}H-NMR (DMSO δ ppm): 8.62 (1H, S,HC=N), 7.3-7.8 (4H, Ar-H), 7.1-7.3 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S, -CH_2).

44' Methylenebis(*N*-(3-bromo benzylidine)-2-methyl aniline) (Mj):
IR (KBr cm-1): 1629.38 (HC=N), 3008.97 (-CH_2),652.0 (C-BrArstr).

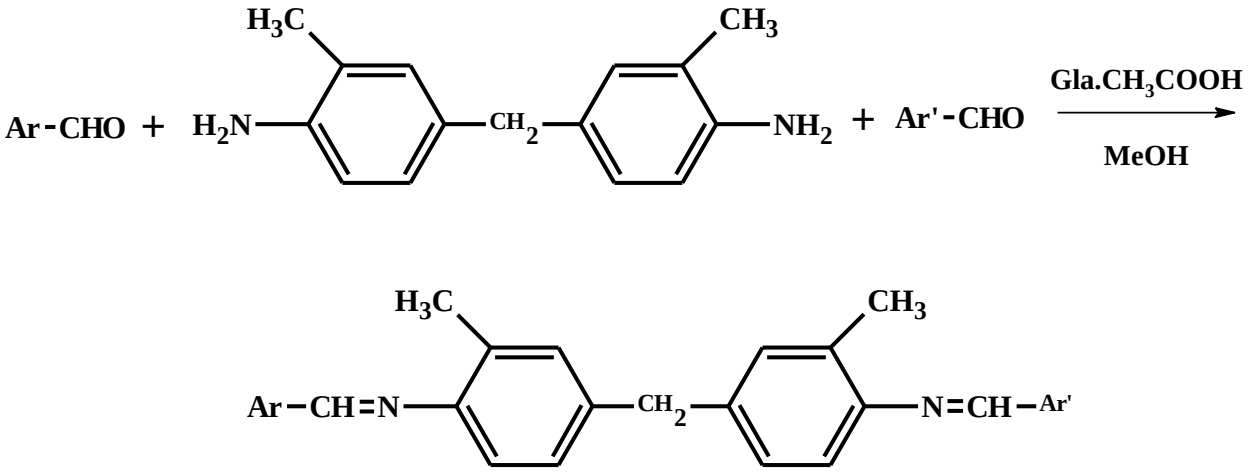
^{1}H-NMR (DMSO δ ppm): 8.6 (1H, S,HC=N), 7.4-7.8 (4H, Ar-H), 6.9-7.1 (4H, Arbenzylidinimine ring),2.3 (1H,S,-CH_3) 3.9 (1H, S,-CH_2).

RESULTS AND DISCUSSION

All the synthesized compounds (Ma-Mj) were purified by successive recrystallization using Methanol. The purity of the synthesized compounds was checked by performing TLC. The structures of the synthesized compounds were determined on the basis of their FT-IR and ^{1}HNMR data.



Scheme 1. Preparation of Intermediate



Scheme 2. Preparation of Schiff Bases (Ma- Mj)

Where Ar and Ar' is

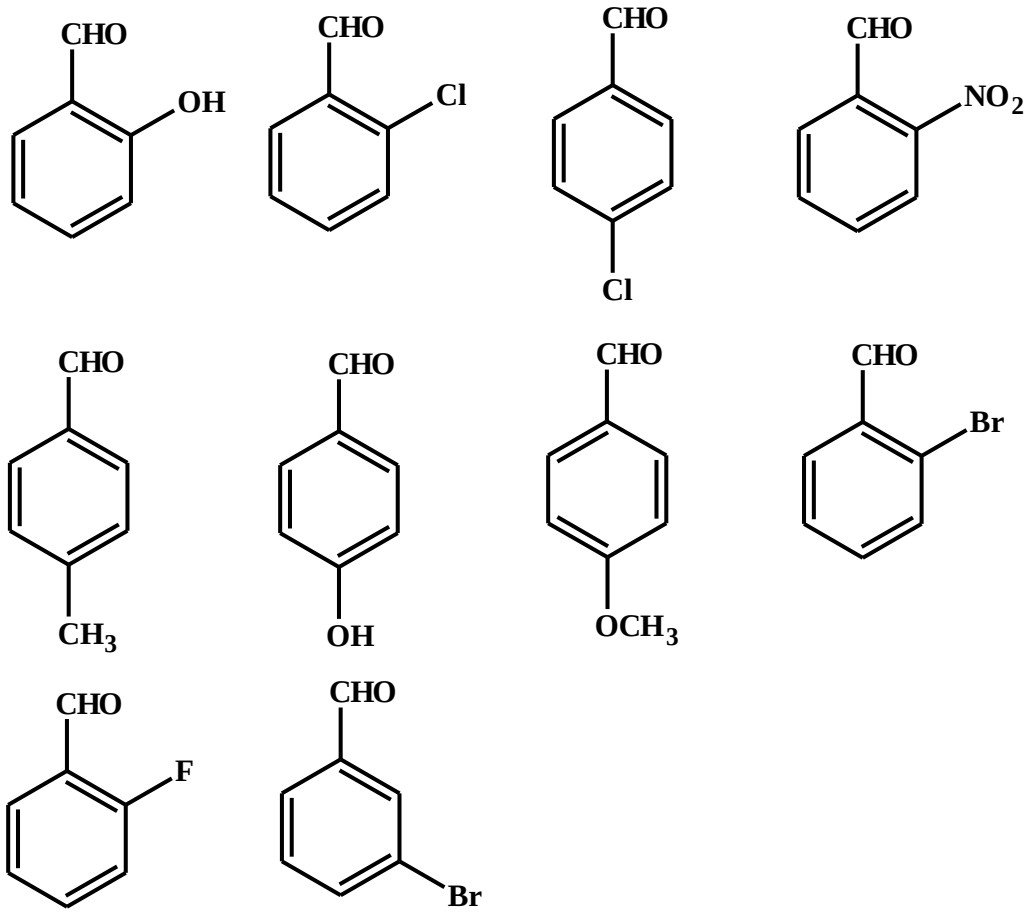


Table 1 : Physical constant data of synthesized compounds (Ma to Mj)

Compounds	Ar & Ar'	Mol.Formula	Yield%	M.P(°C)
Ma	2-OHC_6H_5CHO	$C_{29}H_{26}N_2O_2$	80%	174-176
Mb	2-ClC_6H_5CHO	$C_{29}H_{24}Cl_2N_2$	85%	96-98
Mc	4-ClC_6H_5CHO	$C_{29}H_{24}Cl_2N_2$	85%	124-126
Md	2-$NO_2C_6H_5CHO$	$C_{29}H_{24}N_4O_4$	80%	118-120
Me	4-$CH_3C_6H_5CHO$	$C_{31}H_{30}N_2$	75%	188-190
Mf	4-OHC_6H_5CHO	$C_{29}H_{26}N_2O_2$	70%	92-94
Mg	4-$OCH_3C_6H_5CHO$	$C_{31}H_{30}N_2O_2$	70%	132-134
Mh	2-BrC_6H_5CHO	$C_{29}H_{24}Br_2N_2$	75%	100-102
Mi	2-FC_6H_5CHO	$C_{29}H_{24}F_2N_2$	85%	96-98
Mj	3-BrC_6H_5CHO	$C_{29}H_{24}Br_2N_2$	80%	116-118

Table 2: Zone of inhibition (mm) data of synthesized compounds.

Sample code	Zone diameter in millimeter (mm)					
	Escherichia coli	***Proteus vulgaris***	***Staphylococcus aureus***	***Bacillus subtilis***	***Candida albicans***	***Saccheromyces cervecieaceae***
M – a	R	R	S(18)	R	S(15)	R
M – b	R	S(17)	R	R	R	R
M – c	R	R	S(17)	R	R	R
M – d	S(17)	R	R	R	R	R
M – e	S(18)	R	R	R	R	R
M – f	R	R	R	R	R	R
M – g	S(19)	R	R	R	R	R
M – h	S(20)	R	S(20)	R	R	S(15)
M – i	R	R	R	R	R	R
M - j	R	R	R	R	R	R

R = RESISTANT (No zone of inhibition seen)
S = SENSITIVE (Zone of inhibition seen)

Antimicrobial activity

The antimicrobial activity of all the synthesized compounds (Ma -Mj) were examined against different Gram-positive(*Bacillus subtilis* and *Staphylococcus aureus)* and Gram-negative
(*Escherichia coli* and *proteus vulgaris*) and fungal strains *Sqccheromyce scervecieaceae* and *Candida albicans* organisms by measuring zone of inhibition. The antimicrobial activity was performed by Kirby baurer method at the concentration level of 50µg/ml.Ciprofloxacin, Penicillin and Cefotaxime as standard drug at a concentration of 50µg/ml (23-25) The results of the antimicrobial activity are shown in Table 2

ACKNOWLRDGEMENT
The authors are thankful to Dr K C Patel for providing laboratory facilities. Authors are also thankful to Dr. Paresh S Patel, Narmada College of Science and Commerce, Zadeshwar, Bharuch for constant support in this work. Authors also thankful to Samarth clinical laboratory,Surat for antimicrobial activity.SAIF Chandigarh for spectral

data.One of the authors (Mayank S Patel) is thankful to the UGC-BSR Research Fellowship(SAP) for financial support.

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