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Ultrasound Assisted Catalyst free Synthesis of Some Novel Bis-Schiff Bases: A Green Approach

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ABSTRACT

Ultrasound assisted catalyst free one pot synthesis of some novel bis-schiff bases is accomplished by condensing hydrazone of 2-hydroxy acetophenone and various aryl aldehydes in good yields.

Keywords: Ultrasound assisted reaction, Bis-Schiff Bases, Hydrazone, Aryl Aldehydes

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INTRODUCTION

Schiff bases are important organic compound. They are first reported by Hugo Schiff in 1864 hence they are named as Schiff bases.They are obtained by condensation reaction of primary amine reacts with an aldehyde or a ketone. They are organic compounds with the general formula RR′C═NR″, where R and R′ represent hydrogen, an alkyl or an aryl. Schiff's bases are also known as imine or azomethine. Various Lewis acids are used as catalyst which accelerates nucleophilic attack of amines on carbonyl carbon as well as serving as dehydrating agent for removal of the water. A large number of Bronsted-Lowry or Lewis acids were used as catalysts for the synthesis of Schiff base include $ZnCl_2$,$TiCl_4$, $MgSO_4$-PPTS, $Ti(OR)_4$, alumina, H_2SO_4,$NaHCO_3$,$MgSO_4$, $Mg(ClO4)_2$, CH_3COOH, $Er(OTf)_3$, P_2O_5/Al_2O_3, [1–12].

The biological activity of Schiff bases have been reported in the literature possessing

Anticancer[13,14]antibacterial[15-21]antifungal ,antiviral[22-24].They have been found to exhibit a broad spectrum of biological activities such as anticonvulsant[25]**,**anti-inflammatory[26-28**]**, analgesic[29], antitubercular[30], antioxidant[31], anthelminthic[32], anticancer[33].

Ultratrasound irradiation has been used as a clean and useful protocol in organic synthesis in the last three decades. This technique is more convenient. A large number of organic reactions can be carried out under milder conditions in shorter reaction times providing higher yields without generation of pollution under ultrasound irradiation. The various advantages are energy efficiency, atom efficiency, environmental friendly, waste minimization etc.

Therefore, we adopted Ultrasound technique for the synthesis of some novel Bis-Schiff base by condensing hydrazone of 2-hydroxy acetophenone [34] and various aromatic and heterocyclic aldehydes under ultrasound irradiation without using any catalyst.

MATERIALS AND METHODS

All the chemicals were purchased from Loba and Merck and used as it is without further purification.All melting points are uncorrected and the temperatures are in centigrade scaleThin -layer chromatography technique was employed for monitoring the progress of the reaction.TLC analyses were carried out on glass plates (6 cm) using silica gel and the plates were analyzed by keeping in iodine chamber.The IR spectra were recorded on KBr disc on Shimadzu FT-IR 8300 spectrometerand absorption was expressed in cm^{-1}.The ^1H NMR spectra were recorded in $CDCl_3$ / DMSO-d_6 on a Brucker instrument at 400 MHz and 300 MHz using tetramethylsilane as the internal standard. Chemical shifts have been expressed in ppm.The mass spectra were recorded on VG 7070 mass spectrometer using ionization energy of 70 ev. .

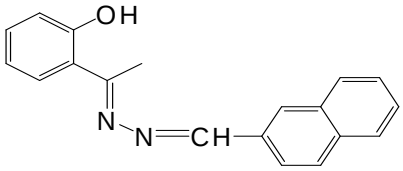
The Ultrasonicator was used having the following specifications.
Electric supply: 230 v A.C .50 Hz, 1Phase
Ultrasonic frequency: 36 + 3 KHz, Ultrasonic power: 100 watts

General procedure for the synthesis of Hyrazone (1):
To a mixture of *o*-hydroxy acetophenone(0.01 mol) and hydrazine hydrate (0.02 mol) in DMSO was added a catalytic amount of $SnCl_2{\cdot}2H_2O$. The reaction mixture was stirred for few minutes. After accomplishment of the reaction (monitored by TLC) the reaction mixture was poured onto crushed ice and stirred for the separation of molecules. The obtained solid product was filtered and purified by recrystallization with ethanol. **(Scheme1)**

General procedure for the synthesis of Bis-Schiff bases (3a-g):
A mixture of hydrazone**1** and various substituted aromatic aldehydes**2a-g** was reacted by using ultrasound radiation under catalyst free condition in presence of ethanolat about 40^0-50^0c. The consumption of reactants was observed within a couple of minute monitored by TLC.The expected product was obtained by addition of ice cold water to the reaction mixture. The separated yellow coloured solid product was purified by crystallization using ethanol producing good yield of the product.(Scheme2)

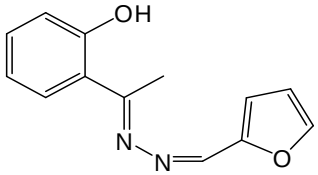
2.5.1. Characterization data for bis-Schiff bases (3a-g)

(3a) 2-{1-[(naphthalene-2-yl methylene) hydrazono] ethyl} phenol



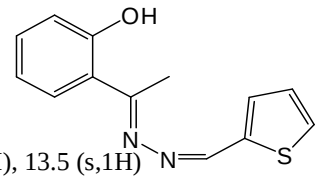
Molecular Formula: $C_{19}H_{16}N_2O$
Molecular Weight: 288
Melting Point: 129^0C
IR (ν max cm^{-1}): 3397 (O-H), 1612 (C=N), 2965 (Ar C-H).
^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.7 (s, 3H), 6.8-8.2 (Ar-H, m, 11 H), 8.70 (s, 1H), 13.4 (s, 1H).
MS (m/z): 289.25

(3b) 2-{1-[(furan -2-yl methylene) hydrazono] ethyl} phenol



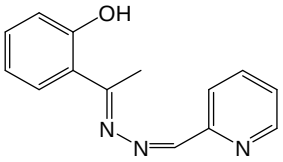
Molecular Formula: $C_{13}H_{12}N_2O_2$
Molecular Weight: 228
Melting Point: 78^0C
IR (ν max cm^{-1}): 1622 (C=N), 2965, 2856, 2853 (Ar-C-H), 3133 (O-H).
^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.7 (s, 3H), 6.6-7.8 (Ar-H ,m 7H), 8.4 (s,1H), 13.2 (s,1H).
MS (m/z): 229.2

(3c) 2-{1-[(Thiophene -2-yl methylene) hydrazono] ethyl}phenol



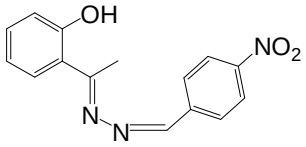
Molecular Formula: $C_{13}H_{12}N_2OS$
Molecular Weight: 244
IR (ν max cm^{-1}): 1607 (C=N), 2963, 2854, 3053 (O-H)
^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.67 (s, 3H), 6.9-7.6 (Ar-H, m, 7H), 13.5 (s,1H)
MS (m/z): 245.17

(3d) 2-{1-[(pyridin-2-yl methylene) hydrazono]ethyl}phenol



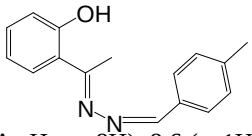
Molecular Formula: $C_{14}H_{13}N_3O$
Molecular Weight: 239
IR (ν max cm^{-1}): 1610 (C=N), 2922, 3049 (O-H).
^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2,7 (s,3H), 6.8-8.6 (Ar-H, m, 8H), 8.49 (s,1H), 13.1 (s,1H)
MS (m/z): 240.22

(3e) 2-{1-[(4-nitrophenyl methylene) hydrazono]ethyl}phenol



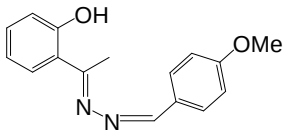
Molecular Formula: $C_{15}H_{13}N_3O_3$
Molecular Weight: 283
IR (ν max cm^{-1}): 1596 (C=N), 2937, 2844, 3417 (O-H)
^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.55 (s, 3H), 6.9-8.3 (Ar-H, m, 8H), 8.8 (s,1H), 12.9 (s,1H)
MS (m/z): 283.1

(f) 2-{1-[(4-toluyl methylene)hydrazono]ethyl}phenol



Molecular Formula: $C_{16}H_{16}N_2O$
Melting Point: 118^0C
IR (ν max cm^{-1}): 1613 (C=N), 2914, 2854
^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.37 (s, 3H), 2.66 (s, 3H,), 6.9-7.8 (Ar-H, m, 8H), 8.6 (s, 1H, -CH), 13.4 (s, 1H, OH)
MS (m/z): 252.1

(3g) 2-{1-[(4-methoxy phenyl methylene)hydrazono]ethyl}phenol



Molecular Formula: $C_{16}H_{16}N_2O_2$
Molecular Weight: 268
IR (ν max cm^{-1}): 1605 (C=N), 3026, 3267 (O-H)
^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.64 (s, 3H),3.4 (S,3H), 6.8-7.7 (Ar-H, m, 8H), 8.5 (s, 1H) 13.5 (s, 1H, OH)
MS (m/z): 268.1

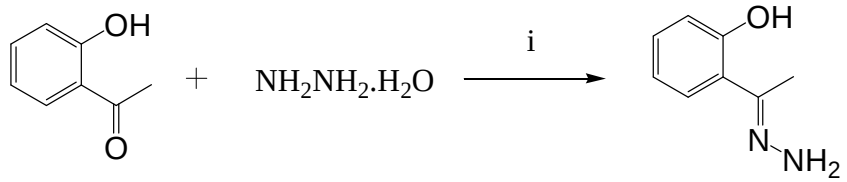
RESULTS AND DISCUSSION

The formation of Schiff's bases is very important due to good electrophilic and nucleophilic property of carbonyl and amine group respectively.

We reported here one pot synthesis of some novel heterocyclic Schiff's bases from condensation of hydrazine of 2-hydroxy acetophenone with various substituted aromatic aldehydes and heterocyclic aldehydes.

Since Hydrazones and their derivatives have interesting biological properties, such as anti-inflammatory, analgesic, anticonvulsant, antituberculous, antitumor and antimicrobial activity. Hydrazones are important compounds for drug design, organo catalysis and also for the syntheses of heterocyclic compounds. Hence the synthesis of Schiff base was carried out by using hydrazone and various aldehyde.

While carrying out the reactions of previously synthesized hydrazone with various substituted aromatic and heterocyclic aldehydes, we observed the smooth conversion of the reactants into products evidenced by TLC. On the basis of TLC, we are able to conclude the progress of reaction within 3-5 minutes in excellent yield and high purity. The product was obtained by filtration and purified by recrystallization using ethanol as a solvent.



Scheme1.Reaction conditions: i) $SnCl_2$, DMSO, RT, Stir, 90 %

R= ARYL/ HETEROARYL

Scheme 2.Reaction conditions: i) Ethanol, 40^0-50^0, Ultra sound, 85 %

In order to explore the scope of this methodology, reaction of hydrazones with various aromatic and heterocyclic aldehydes has been carried out. We did not observe any remarkable difference in the reaction time for various aldehydes (mentioned in Table 1). The newly synthesized molecules were characterized by physical, chemical and spectral analysis (IR, ^{1}H NMR and MASS) data.

Plausible Mechanism

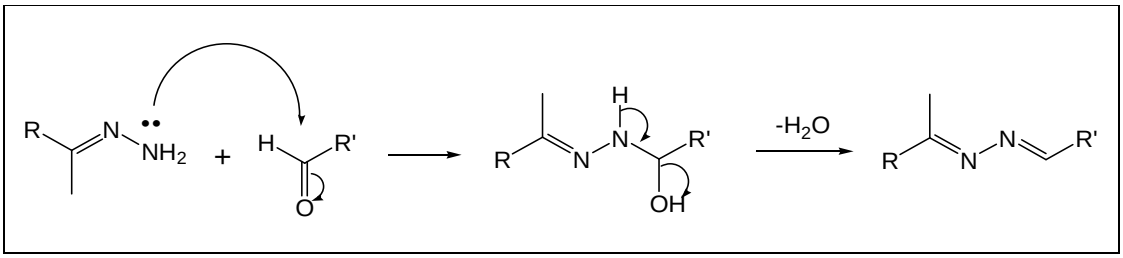
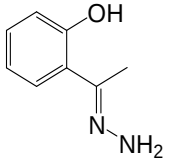
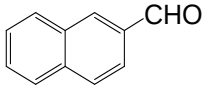
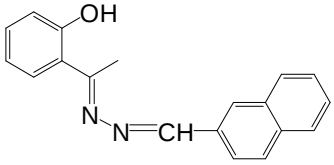
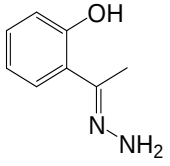
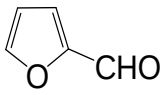
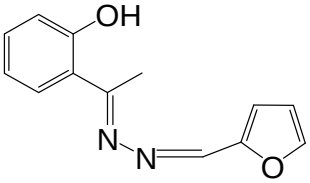
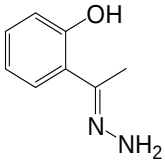
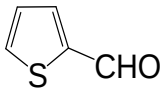
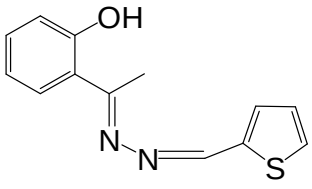
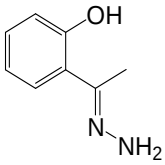
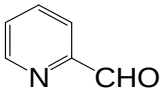
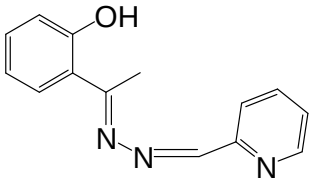
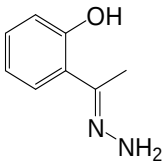
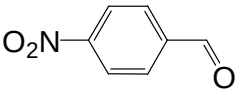
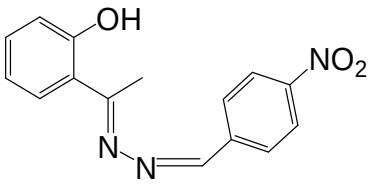
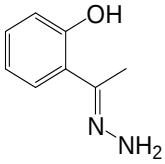
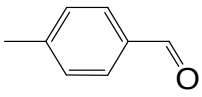
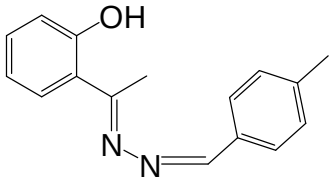
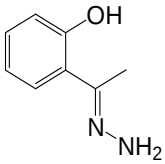
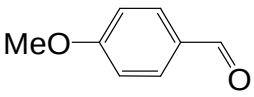
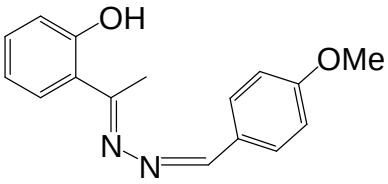


Table 1.Synthesis of bis-Schiff bases (3a-j)

Entry	Hydrazones 1	Aldehyes 2a-j	Bis-schiff bases 3a-j	Yield (%)	M.P. ^{0}C
1	 **1**	 **2a**	 **3a**	**85**	**127-128**
2	 **1**	 2b	 3b	**82**	**75-76**

3	 **1**	 2c	 3c	**79**	**84-85**
4	 **1**	 2d	 3d	**78**	**87-88**
5	 **1**	 2g	 3g	**84**	**172-173**
6	 **1**	 2i	 3i	**79**	**118-119**
7	 **1**	 2j	 3j	**78**	**184-185**

The IR spectrum of **3b** showed absorption bands at 1622 due to -C=N stretching which is the characteristic band for imines. The ^{1}H NMR spectrum of **3b** showed singlet for one proton at 8.4 and singlet for one proton at 13.2 which are the characteristic peaks for -CH=N and –OH respectively. The mass spectrum of **3b** showed m/z at 229.2. The spectral data mentioned above was in agreement with the formation of Schiff's bases.

CONCLUSION

In conclusion, we have presented here a methodology for the synthesis of bis-Schiff bases by the reaction of hydrazone and aromatic and heterocyclic aldehydes under ultrasound irradiation. The process is very simple and the reaction proceeded smoothly with various substituted aryl aldehydes producing good yield of the products in high purity and without using any hazardous solvents. Above all the presented protocol follows the principle of green chemistry

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