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Schiff base synthesis by unconventional route: An innovative green approach

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ABSTRACT

The objective of present research work is to provide green methodologies for synthesis of Schiff bases. Highly efficient and simple methods have been described for the synthesis with excellent yields (95-98%). Synthesis of Schiff base is often carried out with or without acid-catalysed and generally by refluxing the mixture of aldehyde (or ketone) and amine in organic medium. Present synthesis complies with principle of Green chemistry. As part of current studies, we here in reports efficient practical techniques like- sonication (sonochemistry), UV radiations and simple mortal-pastel method (mechanochemistry). The overall progress of the reaction was monitored by TLC and characterized by IR and NMR. Compared with traditional methods, these methods are more convenient and reactions can be carried out in higher yield, shorter reaction time and milder conditions, without generation of pollution and safer to analyst. Low cost, simple to run, maximum efficiency are some advantages of these techniques. Compared with traditional methods, these methods are more convenient and reactions can be carried out in higher yield, shorter reaction time and milder conditions, without generation of pollution and safer to analyst. From these features present methods can be correlated for safer and efficient synthesis of other products.

Keywords: Synthesis by Sonication, Synthesis by Ultra-Violet Radiation, Synthesis by Morter Pastel, mechanochemistry, Green Synthesis, Schiff bases.

INTRODUCTION

Schiff bases are well known in the pharmaceutical industry and have been shown to possess a broad spectrum of biological activities. In light of these significances, a variety of synthetic strategies have been developed for the preparation of Schiff base, despite the progress, the synthesis of these compounds remains less than ideal.[1] Thus, the development of

environmentally friendly benign (*Green Chemistry*), high-yielding and clean approaches for the synthesis of Schiff base is still remains a highly desired goal in organic synthesis.[2]

Here, we try to synthesize derivatives by unconventional techniques. Although many research have been came out in this field but effect of ultrasound waves in chemical reaction have not been fully understood yet.

Wang et al. noticed the effect of acoustic cavitations phenomenon that would be produce in solution because of ultrasonic sound. According to hot spot theory, explosion of bubbles in solution cause local and instant increase in temperature and pressure. Under such condition solvent molecules undergo homolytical bond breakage to generate radicals, H^+ and OH^- for example. Selection of solvent and ambient temperature both are essential for sonication reaction. Ultrasonic-assisted organic synthesis as a green synthetic approach is a powerful technique that is being used more and more to accelerate organic reactions. [3]

Mechanochemistry means mechanical breakage of intramolecular bonds by external force and must be differentiated from molecular solid-state chemistry. Grinding, milling, shearing, scratching and polishing provide the mechanical impact for mechanochemistry, while sonication and shock waving for intramolecular bond breaking are generally described as thermal processes. Here we used simple mortar and pastel for grinding purpose to complete the reaction.[4]

MATERIALS AND METHODS

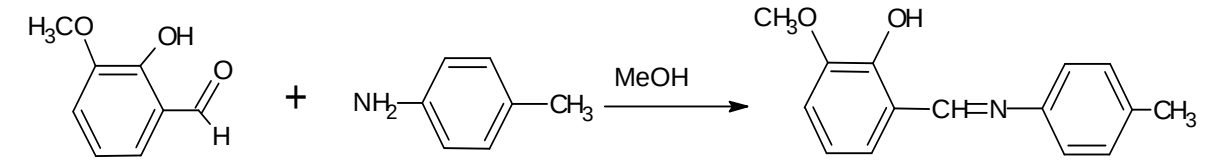
Melting points were obtained using DBK programmed melting point apparatus and are uncorrected. The purification of synthesized compounds was performed by recrytallization with appropriate solvent system. The purity of the compounds was checked using TLC technique, spots were developed by exposure to iodine vapors and UV cabinet, ultraviolet spectra (λ max) were taken on UV 2401 (PC) S 220V double beam UV Spectrophotometer. Infrared spectra were recorded on FTIR spectrophotometer 8400S, Shimadzu corporation. Mass spectra were recorded in QP-2010 PLUS GC-MS system. Nuclear Magnetic Resonance spectra were recorded with AVANCE 300MHz, using $CDCl_3$.

Materials

Ethanol, Methanol, *p*-toluidine, *o*-vanillin, Ethanol, chloroform, DMSO and acetic acid were supplied from Rankem Chemical Co. and they were used as received.

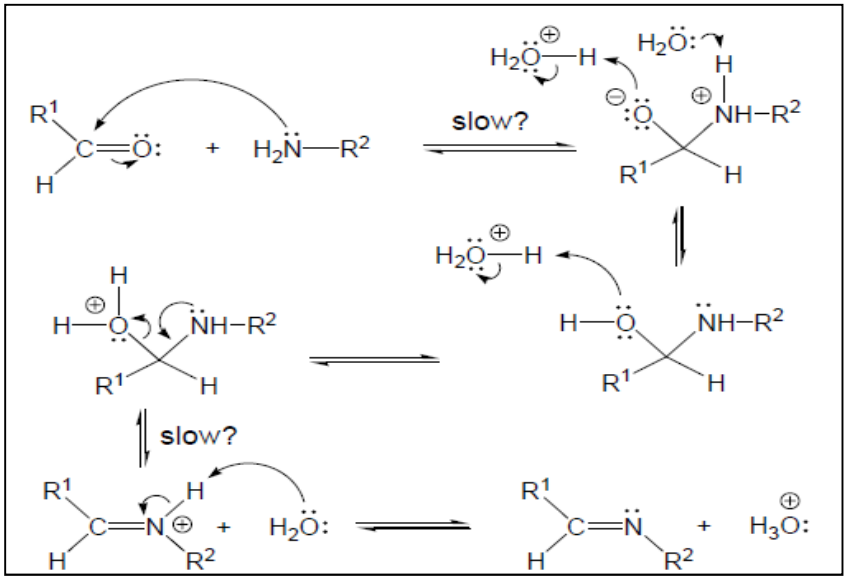
Experimental methods:

Scheme 1: formation of imine[5]



2-hydroxy-3-methoxybenzaldehyde *p*-toluidine 2-methoxy-6-{[(4-methylphenyl)imino]methyl}phenol

Scheme 2: Mechanism for imine formation[5]



1. Synthesis in presence of U. V. Rays [6, 7]

Equimole amount of p-toludine and vaniline were mixed and placed in U. V. Chamber for 15 min. Formation of pale yellow colored product indicates completion of reaction. The synthesized product recrystalized by shock cooling method, using Ethanol as a solvent to get fine crystals of 2-methoxy-6-[(4-methylphenyl) imino] methylphenol (2-M-4-MPIMP). The reaction monitored by TLC and confirmed by IR.

2. By using Sonicator

a) Without catalyst : [8] 0.1 Mole of p-toludine dissolved in 5ml methanol and in another beaker 0.1 Mole of vaniline dissolved in 5ml methanol. Both the contents are mixed in a beaker and place in sonicator at 45^{o}C for 13-15 min. A pale yellow colored product is formed which indicated formation of product. The synthesized product recrystalized by shock cooling method, using Ethanol as a solvent to get fine crystals 2-methoxy-6-[(4-methylphenyl) imino] methylphenol (2-M-4-MPIMP). The reaction monitored by TLC and confirmed by IR.

b) With a catalyst : 0.1 Mole of p-toludine dissolved in 5ml methanol and in another beaker 0.1 Mole of vaniline dissolved in 5ml methanol. Both the contents are mixed in a beaker; a drop of acetic acid is added as a catalyst and beaker place in sonicator at 45^{o}C for 9-10 min. A pale yellow colored product is formed which indicated formation of product. The synthesized product recrystalized by shock cooling method, using Ethanol as a solvent to get fine crystals of 2-methoxy-6-[(4-methylphenyl) imino] methylphenol (2-M-4-MPIMP). The reaction monitored by TLC and confirmed by IR.

3. By using mortar and pastel

Equimole amount of p-toludine and vaniline triturated in mortar for 10-12 min. slight change in color is observed. Product placed in dark room, overnight standing yield the final product. A pale yellow colored product is formed which indicated formation of product. The synthesized product recrystalized by shock cooling method Ethanol as a solvent to get fine crystals of 2-methoxy-6-[(4-methylphenyl) imino] methylphenol (2-M-4-MPIMP). The reaction monitored by TLC and confirmed by IR.

Thin layer chromatography: TLC was performed on silica gel G glass plates using suitable solvents systems to ascertain the purity of these compounds. Mobile phase given in table-1

Table 1: Mobile phase used for determination of R_f value of synthesized compounds.

Sr.No	Mobile Phase
1	$CHCl_3$:MeOH, 90:10

The percentage yield, melting point and analytical data of the synthesized compounds are listed in Table 2.

Table 2: Synthesized conjugates with physical constants

Method No	M.P. (^{0}C)	YIELD (%)	R_f VALUE	Mol. Wt.	EXPERIMENTAL ANALYSIS
1	115-118^{0}C	96.90	0.62	240.27	C:74.98, H:05.83, N:05.83
2a	115-118^{0}C	97.00	0.62	240.27	C:74.98, H:05.83, N:05.83
2b	115-118^{0}C	98.30	0.62	240.27	C:74.98, H:05.83, N:05.83
3	115-118^{0}C	95.80	0.62	240.27	C:74.98, H:05.83, N:05.83

RESULT

Spectroscopical studies [9]

- **λmax**: 276 nm
- **IR:** Characteristic IR (KBr) bands found at:(O-H) 3261 s, (C-H Phenyl) 3029 m, (C-H aliphatic) 2920 s, (C=N) 1616 s, (OCH3) 1456 s, (C=C phenyl) 1595, 1575, 1509 s, (C-O) 1255 s.(νmax/cm-1).
- **1H NMR:** The NMR shows characteristic bands (DMSO): , ppm, 13.35 (s, 1H, -OH), 8.93 (s, 1H, -CH=N-), 7.33 (d, 2H, Ar-Haa'), 7.28 (d, 2H, Ar-Hbb'), 7.13 (d, 1H, Ar-Hc), 6.91 (t, 1H, Ar-Hd), 7.23 (d, 1H, Ar-He)
- **MS (m/z):** 282.12 (100.0%), 283.12 (21.8%), 284.12 (2.4%)

Table 3: Comparison between traditional synthesis and green techniques

Sr. No.	Parameter	Traditional method	Green techniques			
			1	**2a**	**2b**	**3**
1	Time required	1-1.5 hrs	15 min	15min	10 min	17 min
2	% yield	72-78%	96.90%	97.00%	98.30%	95.80%

DISCUSSION

Here we introduced techniques other than conventional route of synthesis for the synthesis of of 2-methoxy-6-[(4-methylphenyl) imino] methylphenol (2-M-4-MPIMP). The synthesized compound complies the spectroscopical studies. Among the different methods used in synthesis, compound 2b shows maximum yield with short duration of reaction. Other compound yields more than traditional route of synthesis in lesser time span.

CONCLUSION

Compared with traditional methods (table 3), these methods are more convenient and reactions can be carried out in higher yield, shorter reaction time with milder conditions, with no generation of pollution and safer to analyst.

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