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Grinding Synthesis of Schiff Bases Combined with Infrared Irradiation

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Solid-phase synthesis combined with infrared irradiation promoted the formation of a series of Schiff bases in the condensation reaction between substituted benzaldehydes and anilines, in the solvent free. Benzaldehydes and anilines, containing either electron withdrawing or electron-releasing groups, were evaluated their substituent effect on the formation of the Schiff bases. Moreover, this new procedure is environmentally benign because no solvent was employed in the transformations.

Key Words: Solid phase synthesis, Infrared irradiation, Solvent free, Imine, Biological activity.

INTRODUCTION

Schiff bases (C=N) play an important role because of their many uses[1], such as organic synthesis, biological activity, *etc*. Especially, imine is exist many compounds, especially nitro linked heterocyclic compounds[2], displayed diversity bioactive[3], for example, they exhibited herbicidal, fungicidal, insecticidal, antimicrobial and antiinflammatory activity. In addition, they are as well as valuable intermediates for the synthesis of biologically active products such as β-lactams, an important class of pharmaceutical compounds[4].

To date, many methods have been described for the preparation of Schiff base. Synthesis of Schiff base is often generally by refluxing the mixture of aldehyde (or ketone) and amine in organic medium[5].

The development of simple, cheap and clean processes in the area of 'green chemistry' is of increasing interest[6]. Chemists meet the controversy of synthetic procedures developing and economic to environment friendship, therefore solvent-free reactions have played strategic roles in methodologies of organic syntheses. Some are using microwave irradiation and ultrasound irradiation. So, we have employed solid phase synthesis combined infrared irradiation as an alternative energy source, working under solvent free conditions.

In this work, we have synthesized the Schiff bases using green method with a proper yield.

EXPERIMENTAL

Melting points were determined using a Yanaco MP-241 apparatus and are uncorrected. Infrared spectra were recorded on a Bruker Equinox55 spectrophotometer as potassium bromide tablets. ^{1}H NMR spectra were measured on a Bruker AC-P500 instrument (300 MHz) using tetramethylsilane as an internal standard and $CDCl_3$ as solvent. infrared irradiation using an apparatus similar to that reported by Pool and Teuben22 during 0-30 min.

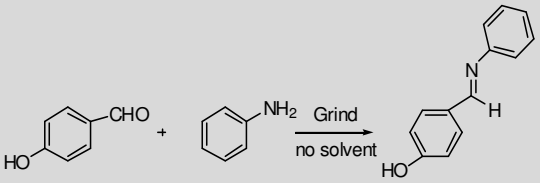
General procedure: The reactants in the molar ratio substitute benzaldehydes/substitute anilines = 1:1 were put in mortar. Then the mixture was exposured to the infrared irradiation under granding. The compound was irradiated for 0-30 min (Table-1) and the completion of the reaction is monitored by TLC examination. Yields are given in Table-1. Almost all derived Schiff base are known compounds and their spectral data, as well as melting points of solids, were in agreement with those known.

RESULTS AND DISCUSSION

Initially, the condensation of *p*-hydroxy benzaldehyde (**1a**) and aniline (**2a**) under solventless conditions was carried out at room temperature during 0.5 h and the corresponding N-benzylidenaniline (**3a**) was obtained in moderate conversion (48 %). However, when the reaction mixture was grinded, then irradiated with an infrared lamp (Guangming, 300 W, 220 V), the product was obtained with excellent conversion in only 10 min (61 %, Table-1). Moreover, the infrared irradiation efficiency was compared with the results obtained under thermal conditions.

In addition, to validate this new method and in order to identify the substituent effect on the formation of the Schiff bases under grinded combined with infrared irradiation and

TABLE-1
COMPARISON OF REACTIVITY BETWEEN *p*-OH BENZALDEHYDE (**1a**) AND ANILINE (**2a**) AT ROOM TEMPERATURE AND PROMOTED BY GRINDING



1a 2a 3a

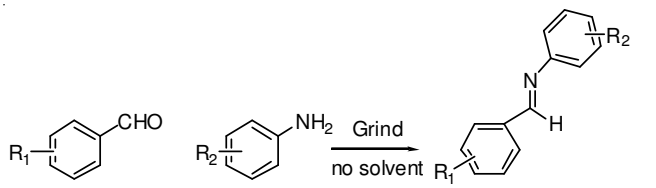
Time (min)	Conversion (%) Grind (20 min)/IR	Conversion (%) Grind
0	13	13
10	61	21
20	88	44
30	91	48

solventless conditions, several reactions using both electron-poor and electron-rich benzaldehydes and anilines (**Scheme-I**) were carried out. When substitute-benzaldehyde (**1b**), bearing an electron-releasing group was irradiated in the presence of **2a**, the conversion rate decreased (Table-2), obtaining **3b** in lower yield (70 %). However, when benzaldehydes with an electron-withdrawing group were employed, a more efficient conversion to the corresponding imine (entries 2 and 3) took place.

TABLE-2
COMPARISON OF YIELDS FOR IMINES **3b-3h** OBTAINED BY GRINDING (20 min)/IR IRRADIATION

No	Imines	R1	R2	Times (min)	Conversion (%)	Yield (%)
1	**3b**	4-$N(CH_3)_2$	H	0	31	71
				10	55	
				20	76	
				30	77	
2	**3c**	2-NO_2	H	0	81	94
				10	100	
				20	100	
				30	100	
3	**3d**	3-OCH_3	H	0	25	61
				10	65	
				20	70	
				30	70	
4	**3e**	H	2-NO_2	0	31	62
				10	46	
				20	69	
				30	68	
5	**3f**	H	3-NO_2	0	33	64
				10	42	
				20	72	
				30	72	
6	**3g**	H	4-NO_2	0	40	63
				10	55	
				20	70	
				30	70	
7	**3h**	H	4-CH_3	0	56	79
				10	65	
				20	85	
				30	82	

Moreover, some imines were obtained just upon mixing the reagents (Tables 1 and 2). These results can be attributed



1a-1g R1: **1a** = 3-CH_3, **2b** = 2-NO_2, **3c** = 2,4-Cl_2, **4d** = 3,4-$(OCH_3)_2$, **5e** = 4-OH, **6f** = 4-$N(CH_3)_2$, **6g** = H

2a-2g R2: **2a** = H, **2b** = 4-Cl, **2c** = 4-CH_3, **2d** = 3-OCH_3, **2e** = 2-NO_2, **2f** = 3-NO_2, 2g = 4-NO_2

3b-3g

R1	R2
3b = 4-$N(CH_3)_2$	H
3c = 2-NO_2	H
3d = 3-OCH_3	H
3e = H	2-NO_2
3f = H	3-NO_2
3g = H	4-NO_2
3h = H	4-CH_3

Scheme-I

to the high reactivity of some benzaldehydes and anilines, particularly those cases in which the reagent is liquid. Indeed, these results suggest that the efficiency of this new method is improved by electron-withdrawing substituents on the benzaldehyde ring and electron-releasing substituents on the aniline ring. Therefore, the rate of condensation of substituted benzaldehydes with anilines promoted by this new method, resembles the corresponding results obtained under a homogeneous phase.

Finally, the versatility of this novel option to obtain the Schiff bases was demonstrated by the preparation of a large number of target molecules **3i-3p** (Table-3). Most yields were high and the products were readily isolated and purified by crystallization. However, for some benzylideneanilines (*e.g.*, **3n** and **3o**), the yields were rather moderate.

TABLE-3
YIELD (%) OF SCHIFF BASES UNDER GRINDING/IR

Substrate	R_1	R_2	Yield
3i	*p*-$CH_3C_6H_4$	*p*-$NO_2C_6H_4$	80.4
3j	*p*-$OCH_3C_6H_4$	*m*-$NO_2C_6H_4$	75.6
3k	2,4-$Cl_2C_6H_3$	*o*-Cl C_6H_4	84.2
3l	*p*-OHC_6H_4	*p*-$OCH_3C_6H_4$	83.1
3m	*o*-$OCH_3C_6H_3$	*p*-$OCH_3C_6H_4$	82.6
3n	3,4-di$CH_3C_6H_3$	*o*-$OCH_3C_6H_3$	74.3
3o	3,4-diOCH_3 C_6H_3	*o*-$OCH_3C_6H_3$	72.6
3p	$N(CH_3)_2C_6H_4$	*p*-$CH_3C_6H_4$	82.3

Conclusion

A new, simple, efficient and environmentally benign method for the preparation of substituted N-benzylideneaniline derivatives, *via* condensation of several benzaldehydes and anilines, by means of grinding combined with infrared irradiation under solvent-free conditions, was developed. Additional advantages of the method were lower cost, ease of work-up and the fact that activation of the reaction by an acid catalyst was unnecessary.

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