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Synthesis of Schiff Bases via Environmentally Benign and Energy-Efficient Greener Methodologies

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Abstract: Non classical methods (water based reaction, microwave and grindstone chemistry) were used for the preparation of Schiff bases from 3-chloro-4-fluoro aniline and several benzaldehydes. The key raw materials were allowed to react in water, under microwave irradiation and grindstone. These methodologies constitute an energy-efficient and environmentally benign greener chemistry version of the classical condensation reactions for Schiff bases formation.

Keywords: Schiff bases, Microwave irradiation, Grinding, Greener chemistry approaches.

Introduction

Among the challenges for chemists include discovery and development of novel and simple environmentally safe chemical processes for selective synthesis by identifying alternative reaction conditions and solvents for much improved selectivity, energy conservation and less or no toxic waste generation and inherently safer chemical products. Therefore, to address depletion of natural resources and preservation of ecosystem it is just urgent to adopt so called “greener technologies” to make chemical agents for well being of human health. Schiff's bases are reported to show characteristic biological activities including antibacterial, antifungal, anticancer and herbicidal properties¹⁻⁶. Other application of Schiff's bases includes industrial synthesis of high value life saving beta lactam⁷ antibiotics from class of penicillins and cephalosporins.

In recent years, environmentally benign synthetic methods have received considerable attention. Verma *et al*⁸ reported synthesis of enamines and imines under microwave irradiation accompanied with solvent less conditions. Kaupp *et al*⁹ reported the synthesis of Schiff bases using water as a solvent. In continuation of our ongoing program¹²⁻¹³ towards

ecofriendly green synthesis, it was thought worthwhile to synthesize Schiff bases utilizing greener methodologies.

Experimental

Melting points were determined in open capillary tubes and are uncorrected (Table 1). The purity of the compound was checked on silica-gel-coated Al plates (Merck). IR spectra were recorded in KBr on a Perkin Elmer Spectrum RX-1 FT-IR spectrophotometer. ^1H -NMR spectra was measured on Advance Bruker DRX-300 and JEOL AL300 FTNMR using solution in hexadeuterio dimethyl sulfoxide (DMSO) with trimethyl silane (TMS) as the internal standard, chemical shifts are given in δ (ppm). The values are recorded in the Table 2. Nitrogen was estimated by Dumas method. Microwave irradiations were carried out in an unmodified IFB domestic microwave oven. All chemicals were of analytical grade.

General procedure

3 Different greener methodologies that were adopted and studied for preparing Schiff bases are described below (Scheme 1).

Water based synthesis (Method A)

A mixture of 3-chloro-4-fluoro aniline (5 mmol, 0.71 g) and substituted benzaldehydes¹⁻⁹ (5 mmol) was stirred in 10 mL water for 30 min at room temperature in a few minutes, the temperature of the reaction mixture rises due to the heat evolved during this exothermic reaction, but it should not allowed to exceed 20 °C above the room temperature. The crystalline product so obtained was filtered, washed with water and dried. The product was obtained in good yield (80-90%).

Microwave “jump start” synthesis (Method B)

A mixture of 3-chloro-4-fluoro aniline (0.145 g, 0.1 mmol), substituted benzaldehydes¹⁻⁹ (0.1 mmol), and piperidine (0.02 mmole) were taken in DMSO (3 mL) in a round bottom flask. Reaction mixture was irradiated in MW oven for 3-6 min. On cooling the reaction mixture, a good yield (73-86%) of Schiff bases was obtained which was recrystallized from absolute ethanol.

Grindstone “friction activated” synthesis (Method C)

A mixture of 3-chloro-4-fluoro aniline (1 mmol, 0.15 g) and substituted benzaldehydes¹⁻⁹ (1 mmol) was grinded in a mortar with a pestle made of porcelain for 5-10 min. The mixture turns pasty after few minutes of grinding. Leave the reaction mixture for overnight. The solid product thus obtained (53-70%) was recrystallized from absolute ethanol.

Scheme 1.

Results and Discussion

Formation of Schiff base is an exothermic reaction. So rather than providing energy in the form of heat, their synthesis has been scaled up towards green chemistry domain by circumventing the use of water as a solvent, microwave irradiations and friction activated

synthesis by grinding. And out of the above adopted greener methodologies, water based reactions have a great virtue as water is the abundantly available solvent, indeed a cheaper medium for reactions. Reactions in aqueous media are not only environmentally benign but easy to handle and devoid of any corrosive or carcinogenic effect. Moreover, in this protocol, the products obtained are in high yield, pure and easily isolable. In conclusion, from our point of view, water has been proved here as a suitable “green solvent” for the synthesis of Schiff bases and increase in % yield is in following order: Method C < Method B < Method A.

Table 1. Physical and analytical data of compounds.

S.No	Aldehydes *	M.P, °C	Colour	N, % Found, Calcd.	Yield, %		
					A	B	C
1	3,4-Di-OCH ₃ BD	110	White	4.38(4.43)	81.37	73.64	57.00
2	2-Cl BD	63	Peach	2.96(2.98)	82.00	77.10	53.72
3	4-Cl BD	124	White	2.96(2.99)	90.00	79.52	68.40
4	Piperonal	88	White	3.22(3.24)	89.36	84.30	65.16
5	Vanillin	86	White	5.57(5.52)	87.20	85.12	69.23
6	2-OH BD	138	Yellow	3.58(3.60)	87.79	79.00	70.25
7	4-OH BD	172	Cream	3.58(3.62)	84.65	83.42	63.80
8	3-NO ₂ BD	140	White	10.05(9.98)	89.72	84.89	64.32
9	2-OH-1-ND	122	Yellow	4.63(4.68)	85.81	86.14	55.93

Note*: BD=Benzaldehyde, ND=Naphthaldehyde

Table 2. Characterization (IR and ¹H NMR) data of compounds.

Compd No.	IR (ν in cm ⁻¹)	¹ H NMR (δ in ppm)
1	1018 (C-Cl), 1264-1138 (C-F), 1576 (-CH=N-), 1620 (Ar-(C-C)), 2935(-OCH ₃).	2.51 (DMSO), 3.36 (s, 3H, OCH ₃), 3.83 (s, 3H, OCH ₃), 7.54-7.24(m, 6H, Ar-H), 8.54(s, 1H, -CH=N-).
3	1057 (C-Cl), 1412-1171 (C-F), 1571 (-CH=N-), 1617 (Ar-(C-C)).	2.51 (DMSO), 7.33-7.95(m, 7H, Ar-H), 8.67(s, 1H, -CH=N-)
6	976 (C-O), 1052 (C-Cl), 1273-1150 (C-F), 1494 (-OH), 1510 (-CH=N-), 1618 (Ar-(C-C)).	2.51 (DMSO), 6.96-7.54(m, 7H, Ar-H), 8.96(s, 1H, -CH=N-), 12.59(s, 1H, OH).

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