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RESEARCH ARTICLE

Novel Synthesis of Schiff Base of 4 - Nitro Toluene with Aldehyde

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ABSTRACT

In the present study an intermolecular reductive Schiff base formation from nitroarenes and benzaldehydes to yield diarylimines is carried out in the presence of iron powder and dilute acid In this paper we propose the synthesis of (*E*)-4-methyl-N-(3,4,5-trimethoxybenzylidene) benzenamine in different methods and compare economically attractive method for synthesis of Schiff bases.

KEYWORDS

4-nitro toluene**,** Synthesis, Schiff base, Comparison

INTRODUCTION

The classical synthesis of imines, originally reported by Schiff, involves condensation of a carbonyl compound with an amine under azeotropic distillation to separate the liberated water.

Imine bond formation proceeds with dehydration within a single molecule, or between two molecules containing amino and carbonyl groups and a C=N bond is formed either intra- or in It is common to drive the reaction towards completion by removing H_2O as it is formed, either by separating it physically or by adding a drying agent.

Note that in the reaction between a nucleophile and a carbonyl group the carbon atom changes hybridization from sp2 (trigonal planar) to sp3 (tetrahedral). That means that the attack of the nucleophile occurs at an angle of approximately 109° (tetrahedral angle) to the existing C=O bond.

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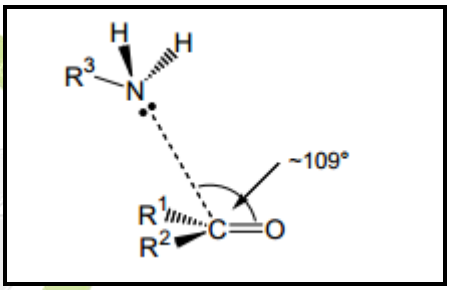


Schiff bases are typically formed by the condensation of a primary amine and an aldehyde. Schiff bases are important intermediates for the synthesis of various bioactive compounds. Furthermore, they are reported to show a variety of biological activities including antibacterial, antifungal, anti cancer and herbicidal activities[1-5].

On the other hand, Primary amines are fundamental material for synthesis of various Schiff base ligands which used as chiral auxiliaries in asymmetric synthesis. Metal complex Schiff bases have also been used in oxidation reactions [6].

In view of these facts we can clear about that Schiff base are important not only in medical chemistry, but also in organic synthetic

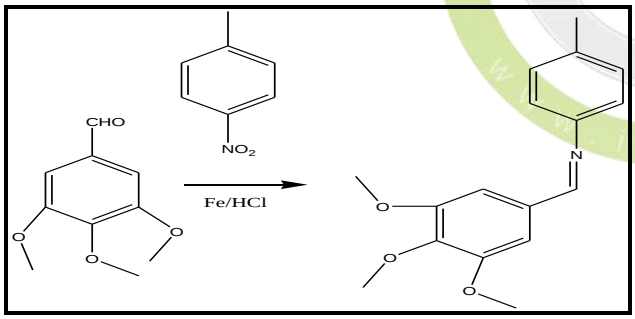
chemistry. Schiff base perhaps are synthesized in various method.

Traditional formation of Schiff bases from nitroarene starting materials requires a two-step process in which the nitroarene is first reduced to the aniline, then isolated, and subsequently condensed with the desired carbonyl. Recently, catalytic Schiff base formation from nitroarenes and carbonyls has been reported.[7,8]

Tandem nitroarene reduction and intramolecular Schiff base condensation to give heteroarenes has been reported using iron in aqueous media.[9-11] surprisingly, the breadth of this methodology in an intermolecular application has not been previously reported.

Herein we wish to report our findings of a tandem iron reduction of nitroarenes and subsequent condensation of arylaldehydes under mild reaction conditions.

In this paper, we will research which the simple way to synthesize Schiff base of 4 nitro toluene with 3, 4, 5 tri methoxy benzaldehyde via reduction spontaneously condense with an aldehyde *in situ.*



EXPERIMENTAL

Melting points were uncorrected and were measured with micro-melting point apparatus XT-4. IR spectra (KBr) were obtained on a Thermo Nicolet Nexus 470 FT-IR spectrometer. 1H NMR spectra were determined on a Varian Mecurry 300 spectrometer using CDCl3 as solvent and tetramethylsilane (TMS) as internal reference. Microwave irradiation was carried out with commercial LG domestic microwave oven (1000W). All reagents were commercially available.

Preparation of Schiff Base ((*E*)-4-methyl-N-(3,4,5-Trimethoxy benzylidene)benzenamine)

Method 1

A mixture of p-nitro toluene (0.107g, 1mmol), 3,4,5-trimethoxybenzaldehyde(0.196g, 1mmol), neutral alumina(1g) and dichloromethane(2ml) in conical flask was introduced into the microwave oven and irradiated for 4min (output power at 20%). After cooling, the solid was recrystallized from ethyl acetate/petroleum ether to provide (0.242g, 85%) of the title compound as a white lamellar crystal.

Method 2

A solution of 3,4,5-trimethoxybenzaldehyde(1g, 5.09mmol) in benzene (10mL) was added dropwise in a solution of p-nitro toluene (0.54g, 5.09mmol) in benzene (5mL). The mixture was heated in reflux temperature, until no water appear (monitor with a Barrett distilling receiver). The solvent was removed in vacuo, and the residual was recrystallized from EtOAc to obtain the title compound (1.05g, 72%) as a white lamellar crystal.

Method 3

To a stirred solution of 3,4,5-trimethoxybenzaldehyde (1g, 5.09mmol) and p-nitro toluene (0.54g, 5.09mmol) in 10ml DCM, anhydrous MgSO4 was added. The reaction mixture was stirred 2 hours at room temperature. The resulting mixture was filtered through a sintered glass funnel with the aid of two 2ml portions of DCM, and then the filtrate was concentrated under reduced pressure by rotary evaporation at room temperature to afford yellow oil. The residual was dissolved in ethanol heated in an 80°C water bath while hot water was added with stirring. The resulting solution was allowed to cool to room temperature and then was cooled in an ice-water bath for 2 hr. Filtration provide the title compound (1.09 g, 75%) as white lamellar crystal.

Method 4

HCl (0.13 mL, 4.5 mmol) was added to a mixture of 4 nitro toluene (0.986 gr, 0.72 mmol)

3, 4, 5-trimethoxybenzaldehyde (1.41gr, 0.72 mmol), and iron powder (0.409 g, 7.32 mmol) in 24 mL of EtOH–H2O (2:1 v/v) solution. The reaction was heated to 65 °C for 1.5 h before being filtered while hot. The filtrate was extracted using CH2Cl2 (2 × 20 mL) after which the organic layers were combined, dried over MgSO4, filtered, and concentrated in vacuo to yield 2.04g (85%).

RESULTS AND DISCUSSION

Compared with other methods of synthesis, method 4 is excellent yield of products in crystalline form, short reaction time, simplicity of work up procedure and no use of any type of hazardous solvents. Simply this reaction is economically attractive method for synthesis of Schiff base compounds. It is very suit for industrial manufacture which consumes the least time to finish the synthesis of Schiff base. Diarylimine have been prepared by a simple and environmentally friendly reductive imination procedure. This process tolerates various functional groups and often proceeds quantitatively with no need for purification. This methodology uses only Fe (0) in acidic $EtOH/H_2O$ as a reductant for nitroarenes, which upon reduction spontaneously condense with an aldehyde *in situ*. Above Schiff base compounds shows inherent new generation of series of pharmaceutically important compounds.

Table 1: The compare of three way of synthesis of Schiff base

Method	Reaction conditions	Time	Yield
1	Microwave irradiation	4-6 min	85%
2	Reflux	7-8 h	72%
3	Rt stirr	4 h	75%
4	*In situ* red	4 h	85%

Melting Point: 91–93ºC.

TLC: Rf (silica; ethyl acetate: petroleum ether, 1:4) 0.40.

IR(KBr cm^{-1}): 2954, 2934, 2835, 1624, 1558, 1506, 1460, 1330, 1127, 1003.

1H-NMR (300 MHz, $CDCl_3$): δ= 2.35 (s, 3H, -CH_3). 3.90 (s, 9H,-(OCH_3)3), 7.11(s, 6H, PhH). 8.31 (s, 1H, N=CH).

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