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NOVEL ONE POT TANDEM APPROACH FOR THE RAPID AND EFFICIENT SYNTHESIS OF SCHIFF BASES

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ABSTRACT

In the present study of one pot tandem reductive Schiff base formation from nitroarenes carried out in the presence of iron powder and dilutes acid. A new efficient and environmental friendly procedure for the synthesis of salicylaldehyde-based Schiff bases. The present work involves condensation of salicylaldehyde with various aromatic nitro derivatives. All the compounds synthesized were adequately characterized by their elemental analyses and spectral IR, ¹H-NMR. All the structures of the above compounds were in good agreement with spectral and analytical data.

KEY WORDS: Tandem reaction, Intermolecular reductive Schiff base, Green chemistry, Spectral studies, Nitro derivatives.

INTRODUCTION

The chemistry of biological science has produced a number of compounds that are now employed as antibacterial agents. Such type of compounds revealed great promise in this area is the Schiff bases. 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. Multistep synthesis of specialty chemicals normally requires stoichiometrically excess reagents, leading to high effluent loads.

Hence, search is now on for clean, non-hazardous and 'green' chemical transformations, which will have negligible bi-products and high selectivity. There has been growing concern over the environmental impact of chemicals so that cleaner green reaction conditions in synthetic processes have been advocated. The tight legislation to maintain greenness requires us to prevent the generation of waste, avoid use of auxiliary substances (e.g., organic solvents, additional reagents), and minimize the energy requirement. The chemistry of the carbon-nitrogen double bond plays a vital role in the progress of chemical science. Schiff-base compounds are used as fine chemicals and medical substrates [1].

Schiff base compounds are very popular ligands because of their easy formation and rich coordination chemistry with a large variety of metal ions that has allowed their use as catalysts in different asymmetric reactions [2, 3]. Salicylaldehyde-based Schiff bases have been screened for antibacterial activity against several bacterial strains such as *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* [4].

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 [5, 6]. It is worthwhile to mention here that the synthesis of these Schiff bases is known [7–10] in the literature involving tedious process using methanol/ethanol as solvent and requires longer reaction time. In general the reported syntheses of Schiff bases involving condensation reactions requires drastic conditions namely, use of Dean Stark apparatus, use of catalyst, higher temperature, and longer reaction time [11,12]. In conclusion, we describe a green and efficient method for the synthesis of Schiff bases with easy workup; facile conditions, fast reaction rates, good yields, and selectivity of the reaction make the present methodology attractive.

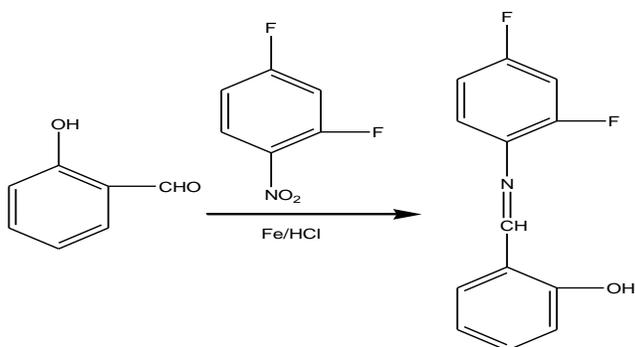
MATERIALS AND METHODS

Experimental

Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded in KBr on a Perkin Elmer Spectrum RX-1 FTIR spectrophotometer. ¹H-NMR spectra were measured on Jeol JNM-ECX400P at 400 MHz. All chemicals used were of analytical grade.

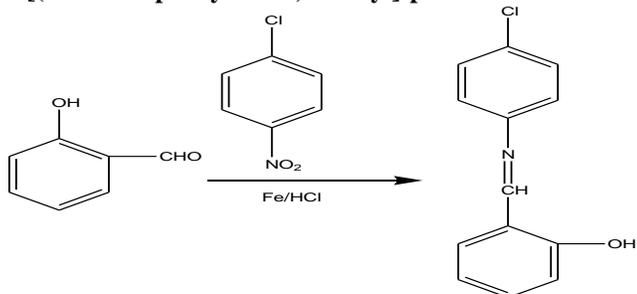
Synthesis of Schiff base

2-[(2, 4-Difluoro-phenylimino)-methyl]-phenol



Hydrochloric Acid (4.5 mmol) was added to a mixture of 2, 4 difluoro nitro benzene (0.72 mmol), salicylaldehyde (0.72 mmol), and iron powder (7.32 mmol) in 26 mL of MeOH– H₂O (2:1 v/v) solution. The reaction was heated to 65°C for 4-5 h before being filtered while hot. The filtrate was extracted using chloroform (100 ml) after which the organic layers were combined, dried over MgSO₄, filtered, and concentrated in vacuo to yield Yellow crystals (68%) ; mp . 96–98°C. IR (KBr, cm⁻¹): 2915, 1619, 1495, 1288, 1149, ¹HNMR (400 MHz, CDCl₃): δ 12.79 (1H, s), 8.72 (1H, s), 7.48 (2H, d), 7.20 (1H, m), 7.14 (1H, t), 6.90 (3H, m).

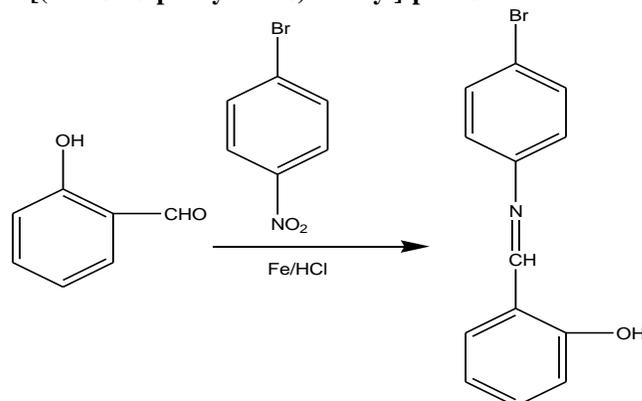
2-[(4-Chloro-phenylimino)-methyl]-phenol



Hydrochloric Acid (4.5 mmol) was added to a mixture of 4 chloro nitro benzene (0.72 mmol), salicylaldehyde (0.72 mmol), and iron powder (7mmol) in 30 mL of MeOH– H₂O (2:1 v/v) solution. The reaction was heated to 65°C for 4.5 h before being filtered while hot. The filtrate was extracted using chloroform (100 ml) after which the organic layers were combined, dried over MgSO₄, filtered, and concentrated in vacuo to yield golden solid (60%) M.p. 70–72 °C, IR (KBr, cm⁻¹): 2929, 1619, 1488, 1289, 838, ¹HNMR (400 MHz, CDCl₃): 13.14 (1 H,

s), 8.39 (1 H, s), 7.48 (2 H, d), 7.32 (2 H, d), 7.27(2 H, dd), 7.12 (1 H, d), 6.90 (1 H, t).

2-[(4-Bromo-phenylimino)-methyl]-phenol



Hydrochloric Acid (4.5 mmol) was added to a mixture of 4 bromo nitro benzene (0.72 mmol), salicylaldehyde (0.72 mmol), and iron powder (7.32 mmol) in 26 mL of MeOH– H₂O (2:1 v/v) solution. The reaction was heated to 65°C for 4-6 h before being filtered while hot. The filtrate was extracted using chloroform after which the organic layers were combined, dried over MgSO₄, filtered, and concentrated in vacuo to yield greenish crystals (yield 60%); M.p. 98–100 °C, IR (KBr, cm⁻¹): 2929, 1617, 1481, 1285, 826, 753. ¹HNMR (400 MHz, CDCl₃): (1H, s), 8.57 (1H, s), 7.52 (2H, d), 7.30 (2H, m), 7.18 (2H, d), 7.07 (1H, d), 6.98 (1H, t).

CONCLUSION

This methodology uses only Fe powder in acidic MeOH/H₂O as a reducing agent for nitro derivatives which upon reduction spontaneously condense with an aldehyde in situ.

Our present work brings forth a novel method for the synthesis of Schiff bases in which offers significant improvements over existing conventional procedures. This simple technique affords various Schiff base derivatives with short reaction times, excellent yields and without formation of undesirable side products, operation simplicity, cleaner reaction and easy work-up. All spectroscopic analysis confirmed the proposed structures for these compounds.

The synthesized compounds therefore, present a new scaffold that can be used to yield potent antimicrobial compounds. It can be concluded that these compounds certainly holds great promise towards good active leads in medicinal chemistry.

ACKNOWLEDGEMENTS

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