Improved Synthesis of *Ferrocenyl aniline*

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Summary: Comparative synthesis of ferrocenyl aniline from nitro phenyl ferrocene using different reducing agents, like Sn/HCl, Zn/HCl, Pd-charcoal/NH_2-NH_2 and Zn/formic acid, has been studied and found that Zn/formic acid system yields highest ferrocenyl aniline as compare to the rest of reducing agents.

Introduction

The ferrocene has several novel applications due to its ease of derivatization, stability, redox activity and spectroscopic properties. Ferrocene derivatives have potential application as biosensors [1-3], potential unnatural anticancer [4-6] and anti malarial drugs [7], the substitution of ferrocene in anti cancer drugs enhance their activity [8, 6]. Ferrocene derivatives also have potential for use as surfactant [9], corrosion inhibitors [10] and catalyst for the free radical polymerization of methyl methacrylate and styrene [11]. Polymeric materials containing ferrocene derivatives have novel properties and play an important role in the synthesis of conducting organic materials [12] and Supra molecular Synthon [13].

Due to the novel characteristics of ferrocene derivatives the synthetic procedure used for attaining high attention. Lot of work has been done in derivatizing the ferrocene [14]. To derivatize ferrocene; amine, carbonyl and carboxylic acid functionalities are introduced [15]. Ferrocenyl aniline is synthesized by the reduction of nitro phenyl ferrocene. Ferrocenyl aniline is the intermediate for the synthesis of ferrocene containing liquid crystals and ferrocene containing Schiff bases etc. [16].

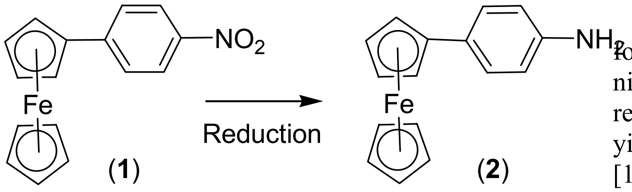

Fig. 1: Reaction for the synthesis of ferrocenyl aniline.

Results and Discussion

The synthesized ferrocenyl aniline (**2**) is characterized by melting point, FT-IR and NMR spectroscopic techniques. The results are in agreement with literature [17-18].

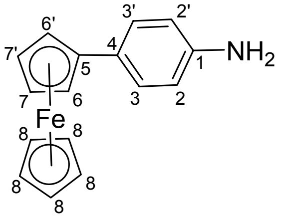

Fig. 2: Labeling of ferrocenyl aniline for ^{1}HNMR and ^{13}CNMR.

Table-1: ^{1}HNMR and ^{13}CNMR data of ferrocenyl aniline.

Carbon no.	δ value in ppm	Proton no.	δ value in ppm
1	**144.57**	**NH_2**	**3.66 (s)**
2, 2'	**115.21**	**2, 2'**	**7.33 (m)**
3, 3'	**127.18**	**3,3'**	**6.67 (m)**
4	**129.00**	**6,6'**	**4.56 (t, 1.8Hz)**
5	**86.56**	**7,7'**	**4.26 (t, 1.8Hz)**
6, 6'	**68.23**	**8**	**4.06 (s)**
7, 7'	**65.83**		
8	**69.42**		

Different reduction procedures are reported for the synthesis of ferrocenyl aniline from 4-nitrophenyl ferrocene (**1**). Hu Ping, *et al.* (2001) [17] report the reduction of (**1**) with granular tin and HCl yielding 76% ferrocenyl aniline, Zaheer M. (2008) [18] reduce (**1**) using Pd-charcoal and hydrazine with 78% yield, but we reduce (**1**) with Zn/formic acid which show much higher (94%) yield than ever reported, we also tried Sn-powder/HCl and Zn-dust/HCl for the reduction (**1**), comparative results are shown in Table-2.

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Table-2: Comparative yields of reduction of 4-nitrophenyl ferrocene (**1**).

Entry no.	Reducing agent	Conditions	Yield	Reference
1	**Zn dust + conc. HCl**	**8 hours reflux**	**65 %**	**This work**
2	**Sn Powder + conc. HCl**	**8 hours reflux**	**79 %**	**This work**
3	**Zn dust + HCOOH in methanol**	**3 hours stirring**	**90 %**	**This work**
4	**Zn dust + HCOOH as solvent**	**5 minutes stirring**	**94 %**	**This work**
5	**Sn Granular + conc. HCl**	**8 hours reflux**	**76 %**	**Hu Ping, *et al.* (2001) [17]**
6	**Pd charcoal + hydrazine**	**8 hours reflux**	**78 %**	**Zaheer M. (2008) [18]**

This work shows the better reducing properties of Zn/formic acid system for the nitro functionality which in agreement with the work of D. Gowda *et al*. (2001) [19] this is because, the nitro group has good oxidizing behavior due to which strong reducing agents like Sn/HCl, Pd-charcoal/hydrazine and Zn/HCl gives much quantities of side products lowering the yield of reaction. But as the Zn formic acid system has mild reducing properties so gives higher yield of amino product. Due to the good oxidizing properties of nitro group and mild reducing property of Zn formic acid system this system is selective for the reduction of nitro group, other functionalities like COOH, CO, CONH2, CN, CHO, OH and un-saturation etc. dose not reduce with this system [19].

Experimental

Materials

Ferrocene, p-nitro aniline, sodium nitrite and all the other chemicals including solvent are purchased from Aldrich and used as such. 4-nitrophenyl ferrocene synthesized by literature reported method.[20] Melting points measure with BIO COTE Model SMP10 melting point apparatus, FTIR spectra taken with Thermo Scientific Nicolet-6700 FTIR spectrometer and NMR spectrum taken on BRUKER AVANCE 300MHz NMR spectrometer.

Synthesis of Ferrocenyl aniline (**2**)

Conc. HCl (30 mL) added to the suspension of Zn dust (2.62 g, 40.0 mmol) in solution of 4-nitrophenyl ferrocene (2.0 g, 7.0 mmol) in ethanol (100 mL). The reaction mixture refluxed for 8 hours and monitored on TLC. Reaction completed with changing color from violet to orange. Reaction mixture filtered in hot and volume of filtrate reduced to 30ml using rotary evaporator and further diluted with water NaOH solution by adjusting pH at 14. Ferrocenyl aniline then extracted from that mixture with CH2Cl2 (6 x 50 mL). Solvent evaporated and product re-crystallized from pet ether of boiling range (60-80 ºC) to give 4-ferrocenylaniline as a red-orange solid. (1.17 g, 65%)

Same procedure adopted as in entry 1. By replacing Zn dust with Sn powder (4.50 g, 40.0 mmol). Yield (1.42 g, 79%)

Suspension of Zn dust (2.62 g, 40.0 mmol) was made in solution of 4-nitrophenyl ferrocene (2.0 g, 7.0 mmol) in 100 mL methanol. Formic acid (3.82 mL, 100 mmol) added drop wise to the suspension, stirred for 3 hours and monitored on TLC. On completion reaction mixture was rotary evaporated, orange yellow crude solid dissolved in 100 mL CH_2Cl_2 and washed with water (4 x 100 mL). Solvent evaporated and product re-crystallized from pet ether of boiling range (60-80 ºC) to give 4-ferrocenylaniline as a red-orange solid. (1.62 g, 90%)

Zn dust (2.62 g, 40.0 mmol) was added to the solution of 4-nitrophenyl ferrocene (2.0 g, 7.0 mmol) in 50 mL Formic acid, stirred vigorously for 5 minutes and monitored on TLC. On completion reaction mixture was rotary evaporated, orange yellow crude solid dissolved in 100 mL CH_2Cl_2 and washed with 2.0% NaOH solution (3 x 100 mL) and the water (4 x 100 mL). Solvent evaporated and product re-crystallized from pet ether of boiling range (60-80 ºC) to give 4-ferrocenyl aniline as a red-orange solid (1.69 g, 94%). Melting point of the product of all entries was in the range of 156-159 ºC. FT-IR (cm^{-1}): 3435, 3372, 3354, 1616, 1528, 1455, 1103, 999, 814.

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