

PREPARATION OF 4-AMINODIPHENYLAMINE BY A ONE-POT REACTION

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Abstract: Aminodiphenylamine and its derivatives have been known to be used as dye intermediates and antioxidant of rubber. This study investigated the preparation of 4-aminodiphenylamine via two step reaction in a one pot procedure. For the first step, the coupling reaction of nitrobenzene and aniline was carried out in an aqueous solution of tetramethylammonium hydroxide, sodium hydroxide, and potassium hydroxide as the base. The major products of this one step reaction include nitro-, nitroso-, and diphenylamine derivatives. Azobenzene and its derivatives were by-products. The effect of catalyst on the reaction of nitrobenzene with aniline was investigated. It was also observed that the property and position of nitroarene and aminoarene substituent groups impacted product yield. Subsequently, the intermediate product mixture without workup could be reduced with Raney Ni-Al alloy and Al powder in a dilute aqueous alkaline solution, affording the objective aminodiphenylamine derivatives. A high yield of 4-aminodiphenylamine can be obtained in a one pot operation via aniline and nitrobenzene reactions as well as reduction of crude mixture using a Raney Ni-Al alloy and aluminum powder as the reductive agents in a dilute aqueous alkaline solution.

Keywords: 4-Aminodiphenylamine, coupling reaction, one-pot reaction, Raney Ni-Al alloy, aniline, nitrobenzene

Introduction

4-Aminodiphenylamine (4-ADPA) is a useful intermediate in the synthesis of dye intermediates and rubber antioxidants. Many processes can yield this compound¹⁻⁶. However, these processes often require several steps that heavily depend on halogenated reagents. A new route to synthesize 4-ADPA was reported, via reactions with aniline and nitrobenzene³⁻⁴. This process, however, must be conducted under anhydrous conditions in the first step, while the second step, a reduction, must be carried out by using a Pt catalyst and hydrogen under high pressure. Its high cost is not attractive for commercial processes. It has been reported that Raney Ni-Al alloy in aqueous solution was effective for dehalogenation of aromatic halides⁷⁻⁸. This study focuses on improving this reaction process, reporting a convenient and economic preparation of 4-ADPA **3** with aniline **1** and nitrobenzene **2** in a one-pot procedure (Scheme 1).

Experimental

In a typical procedure, aniline **1** (5mL, 54mmol) and nitrobenzene **2** (0.5mL, 4.9mmol) were added to a stirred mixture solution of 25wt% aqueous solution of tetramethylammonium hydroxide (1.8g, 4.9mmol) and sodium hydroxide (2.9g, 70mmol). A dark purple solution formed immediately after contact. The reaction mixture was stirred at 80°C for 2 h. Analysis of the reaction mixture by GC indicated relative product yields and nitrobenzene conversion. The relative yields of products were 4-nitrodiphenylamine (4-NDPA) **4** (43%), 4-nitrosodiphenyleamine (4-NODPA) **5** (31%), 4-ADPA **3** (19%), azobenzene **6** (7%) and azoxybenzene (trace). 92% of nitrobenzene had been consumed. Subsequently, water (80mL) was added to the reaction mixture. The Raney Ni-Al alloy (1g, 27mmol) and Al powder (1.5g, 56mmol) with water (55mL) was gradually added to the reaction mixture over 30 min. After the reaction had been stirred at 80 °C for 3h, the reaction mixture was found by GC analysis to consist of 4-ADPA and aniline. The reaction mixture was cooled to room temperature, filtered through Celite, and washed with dichloromethane (50mL). The metal powders were

filtrated out and the resultant was extracted with dichloromethane (50mL). The organic layer was dried over anhydrous MgSO_4 , evaporated *in vacuo*. The residue was subjected to distillation under reduced pressure (100°C at 0.5-1Torr) to yield 4-ADPA (0.78g, 4.2mmol, 86%) and aniline (3.91g, 42mmol, 78%).

Techniques used: GC, GCMS, ^1H NMR

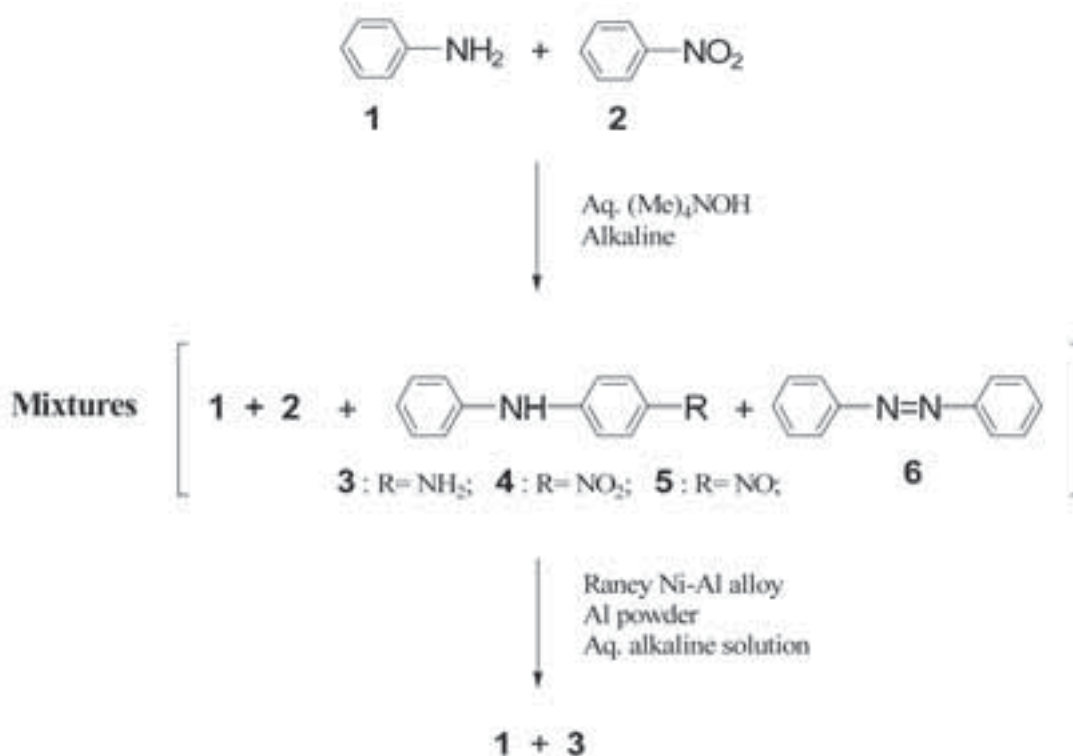
Results and Discussion

4-ADPA **3** was prepared in two subsequent reaction steps carried out in a one-pot operation (Scheme 2). Nitrobenzene **2** was first reacted with aniline **1** at $80-100^\circ\text{C}$ for 2-4 hours in the presence of 10-35 wt% aqueous solution of tetramethylammonium (TMA) hydroxide and sodium hydroxide, as additional base. The major products in this first step were 4-NDPA **4**, 4-NODPA **5**, targeted product 4-ADPA **3** as well as byproduct azobenzene **6**. A nitrobenzene **2**

conversion of near 100% was achieved under these mild reaction conditions. It was observed that with an increasing reaction temperature under otherwise identical reactions, yields of compounds **4**, **5** and **3** were increased. The amount of TMA hydroxide also affected the yields of compounds **4**, **5** and **3**. As shown in Table 1, with an increase of the mole ratio of TMA hydroxide to **2** from 0.3 to 1, the conversion of nitrobenzene **2** was increased from 30% to 91%. On the other hand, it has been reported³⁻⁵ that the amount of water in the reaction system of nitrobenzene - benzamide and nitrobenzene - aniline, in the presence of TMA hydroxide dehydrate, have a significant effect on the yield of these products. It has been previously shown that the upper limit of protic material allowed in the reaction was 4% H_2O , based on the volume of the reaction mixture³. However, in this study, 10wt% TMA hydroxide was added to the reaction mixture



Scheme 1



Scheme 2

with adequate yield, and a suitable amount of base, for example, sodium hydroxide was added as well. Although the amount of water was close to 40 v/v%, over 90% conversion of nitrobenzene **2** was obtained (Entry 4, 5). The total yield of 4-NDPA **4**, 4-NODPA **5** and 4-ADPA **3**, which were products that might be reverted to 4-ADPA **3** in the second step of the procedure, was over 80%. The key factor is to control the amount of added base. It is also interesting to note that 4-ADPA **3** is already present after the first step reaction.

The effect of substituent group in nitrobenzene on the reaction was investigated in the past study ⁹. The nitrobenzene derivatives such as *o*-, *m*- and *p*-nitrotoluenes, nitroanisoles and nitrochlorobenzene were reacted respectively with aniline at the same condition. It was observed that the property and the position of substituent group in nitrobenzene effected on the kind and the yield of products. This result is similar to the reaction of aniline with nitrobenzene. In this study, we used the Raney Ni-Al alloy as well as Al powder in a dilute aqueous alkaline solution as the hydrogenation source. Since a base had already been added in the first reaction step, the concentration of base in the alkaline aqueous solution in the second reaction step was adjusted by adding various

amounts of water. The reduction of 4-NDPA **4** and 4-NODPA **5** was carried out easily in a dilute aqueous alkaline solution. The reaction mixture of the first step could be used without workup for the second reaction step. The nitro- and nitroso- moieties could be reduced. Additionally, azobenzene **6** and unreacted nitrobenzene **2** could be recycled to aniline **1** by the reduction step. The best yield of 4-ADPA **3** was 94% based on nitrobenzene **2**, where over 70% aniline **1** could be recycled.

Conclusion

High yield 4-ADPA can be obtained in a one-pot procedure by coupling aniline and nitrobenzene reactions with reduction of the crude reaction mixture via Raney Ni-Al alloy and aluminum powder as reductive reagent in a dilute aqueous alkaline solution. The yield of 4-ANPA is 94%. A 10% aqueous solution of tetramethylammonium hydroxide can be used as catalyst in the first step coupling reaction. The nitro-, nitroso- and azo- groups can reduced effectively to amino and amine by Raney Ni-Al alloy and aluminum powder in dilute aqueous alkaline solution.

Acknowledgement:

Research was completed under meticulous

TABLE 1 Preparation of 4-ADPA by one-pot reaction ^{a)}

Run	Synthesis						Reduction			
	A / 2	water / A	Relative ratios [%] ^{b)}			Conversion of 2	Metal / 2	[g/mmol]	NaOH	Yield of 3 ^{c)}
	[mol/mol]	[mol/mol]	4 + 5	3	6	[%]	Raney Ni-Al	Al	[%]	[%]
1	0.3	45	78	14	8	30				
2	0.5	45	75	17	8	64	0.07	0.14	0.5	40
3	0.5	9	34	59	7	78	0.09	0.13	0.5	57
4 ^{d)}	1	45	67	10	23	91	0.2	0.2	2	68
5 ^{e)}	1	45	86	4	4	94	0.3	0.3	4	88
6	1	15	75	19	6	92	0.2	0.3	2	86
7	1	9	49	37	14	100	0.14	0.16	1	90
8 ^{f)}	1	9	47	42	10	100	0.29	-	1	94

a) **1** : **2** = 11 [mol/mol], **2** = 4.9 [mmol]; synthesis reaction time = 2 [h] and reaction temperature = 80 [°C];

b) Ratios were determined by GC;

c) Isolated molar yield of **3** was calculated from used **2**;

d) Reaction time was 4 hours;

e) The reaction temperature in first step was 100 [°C];

f) **1** : **2** = 22 [mol/mol].

A : Tetramethylammonium hydroxide.

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