



A MILD, ENVIRONMENTALLY FRIENDLY METHOD FOR REDUCTION OF AROMATIC NITRO COMPOUNDS USING TETRABUTYLAMMONIUM FLUORIDE AND POLYMETHYLHYDROSILOXANE

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ABSTRACT

A mild, environmentally friendly method for reduction of aromatic nitro compounds to the corresponding amines is reported, using polymethylhydrosiloxane, PMHS, in the presence of catalytic tetrabutylammonium fluoride, TBAF. A range of aromatic nitro compounds such as (*m*-Nitroaniline **1a** and *p*-Nitroaniline **2a**) have been converted efficiently to the corresponding aromatic amines: 1,3-diaminobenzene (**1b**), and 1,4-diaminobenzene (**2b**) with > 61% yield.

KEY WORDS: Reduction, PMHS, TBAF, aromatic, nitro compounds.

1-INTRODUCTION

Aromatic nitro compounds are an important class of compounds in that they are valuable intermediates for the preparation of different organic compounds like amines, azo compounds, hydroxyl amines etc. In related papers the use of polymethylhydrosiloxane in combination with TBAF has been studied^{i-iiiv}. Corriu and Co-workers have shown that PMHS with fluoride or alkoxide-can be used for the reduction of esters to alcohols^{viii}. This was followed by the description of use of PMHS and titanium isopropoxide, again for the reduction of esters^{ix}.

In 1991 Buchwald's group have used PMHS in combination with Cp₂TiCl₂, n-BuLi for the reduction^{x-xii}. These processes, which are usually carried out in polar solvents such as DMSO or DMF, are described as heterogeneous and generally require an excess of fluoride. In 1999, N. J. Lawrence and Co-workers described the efficient reduction of esters to the corresponding alcohols with polymethylhydrosiloxane (PMHS) [Me₃SiO(Me₃HSiMe₃)_nSiMe₃] in the presence of titanium (IV) isopropoxide or zirconium alkoxide^{ix}. This was followed by the description of the use of PMHS and catalytic fluoride^{xiii-xiv}.

In contrast, many methods for the selective reduction of nitro compounds have been reported in the literature, including homogeneous and heterogeneous catalytic hydrogenation^{xxv-xxiv}. More recently, catalytic hydrogenation using hydrogen donors has been widely reported for different substrates^{xxiv}.

However, the significant disadvantages associated with these methods include (i) prolonged reaction time, (ii) potential halogenation, (iii) formation of by-products, and (iv) incompatibility with acid-sensitive groups and other reducible groups. Here we report on an efficient method for the reduction can be achieved with a nitro group $-NO_2$. This work is a part of project seeking new uses of PMHS in reduction a nitro group $-NO_2$ using tetrabutylammonium fluoride and polymethylhydrosiloxane with some modifications in our method reported recently, described the efficient reduction of α -aminoacids to the corresponding aminoalcohols with polymethylhydrosiloxane (PMHS) in the presence of catalytic tetrabutylammonium fluoride^{xxvi}. The attractive features of this new method are: (i) PMHS is cheap (ii) commercially is available (iii) non-toxic salane.

2-EXPERIMENTAL

2.1- Methods

The nitro compounds **1a** and **2a** used for reduction were purchased from Aldrich. They were used without further purification. The solvents used were of synthesis grade. They were used without further purification. Thin-chromatography (TLC) was performed using precoated plates (Aluminium foil, silica gel 60 F254 Merck, 0.25mm). Merck 60 silica gel (230-400 mesh) was used for flash chromatography. All reactions were carried out under nitrogen. Solutions were dried over anhydrous magnesium sulphate ($MgSO_4$) and evaporated under reduced pressure using a rotary evaporator (rotary evaporator (IKA Evaporator RV 06-ML)).

All the products reported here are known compounds and their identity were determined using authentic samples and also melting or boiling points from the literature including Merck index.

2.2- Physical measurements

1H NMR spectra were recorded on BRUCKER AC 400 MHz spectrometer at $0^\circ C$, and the chemical shifts are reported in ppm relative to the central line of the singlet for $CDCl_3$ at 7.26 ppm. Coupling constants (J values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). ^{13}C NMR and DEPT were recorded on BRUCKER AC 101 MHz spectrometer at $0^\circ C$ and all are reported in ppm relative to the central line of the triplet for $CDCl_3$ at 77.16 ppm. The spectra reported are proton decoupled.

IR spectra were recorded on SHIMADZU 830-FTIR spectrometer using KBr pellets. Melting points were recorded on a Gallenkamp melting point apparatus, and are uncorrected. Thin layer chromatography (TLC) was performed on precooked 0.25 mm silica gel plates 60F254 purchased from Merck.

2.3- Reduction of Aromatic nitro compounds:

2.3.1 Standard procedure

Three-necked round bottomed flask was fitted with magnetic stirrer bar and an addition funnel. The flask was then charged with aromatic nitro compounds (5.0 mmol) and tetrabutylammonium fluoride (0.2 mmol) in dry tetrahydrofuran (THF) (40 ml) and polymethylhydrosiloxane (PMHS) (3.5 ml, 15.0 mmol) was added dropwise. The remaining neck was sealed with a septum and a

nitrogen line attached; the flask was heated to 55°C in oil bath. The mixture was stirred vigorously at room temperature for two hours and the reaction was followed (by TLC). Sodium hydroxide (70 ml of a 3N solution) was added dropwise. After stirring vigorously overnight the solvent was evaporated *in Vacuo* and the precipitate was removed by filtration. The pH of the filtrate was adjusted at 4.12 by adding HCl (3N) and the aqueous solution was extracted with dichloromethane (1X150 ml). The Solvent was evaporated *in Vacuo* and the residue was identified to be the rest of unreacted *m*-nitroaniline. The pH of the aqueous solution was adjusted at 1.84 by adding NaOH (1N) and then extracted with dichloromethane (3X70 ml). The combined organic extracts were dried (MgSO₄) and evaporated *in Vacuo*. The red residue of 1,3-diaminobenzene was purified chromatography (SiO₂). Typical pure yield after purification is (50-55%).

2.3.2 Reduction of *m*-Nitroaniline **1a**:

Three-necked round bottomed flask was fitted with magnetic stirrer bar and an addition funnel. The flask was then charged with *m*-nitroaniline (0.5g, 3.6 mmol) and tetrabutylammonium fluoride (0.0457 mg, 0.145 mmol) in dry tetrahydrofuran (THF) (30 ml) and polymethylhydrosiloxane (PMHS) (2.5 ml, 10.8 mmol) was added dropwise. The remaining neck was sealed with a septum and a nitrogen line attached; the flask was heated to 55°C in oil bath. The mixture was stirred vigorously at room temperature for two hours and the reaction was followed (by TLC). Sodium hydroxide (50 ml of a 3N solution) was added dropwise. After stirring vigorously overnight the solvent was evaporated *in Vacuo* and the precipitate was removed by filtration. The pH of the filtrate was adjusted at 4.12 by adding HCl (3N) and the aqueous solution was extracted with dichloromethane (1X150 ml). The Solvent was evaporated *in Vacuo* and the residue was identified to be the rest of unreacted *m*-nitroaniline. The pH of the aqueous solution was adjusted at 1.84 by adding NaOH (1N) and then extracted with dichloromethane (3X50 ml). The combined organic extracts were dried (MgSO₄) and evaporated *in Vacuo*. The red residue of 1,3-diaminobenzene was purified chromatography (SiO₂). Typical pure yield after purification is (50-55%). The product 1, 3-Diaminobenzene was identified by comparison its spectroscopic data with those of an authentic sample^{xxvii}.

The IR spectrum showed the absence of nitro group and the presence of -NH₂.

IR (v cm⁻¹): 3195.8-3400 (v_{NH}); 1624.0 (vc=c); 1521.7(F,v_{N-H}); 1267.1 (vc-N) aryl; 734.8 (v_{NH}).

2.3.2 Reduction of *p*-Nitroaniline **2a**:

p-Nitroaniline was reduced using *m*-nitroaniline (0.5g, 3.6 mmol), tetrabutylammonium fluoride (0.0457 mg, 0.145 mmol) in dry tetrahydrofuran (THF) (30 ml) and polymethylhydrosiloxane (PMHS) (2.5 ml, 10.8 mmol) in similar way to *m*-Nitroaniline.

1, 4-Diaminobenzene (46.6% yield) was obtained as yellow-green solid which has the following IR spectroscopic properties:

IR (v cm⁻¹): 3101.3-3480 (v_{NH}); 1598.9 (vc=c); 1477.4(v_{N-H}); 1292.2 (vc-N) aryl; 769.5 (v_{NH}).

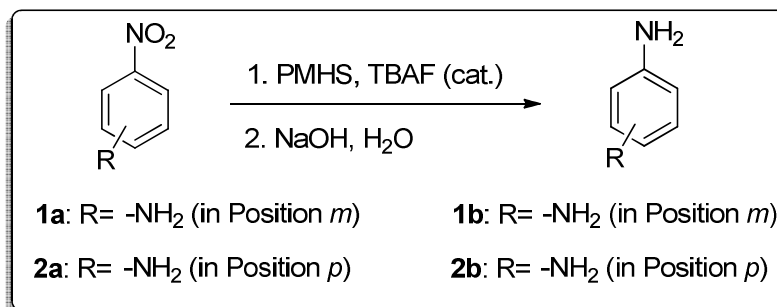
The product 1, 4-Diaminobenzene was confirmed by comparison its other spectroscopic data with those of an authentic sample^{xxvii}.

3-RESULTS AND DISCUSSION

As part of our studies on the reduction of nitro compounds with PMHS, we found that catalytic tetrabutylammonium fluoride (TBAF) (0.02 mole %) is a remarkable homogeneous catalyst for this process^{xxxi}^{v-xxvii}. Here we report on an efficient method for the reduction of aromatic nitro compounds to the corresponding amines using PMHS with catalytic

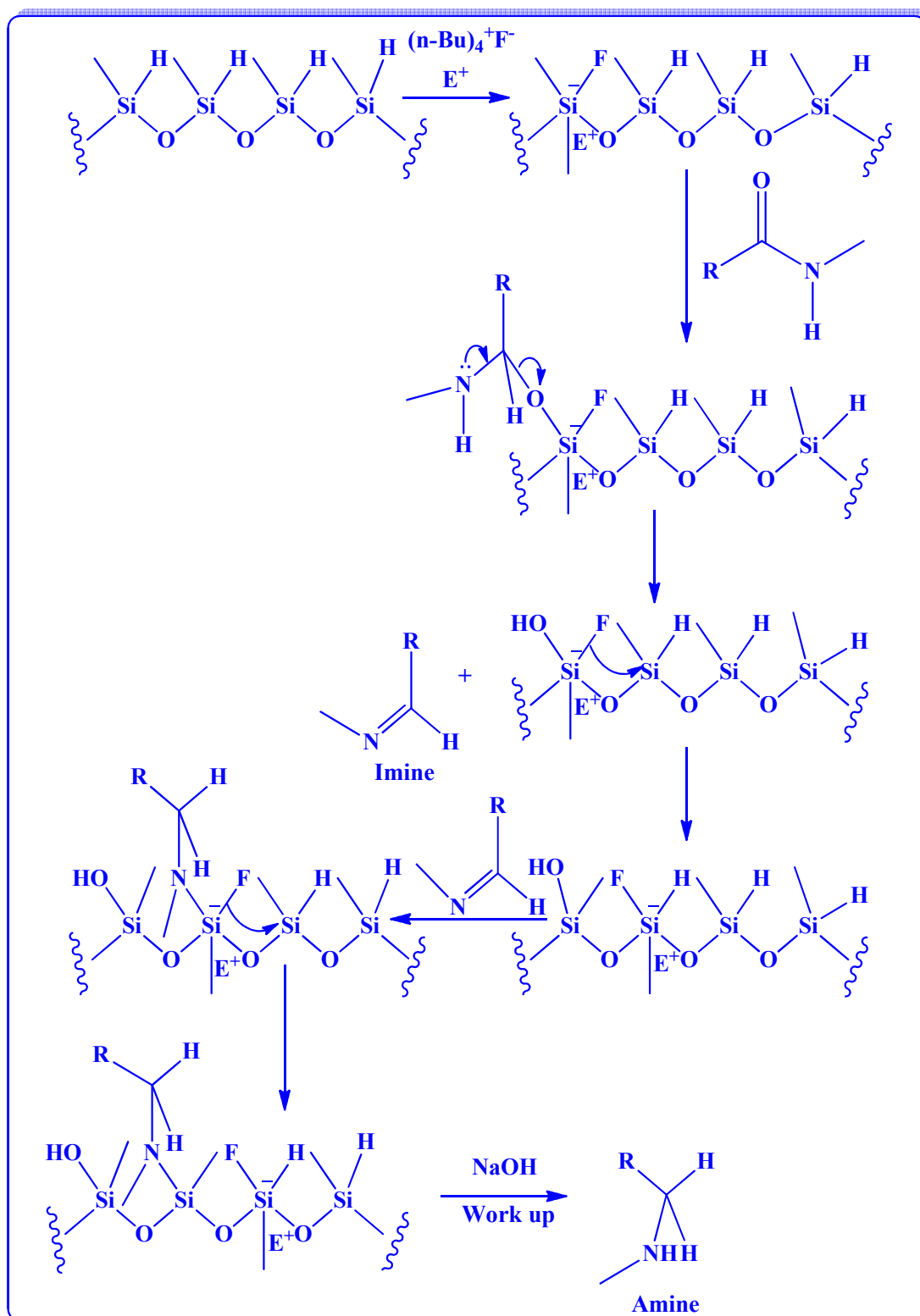
tetrabutylammonium fluoride (TBAF) (**Scheme-1**). The reaction was accomplished at neutral pH and preceded with excellent chemo-selectivity and yields. As is typical for PMHS reactions, a significant excess of reagents is used to assure complete reduction.

It serves as a new method for the reduction of nitro compounds. In our protocol, the use of polymethylhydrosiloxane, PMHS, provides an alternative method for the reduction of nitro compounds. For such reduction, PMHS, can often successfully applied unlike other reducing agents for such reductions occurs with unsaturated derivatives, since these reducing agents rapidly add to double bond.



Scheme1: Reduction of aromatic nitro compounds using PMHS with (TBAF)

As expected two equivalents of Si-H are required for the reduction one nitro compound to the corresponding amine. The first to reduce a nitro compound to the corresponding nitroso compound, and the second to reduce this nitroso compound to the corresponding amine. The impressive rate acceleration is possibly due to the intermolecular transfer of nucleophile from the silicate to another silicon atom, as illustrated in Scheme-2 via 1,3-mode of transfer, a process that is repeated over and over again as the nucleophile travels along the polymer backbone. The corresponding process of nucleophile transfer in an intermolecular sense is presumably much slower. This process is called “Zipper”^{xxiv-xxviii} catalysis, in detail (**Scheme-2**).



Scheme 2: Proposed mechanism of nucleophile-promoted "zipper catalysis"

3-CONCLUSION

By using polymethylhydrosiloxane in combination with catalytic TBAF, an environmentally benign, efficient, simple, economically, and chemo-selective method for the reaction of aromatic nitro compounds to amino compounds was reported. This method is suitable for use with other reducible groups, and polymethylhydrosiloxane in combination with catalytic TBAF is an excellent reducing agent for the mild reduction of nitro compounds.

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