Polymer-supported formate and zinc: A novel system for the transfer hydrogenation of aromatic nitro compounds

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A mild and efficient catalytic transfer hydrogenation (CTH) system has been developed for the facile reduction of aromatic nitro compounds using recyclable polymer-supported formate in the presence of commercial zinc dust at room temperature. This method is found to give the product amine in excellent yield (92-98%) without the need for any chromatographic purification steps. Many other sensitive functional groups such as halogen, alkene, nitrile, carbonyl, ester and amide are compatible with the present system.

Reduction of nitroarenes to the corresponding amines is synthetically important transformation, both in the laboratory and in industry. Although there are a good number of methods available for the reduction of nitro compounds[1], limitations include the use of harsh conditions and/or costly reagents. Catalytic hydrogenation[2] is also commonly used, although the success of reaction is sensitive towards catalyst, solvent and substrate. Furthermore, catalytic hydrogenation employs highly diffusible, low molecular weight, flammable hydrogen gas and requires pressure equipment.

In comparison with all other reduction processes, catalytic transfer hydrogenation (CTH) using a stable hydrogen donor in conjunction with a metal catalyst has real and potential advantages[3]. Several recent advances in the field of CTH, which involves the use of microwave[4], ionic liquids[5], transition metal-based mesoporous silicate and aluminophosphate molecular sieves as catalysts[6], and supported reagents[7] are reported. The industrial application of CTH for large scale reduction process is also reported[8]. The CTH method of reduction is safer, highly selective, cost-effective, mild, and proceeds under ambient conditions of pressure and temperature without the need for any elaborate experimental set up. In addition, the rate and specificity of reduction are amenable to control through choice of hydrogen donor. As a result, various hydrogen donors such as cyclohexene[9a,b], 1,4-cyclohexadiene[9c,d], hydrazine[9e,f], formic acid[3c,9g], propan-2-ol[6,9h], ammonium formate[3b-d,4,5,6b,9i], triethylammonium formate[3g,h,9j], and hydrazinium monoformate[9k,l] have been developed for the transfer hydrogenation of various functionalities. Of all the hydrogen donors available for CTH, ammonium formate is the most versatile and widely employed. Although efficient, these ammonium formate-CTH reactions are often troublesome since ammonium formate can sublime and block the reaction apparatus. Also, the reaction leads to the release of ammonia and could create significant problems when performed on large scale. Moreover, the use of formate salts as hydrogen donors poses complication during isolation and purification of water-soluble products.

We reasoned that a facile and versatile CTH system could be developed if the hydrogen donor is immobilized on a solid support. In recent years, polymer-supported reagents, catalysts, and scavengers are ubiquitous throughout the fields of combinatorial chemistry, organic synthesis and catalysis[10,11]. The use of polymer-supported reagents couples the advantages of solution phase chemistry (ease of monitoring the progress of the reaction by using chromatographic and spectroscopic techniques) with those of solid phase methods (use of excess reagents and easy isolation

and purification of products). The utility and power of such reagents has been exquisitely demonstrated by the groups of Ley and others in synthesizing several complex natural products by multi-step sequences requiring many different kinds of heterogenized reagents, which can be removed by simple filtration[10-12]. In this paper, we report that the polymer-supported formate can be conveniently employed as hydrogen donor for the clean and efficient reduction of aromatic nitro compounds to the corresponding amines in excellent yields using commercial zinc dust as catalyst at room temperature (**Scheme I**).

The scope of this new system is illustrated in **Table I**, where we examined series of aromatic nitro compounds with a variety of substituents. All the products were characterized by comparison of their TLC, m. p., IR and ^{1}H NMR with authentic samples. The reactions are, on the whole, reasonably fast and high yielding (92-98%). It is worth noting that the present system selectively reduced aromatic nitro compounds to the corresponding amines in the presence of other sensitive functional groups such as halogen[9f,i] (**Table I**, entries 1-3), alkene[3d] (**Table I**, entry 4), nitrile[9k,13] (**Table I**, entry 5), and carbonyl[6a,9h] (**Table I**, entries 6 and 7), groups which are susceptible to reduction under transfer hydrogenation conditions. In addition, many other functional groups such as ester, amide, methoxy, acid and hydroxyl are also compatible with the present system.

The separation of products from the reaction mixture is simple and involves, in most of the cases, direct removal of the catalyst and resin by filtration and evaporation of the solvent under vacuum. The crude product, so isolated, was of excellent purity for most purposes. Hence, this procedure is highly advantageous to obtain water-soluble aromatic amines in high yields (**Table I**, entries 1, 3, 7, 12-15).

For this study, the polymer-supported formate was prepared by washing aminomethyl polystyrene (2 mmole/g) with an excess of 50% solution of formic acid in dichloromethane. The resulting polymer was washed thoroughly and successively with dichloromethane and ether, and dried under vacuum. The obtained resin was used as such for the reduction.

It is noteworthy here that the polymer-supported formate was regenerated and could be reused for further hydrogenolysis process. In total, ten successive recycle runs were possible before there was an appreciable decrease in the reaction yield (**Table II**).

In conclusion, a novel CTH system for the clean and efficient reduction of aromatic nitro compounds to the corresponding amines using polymer-supported formate and zinc has been developed. The major advantages of this method include the ability to obtain aromatic amines in pure form with no work-up, and the enhanced chemoselectivity. Thus, the use of resin bound hydrogen donor combines the advantages of polymer-supported chemistry with the flexibility of CTH technique. Further, application of this polymer-supported formate to many other key reductive functional group transformations *via* CTH are in progress and will be the subject of future reports.
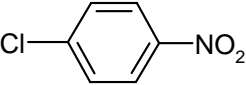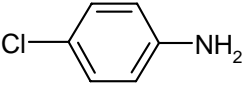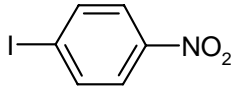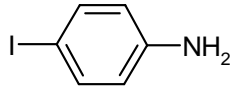
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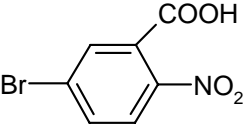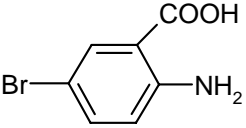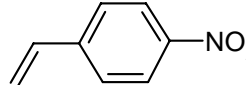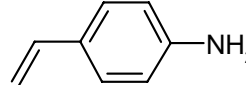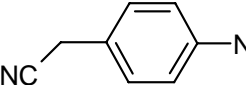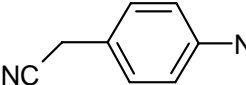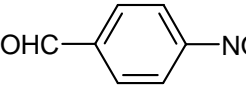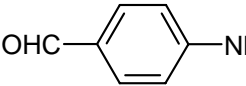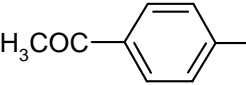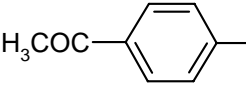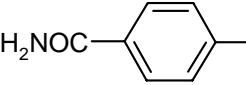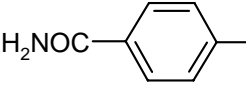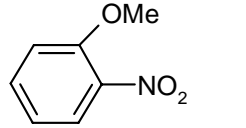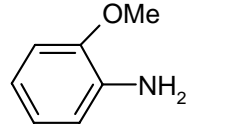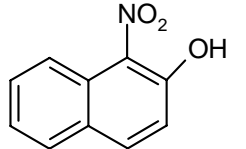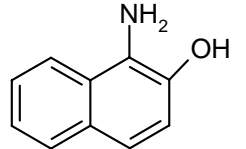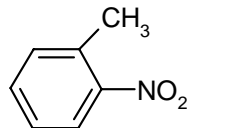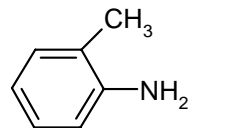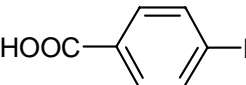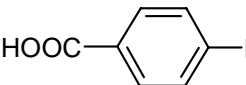
General. The ^{1}H NMR spectra were recorded on an AMX-400 MHz spectrometer using $CDCl_3$ as the solvent and TMS as internal standard; and IR spectra on a Shimadzu FTIR-8300 spectrometer. The melting points were determined by using Thomas–Hoover melting point apparatus and are uncorrected. Thin layer chromatography was carried out on silica gel plates obtained from Whatman Inc. The substrates were either commercial products and were used as purchased or were prepared according to literature procedures. Aminomethyl polystyrene resin was purchased from Advanced Chemtech (1% DVB cross-linked, 100-200 mesh, 2 mmole/g). Zinc dust (particle size < 45 μm) was purchased from E-Merck (India) Ltd. All the solvents used were of analytical grade or were purified according to standard procedures.

General procedure for the reduction of aromatic nitro compounds. To a solution of nitro compound (1 mmole) in methanol (15 mL) taken in a horizontal solid phase vessel, polymer-supported formate (1 g) and zinc dust (1 mmole) were added. The suspension was shaken well[14] for the specified time at room temperature (**Table I**). After consumption of the starting material, as monitored by TLC, the reaction

R = halogen, -CH=CH$_2$, -CN, -CHO, -COR, -COOR, -CONH$_2$, -OCH$_3$ and -OH.
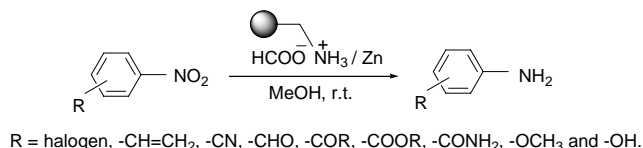
Scheme I

Table I — Catalytic transfer hydrogenation of aromatic nitro compounds using polymer-supported formate/zinc

Entry	Substrate	Time (hr)	Product	Yield[a] (%)	m.p. °C
1	Cl—C6H4—NO2	1.0	Cl—C6H4—NH2	96	71[15]
2	I—C6H4—NO2	1.5	I—C6H4—NH2	98	62[15]
3	Br, COOH, NO2	2.5	Br, COOH, NH2	93	217-19[16]
4	CH2=CH—C6H4—NO2	2.0	CH2=CH—C6H4—NH2	95	212-14[b,c]
5	NC-CH2—C6H4—NO2	1.5	NC-CH2—C6H4—NH2	98	46-48[15]
6	OHC—C6H4—NO2	1.5	OHC—C6H4—NH2	97	70-72[15]
7	H3COC—C6H4—NO2	1.0	H3COC—C6H4—NH2	96	104-06[16]
8	H2NOC—C6H4—NO2	1.0	H2NOC—C6H4—NH2	95	114-16[15]
9	OMe, NO2	1.5	OMe, NH2	94	86-87[d,15]
10	NO2, OH (naphthalene)	2.0	NH2, OH (naphthalene)	92	205-07[15]
11	CH3, NO2	1.5	CH3, NH2	97	110-12[d,15]
12	HOOC—C6H4—NO2	2.5	HOOC—C6H4—NH2	96	186-87[15]

— Contd

Table I — Catalytic transfer hydrogenation of aromatic nitro compounds using polymer-supported formate/zinc — *Contd*

Entry	Substrate	Time (hr)	Product	Yield[a] (%)	m.p. °C
13		3.0		95	57-58[16]
14	H_3COCHN—〈 〉—NO_2	1.5	H_3COCHN—〈 〉—NH_2	98	163-64[15]
15		2.0		96	150-52[16]

[a]Yields of isolated products
[b]Boiling point
[c]The spectra were compared to those of a commercial sample
[d]Isolated as acetyl derivative

Table II — Recycling of polymer-supported formate for the reduction of *p*-chloronitrobenzene

Cycle	Time (hr)	Yield (%)
1	1.0	96
2	1.0	95
3	1.0	95
4	1.0	94
5	1.5	94
6	1.5	94
7	1.5	93
8	2.0	94
9	2.0	93
10	2.5	93

mixture was filtered and washed thoroughly with methanol. The combined washings and filtrate were evaporated under reduced pressure. The crude product was found to be analytically pure in most cases. Where necessary, the crude product was taken into organic layer and washed with saturated sodium chloride.

For recycling purposes, the residue containing polymer-supported formate and the catalyst was washed thoroughly and successively with DMF, dichloromethane, 50% solution of formic acid in dichloromethane, dichloromethane and ether. Thus activated resin along with the catalyst was dried under vacuum and used as such for further reduction reactions.

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