Research Article

RECYCLABLE POLYMER SUPPORTED FORMATE (PSF) AND TIN: A NOVEL REAGENT SYSTEM FOR THE TRANSFER HYDROGENATION OF AZO COMPOUNDS TO HYDRAZO COMPOUNDS

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Abstract

A novel and efficient catalytic transfer hydrogenation (CTH) system for the reduction of both symmetrical and unsymmetrical azo compounds to respective hydrazo compounds by using recyclable polymer supported formate as hydrogen donor in the presence of low cost tin powder as catalyst at room temperature in methanol medium has been reported. Many other sensitive functional groups like -OH, -CH$_3$, -OCH$_3$, -OC$_2$H$_5$, -COOH and halogens are compatible with the present system. The present method is found to give the product in excellent yield (90-95%) without any need for chromatographic purification steps.

Key Words: Azo compounds, reduction, recyclable polymer supported formate, tin, hydrazo compounds

Introduction

Reduction of aromatic azo compounds to hydrazo compounds has received a good deal of attention, both preparatively and analytically (Jnaneshwara G K et al. 1998). Although, there are several methods of reagents that have been reported in the literature for the reduction of azo compounds to

hydrazo compounds (Bavin P M G 1958; Furst A and Moore R E 1957; Hornsby S and Peacock W L 1958; Vogel A I et al. 1958; Gilchrist T L 1991), limitations include the use of harsh conditions or costly reagents. In earlier methods, the conversion of azo compounds to hydrazo compounds required longer reaction time, highly expensive and employed pyrophoric catalysts such as Pd-C (Bavin P M G 1958) and Raney Ni (Furst A and Moore R E 1957). In addition, if the azo compounds contain reducible or hydrogenolysable groups like halogen or nitrile, then systems like 10% Pd-C/HCOONH$_4$ (Brown G R and Foubister A J 1982) and 10% Pd-C/triethylammonium formate (Cortese N A and Heck R F 1977) reduce the nitrile group to a methyl group and remove the halogen from aromatic rings. Moreover, poor yields were reported during the reduction of azo compounds to hydrazo compounds.

Polymer supported reagents, catalysts and scavengers are ubiquitous throughout the fields of combinatorial chemistry and catalysts in organic synthesis (Ley S V et al. 2000; Kirschning A et al. 2001; Clapham B et al. 2001; Gladysz J A 2002; Ley S V 2002; Hodge P 2003; Gonthier E and Breinbauer R 2003; Strohmeier G A and Kappe C O 2004; Burt J et al. 2004; MacCoss R N et al. 2004; Coppo F T et al. 2004; Choi M K W and Toy P H 2004; Baxendale I R et al. 2002). The use of polymer-supported reagents couples the advantages of solution phase chemistry. 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 (Storer R I et al. 2003). Earlier, the use of polymer supported formate as hydrogen donor for the transfer hydrogenation of alkenes in the presence of Wilkinson's catalyst or Pd(OAc)$_2$ is reported (Desai B and Danks T N 2001; Basu B et al. 2003). However, it has been observed that controlling the reduction rates is difficult with these active homogeneous catalysts. In our laboratory, the use of polymer supported formate as a hydrogen donor and the use of heterogeneous catalyst for various functional group transformations in organic synthesis were reported (Abiraj K et al. 2005; Srinivasa G R et al. 2004). On the other hand, the use of heterogeneous catalysts offer several advantages over homogeneous systems such

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as easy recovery and recycling of catalyst, high selectivity, easy product isolation, and minimization of undesired toxic wastes.

Tin powder is non-toxic, widely available and inexpensive. The application of tin and organotin compounds are widely employed in organic synthesis (Pereyre M et al. 1987; Lopez R. M and Fu G C 1997; Shanmugam P et al. 1997). To the best of our knowledge, tin has not been used in conjunction with polymer supported formate for reduction of azo compounds to hydrazo compounds.

In this regard, we have developed a novel and efficient system which included recyclable polymer supported formate as hydrogen donor for the clean and efficient reduction of azo compounds to hydrazo compounds in excellent yields using readily available inexpensive tin powder as catalyst under ambient temperature in methanol as shown in **Scheme 1.**

X or Y= -H, OH, CH_3, OCH_3, OC_2H_5, COOH and halogen.
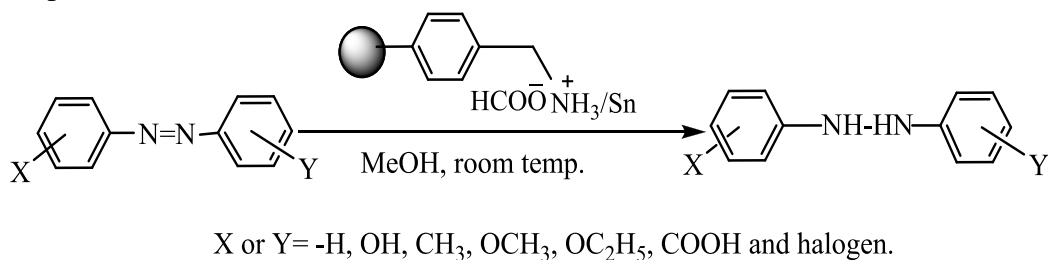
Scheme 1

Meterials and Methods

The ^{1}H–NMR spectra were recorded on an AMX-400 MHz spectrometer using $CDCl_3$ as the solvent and TMS as internal standard. IR spectra were recorded on Shimadzu FTIR- 8300 spectrometer. Elemental analysis was performed on a model Vario EL III elemental analyzer. 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 reported procedures. Merrifield resin was purchased from Advanced Chemtech (1% DVB

crosslinked, 100-200 mesh, 2 mmol/g) and tin metal powder was Purchased from E-Merck Mumbai (India) Ltd, Mumbai. All the solvents used were of analytical grade or were purified according to standard procedures.

Preparation of polymer supported formate

The polymer-supported formate was prepared by washing (aminomethyl) polystyrene (2 mol/g) with an excess of 50% solution of formic acid in dichloromethane and washed thoroughly, successively with dichloromethane, ether and dried under vacuum. The resulting (aminomethyl) polystyrene formate is used directly for catalytic reduction (Abiraj K et al. 2005).

General procedure for the synthesis of azo compounds to hydrazo compounds

To a solution of azo compound (5 mmol) in methanol (15 mL) taken in a round bottomed flask and polymer supported formate (1 g) and tin (5 mmol) were added. The suspension was stirred for the specified time at room temperature. After consumption of the starting material, as monitored by TLC, the reaction 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.

Results and Discussion

The scope of this new system is illustrated in **Table 1**, where we examined series of azo compounds with a variety of substituents. The reactions are reasonably fast and high yielding (90-95%). This procedure is found to be compatible with several sensitive functional groups such as –OH, -CH$_3$ -OCH$_3$, -

OC_2H_5, -COOH and halogens. All the products were characterized by comparison of their TLC, melting points, IR spectra, elemental analysis and ^{1}H-NMR spectra with authentic samples. The disappearance of a strong absorption band between 1630-1575 cm^{-1} due to –N═N– stretching and the appearance of strong absorption band between 3290-3440 cm^{-1} due to the –NH–NH– group, clearly showed that azo compounds have been reduced to hydrazo compounds and also observed that there was no reductive cleavage of azo compounds to anilines at room temperature, even after several hours of reaction.

It should be emphasized that in the absence of tin, the reaction did not proceed and mainly resulted in the recovery of the starting materials. Similarly, the reduction of azo compounds in the absence of polymer supported formate salt did not yield the product. In order to obtain optimum reduction condition, a number of trails with a range of solvents, which are commonly employed for reduction reactions were carried out. Methanol was found to be the best choice as for as the solubility of substrate and rate of reaction is concerned. To interpret the role of methanol, reaction was carried out for several hours in the absence of polymer supported formate and it failed to give any reduced product indicating clearly that methanol serves only as solvent.

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Table 1: Catalytic transfer hydrogenation of azo compounds to hydrazo compounds by using PSF/Sn

X or Y= -H, OH, CH_3, OCH_3, OC_2H_5, COOH and halogen.
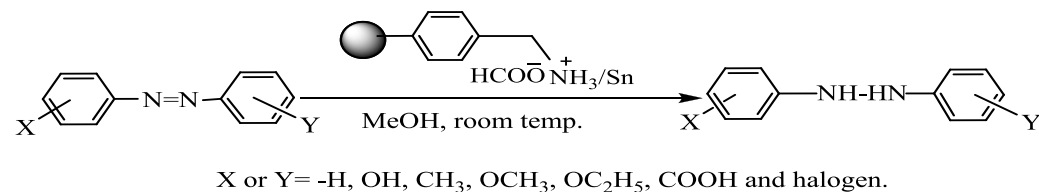
Entry	Substrate	Product	Time (hr)	Yield (%)[a]	Melting point (°C) Found	Melting point (°C) Lit.[30]
1	Azobenzene	Hydrazobenzene	4.0	90	125-126	127[30]
2	4,4′-Dimethyl azobenzene	4,4′-Dimethyl hydrazobenzene	4.0	92	133-135	134[30]
3	3,3′-Dimethyl azobenzene	3,3′-Dimethyl hydrazobenzene[b]	4.2	90	oil	38[30]
4	4,4′-Diethoxy azobenzene	4,4′-Diethoxy hydrazobenzene	4.0	93	83-85	86[30]
5	3,3′-Diethoxy azobenzene	3,3′-Diethoxy hydrazobenzene	4.5	90	121-122	119[30]
6	2,2′-Dimethoxy azobenzene	2,2′-Dimethoxy hydrazobenzene	4.3	92	99-101	102[30]
7	2,2′-Azodiphenol	2,2′-Hydrazodiphenol	4.5	90	149-151	148[30]
8	2,2′-Azonaphthalene	2,2′-Hydrazonaphthalene	4.0	90	140-142	141[30]
9	3,3′-Dichloroazobenzene	3,3′-Dichlorohydrazobenzene[b]	4.0	95	89-91	—
10	Methylorange	N,N′- Dihydromethylorange[b]	4.5	50[c]	oil	—
11	Methylred	N,N′- Dihydromethylred[b]	4.5	56[c]	oil	—
12	Azobenzene -4-carboxylic acid	N,N′- Dihydroazobenzene-4-carboxylic acid[b]	4.2	60[c]	176-178	—

[a]Isolated yields are based on single experiment and the yields were not optimized
[b]Satisfactory elementary analyses is obtained for these compounds
[c]The low yield is due to water soluble nature of these compounds, but TLC analyses showed more than 90% reduction

Table 2: Recycling of polymer supported formate for the reduction of 3,3'-dichloro azo benzene.

Cycle	1	2	3	4	5	6	7	8	9	10
Time (hr)	4.0	4.0	4.0	4.0	4.5	4.5	4.5	5.0	5.0	5.0
Yield (%)	95	95	94	94	94	93	93	92	92	90

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. It is noteworthy here that the polymer-supported formate was regenerated and could be reused for further hydrogenation process **(Table-2)**. In total, ten successive recycle runs were possible before there was an appreciable decrease in the reaction yield.

Conclusion

In summary, a novel and efficient recyclable polymer supported formate and tin reagent system was developed for the smooth reduction of azo compounds to hydrazo compounds. The use of polymer supported formate combines the advantages of polymer-supported chemistry with the flexibility of CTH technique. The advantages include safe reaction medium, high selectivity, ease of operation, simple recovery of hydrogen donor and the use of inexpensive heterogeneous catalyst.

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