Polymer-supported formate and magnesium: an efficient transfer hydrogenation system for the facile reduction of azo compounds

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A mild and efficient method was developed for the chemo-selective reduction of azo compounds to the corresponding amine/s using recyclable polymer-supported formate as hydrogen donor in the presence of low cost magnesium powder at room temperature.

Keywords: reduction, polymer-supported formate, magnesium, azo compounds, amines

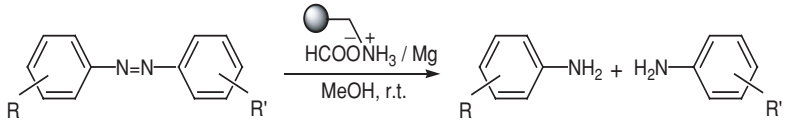
Reduction of azo compounds to the corresponding amine/s is a synthetically important transformation, both in the laboratory and in industry. Although there are a number of good methods available for the reduction of azo compounds,[1] limitations include the use of harsh conditions and/or costly reagents. In comparison with all other reduction processes, catalytic transfer hydrogenation (CTH) employing hydrogen donors, *e.g.*, ammonium formate, is safer, cost-effective, highly selective, rapid, and environmentally friendly.[2] Various catalytic transfer hydrogenation systems such as cyclohexene/ 5% Pd on asbestos,[3a] ammonium formate/ 10% Pd–C,[3b] ammonium formate/ zinc,[3c] ammonium formate/ magnesium,[3d] hydrazinium monoformate/ zinc[3e] and ammonium chloride/ zinc[3f] have been developed for the reduction of azo compounds to the corresponding amine/s. However, ammonium formate aided CTH systems are the most versatile and widely employed. Though 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.

The use of polymer-supported reagents, catalysts, and scavengers as an aid to synthesis is becoming an increasingly common feature in both academic and industrial synthesis laboratories.[4,5] The immobilisation of reagents on a polymeric support 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). Danks *et al.*[6a] and Basu *et al.*[6b] performed the transfer hydrogenation of alkenes using polymer-supported formate as hydrogen donor in the presence of Wilkinson's catalyst or $Pd(OAc)_2$. However, it has been observed that controlling the reduction rates is difficult with these active homogeneous catalysts. On the other hand, the use of heterogeneous catalysts offers several advantages over homogeneous systems such as easy recovery and recycling of catalyst, high selectivity, easy product isolation, and minimisation of undesired toxic wastes. In this context, we probed the reduction of azo compounds employing polymer-supported formate as hydrogen donor in the presence of magnesium as heterogeneous catalyst. Our investigations revealed that the use of polymer-supported formate in conjunction with magnesium is highly efficient for the facile reduction of substituted azo compounds to the corresponding amine/s (Scheme 1).

A wide range of structurally varied azo compounds, both symmetric and unsymmetric underwent reduction by this procedure to furnish the corresponding amine/s. The results are summarised in Table 1. All the products were characterised by comparison of their TLC, melting points, IR spectra, and ^{1}H NMR spectra with authentic samples. The IR spectra of all the products showed sharp doublet between 3500 and 3300 cm^{-1} ascribed for NH_2 group and no absorption bands were noticed for the substrate azo compound (between 1630 and 1575 cm^{-1}) and intermediate hydrazo compound (2290–2440 cm^{-1}) indicating clearly the complete conversion of the azo compounds to their corresponding amino-derivate/s. Further, the appearance of a broad singlet between δ 4.5– 6.5 due to NH_2 protons in the ^{1}H NMR spectra confirmed the nature of the products.

The reactions are, on the whole, rapid (10–20 min) and high yielding (88–97%). It is worth noting that our system selectively reduced azo compounds to the corresponding amines in the presence of other sensitive functional groups such as halogen[2a,2b] (Table 1, entries 2–4), alkene[2a,2f] (Table 1, entry 5), nitrile[2a,7] (Table 1, entry 6), and carbonyl[2a,8] (Table1, entries 7 and 8), groups which are susceptible to reduction under transfer hydrogenation conditions. In addition, many other functional groups such as amide, methoxy, acid, and hydroxyl groups are compatible with the present system.

In the case of symmetrically-substituted azo compounds, the separation of products from the reaction mixture is simple and involves, in most 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 1, entries 2, 8, 11–13). Further, it is noteworthy here that the polymer-supported formate was regenerated and could be reused for further hydrogenolysis process. In total, eight successive recycle runs were possible before there was an appreciable decrease in the reaction yield (Table 2).



R or R' = halogen, -CH=CH$_2$, -CN, -CHO, -COR, -CONH$_2$, -OCH$_3$ and -OH.

Scheme 1

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Table 1 Reductive cleavage of azo compounds using polymer-supported formate/magnesium

Entry	R	R′	Time/min	Yield /%[a]	M.p.°C	
					Found	Literature
1	H	H	15	97[b]	112–114	114[10]
2	4-Cl	4′-Cl	10	95	68–70	70[10]
3	2-Br	2′-Br	12	94[b]	99–100	99[10]
4	4-I	4′-I	12	96	62–64	63[10]
5	4-CH_2=CH_2	4′-CH_2=CH_2	20	93[c]	211–212[d]	213–214[10]
6	4-CH_2-CN	4′-CH_2-CN	16	94	48–50	45–48[10]
7	4-CHO	4′-CHO	15	92	70–71	72[10]
8	4-$COCH_3$	4′-$COCH_3$	18	94	104–106	106[11]
9	2-CH_3	2′-CH_3	20	95[e]	145	144[10]
10	4-$CONH_2$	4′-$CONH_2$	14	93	114	114[10]
11	4-OCH_3	4′-OCH_3	12	95[b,f]	58–59	57[10]
12	2-OH	2′-OH	16	96	174	174[10]
13	4-COOH	4′-COOH	17	95	184–185	188[10]
14	4-NH_2, 3-CH_3	2′-CH_3	20	89, 91[e]	64–66, 144	64,[10] 144[10]
15	4-NH_2	H	15	88, 93[b]	145, 113–114	145–147,[11] 114[10]

[a]Yields of isolated products.
[b]Isolated as acetyl derivative.
[c]The spectra were compared to those of a commercial sample.
[d]Boiling point.
[e]Isolated as benzoyl derivative.
[f]*Typical IR and ^{1}H NMR spectra for p-anisidine:* IR (Nujol) ν_{max} = 3346, 3421 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.82 (3H, s, OCH_3), 4.95 (2H, br s, NH_2), 6.85 (2H, d, *J* = 6.0 Hz, ArH), 7.12 (2H, d, *J* = 6.0 Hz, ArH).

Table 2 Recycling of polymer-supported formate for the reduction of azobenzene

Cycle	1	2	3	4	5	6	7	8
Time /min	15	15	15	15	20	20	30	30
Yield /%	97	97	95	95	94	92	91	90

In conclusion, a simple polymer-supported formate/magnesium system has been developed for the smooth reduction of azo compounds to the corresponding amine/s. 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, rapidity, ease of operation, and simple recovery of hydrogen donor. In addition, this approach is highly helpful for the reduction of symmetric azo compounds to obtain the corresponding amines in pure form with no work-up.

Experimental

Preparation of polymer-supported formate: The aminomethyl polystyrene (Advanced Chemtech, 1% DVB cross-linked, 100–200 mesh, 2 mmol/g) was washed 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.

General procedure for the reduction of azo compounds: To a solution of azo compound (1 mmol) in methanol (15 ml) taken in a horizontal solid phase vessel, polymer-supported formate (1 g) and magnesium powder (1 mmol) were added. The suspension was shaken well[9] for the specified time at room temperature (Table 1). 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 the 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 was dried under vacuum and used as such for further reduction reactions.

In the case of reduction of unsymmetrically substituted azo compounds, the crude product was subjected either to preparative TLC or to column chromatography in order to separate two different constituent amines.

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