SHORT PAPER

J. Chem. Research (S), 2003, 299-300

Magnesium-catalysed cost effective and rapid reductive cleavage of azo compounds using ammonium formate†

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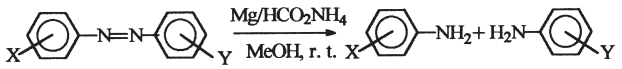
Azo compounds, both symmetrically and unsymmetrically substituted, are reduced to the corresponding amine/s with low cost magnesium powder using ammonium formate within 20 minutes.

Keywords: azo compounds, catalytic transfer hydrogenation, magnesium powder, ammonium formate, reductive cleavage.

In recent times, the heterogeneous catalytic transfer hydrogenation[1-4] method has proved to be a potent choice for reduction of organic compounds compared with traditional hydrogenation or other methods of reduction[5] due to its simple work-up and high degree of selectivity. There are many methods available in literature[5-9] for the reductive cleavage of azo compounds, which employ strongly acidic or basic conditions and systems like cyclohexene/5% Pd on asbestos,[7] cyclohexene/10% Pd–C,[8] ammonium formate/10% Pd–C,[9] hydrazine/10% Pd–C[10] or hydrazine/ Raney Ni[10] which require a duration as long as 16–48 hours at reflux temperature and use expensive catalysts.

Recently, we have reported the use of magnesium powder for removal of protecting groups which are commonly used in peptide synthesis.[11] Now we wish to report that the magnesium/ammonium formate system effectively cleaves the symmetrical and unsymmetrical azo compounds giving their constituent amine/s as depicted in Scheme 1. Many primary and secondary functional groups like halogens, –OH, $–OCH_3$, –COOH, $–CH_3$ and $–COCH_3$ are tolerated.



X or Y = -H, halogen, -OH, $-OCH_3$, -COOH, $-CH_3$ and $-COCH_3$.

Scheme 1

The cleavage of azo compounds in the presence of magnesium powder and ammonium formate was completed within five to twenty minutes. The course of reaction was monitored by TLC and IR spectra. The work-up and isolation of the products were easy. Thus, the azo compounds reduced (a few examples are listed in Table 1) by this system were obtained in good yields (90–95%). The products were characterised by comparison of their melting points, TLC and IR spectra with authentic samples. The disappearance of the strong absorption band between 1630–1575 cm^{-1} due to –N=N– stretching and the appearance of a strong absorption band between 3500–3300 cm^{-1} of the $–NH_2$ group clearly shows that the azo compounds are cleaved to their constituent amine/s. Further, there is no absorption between 2290 and 2440 cm^{-1}, which clearly indicates the absence of the –NH–NH– group. A control experiment was carried out using azo compounds with ammonium formate, but without magnesium powder, does not yield the desired product. The appearance of one spot, in the case of symmetrical azo compounds and two spots, in the case of unsymmetrical azo compounds in TLC also indicates that no hydrazo compounds were formed as intermediates during the reductive cleavage of azo compounds. In order to test the selectivity, the reduction was attempted with *p*-dichlorobenzene, *p*-chloro-*m*-cresol, β-naphthol, acetanilide, benzoic acid, anisole, phenyl acetate at reflux temperature. However, the reaction failed to give any reduced product.

Thus the cleavage of azo compounds can be accomplished at room temperature in a short time with magnesium powder instead of expensive platinum or palladium *etc*., without affecting the reduction of any of the reducible or hydrogenolysable substituents. The yields are virtually quantitative and analytically pure. This procedure will therefore be of general use, especially in the cases where, rapid, mild and selective reduction or cleavage is required.

Experimental

Caution: Magnesium had initially been added to the solvent slowly and in portions to prevent unacceptable temperature rise.

Reductive cleavage of azo compounds. general procedure: A suspension of azo compound (1g), ammonium formate (2.5g) and magnesium powder (2g) in methanol (10ml) was stirred at room temperature, under nitrogen until completion of the reaction. After the completion of the reaction (monitored by TLC or by the disappearance starting material colour), the reaction mixture was filtered through a celite pad, washed with solvent and then the combined filtrate and washings were evaporated under vacuum. The residue was taken into chloroform or ether, washed twice with saturated brine solution and finally with water. The organic layer was dried over anhydrous sodium sulfate and evaporation of the organic layer followed by purification/separation either by preparative TLC or by column chromatography (using two different solvents systems such as chloroform:benzene and chloroform:methanol:acetic acid in different ratios) produced the constituent amine/s. Thin layer chromatography was carried out using the solvent systems; chloroform:benzene (60:40), chloroform:methanol:acetic acid (95:5:3), chloroform:methanol:acetic acid (90:10:3), chloroform:methanol:acetic acid (85:15:3) and the R_f values are reported as R_f^1, R_f^2, R_f^3, R_f^4 respectively. In the cases, where the products obtained are liquids, the unstable liquid amine/s has been converted into a stable derivative. The reaction duration, yields, R_f values and melting points are shown in Table 1.

In conclusion, ammonium formate/magnesium system is more effective than either cyclohexene/5% Pd on asbestos,[7] cyclohexene/10% Pd–C,[8] ammonium formate/10% Pd–C,[9] hydrazine/10% Pd–C[10] or hydrazine/Raney Ni.[10] Most of the reactions are complete in less than 15 min at room temperature. Further investigations of other useful applications related to cleavage of peptides from resin support in solid phase peptide synthesis are in progress.

The authors wish to thank University Grants Commission, New Delhi, India for financial assistance.

Received 1 April 2002; accepted 28 October 2002
Paper 02/1321

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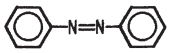
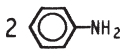
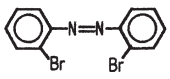
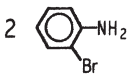
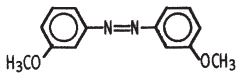
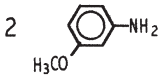
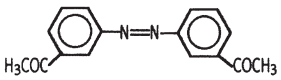
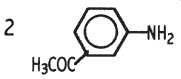
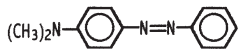
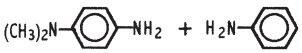
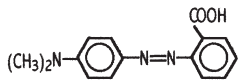
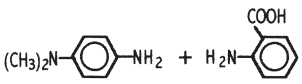
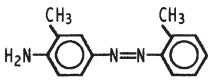
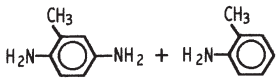
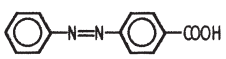
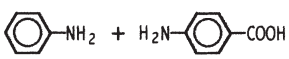
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Magnesium catalysed reductive cleavage of azo compounds using ammonium formatea

Substrate	Product	Duration /min	Yield /%[b]	R_f Values	Melting point/ °C		
					Found	Literature	Ref.
		3	95[d]	0.39 (R_f^1)	112	114	12
		8	92[c]	0.69 (R_f^1)	115	116	12
		12	92[d]	0.64 (R_f^2)	78	80	12
		9	91	0.61 (R_f^2)	100	99	12
		15	90[d], 92[d]	0.24, 0.91 (R_f^3)	50, 112	53, 114	13, 12
		20	88[d], 80[e]	0.30, 0.68 (R_f^4)	52, 144	53, 145	13, 12
		15	90, 93[c]	0.51, 0.65(R_f^2)	62, 144	64, 144	12, 12
		18	90, 75[d,e]	0.82, 0.30 (R_f^2)	113, 188	114, 186	12, 12

In the case of unsymmetrical azo compounds, the first mentioned data refer to the left hand fragment and the next mentioned data refer to the right hand fragment of the reductively cleaved azo compound.
[a] More than 20 azo compounds are reductively cleaved, only representative examples are given.
[b] Isolated yields are based on single experiment and the yields were not optimised.
[c] Isolated as benzoyl derivative.
[d] Isolated as acetyl derivative.
[e] The low yield is due to its water-soluble nature; TLC analysis indicates complete cleavage.

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