

Catalytic transfer reductive cleavage of azo compounds to amines using chitosan-supported formate and zinc

Y.Q. Han^{a,b}, X.H. Yu^{a,b,*}, L. Xu^{a,b}, H. Song^{a,b}, G.F. Yan^a, X.J. MA^a and Y.Z. Zhen^a

^aCollege of Chemistry and Chemical Engineering, Hexi University, Zhangye, 734000, P. R. China

^bKey Laboratory of Resources and Environment Chemistry of West China, Zhangye, 734000, P. R. China

A convenient method for the cleavage of azo derivatives to the corresponding amines using chitosan-supported formate as hydrogen donors in conjunction with zinc is described.

Keywords: catalytic transfer hydrogenation, azo compounds, chitosan-supported formate, zinc

Catalytic transfer hydrogenation (CTH), using stable hydrogen sources in the presence of metal catalyst is a useful method for reductive functional group transformations in organic synthesis. Several hydrogen donors such as cyclohexene,¹ 1, 4-cyclohexadiene,² 2-propanol,³ hydrazine,⁴ formic acid,⁵ ammonium formate,⁶ triethylammonium formate⁷ and hydrazinium monoformate⁸ have been employed as the hydrogen source in transfer hydrogenation. Ammonium formate was the more convenient and efficient reductant for the cleavage of organic compounds compared to other hydrogen sources. However ammonium formate itself did have some limitations. This reagent could sublime and block apparatus, and it released the gaseous by-products (ammonia and carbon dioxide) by decomposition. It gave deposits on the cold surfaces of the reactor lines, which created significant problems when performed on a large scale. In addition, the use of ammonium formate as hydrogen donor often posed complications during the isolation and purification of water-soluble products. Immobilised formate on polymeric supports has been developed to solve these problems. It offers advantages over the conventional solution phase reactions in terms of clean and green processes. In the past few years, several strategies have been reported using the polymer-supported formate as a hydrogen donor in CTH.^{9–13} In the past, most of the studies have been performed using synthetic polymers; but this type of polymer supports is not environmentally friendly and is rather complicated to prepare. Consequently, the development of biodegradable, non-toxic, readily and cheaply available supports is highly desirable.

Chitosan is an abundant and renewable biopolymer which contains amino groups that account for its unique properties¹⁴. This biopolymer can be prepared in different forms such as flakes, gel beads, membranes, fibers, hollow fibres and sponge.¹⁵ Hence chitosan and its derivatives have attracted attention as polymeric supports in various fields, especially in oxidation^{16–19} and reductive hydrogenation reactions.^{20–24} Despite the rapid development of chitosan-supported chemistry over the last few years, there are few reports of chitosan-supported formate (CSF) as hydrogen donors in CTH. The major limitation of chitosan is its solubility in most dilute mineral and organic acid solutions.²⁵ Many attempts have been made to improve its chemical stability through chemical modification using different cross-linking agents. In our work, we prepared a highly porous chitosan resin using epichlorohydrin (ECH) as a cross-linking agent by reacting the hydroxyl groups while retaining the amine groups of chitosan. This prevents the dissolution of chitosan in acid and other chemicals. When the cross-linked chitosan resins were treated with a formic acid solution, the CSF were obtained. Our investigations revealed that the use of CSF as a hydrogen donor in conjunction with zinc cleaved the azo derivatives to the corresponding amine (s) in a cost-effective, rapid and simple reaction.

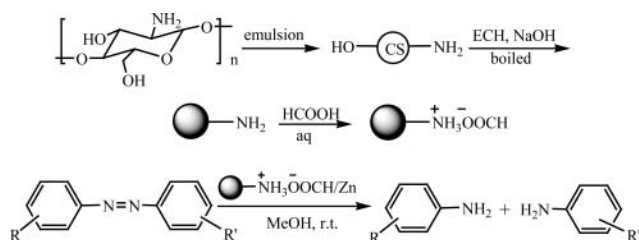
The highly porous chitosan resins were made by emulsion method using chitosan powder dissolved in 2.0% aqueous

acetic acid and paraffin oil with Span 80²⁵. A volume of 10 mL of 12.5 mol L⁻¹ ECH was added to the chitosan solution and the temperature was maintained at 60 °C for 2 h. Subsequently, 50 mL of 0.1 mol L⁻¹ NaOH was added dropwise and the system was boiled for 3 h under constant stirring. The product which was obtained was filtered, washed several times with distilled water and ethanol, and then dried in a vacuum. Finally, the resin was packed in a column and treated with an excess of 50% solution of formic acid repeatedly to give the CSF. The resulting resin was washed with water several times, dried under vacuum and used directly for a catalytic reduction (Scheme 1).

The generality of this catalytic reduction methodology has been investigated with series of azo compounds (Table 1). All the products were purified by column chromatography over silica gel and characterised by comparison of their TLC, melting points, IR spectra, and ¹H NMR spectra. We first examined the reduction of substituted azo compounds ((Table 1) with CSF and zinc in methanol. The reactions were rapid (20–40 min) and high yielding (84–95%) and there was a selective reduction of the azo compounds to the corresponding amine(s). Substituents such as –Me, –OMe, –OH, –C(CH₃)₃ and –CONH₂ were not affected under the reaction conditions. Based on these encouraging results, the scope of this catalytic reduction was further extended. As seen in Table 1, other functional groups, such as alkene, nitrile, carbonyl and halogens, all of which are known to be susceptible to catalytic hydrogenation were also compatible with the reaction conditions. However interestingly, when the substrate contained a carbonyl group, Schiff base complexes were observed in the reduction products, revealing the formation of an imine from an amino group and carbonyl group.

In addition, we discovered the reactions were sensitive to steric and electronic effects from the substituents. The reduction of alky-substituted azo compounds (Table 1, entries 2 and 3) to the corresponding amine (s) proceeded in good yields at room temperature. While the cleavage of the more sterically hindered azo compounds was inefficient at room temperatures, a good conversion was obtained at reflux with longer reaction times (Table 1, entry 4). The results also revealed that electron-donating groups facilitated the reaction while electron-withdrawing groups lengthened the reaction time.

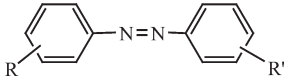
In order to improve the yields, reactions were performed using different amounts of reagents. The best results were obtained at mass ratio 1:0.1:0.5 of CSF, zinc power, and azo compound. Experiments in the absence of either CSF or zinc



Scheme 1

* Correspondent. E-mail: yuxinghai455@163.com

Table 1 Hydrogenative cleavage of azo compounds using chitosan-supported formate and zinc

Entry		Temp/ °C /Time/min	Yield/% ^a	M.p./ °C	
				Found	Lit.
1	R=H, R'=H	25/8	95	112 ^b	114 ²⁶
2	R= 3-CH ₃ , R'= 3'-CH ₃	25/8	95	124–125 ^c	125 ²⁶
3	R= 2-CH ₃ , R'= 2'-CH ₃	25/10	93	142–143 ^c	144 ²⁶
4	R= 2-C(CH ₃) ₃ , R'= 2'-C(CH ₃) ₃	65/15	91	231–232 ^d	233 ²⁷
5	R= 4-OCH ₃ , R'= 4'-OCH ₃	25/13	90	58–59	57 ²⁶
6	R= 4-OH, R'= 4'-OH	25/10	96	189–191	189 ²⁶
7	R= 4-CONH ₂ , R'= 4'-CONH ₂	25/12	94	181	183 ²⁶
8	R= 2-Br, R'= 2'-Br	25/15	87	28–30	30 ²⁶
9	R= 4-Cl, R'= 4'-Cl	25/12	89	71	72 ²⁶
10	R= 4-vinyl, R'= 4'-vinyl	25/10	93	242 ^d	249 ²⁶
11	R= 4-CHO, R'= 4'-CHO	25/12	90	70–71	71 ²⁶
12	R= 4-CN, R'= 4'-CN	25/13	89	84–85	86 ²⁷
13	R= 3-COCH ₃ , R'= 3'-COCH ₃	25/15	91	98–99	99 ²⁶
14	1,2-di(naphthalen-1-yl)diazene	25/9	96	50	50 ²⁸
15	1,1'-(diazene-1,2-diyl)bis(naphthalen-2-ol)	25/10	95	50	51 ²⁸

^aYield refer to pure isolated products.^bIsolated as acetyl derivative.^cIsolated as benzoyl derivative.^dBoiling point.

powder did not yield the reduced compound. The results showed that the combination of CSF and zinc powder is essential to carry out the reduction. The probable reduction mechanism proceeded through the degradation of CSF into hydrogen which induced the reduction of azo compounds. Furthermore, it is worth noting that the CSF could be regenerated and reused for further hydrogenolysis processes. In most of the reactions, we found the reaction yields retained the typical values throughout six successive recycle runs.

In conclusion, the use of CSF and zinc powder provides a very simple and efficient procedure for the smooth hydrogenative cleavage of azo compounds to the corresponding amine(s). The method combines the advantages of polymer-supported chemistry with the flexibility of the CTH technique, including a cost effective safe reaction medium, rapidity, ease of operation, and a simple recovery of the hydrogen donor. This distinguishes this procedure from others catalytic transfer hydrogenation and will hopefully prove to be of wide use in organic synthesis.

Experimental

Chitosan with a deacetylation percentage of approximately 99% was a product of Shanghai Fuqiang Biochemical Co. Ltd. (China). It was purified before use by dissolving it and precipitating several times, then extracting it in a Soxhlet apparatus with acetone for 24 h, and dried at 40 °C under vacuum. Epichlorohydrin and formic acid were obtained from Shanghai Chemical Ltd (China). Zinc dust was purchased from Beijing Chemical Ltd (China). The other substances were either commercial products and were used as purchased or were prepared according to literature procedures. All of the solvents used were analytical grade and purified according to standard procedures.

TLC was carried out on silica gel plates obtained from Shanghai chemical Ltd (China). The melting points were determined by using a TX-4 melting point apparatus and are uncorrected. IR spectra were taken with KBr pellets on a Perkin-Elmer FTIR 1725 spectrometer. The ¹H NMR spectra were recorded on a Mercury-Plus 400 MHz spectrometer using CDCl₃ as the solvent and TMS as internal standard.

Reductive cleavage of azo compounds; general procedure

Zinc dust (5 mmol) was added to a suspension of the appropriate azo compound (5 mmol) in methanol (15 mL), CSF (1g), and stirred under nitrogen atmosphere at room temperature. The progress of the reaction was monitored by TLC. The separation of products from the reaction mixture and involved in most of the cases, direct removal of the catalyst and resin by filtration and evaporation of the solvent under vacuum. The crude product, as isolated, was of excellent purity for most purposes. Water-soluble aromatic amines were obtained in high yields.

For recycling purposes, the residue of the catalyst containing the CSF was washed thoroughly and successively with dimethylformamide (DMF), dichloromethane, and a 50% solution of formic acid. The activated resin was dried under vacuum and used as such for further reduction reaction.

We thank the Key Laboratory of Resources and Environment Chemistry of West China, and Hexi University for the financial assistance. We are also grateful to Dr G. R. Yue for his encouragement.

Received 31 October 2012; accepted 27 November 2012

Paper 1201600 doi: 10.3184/174751912X13553360452222

Published online: 15 January 2013

References

- M.C. Daga, M. Taddei and G. Varchi, *Tetrahedron Lett.*, 2001, **42**, 5191.
- J.S. Bajwa, *Tetrahedron Lett.*, 1992, **33**, 2299.
- R.C. Mebane, D.R. Jensen, K.R. Rickerd and B.H. Gross, *Synthetic Commun.*, 2003, **33**, 3373.
- P.P. Cellier, J.F. Spindler, M. Taillefer and H.J. Cristau, *Tetrahedron Lett.*, 2003, **44**, 191.
- K. Prasad, J.S. Slade, J. Clemens, O. Repic and T.J. Blacklock, *Adv. Synth. Catal.*, 2005, **347**, 1769.
- A. Saha and Brindaban.C. Ranu, *J. Org. Chem.*, 2008, **73**, 6867.
- K. Abiraj, D.C. Gowda and S. Gowda, *Synlett.*, 2004, 877.
- S. Gowda, K. Abiraj and D.C. Gowda, *J. Chem. Res. (S)*, 2002, 384.
- B. Basud, M.M.H. Bhuiyan, D. Pralay and H. Ismail, *Tetrahedron Lett.*, 2003, **44**, 8931.
- B. Desai and T.N. Danks, *Tetrahedron Lett.*, 2001, **42**, 5963.
- G.R. Srinivasa, K. Abiraj and D.C. Gowda, *Synth. Commun.*, 2005., **35**, 1161.
- B. Desai, T.N. Danks and G. Wanger, *Tetrahedron Lett.*, 2005, **46**, 955.
- G.R. Srinivasa, K. Abiraj and D.C. Gowda, *Synthetic Commun.*, 2005, **35**, 1161.
- R. GAF, *Chitin chemistry*. MacMillan, London, 1992.
- E. Guibal, *Sep. Purif. Technol.*, 2004, **38**, 43.
- E. Chiessi and B. Pispisa, *J. Mol. Catal. A: Chem.*, 1994, **87**, 177.
- G. Paradossi, E. Chiessi, F. Cavalieri, D. Moscone and V. Crescenzi, *Polym. Gels. Netw.*, 1997, **5**, 525.
- N.V. Kramareva, A.Y. Stakheev and O. Tkachenko, *J. Mol. Catal. A: Chem.*, 2004, **209**, 97.
- C.C. Guo, G. Huang, X.B. Zhang and D.C. Guo, *Appl. Catal. A: Gen.*, 2003, **247**, 261.
- X.X. Wang, M.Y. Huang and Y.Y. Jiang, *Macromol. Chem. Macromol. Symp.*, 1992, **59**, 113.
- M. Adlim, M.B. Abut, K.Y. Liew and J. Ismail, *J. Mol. Catal. A: Chem.*, 2004, **212**, 141.
- G. Yuan and M.A. Keane, *Catal. Commun.*, 2003, **4**, 195.
- L.M. Tang, M.Y. Jiang and Y.Y. Huang, *Chin. J. Polym. Sci.*, 1996, **14**, 57.
- H.S. Han, S.N. Jiang, M.Y. Huang and Y.Y. Jiang, *Polym. Adv. Technol.*, 1996, **7**, 704.
- C.Q. QIN, L. XIAO and Y.M. DU, *Chin. Chem. Lett.*, 2001, **12**, 1051.
- I. Vogel, *Text-book of practical organic chemistry*, 5th, edn. Addison Wesley Longman Limited, 1997.
- Dictionary of organic compounds*, 6th edn, Chapman & Hall, London, 1996.
- Handbook of fine chemicals and laboratory equipment 2000–2001*, Aldrich Chemical Company Inc., Milwaukee.

Copyright of Journal of Chemical Research is the property of Science Reviews 2000 Ltd. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.