Pergamon

Tetrahedron Letters 44 (2003) 8931–8934

TETRAHEDRON
LETTERS

Catalytic transfer reduction of conjugated alkenes and an imine using polymer-supported formates

Basudeb Basu,* Md. Mosharef H. Bhuiyan, Pralay Das and Ismail Hossain

Department of Chemistry, University of North Bengal, Darjeeling 734 430, India

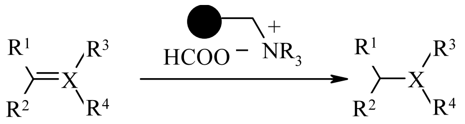
Received 22 August 2003; revised 23 September 2003; accepted 3 October 2003

Abstract—An efficient and mild method for catalytic transfer hydrogenation of C=C and C=N double bonds with the aid of resin-supported formate (PSF) as the hydrogen donor and palladium acetate as the catalyst is reported.

Catalytic transfer hydrogenation (CTH) with the aid of a stable hydrogen donor is a useful alternative method to catalytic hydrogenation by molecular hydrogen.[1] In transfer hydrogenation, several organic molecules such as hydrocarbons,[2] primary and secondary alcohols,[3] and formic acid and its salts[4] have been employed as the hydrogen source. The use of reagents such as hydrazine is less frequent.[1b] The use of a hydrogen donor has some advantages over the use of molecular hydrogen since it avoids the risks and the constraints associated with hydrogen gas as well as the necessity for pressure vessels and other equipment. During the last decades, asymmetric transfer hydrogenation has been accomplished using chiral metal complexes.[5]

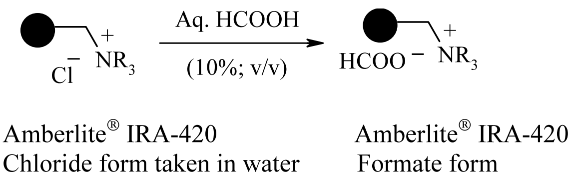
Functionalized polymers have emerged as potent tools for solution-phase chemistry and automated parallel synthesis.[6] Reagents immobilized on solid supports offer advantages in terms of clean and green reactions, ease of separation of the product and reusability. While polymeric supports have been used for anchoring several reducing agents such as borohydrides,[7] tin hydrides[8] etc., solid supported hydrogen donors have rarely been employed in CTH. Desai and Danks reported that polymer supported formate (PSF) can be used in Rh(I)-catalyzed reduction of cinnamic acids, but their method lacks optimization with substrates bearing other reducible groups and other multiple bonds.[9] In connection with our interest in palladium-catalyzed transfer hydrogenation of alkenes and imines using potassium formate,[10] we wanted to develop a stable hydrogen donor anchored to a solid surface to be used in CTH. Herein we disclose our results illustrating the synthetic utility of PSF in palladium-catalyzed transfer hydrogenation of a variety of electron deficient alkenes and an imine (Scheme 1).

The PSF was prepared by washing Amberlite resin (IRA 420, Cl^-) packed in a column with 10% aqueous formic acid solution repeatedly until the washings gave a negative response for chloride ion (Scheme 2). Finally the solid was washed with water several times and then dried under vacuum. The resulting resin formate was used directly for catalytic reduction. A mixture of unsaturated compound, palladium acetate (2 mol%) and resin formate in DMF was stirred at 70–75°C for 10–16 h (Table 1). After being cooled and diluted with water the mixture was filtered and extracted with ether, which on evaporation afforded the desired product.



$R^1 = R^2 =$ Ph, Ar, H X = C, N
$R^3 = R^4 =$ CN, COOEt, COOMe, NHBoc, H, Ph

Scheme 1.



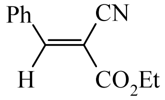
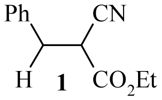
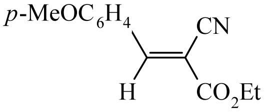
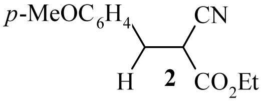
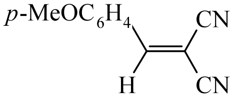
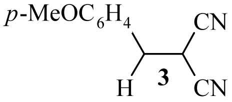
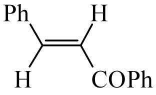
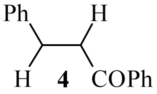
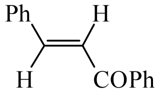
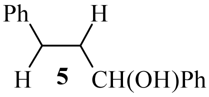
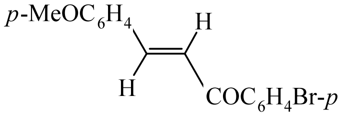
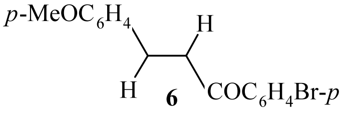
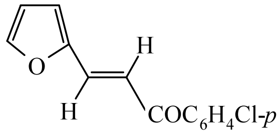
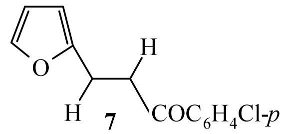
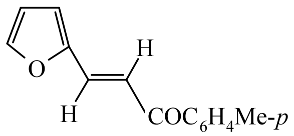
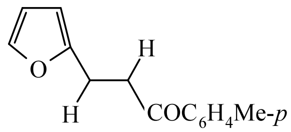
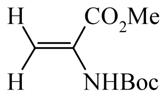
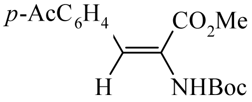
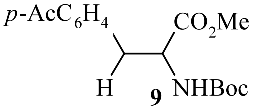
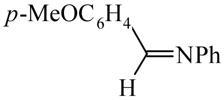
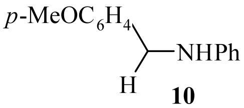
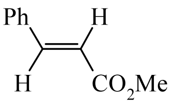
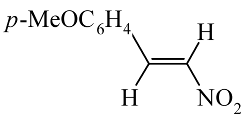
Scheme 2.

Keywords: catalytic transfer hydrogenation; polymer-supported formate; palladium acetate; unsaturated alkenes, imines.

* Corresponding author: Fax: +91-353-2581546; e-mail: basu_nbu@indiatimes.com

0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2003.10.019

Table 1. Palladium-catalyzed transfer reduction of alkenes and an imine using PSF

Entry	Substrate	Temp./ Time	Product[a]	%Yield[b]
1.		70 °C / 10 h	 **1**	85
2.		70 °C / 12 h	 **2**	75
3.		75 °C / 10 h	 **3**	81
4a.		70 °C / 10 h	 **4**	82
4b.		75 °C / 16 h	**4** +  **5**	56+31
5.		70 °C / 12 h	 **6**	60
6.		70 °C / 14 h	 **7**	77
7.		70 °C / 14 h	 **8**	70
8.		70 °C / 14 h	No reaction	
9.		70 °C / 10 h	 **9**	70
10.		70 °C / 12 h	 **10**	85
11.		75 °C / 14 h	No reaction	
12.		75 °C / 14 h	No reaction	

---

[a] All the products gave satisfactory spectral data (^{1}H- and ^{13}C-NMR); [b] Yields refer to the average from 2-3 runs.

The generality of this methodology has been investigated with different types of electron-deficient alkenes and an imine (Table 1). We first examined reduction of alkylidene cyanoacetates (entries 1, 2) using PSF and palladium acetate (2 mol%) in DMF. The PSF was employed in excess anticipating that other functional groups would not react. The reduction of the C–C double bond proceeded smoothly at 70–75°C requiring only gentle agitation; work-up was then achieved by simple filtration, extraction with diethyl ether and evaporation. The reduced product was purified by column chromatography over silica gel. Both the cyano and ester groups remained unaffected under the reaction conditions. The reduction of a dicyanoalkylidene derivative (entry 3) was found to occur with similar efficiency.

Based on these encouraging results, the scope and limitations of this transfer hydrogenation were further extended. As seen in Table 1, α,β-unsaturated ketones (entries 4–7) bearing potentially reducible groups were hydrogenated efficiently. The reaction, if continued for a longer period, resulted in partial reduction of the carbonyl function as well (31%) (entry 4b).

Since dehydroamino acid derivatives are potential precursors to phenylalanine or alanine based amino acids and their synthesis is one of our major interests,[11] we attempted reduction of enamides (entries 8, 9) using PSF and catalytic palladium acetate. Interestingly, while methyl 2-(*tert*-butoxycarbonylamino)-acrylate (entry 8) was not reducible under the present conditions, the *p*-acetyl compound (entry 9) underwent smooth reduction in good yield (70%). Although this selectivity is difficult to explain without further evidence, the enhanced electrophilicity at the β-carbon of the alkene and involvement of the 'hydridic route' might be the possible reasons.

In order to broaden the scope of this study, we carried out reduction of the C=N double bond of an imine. The (4-methoxybenzylidene)-phenylamine (entry 10) under similar conditions afforded the secondary amine **10** in excellent yield (85%). Since the imine was derived from the corresponding carbonyl compound, this overall one-pot protocol may be seen as a direct reductive amination of carbonyl compound using PSF and catalytic palladium acetate. Further studies are in progress in this direction.

Surprisingly, a simple alkyl cinnamate (entry 11) and a nitro olefin (entry 12) failed to undergo CTH using the optimized condition. Desai and Danks carried out reduction of alkyl cinnamates using PSF and $RhCl(PPh_3)_3$ (2.5 mol%) as the catalyst under microwave irradiation.[9] Dehalogenation of aromatic halides under CTH methods has been observed[12] and the process is rapid while using microwaves.[13] Nitro olefins are known to produce oximes under CTH using ammonium formate.[14] We, however, obtained no change of the starting material while carrying out the reaction using PSF.

In conclusion, we have shown that palladium-catalyzed transfer hydrogenation can be performed on a variety of electron-deficient alkenes as well as an imine using polymer supported formate (PSF) as the source of hydrogen. The method is operationally simple and applicable to a variety of unsaturated organic compounds. Other advantages are clean work-up, high yields and environmentally benign conditions. The use of a palladium catalyst showed some substrate selectivity and the transfer hydrogenation appears to proceed at a slower rate in comparison to that of potassium formate. Future studies on the mechanistic aspects including the use of other transition metal complexes with chelating phosphine ligands are of major interest.

Representative procedure for catalytic transfer hydrogenation of functionalized alkenes using PSF: To a solution of methyl 3-(4-acetophenyl)-2-(*tert*-butoxycarbonylamino)-acrylate (entry 9) (321 mg, 1 mmol) in DMF (3 mL) was added $Pd(OAc)_2$ (5 mg, 2 mol%). The reaction mixture was flushed with nitrogen and PSF (resin formate, 1 g) was added in one portion. The reaction mixture was stirred in a screw-cap sealed tube at 70°C for 10 h. After cooling, the reaction mixture was diluted with water and the solid resin was removed by filtration. The filtrate was extracted with ether (3×15 mL). The combined ethereal layer was washed with brine, dried over Na_2SO_4 and evaporated to dryness under reduced pressure. The residue was purified by column chromatography over silica gel using petroleum ether:EtOAc (4:1) to furnish methyl 3-(4-acetophenyl)-2-(*tert*-butoxycarbonylamino)propionate **9** as colorless crystals (224 mg, 70%); mp 72–73°C; UV (MeOH): λ_{max} 248 nm; IR (neat): ν_{max} 3360, 2996, 1752, 1670, 1609, 1516, 1455, 1373 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.87 (d, 2H, $J=8.1$ Hz), 7.23 (d, 2H, $J=8.1$ Hz), 5.05 (d, 2H, $J=7.7$ Hz), 4.59 (t, 1H, $J=7.7$ Hz), 3.69 (s, 3H), 2.55 (s, 3H), 1.38 (s, 9H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 197.7, 171.9, 154.9, 141.7, 135.8, 129.5, 128.5, 54.1, 52.3, 38.3, 29.6, 28.2, 26.5.

Acknowledgements

The authors are appreciative of the financial support provided by The Department of Science & Technology, Govt. of India (Grant No. SP/S1/G-13/97) and The Council of Scientific and Industrial Research, New Delhi (Grant No. 01-1863/03-EMR-II).

References

1. (a) Brieger, G.; Nestrick, T. J. *Chem. Rev.* **1974**, *74*, 657; (b) Johnstone, R. A. W.; Wilby, A. H.; Entwistle, I. D. *Chem. Rev.* **1985**, *85*, 129.
2. Braude, E. A.; Linstead, R. P. *J. Chem. Soc.* **1954**, 3544.
3. Noyori, R.; Yamakawa, M.; Hashiguchi, S. *J. Org. Chem.* **2001**, *66*, 7931 and references cited therein.
4. (a) Fache, F.; Schilz, E.; Tommasino, M. L.; Lemaire, M. *Chem. Rev.* **2000**, *100*, 2159; (b) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345; (c) Ram, S.; Ehrenkaufer, R. E. *Synthesis* **1988**, 91.

5. Zassinovich, G.; Mestroni, G.; Gladiali, S. *Chem. Rev.* **1992**, *92*, 1051.
6. Kirschning, A.; Monenschein, H.; Wittenberg, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 650.
7. (a) Gibson, H. W.; Baily, F. C. *J. Chem. Soc., Chem. Commun.* **1977**, 815; (b) Yakabe, S.; Hirano, M.; Morimoto, T. *Synth. Commun.* **1999**, *29*, 295.
8. Delmond, B.; Dumartin, G. In *Solid State Organometallic Chemistry: Methods and Applications*; Gielen, M.; Willem, R.; Wrackmeyer, B., Eds.; Wiley: Chichester, 1999; p. 445.
9. Desai, B.; Danks, T. N. *Tetrahedron Lett.* **2001**, *42*, 5963.
10. (a) Basu, B.; Bhuiyan, M. M. H.; Jha, S. *Synth. Commun.* **2003**, *33*, 291; (b) Basu, B.; Jha, S.; Bhuiyan, M. M. H.; Das, P. *Synlett* **2003**, 555.
11. (a) Basu, B.; Frejd, T. *Acta Chem. Scand.* **1996**, *50*, 316; (b) Basu, B.; Chattopadhyay, S. K.; Ritzen, A.; Frejd, T. *Tetrahedron: Asymmetry* **1997**, *8*, 1841; (c) Ritzen, A.; Basu, B.; Chattopadhyay, S. K.; Dossa, F.; Frejd, T. *Tetrahedron: Asymmetry* **1998**, *9*, 503.
12. Sasson, Y.; Blum, J. *J. Am. Chem. Soc.* **1975**, *40*, 1887.
13. Banik, B. K.; Barakat, K. J.; Wagle, D. R.; Manhas, M. S.; Bose, A. K. *J. Org. Chem.* **1999**, *64*, 5746.
14. Entwistle, I. D.; Jackson, A. E.; Johnstone, R. A. W.; Telford, R. P. *J. Chem. Soc., Perkin Trans. 1* **1977**, 443.