Pergamon

Tetrahedron Letters 41 (2000) 7847–7849

TETRAHEDRON
LETTERS

Palladium-catalyzed transfer hydrogenation in alkaline aqueous medium

Jeffrey B. Arterburn,[a,]* Madhavi Pannala,[a] Anicele M. Gonzalez[a] and
Rebecca M. Chamberlin[b]

[a]*Department of Chemistry and Biochemistry MSC 3C, New Mexico State University, PO Box 30001, Las Cruces, NM 88003, USA*
[b]*Nuclear and Radiochemistry Group, CST-11, Los Alamos National Laboratory, Los Alamos, NM 87545, USA*

Received 29 June 2000; revised 7 August 2000; accepted 8 August 2000

Abstract

Catalytic transfer hydrogenation using palladium(II) chloride, formate and aqueous sodium hydroxide is effective for the reduction of unsaturated carboxylic acids, azalactones, and α-ketocarboxylic acids. This method is convenient, economical, avoids organic solvents, and uses a stable, nonpyrophoric catalyst.

Catalytic transfer hydrogenation can be an effective method for reducing a variety of organic substrates, which avoids some of the technical and safety concerns associated with using compressed hydrogen gas.[1] The heterogeneous mixture of Pd–C and ammonium formate in alcohol solvent has proven to be a particularly effective reagent in organic synthesis.[2] Replacing organic solvents with water offers economic advantages, improves safety, reduces the environmental impact of the waste stream, and in combination with the development of catalytic processes offers great opportunities for 'green' chemistry.[3] We have studied transfer hydrogenation in alkaline aqueous conditions as part of a broad investigation of noble metal-catalyzed reactions of organic substrates in water. Herein, we report a convenient, effective method for reducing unsaturated carboxylic acids using the nonpyrophoric catalyst palladium(II) chloride, formic acid, and sodium hydroxide base in water.

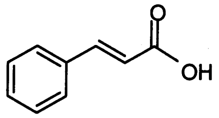
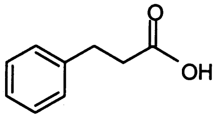
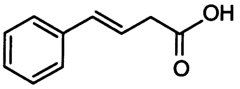
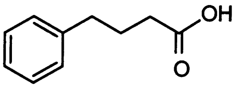
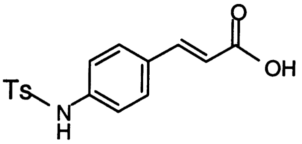
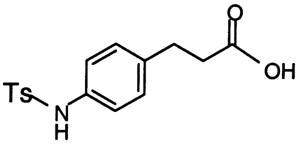
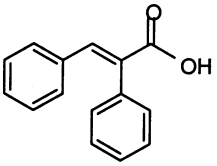
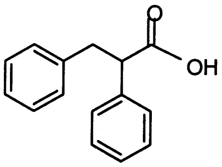
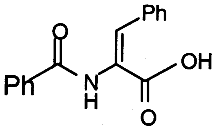
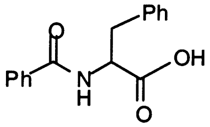
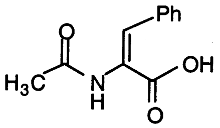
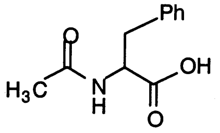
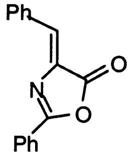
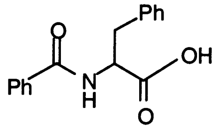
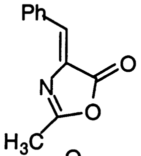
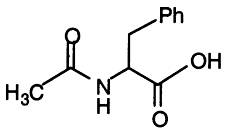
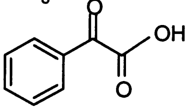
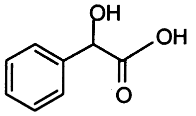
The reduction of cinnamic acid **1** was carried out using 10 mol% $PdCl_2$ and 4 equivalents of hydrogen donor, in 2.5 M aqueous NaOH solution, heated to 65°C for 16 h. A series of potential hydrogen donors was investigated, from which formic acid was the most effective (yield of hydrocinnamic acid **2** = 98%), followed in decreasing order of effectiveness by: glyoxylic acid (80%), gluconic acid (35%), *N*-(2-hydroxyethyl)ethylenediaminetriacetic acid (20%), glycolic

---

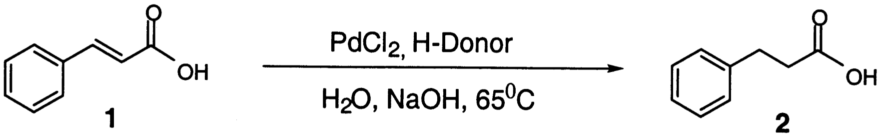
* Corresponding author.

0040-4039/00/$ - see front matter © 2000 Published by Elsevier Science Ltd.
PII: S0040-4039(00)01365-4

Table 1
Pd-catalyzed transfer hydrogenation with alkaline aqueous formate

Entry	Substrate	Product	Yield (%)
1			98 %
2			98 %
3			95 %
4			96 %
5			85 %
6			82 %
7			85%
8			80 %
9			80 %

acid (20%), and formaldehyde (5%). Formaldehyde is known to produce hydrogen under alkaline aqueous conditions,[4] but was ineffective for the reduction under these conditions. The reaction was also successful using varying hydroxide concentrations ranging from 0.5 to 5 M; however, no reduction was evident when 2.5 M Na_2CO_3 was used as base.[5,6]



A variety of other unsaturated carboxylic acids were also reduced under these conditions in excellent yields (Table 1, entries 2–4).[7] The α-*N*-acyldehydroamino acids (entries 5, 6) were converted to the corresponding *N*-acylphenylalanine derivatives in very good yields. The readily available azalactones (entries 7, 8) were also converted directly to the *N*-acyl amino acids. This procedure was also effective for reducing the α-keto group of phenylpyruvic acid, giving the product mandelic acid in very good yield (entry 9).

In summary, $PdCl_2$ is an effective catalyst for transfer hydrogenations using formic acid in alkaline aqueous media. This procedure is advantageous because no organic solvent is required, the reagents are inexpensive, and the catalyst is nonpyrophoric. These reaction conditions should be suitable for the reduction of a wide variety of organic substrates, and offers an economical, safe, and environmentally benign alternative to available procedures.

Acknowledgements

This research was supported by the Department of Energy Environmental Management Science Program.

References

1. (a) Brieger, G.; Nestrick, T. J. *Chem. Rev.* **1974**, *74*, 567–580; (b) Nishiguchi, T.; Tagawa, T.; Imai, H.; Fukuzumi, K. *J. Am. Oil Chem. Soc.* **1977**, *54*, 144–149; (c) Johnstone, R. A. W.; Wilby, A. H.; Entwistle, I. D. *Chem. Rev.* **1985**, *85*, 129–170; (d) Palmer, M. J.; Wills, M. *Tetrahedron: Asymmetry* **1999**, *10*, 2045–2061.
2. (a) Ram, S.; Ehrenkaufer, R. E. *Synthesis* **1988**, 91–95; (b) Rao, H. S. P.; Reddy, K. S. *Tetrahedron Lett.* **1994**, *35*, 171–174; (c) Dragovich, P. S.; Prins, T. J.; Zhou, R. *J. Org. Chem.* **1995**, *60*, 4922–4924; (d) Pande, P. P.; Joshi, G. C.; Mathela, C. S. *Syn. Commun.* **1998**, *28*, 4193–4200; (e) Ranu, B. C.; Sarkar, A.; Guchhait, S. K.; Ghosh, K. *J. Ind. Chem. Soc.* **1998**, *75*, 690–694; (f) Ranu, B. C.; Guchhait, S. K.; Ghosh, K. *J. Org. Chem.* **1998**, *63*, 5250–5251; (g) Banik, B. K.; Barakat, K. J.; Wagle, D. R.; Manhas, M. S.; Bose, A. K. *J. Org. Chem.* **1999**, *64*, 5746–5753.
3. (a) Hanson, B. E. *Coord. Chem. Rev.* **1999**, *186*, 795–807; (b) Lubineau, A.; Auge, J. *Top. Curr. Chem.* **1999**, *206*, 1–39; (c) Sinou, D. *Top. Curr. Chem.* **1999**, *206*, 41–59; (d) Genet, J. P.; Savignac, M. *J. Organomet. Chem.* **1999**, *576*, 305–317.
4. Ashby, E. C.; Doctorovich, F.; Liotta, C. L.; Neumann, H. M.; Barefield, E. K.; Konda, A.; Zhang, K.; Hurley, J.; Siemer, D. D. *J. Am. Chem. Soc.* **1993**, *115*, 1171–1173.
5. The weak base sodium carbonate is an effective base for Heck reactions in water: Bumagin, N. A.; More, P. G.; Beletskaya, I. P. *J. Organomet. Chem.* **1989**, *371*, 397–401.
6. Palladium catalysts convert aryl halides to biaryls with aqueous sodium formate, hydroxide, and surfactant: (a) Bamfield, P.; Quan, P. M. *Synthesis* **1978**, 537–538; (b) Rajagopal, S.; Spatola, A. F. *J. Org. Chem.* **1995**, *60*, 1347–1355.
7. Typical procedure: To a stirred solution of cinnamic acid (50 mg, 0.33 mmol) in 2.5 M aqueous NaOH (4 mL) was added $PdCl_2$ (6.0 mg, 0.025 mmol). Formic acid (50 μL, 1.3 mmol) was added dropwise, then heated to 65°C for 16 h. The reaction mixture was neutralized with 2 M HCl, extracted with diethyl ether (2×5 mL), washed with water (10 mL), and dried (Na_2SO_4). The product was then purified by a short column of silica gel eluted with 25% ethyl acetate in hexanes. Removal of solvent in vacuo gave hydrocinnamic acid (50 mg, 98% yield).