PERKIN 1 COMMUNICATION

Easy and partial hydrogenation of aromatic carbonyls to benzyl alcohols using Pd/C(en)-catalyst

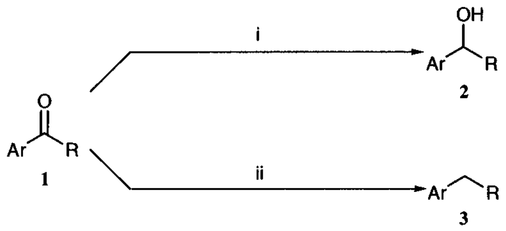
Hironao Sajiki, Kazuyuki Hattori and Kosaku Hirota *

Laboratory of Medicinal Chemistry, Gifu Pharmaceutical University, Mitahora-Higashi, Gifu 502-8585, Japan

Received (in Cambridge) 29th September 1998, Accepted 9th November 1998

Although 10% Pd/C catalyzed hydrogenolysis of aromatic ketones and aldehydes readily affords methylene compounds *via* intermediary benzyl alcohols, the employment of 10% Pd/C–ethylenediamine complex [Pd/C(en)] as a catalyst eased the formation of benzyl alcohols.

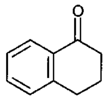
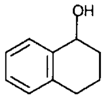
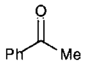
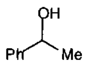
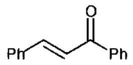
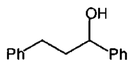
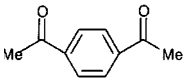
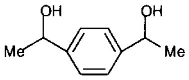
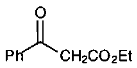
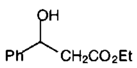
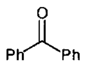
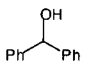
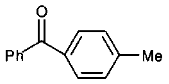
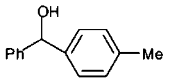
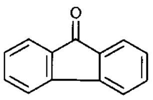
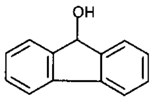
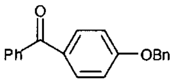
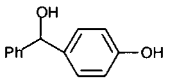
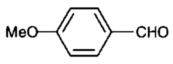
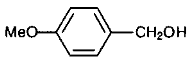
The preparation of alcohols through reduction of ketones and aldehydes is among the most fundamental subjects in organic synthetic chemistry. This significant transformation has been mainly accomplished by stoichiometric metal hydride reagents.[1] In contrast to a large number of effective stoichiometric reagents and some catalytic homogeneous hydrogenation catalysts[2–4] available for carbonyl reduction, few heterogeneous hydrogenation catalysts for reduction of aldehydes and ketones to alcohols have been developed.[1] Although the heterogeneous hydrogenation of aliphatic carbonyls does not occur easily as a rule, aromatic carbonyls hydrogenolyze to methylene compounds smoothly *via* formation of the intermediate benzyl alcohol (Scheme 1, **1**→**3**).[5,6] Therefore, it is extremely difficult to isolate the intermediate benzyl alcohol selectively when hydrogenating aromatic carbonyl compounds using a palladium catalyst.[7] While Ram and Spicer reported a transfer hydrogenation method for the partial reduction of aromatic carbonyls using 10% Pd/C and ammonium formate,[8] the main reduction tends to be accompanied by a reductive amination reaction with nucleophilic ammonia released from ammonium formate. Therefore, the development of heterogeneous palladium catalysts with excellent chemoselectivity between aromatic carbonyls and intermediary benzyl alcohols is highly desirable because of a series of practical benefits.[5]



Scheme 1 *Reagents and conditions*: i, 10% Pd/C(en), H_2 (balloon), MeOH, 24 h; ii, 10% Pd/C, H_2 (balloon), MeOH, <24 h.

We have recently established that a Pd/C catalyst formed an isolable complex with ethylenediamine (en) employed as a catalytic poison and the complex catalyst [Pd/C(en)] selectively catalyzed the hydrogenation of various functional groups (*e.g.* olefin, nitro, benzyl ester, or azido) without the hydrogenolysis of the *O*-benzyl protective group or the *N*-Cbz protective group of aliphatic amines.[9] We are now in a position to disclose that the Pd/C(en) catalyst is very efficient for the partial reduction of aromatic carbonyl compounds (Scheme 1, **1**→**2**).

Table 1 Pd/C(en)-catalyzed partial hydrogenation of aromatic ketones and aldehyde to benzyl alcohols

Entry	Substrate	Product	Yield (%)[a,b]
1			91
2			93
3			99
4			97
5			98
6			89
7			90
8			86
9			86
10			94

[a] The reaction was carried out using 0.5 mmol of the substrate in MeOH (2 mL) with 10% Pd/C(en) (10% of the weight of the substrate) under a hydrogen atmosphere (balloon) for 24 h and the structures of all the new compounds were determined by their IR, MS, and ^1H NMR spectra and HRMS or elemental analyses. [b] Upon the use of commercial 5 or 10% Pd/C instead of 10% Pd/C(en), the hydrogenolysis of the aromatic carbonyl compounds readily proceeded to give fully hydrogenolyzed methylene products in excellent yields.

First, the catalytic hydrogenation of 1-tetralone was carried out smoothly using the 10% Pd/C(en) catalyst† (10% of the weight of the substrate) in MeOH under a hydrogen atmosphere (balloon) for 24 h to provide partially reduced 1-hydroxytetralin in 91% isolated yield without formation of the fully hydrogenated tetralin (run 1 in Table 1). In addition, a competition experiment using a 1 : 1 mixture of 1-tetralone and cyclohexanone as a substrate indicated that only 1-tetralone was reduced to the corresponding 1-hydroxytetralin and the non-aromatic ketone, cyclohexanone, was quantitatively recovered unchanged. However, upon using a 10% Pd/C catalyst such a selective hydrogenation failed and tetralin was readily formed in 92% yield. To investigate the synthetic utility of this new finding, the selective hydrogenation of aromatic carbonyl groups to hydroxy groups was conducted on a variety of substrates (Table 1). The results show that the aromatic carbonyl compounds can be readily converted to the corresponding benzyl alcohols in excellent yields. In addition, the reactions of the *mono*-aromatic carbonyl group (runs 1–5 and 10) were very clean, and no chromatographic separation was required to obtain spectrally pure products. Although the resulting products from *di*-aromatic ketones (runs 6–9) were contaminated by a trace quantity of over-reduction product, the less polar methylene contaminant could be removed easily by simple flash column chromatography.[10] The reaction conditions were compatible with the hydrogenation of an olefin functionality (run 3). On the other hand, the *O*-benzyl protective group of 4-(benzyloxy)benzophenone, which possesses an electron withdrawing benzoyl group at the *p*-position, did not survive under these conditions (run 9).[9]

The chemoselectivity of the hydrogenation could be attributable to the difference of the coordination affinity between longer-conjugated aromatic carbonyls and benzyl alcohols to ethylenediamine-coordinated palladium. In Pd/C(en) catalyst, the original affinity of palladium for π-electrons should be reasonably reduced by ethylenediamine.

In summary, we have developed an efficient chemoselective hydrogenation of aromatic carbonyl groups to benzyl alcohols using the heterogeneous and easily handled Pd/C(en) catalyst under neutral conditions. The hydrogenolysis of the intermediate benzyl alcohols to methylene compounds could be mostly overcome. The chemoselectivity observed for aromatic carbonyl groups over intermediate benzyl alcohols and the general utility of this methodology will make this simple technique an attractive addition to the range of procedures already known for this general transformation.[1]

Experimental

General procedure for the partial hydrogenation of aromatic carbonyls

A mixture consisting of aromatic carbonyl compounds (1.0 mmol), 10% Pd/C(en) (10% of the weight of the substrate) and methanol (2 ml) was stirred at room temperature under a hydrogen atmosphere for 24 h. The reaction mixture was filtered using a membrane filter (Advantec DISMIC-13CP) and the filtrate was concentrated *in vacuo* to give in most cases an analytically pure product. If the product were not analytically pure, the residue was purified by flash column chromatography.[10]

Acknowledgements

This work was supported by the Research Foundation of Gifu Pharmaceutical University, Japan.

Notes and references

† 10% Pd/C(en) catalyst was prepared from 10% Pd/C according to the reported method for the preparation of 5% Pd/C(en) catalyst.[9]

1 R. C. Larock, *Comprehensive Organic Transformations*, VCH, NY, 1989, p. 527.

2 For non-asymmetric hydrogenation, see: M. J. Burk, T. G. P. Harper, J. R. Lee and C. Kalberg, *Tetrahedron Lett.*, 1994, **35**, 4963, and references cited therein.

3 For asymmetric hydrogenation using homogeneous catalysts, see, R. Noyori and H. Takaya, *Acc. Chem. Res.*, 1990, **23**, 345; H. Takaya and T. Ohta, *J. Synth. Org. Chem., Jpn.*, 1993, **51**, 1013; H. Doucet, T. Ohkuma, K. Murata, T. Yokozawa, E. Katayama, A. F. England, T. Ikariya and R. Noyori, *Angew. Chem., Int. Ed.*, 1998, **37**, 1703 and references cited therein.

4 For reviews on asymmetric transfer hydrogenations using homogeneous catalysts, see, G. Zassinovich, G. Mestroni and S. Gladiali, *Chem. Rev.*, 1992, **92**, 1051; R. Noyori and S. Hashiguchi, *Acc. Chem. Res.*, 1997, **30**, 97.

5 For reviews on hydrogenation, see, M. Freifelder, *Practical Catalytic Hydrogenation Techniques and Applications*, Wiley-Interscience, NY, 1971, p. 398; P. N. Rylander, *Catalytic Hydrogenation in Organic Synthesis*, Academic Press, NY, 1979, p. 271; P. N. Rylander, *Hydrogenation Methods*, Academic Press, NY, 1985, p. 157; S. Siegel, *Comprehensive Organic Synthesis*, eds. B. M. Trost and I. Fleming, Pergamon Press, NY, 1991, vol. 8, p. 417; M. Hudlicky, *Reductions in Organic Chemistry*, American Chemical Society, Washington, DC, 1996.

6 W. H. Hartung and R. Simonff, *Org. React.*, 1953, **7**, 263.

7 L. M. Werbel, E. F. Elslager and W. M. Pearlman, *J. Org. Chem.*, 1964, **29**, 967.

8 S. Ram and L. D. Spicer, *Synth. Commun.*, 1992, **22**, 2673.

9 H. Sajiki, K. Hattori and K. Hirota, *J. Org. Chem.*, 1998, **63**, 7990.

10 W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.

Communication 8/07486K