# Selective transfer dehydrogenation of aromatic alcohols on supported palladium

**Csilla Keresszegi, Tamas Mallat and Alfons Baiker***

*Laboratory of Technical Chemistry, Swiss Federal Institute of Technology, ETH Hönggerberg-HCl, CH-8093 Zürich, Switzerland. E-mail: baiker@tech.chem.ethz.ch; Fax: +411 632 1163*

***Received (in Montpellier, France) 15th March 2001, Accepted 18th June 2001***
***First published as an Advance Article on the web 17th August 2001***

Transfer dehydrogenation of various alcohols has been investigated over heterogeneous palladium catalysts using olefins as hydrogen acceptors. $Pd/Al_2O_3$ together with cyclohexene is the most active and selective system, affording a simple and convenient laboratory synthesis of aromatic ketones in refluxing cyclohexane. Hydrogenolysis-type side reactions can be suppressed by minute amounts of a tertiary amine (selective poisoning of Pd). Aliphatic and cycloaliphatic alcohols are barely reactive under these conditions, a difference which offers the possibility of the selective transformation of aromatic alcohols even in the presence of an aliphatic OH group.

Oxidation of alcohols to carbonyl compounds is an essential route in synthetic chemistry. A broad range of homogeneous and heterogeneous catalysts have been found to be useful for alcohol oxidation in the past decades.[1–6] From an environmental point of view, a highly attractive method is oxidative dehydrogenation over heterogeneous noble metal catalysts in aqueous media, using molecular oxygen as the oxidant. The procedure is particularly useful in carbohydrate chemistry.[7–11] Aerobic oxidation of water-insoluble alcohols can be performed in organic solvents but safety problems may hinder its practical application. Another drawback of the method is the limited possibility of tuning the selectivity according to special requirements, for example, differentiation between aromatic and aliphatic OH functional groups.

Replacing molecular oxygen with a readily available unsaturated organic compound as hydrogen acceptor, that is changing from oxidative dehydrogenation to transfer dehydrogenation, offers the possibility to overcome these limitations. Transfer dehydrogenation of alcohols over heterogeneous metal catalysts in the presence of nitrobenzene, phenol, cyclohexanone and ethylene was proposed many years ago[12,13] but the synthetic potential of the method has barely been exploited yet. Hayashi and coworkers[14,15] reported very recently that Pd/C in an ethylene atmosphere offers good yields in the dehydrogenation of aromatic alcohols to ketones at close to ambient conditions, though the reaction times were usually in the range of days. Here we show that the use of a liquid olefin as the hydrogen acceptor is more convenient and the reactions are remarkably faster. Application of $Pd/Al_2O_3$ with cyclohexene in refluxing cyclohexane provides a convenient and highly selective synthesis of aromatic ketones.

## Results

### Influence of catalysts and reaction conditions

Preliminary studies revealed that only a few olefins are really active as hydrogen acceptors in the transfer dehydrogenation of 1-phenylethanol (**1**) to acetophenone, a test reaction for the synthesis of aromatic ketones (Table 1). Over a 5 wt% $Pd/Al_2O_3$ catalyst the reactivity order is cyclohexene > vinyl acetate ≫ methyl acrylate > 1-hexene. The reaction rate increased at higher cyclohexene : **1** ratios, though over 90% acetophenone yield could be achieved in 5 h even with the lowest ratio applied (1.2) . For comparison, without a hydrogen acceptor the acetophenone yield was 35% in 1 h and the selectivity was also lower (93.7%). We conclude from Table 1 that only cyclohexene and vinyl acetate could accelerate the dehydrogenation of **1**, the other olefins rather poisoned the catalyst. Blocking of active sites by oligomers is a feasible explanation, though the different reactivity of olefins in transfer dehydrogenation reactions may also be due to differences in the adsorption strength relative to that of the substrate.[16,17]

Among the platinum metals, Pd was by far the most active in the dehydrogenation of **1**. When using cyclohexene in the presence of various supported Rh, Ru or Pt catalysts, the acetophenone yields were 3% or less after 1 h reaction time. A comparison of various commercially available supported Pd catalysts indicates that all catalysts afforded reasonable reaction rates and selectivity (Table 2). The rate of dehydrogenation increased and the selectivity decreased slightly with increasing catalyst concentration. For the following experiments a catalyst : alcohol mass ratio of 10% has been employed. The lower selectivity of some catalysts, in particular with Pd/C (Table 2), is due to the formation of ethylbenzene by hydrogenolysis of **1**. This disproportionation-type side reaction may be considered as a transfer dehydrogenation reaction in which the reactant acts both as a hydrogen donor and an acceptor (Scheme 1). This side reaction reveals a crucial requirement that the Pd catalyst–olefin system has to

**Table 1** Effect of H-acceptor on the transfer dehydrogenation of 1-phenylethanol (**1**) over $Pd/Al_2O_3$ [a,b]

| H-acceptor | H-acceptor : **1** mol ratio | Yield (%) |
|---|---|---|
| Cyclohexene | 5 | 77 |
| Cyclohexene | 2 | 72 |
| Cyclohexene | 1.2 | 69 |
| Vinyl acetate | 2 | 41 |
| Methyl acrylate | 2 | 9 |
| 1-Hexene | 2 | 6 |
| Cyclopentene[c] | 5 | <1 |
| Styrene | 5 | <1 |
| Methyl vinyl ketone | 2 | <1 |

[a] Conditions: 0.10 g 5 wt% $Pd/Al_2O_3$, 1.0 g **1**, 30 ml cyclohexane, 1 h, 80 °C. [b] The chemoselectivity to acetophenone is always 100%. [c] $T = 71\,°C$.

DOI: 10.1039/b102463a

**Table 2** Transfer dehydrogenation of 1-phenylethanol (**1**) to acetophenone with cyclohexene over various supported Pd catalysts and the effect of triethylamine as a selective poison[a]

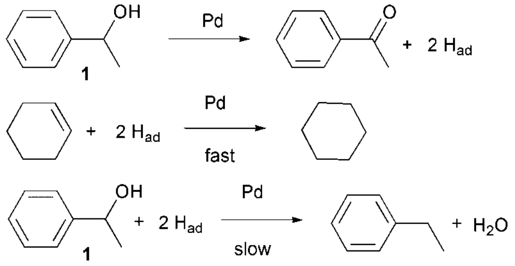
| | Amount of amine[b]/wt% | Time/h | Conv. (%) | Select.[c] (%) |
|---|---|---|---|---|
| $Pd/Al_2O_3$ | — | 1 | 77 | 100 |
| | | 5 | 93 | 100 |
| $Pd/CaCO_3$ | — | 1 | 47 | 100 |
| | | 5 | 79 | 100 |
| $Pd/TiO_2$ | — | 1 | 75 | 98.5 |
| | | 5 | 93 | 97.5 |
| Pd/organopolysiloxane | — | 1 | 84 | 99 |
| | | 5 | 96 | 99 |
| Pd/C | — | 1 | 93 | 93 |
| | 1 | 1 | 91 | 99.5 |
| | 1 | 2 | 95 | 99.5 |
| | 2 | 1 | 89 | 99.5 |
| | 2 | 2 | 93 | 99.5 |

[a] Conditions: 0.10 g catalyst (5 wt% metal), 1.0 g (8.2 mmol) **1**, 30 ml cyclohexane, alternatively 0.01 or 0.02 g (0.1–0.2 mmol) triethylamine, alcohol : cyclohexene mol ratio = 1 : 5, reflux (80 °C). [b] Relative to the amount of **1**. [c] The other product was ethylbenzene.

fulfill, namely, that the hydrogen consumption by the olefin should be much faster than the hydrogenation of the reactant. When necessary, the hydrogenolysis reaction can be selectively poisoned by addition of small amounts of a tertiary amine promoter (*e.g.*, $Et_3N$). Organic bases are known to poison hydrogenolysis reactions over Pt metals, while acids accelerate them.[18,19] An advantage of this solution is that the overall rate of dehydrogenation of **1** is barely diminished by the amine (Table 2).

In alcohol dehydrogenation the metallic surface sites ($Pd^0$) are much more active than the oxygen-covered Pd or surface Pd oxides formed by exposing the catalyst to ambient air.[9–11] Before the aerobic oxidation of alcohols on Pt or Pd, the catalyst is usually prereduced by hydrogen at room temperature to form the $M^0$ active sites. The alcohol reactant can also reduce the oxidized metal but this process is much slower and incomplete at room temperature.[10] Here we found that prereduction of Pd by hydrogen at room temperature accelerated the reaction at low conversion but the yields after several hours were barely affected, compared to the reaction without this pretreatment. It is important that both the alcohol and the olefin should be added to the catalyst–solvent slurry before heating up the reaction mixture. If the slurry is heated up in the absence of olefin, the selectivity drops due to formation of a mixture of the corresponding carbonyl compound and hydrocarbon according to Scheme 1.

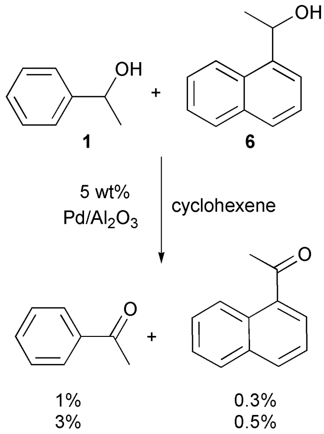
Various solvents may be employed for the reaction. Higher than 90% yields to acetophenone were obtained in 1–3 h over $Pd/Al_2O_3$ in refluxing cyclohexane, heptane and toluene. Transfer dehydrogenation of **1** was facile at 80 °C or higher temperatures but rather slow under ambient conditions. Polar organic solvents that adsorb strongly on Pd retarded the dehydrogenation reaction. Solvents that are reducible and may act as hydrogen acceptors, such as acetonitrile, prevented the complete transformation of **1**.



**Scheme 1** Competitive hydrogenation of cyclohexene (H-acceptor) and 1-phenylethanol (**1**, reactant) explains the apparent disproportionation of **1** as a typical side reaction during transfer dehydrogenation.

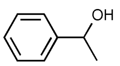
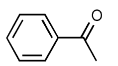
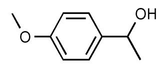
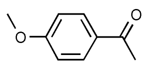
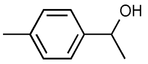
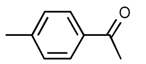
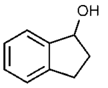
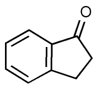
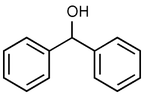
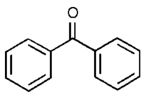
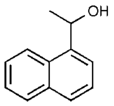
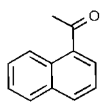
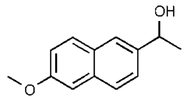
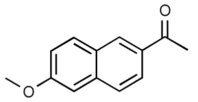
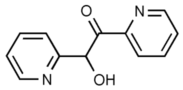
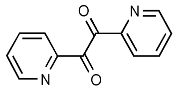
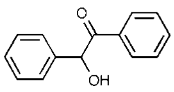
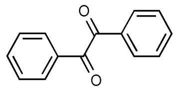
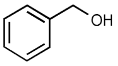
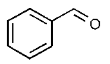
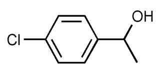
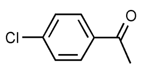
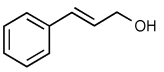
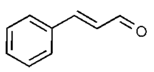
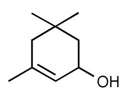
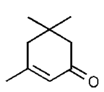
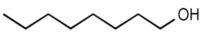
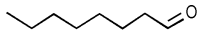
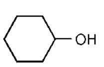
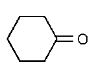
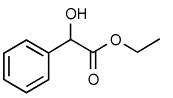
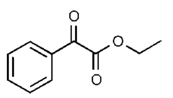
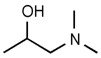
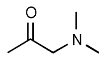
### Scope and limitations of the Pd–cyclohexene system

Application of $Pd/Al_2O_3$ (without any catalyst pretreatment) with cyclohexene in refluxing cyclohexane seems to be a fast and convenient laboratory method for the synthesis of aromatic ketones. Examples on the application range of the method are collected in Table 3. Note that all substrates dissolved in hot cyclohexane, thus the sometimes low reaction rates cannot be attributed to solubility problems. Dehydrogenation of various secondary aromatic alcohols (**1**–**5**) is selective and affords good yields to the corresponding ketones. The slower reaction in the case of two aromatic rings in the reactant (particularly **6**, **7** and **9**) is attributed to a too strong adsorption of the product on the Pd surface. This assumption is supported by the competitive dehydrogenation of **1** and **6** (Scheme 2). Dehydrogenation of **6** is slow with or without **1**, affording less than 1% yield to 1-acetonaphthone. However, the presence of **6** decelerated the initial rate of transformation of **1** by a factor of *ca.* 100. The most likely adsorption mode of 1-acetonaphthone is a flat adsorption of the aromatic ring system and the carbonyl group parallel to the Pd surface, involving the extended delocalized π-electron system of the molecule. Apparently, this adsorption mode is strongly



**Scheme 2** Competitive transfer dehydrogenation of **1** and **6**. Conditions: 0.10 g 5 wt% $Pd/Al_2O_3$, 0.5 g of each alcohol, alcohol : cyclohexene mol ratio = 1 : 2, 30 ml cyclohexane, reflux (80 °C).

**Table 3** Transfer dehydrogenation of various alcohols to ketones with cyclohexene[a]

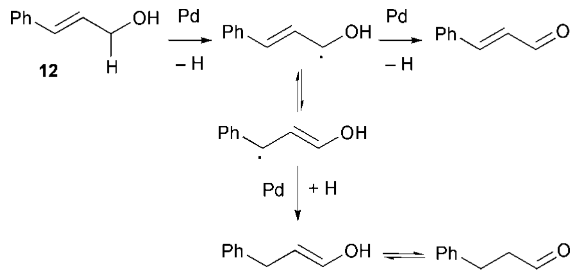
| | Substrate | Time/h | Product | Conv. (%) | Select. (%) |
|---|---|---|---|---|---|
| **1** |  | 3 |  | 92 | 100 |
| **2** |  | 5 |  | 91 | 100 |
| **3** |  | 5<br>15[b] |  | 50<br>82 | 97.5<br>96 |
| **4** |  | 21 |  | 87 | 100 |
| **5** |  | 15 |  | 88 | 100 |
| **6** |  | 5 |  | 0.4 | 100 |
| **7** |  | 5<br>15[b] |  | 8<br>46 | 100<br>100 |
| **8** |  | 8 |  | 50[c] | 100 |
| **9** |  | 7 |  | 2[c] | 100 |
| **10** |  | 15 |  | 20 | 93 |
| **11** |  | 5 |  | 29 | 50 |
| **12** |  | 5 |  | 87 | 20.5 |
| **13** |  | 5 |  | 41 | 7.5 |
| **14** |  | 5 |  | 1 | 100 |
| **15** |  | 5 |  | 1 | 100 |
| **16** |  | 5 |  | 0 | — |
| **17** |  | 5 |  | 0 | — |

[a] Conditions: 0.10 g 5 wt% $Pd/Al_2O_3$, 1.0 g alcohol, 30 ml cyclohexane, reflux (80 °C), alcohol : cyclohexene mol ratio = 1 : 2. [b] 0.30 g 5 wt% $Pd/Al_2O_3$, alcohol : cyclohexene mol ratio = 1 : 5. [c] Determined by $^1H$ NMR analysis in $CDCl_3$.

favored for 1-acetonaphthone compared to **1**; the latter possesses only one aromatic ring and cannot efficiently compete for the active sites.

Dehydrogenation of primary aromatic alcohols (*e.g.*, **10**) to aldehydes is remarkably slower and also less selective than the synthesis of aromatic ketones. A more important limitation of the method is that reducible functional groups, such as aromatic halogen (**11**) or C=C bonds (**12**) are not stable under the reaction conditions. Hydrogenolysis or hydrogenation of these functions by the hydrogen formed in the dehydrogenation of the CH–OH function diminishes the selectivity.

A useful feature of the method is that aliphatic and cycloaliphatic primary and secondary alcohols are not reactive. The same is true for α-functionalized aliphatic alcohols, for example α-hydroxy esters (**16**) and 1,2-aminoalcohols (**17**). An exception is the dehydrogenation of allylic alcohols, such as isophorol (**13**), whose reactions are relatively fast but nonselective. The poor selectivity to ketones is only partly due to



**Scheme 3** Byproduct formation *via* isomerization over Pd during dehydrogenation of allylic alcohols.

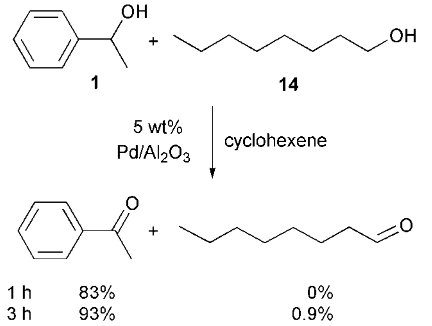
the side reaction depicted in Scheme 1. Another, dominant route may be isomerization *via* the half-dehydrogenated state as shown in Scheme 3.[20] For example, dehydrogenation of cinnamyl alcohol (**12**) afforded a mixture of 3-phenyl-1-propanol, 3-phenyl-1-propanal and cinnamaldehyde as major products.

The low reactivity of aliphatic (**14**) and cycloaliphatic (**15**) alcohols can be exploited for the selective synthesis of aromatic ketones. In the example shown in Scheme 4 a reactant possessing both aromatic and aliphatic OH groups is mimicked by an equimolar mixture of **1** and **14**. As expected on the basis of Table 3, competitive dehydrogenation of **1** and **14** afforded in 3 h higher than 90% yield to acetophenone while **14** remained predominantly unattacked. For comparison, the Pt metal catalyzed aerobic oxidation of aliphatic alcohols is not slower than that of aromatic alcohols. As an example, oxidation of 1-heptanol and 1-dodecanol on $PtO_2$ in heptane at 60 °C afforded 26 and 77% aldehyde yields in 1 and 0.25 h, respectively.[21] Under the same conditions, oxidation of **10** to benzaldehyde afforded 78% yield in 1 h.

## Discussion

The Pt metal-catalyzed aqueous phase oxidative dehydrogenation of alcohols with molecular oxygen affords high yields to ketones and carboxylic acids under mild conditions. A drawback of the method is the high activity of Pt and Pd-based catalysts in the oxidation of almost all types of primary and secondary alcohols. In contrast, transfer dehydrogenation over supported Pd catalysts using cyclohexene as the hydrogen acceptor allows fast and selective synthesis of aromatic ketones only; aliphatic and cycloaliphatic primary and secondary alcohols are barely reactive under the conditions applied. Application of cyclohexene in refluxing cyclohexane is convenient as the coproduct formed from the hydrogen acceptor is identical to the solvent.

Several liquid olefins have been tested together with $Pd/Al_2O_3$ and the conditions have been optimized for cyclohexene, which was the most reactive hydrogen acceptor (Table 1). We have to emphasize that other olefins such as vinyl acetate or 1-hexene may also be used for the synthesis of aromatic carbonyl compounds when lower reaction rates are acceptable. For example, using these two olefins for the synthesis of acetophenone, 97 and 92% yields respectively, were achieved in 5 h, and the only byproduct was ethylbenzene (for conditions see Table 3).



**Scheme 4** Competitive transfer dehydrogenation of **1** and **14**. Conditions: 0.10 g 5 wt% $Pd/Al_2O_3$, 0.5 g of each alcohol, alcohol : cyclohexene mol ratio = 1 : 2, 30 mol cyclohexane, reflux (80 °C).

The high reactivity of cyclohexene as a hydrogen acceptor may be astonishing at first sight, as cyclohexene is widely used as an H-donor in transfer hydrogenation reactions over supported Pd catalysts.[22–25] In fact, when refluxing an acetophenone : 1-phenylethanol = 94 : 6 mixture in cyclohexane solvent over $Pd/Al_2O_3$, the ketone : alcohol ratio increased or decreased depending on the cyclohexene concentration. When the alcohol : cyclohexene ratio was very low, 1 : 40, acetophenone was slowly hydrogenated to 1-phenylethanol (0.5–1% conversion per hour). The double role of cyclohexene can explain our observation that increasing the excess of cyclohexene in transfer dehydrogenation reactions enhanced the initial rate of alcohol conversion but the final yield could not be improved.

We can conclude that transfer dehydrogenation of alcohols with the $Pd/Al_2O_3$–cyclohexene system offers a facile and convenient synthesis of aromatic ketones. The amount of hydrocarbon formed by hydrogenolysis of the CH–OH function can be minimized by selective poisoning with trace amounts of a tertiary amine, such as $Et_3N$.

## Experimental

### Materials

Five wt% Pd/C (Fluka, product no. 75992), 5 wt% $Pd/Al_2O_3$ (Johnson Matthey, product no. 56482), 5 wt% $Pd/CaCO_3$ (Fluka, product no. 76032), 5 wt% $Pd/TiO_2$ (Johnson Matthey) and 5 wt% Pd/organopolysiloxane (Degussa, product no. 1994-8874) catalysts were used for transfer dehydrogenation without any treatment. 1-Phenylethanol (Aldrich, >98%), DL-6-methoxy-α-methyl-2-naphthalenemethanol (Acros, 98%), benzyl alcohol (Fluka, 98%), cinnamyl alcohol (Fluka, 97%), 1-dimethylamino-2-propanol (Fluka, 98%), 1-octanol (Fluka, 99.5%), benzhydrol (Aldrich, 99%), benzoin (Aldrich, 98%), 3,5,5-trimethyl-2-cyclohexene-1-ol (Fluka, 95%), 1-(4-chlorophenyl)ethanol (Aldrich, 98%), 1-(1-naphthyl)ethanol (Fluka, 99%), α-pyridoin (Aldrich, 99%), 1-(4-methoxyphenyl)ethanol (Aldrich, 99%), ethylmandelate (Merck, 98%), 1-(4-methylphenyl)ethanol (Lancaster, 97%), cyclohexanol (Merck, >99%) were used as received. 1-Indanol (Merck, >98%) was purified by sublimation. Analytical grade solvents were used as received. Cyclohexene (Fluka, 99.5% or Merck, >99%), 1-hexene (Fluka, 98%), methyl acrylate (Merck, >99%), cyclopentene (Aldrich, 99%), styrene (Aldrich, 99%), methyl vinyl ketone (Merck, >95%) and vinyl acetate (Aldrich, 99%) were used as H-acceptors. Triethylamine was a Siegfried Synopharm product (99%).

### Methods

Catalyst (0.10 g), alcohol (1.0 g), hydrogen acceptor, 30 ml solvent and $Et_3N$ (0.01–0.02 g), when used as a catalyst poison, were put in a 100 ml glass reactor. Air was replaced by Ar and the reactor was put into a preheated oil bath. The reactions were carried out at reflux temperature with intensive magnetic stirring. Alcohol and cyclohexene conversion and the product distribution were determined by GC analysis (Thermo Quest Trace 2000, equipped with an HP-FFAP capillary column and FID detector). Yields in the dehydrogenation of **8** and **9** were determined by $^1H$ NMR (Bruker Advance DPX300, 300 MHz, in $CDCl_3$). Products were identified by GC-MS, NMR, and GC analysis of authentic samples.

## References

1 I. E. Marko, P. R. Giles, M. Tsukazaki, S. M. Brown and C. J. Urch, in *Transition Metals for Organic Synthesis*, ed. M. Beller and C. Bolm, Wiley-VCH, Weinheim, 1998, vol. 2, p. 350.

2 S. J. H. F. Arts, E. J. M. Mombarg, H. van Bekkum and R. A. Sheldon, *Synthesis*, 1997, 597.

3 R. A. Sheldon, I. W. C. E. Arends and A. Dijksman, *Catal. Today*, 2000, **57**, 157.

4 M. Muhler, in *Handbook of Heterogeneous Catalysis*, ed. G. Ertl, H. Knözinger and J. Weitkamp, VCH, Weinheim, 1997, vol. 5, p. 2274.

5 C. F. de Graauw, J. A. Peters, H. van Bekkum and J. Huskens, *Synthesis*, 1994, 1007.

6 T. Naota, H. Takaya and S.-I. Murahashi, *Chem. Rev.*, 1998, **98**, 2599.

7 K. Heyns, H. Paulsen, G. Rüdiger and J. Weyer, *Fortschr. Chem. Forsch.*, 1968/69, **11**, 285.

8 A. H. Haines, *Methods for the Oxidation of Organic Compounds*, Academic Press, London, 1988.

9 M. Besson and P. Gallezot, in *Fine Chemicals through Heterogeneous Catalysis*, ed. R. A. Sheldon and H. van Bekkum, Wiley-VCH, Weinheim, 2001, p. 507.

10 T. Mallat and A. Baiker, *Catal. Today*, 1994, **19**, 247.

11 H. van Bekkum, in *Carbohydrates as Organic Raw Materials*, ed. F. W. Lichtenthaler, VCH, Weinheim, 1990, p. 289.

12 O. Bayer, in *Methoden der Organischen Chemie* (*Houben-Weyl*), ed. E. Müller, G. Thieme, Stuttgart, 1954, vol. 7/1, p. 160.

13 D. Kramer, in *Methoden der Organischen Chemie* (*Houben-Weyl*), ed. E. Müller, G. Thieme, Stuttgart, 1973, vol. 7/2a, p. 699.

14 M. Hayashi, K. Yamada and S. Nakayama, *Synthesis*, 1999, 1869.

15 M. Hayashi, K. Yamada and S. Nakayama, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1501.

16 T. Nishiguchi, H. Imai, Y. Hirose and K. Fukuzumi, *J. Catal.*, 1976, **41**, 249.

17 Y. H. Kim and J. Y. Choi, *Tetrahedron Lett.*, 1996, **37**, 8771.

18 P. Rylander, *Catalytic Hydrogenation in Organic Syntheses*, Academic Press, New York, 1979.

19 F. Notheisz and M. Bartok, in *Fine Chemicals through Heterogeneous Catalysis*, ed. R. A. Sheldon and H. van Bekkum, Wiley-VCH, Weinheim, 2001, p. 415.

20 M. Y. Sheikh and G. Eadon, *Tetrahedron Lett.*, 1972, **13**, 257.

21 K. Heyns and L. Blazejewicz, *Tetrahedron*, 1960, **9**, 67.

22 M. A. Aramendia, V. Borau, C. Jimenez, J. M. Marinas, M. E. Sempere and F. J. Urbano, *React. Kinet. Catal. Lett.*, 1992, **46**, 279.

23 S. De, N. Jain, H. G. Krishnamurty and Vimal, *Indian J. Chem. Sect. B*, 1994, **33**, 163.

24 V. Sansanwal and H. G. Krishnamurty, *Synth. Commun.*, 1995, **25**, 1901.

25 R. Toplak, J. Svete, B. Stanovnik and S. G. Grdadolnik, *J. Heterocycl. Chem.*, 1999, **36**, 225.