Transfer hydrogenation of olefins catalysed by nickel nanoparticles

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1. Introduction

The reduction of carbon–carbon double bonds is one of the fundamental reactions in organic chemistry. For this transformation, catalytic hydrogenation, either under homogeneous or heterogeneous conditions, is generally preferred to other non-catalytic chemical methods. Homogeneous catalysts have exhibited high activity and selectivity with special applications in asymmetric catalysis, although they are often expensive and their separation and reuse troublesome. In recent years, however, heterogeneous catalysis has experienced an enormous progress, with the catalysts being, in some cases, even more selective than their homogeneous counterparts. Moreover, heterogeneous catalysts are easy to separate and reuse, minimising the presence of metal traces in the product, improving the handling and process control and, therefore, reducing the overall costs. At any rate, catalytic hydrogenation requires special care in the handling of hydrogen (a highly flammable and explosive gas) and, in some cases, rather expensive catalysts and high pressures are mandatory for the reaction to occur.

In this sense, the hydrogen-transfer reduction of organic compounds is an advantageous methodology since: (a) the hydrogen source is easy to handle (no gas containment or pressure vessels are necessary), (b) possible hazards are minimised, (c) the mild reaction conditions used can afford enhanced selectivity and, (d) catalytic asymmetric transfer hydrogenation can be applied in the presence of chiral ligands. In contrast with the reduction of carbonyl compounds, the hydrogen-transfer reduction of olefins has been little studied, mainly involving noble-metal catalysts. Phosphane-ruthenium complexes can transfer hydrogen from alcohols, formic acid, and hydroaromatic compounds to olefins. Formic acid is the hydrogen donor of choice under palladium catalysis (1,4-cyclohexadiene has been recently used), whereas rhodium and iridium complexes have been rarely applied. In the above studies, a narrow substrate scope has been tested, mainly covering activated olefins.

In the search for cheaper catalytic systems, nickel appears as an alternative to the noble metals since it is about 100-fold cheaper than palladium and ruthenium, and much cheaper than rhodium and iridium (referred to their chlorides). As a recent example, clay-entrapped nickel nanoparticles have been found to efficiently catalyse the reduction of styrenes using hydrazine as the hydrogen source. On the other hand, 2-propanol is a very popular hydrogen donor since it is cheap, non-toxic, volatile, possesses good solvent properties and it is transformed into acetone, which is environmentally friendly and easy to remove from the reaction system. Despite the attractiveness of the combination Ni/i-PrOH, only two reports describe its application to the transfer hydrogenation of olefins. In the first one, Raney nickel (10–50 wt % of total substrate) was used under reflux, showing high conversions for cinnamates and cyclic olefins and low conversions for acyclic olefins. In the second report, activated metallic nickel, prepared by thermal decomposition of in situ generated nickel diisopropoxide in boiling 2-propanol, was more effective in the reduction of non-functionalised and non-activated olefins (10–30 mol % Ni, 95–100 °C).

Due to our continued interest on active metals, some years ago, we reported that active nickel, prepared from stoichiometric...
The nickel nanoparticles (NiNPs) were initially generated from anhydrous nickel(II) chloride, lithium powder and a catalytic amount of DTBB (4,4'-di-tert-butylbiphenyl, 5 mol %) in THF at room temperature. A blank experiment, consisting in a standard reaction in the absence of the substrate but in the presence of the hydrogen source (i.e., NiCl₂, Li, DTBB, THF, i-PrOH, 76 °C, 1 h), confirmed the formation of NiNPs. Transmission electron microscopy (TEM) analysis revealed the presence of spherical and highly uniform nanoparticles within the range 0.75–2.88 nm (ca. 1.75±1.00 nm). A preliminary study was carried out using 1-octene as model substrate in order to optimise the amount of catalyst and compare with other nickel catalysts (Table 1). A 1:10 NiNPs/substrate molar ratio at 76 °C was shown to be inactive (entry 1), whereas a quantitative conversion into the product n-octane was observed with a 1:5 NiNPs/substrate molar ratio (20 mol % Ni) (entry 2). Interestingly, the reaction occurred with the latter even at room temperature, albeit with incomplete conversion (entry 3). A series of experiments were performed with commercially available nickel catalysts. Raney nickel behaved similarly to the NiNPs but longer reaction time was needed in order to achieve complete conversion, as shown in entry 4. Nickel on silica–alumina behaved similarly (entry 5). Interestingly, the reaction occurred with Raney nickel even at room temperature with a 1:5 NiNPs/substrate molar ratio (20 mol % Ni) (entry 6). All isolated products were >99% pure (GLC and/or 1H NMR).

2. Results and discussion

The nickel nanoparticles (NiNPs) were initially generated from anhydrous nickel(II) chloride, lithium powder and a catalytic amount of DTBB (4,4'-di-tert-butylbiphenyl, 5 mol %) in THF at room temperature. A blank experiment, consisting in a standard reaction in the absence of the substrate but in the presence of the hydrogen source (i.e., NiCl₂, Li, DTBB, THF, i-PrOH, 76 °C, 1 h), confirmed the formation of NiNPs. Transmission electron microscopy (TEM) analysis revealed the presence of spherical and highly uniform nanoparticles within the range 0.75–2.88 nm (ca. 1.75±1.00 nm). A preliminary study was carried out using 1-octene as model substrate in order to optimise the amount of catalyst and compare with other nickel catalysts (Table 1). A 1:10 NiNPs/substrate molar ratio at 76 °C was shown to be inactive (entry 1), whereas a quantitative conversion into the product n-octane was observed with a 1:5 NiNPs/substrate molar ratio (20 mol % Ni) (entry 2). Interestingly, the reaction occurred with the latter even at room temperature, albeit with incomplete conversion (entry 3). A series of experiments were performed with commercially available nickel catalysts. Raney nickel behaved similarly to the NiNPs but longer reaction time was needed in order to achieve complete conversion, as shown in entry 4. Nickel on silica–alumina behaved similarly (entry 5). Interestingly, the reaction occurred with Raney nickel even at room temperature with a 1:5 NiNPs/substrate molar ratio (20 mol % Ni) (entry 6). All isolated products were >99% pure (GLC and/or 1H NMR).
order to achieve the same conversion at 76 °C (entry 4), while the activity of the former drastically dropped at room temperature (entry 5). Other commercially available nickel catalysts, such as Ni–Al, Ni/SiO2–Al2O3, or NiO, were totally inactive under the above mentioned conditions (entries 6–8). The starting alkene was also the only reaction product when the reaction was carried out in the absence of any nickel catalyst (Li, DTBB, THF, i-PrOH; entry 9).

The optimised reaction conditions (Scheme 1) were first applied to a variety of non-functionalised olefins (Table 2). Terminal alkenes were easily reduced to the corresponding alkanes in quantitative yield (entries 1 and 2). The same behaviour was observed for the internal alkene trans-4-octene (entry 3), whereas trans-5-decene could not be completely reduced (entry 4). Trans-stilbene was readily and quantitatively transformed into 1,2-diphenylethane (entry 5). In contrast, only 40% conversion was achieved for the reaction catalysed by Raney nickel.9 In this case, the authors reported the formation of 1-phenyl-2-cyclohexylethane as a side product on prolonged heating (entry 5, footnote e). Longer reaction time was needed for the geminal alkene 1,1-diphenylethene (entry 7) in comparison with trans-stilbene and α-methylstyrene (entry 6), although the product was also obtained in excellent yield. The cyclic substrates cyclooctene, 1,5-cyclooctadiene, and 1,3-cyclooctadiene were also tested (entries 8 and 9). The results are summarised in Table 3.

Table 3

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkene</th>
<th>t (h)</th>
<th>Product</th>
<th>Yield (%)</th>
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<tr>
<td>1</td>
<td>CO2Et</td>
<td>2</td>
<td>CO2Et</td>
<td>89d</td>
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<tr>
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<td>24e</td>
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<td>48</td>
<td>HO</td>
<td>&gt;99</td>
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<tr>
<td>5</td>
<td>MeO</td>
<td>3</td>
<td>MeO</td>
<td>&gt;99</td>
</tr>
<tr>
<td>6</td>
<td>O</td>
<td>2</td>
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<td>96</td>
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<tr>
<td>9</td>
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<td>51 (90)f</td>
</tr>
<tr>
<td>10</td>
<td>Ph</td>
<td>3</td>
<td>Ph</td>
<td>&gt;99 (0)h</td>
</tr>
<tr>
<td>11</td>
<td>H</td>
<td>2</td>
<td>H</td>
<td>&gt;99 (0)h</td>
</tr>
</tbody>
</table>

*Alkene (5 mmol), NiNPs (1 mmol), 2-propanol (5 mL), 76 °C.
*a All isolated products were ≥99% pure (GLC and/or 1H NMR).
*b Isolated yield.
*c It includes 11% of the transesterified product isopropyl heptanoate.
*d Reaction performed at room temperature.
*e It includes 22% of the transesterified product isopropyl hexanoate.
*f Conversion in parenthesis.
*g Conversion in parenthesis.

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were successfully converted into cyclooctane, with the isolated diene 1,5-cyclooctadiene, a well-known ligand for Ni(0), being more reluctant to react.

We next studied the reduction of a series of functionalised olefins (Table 3). Both terminal and internal unsaturated esters were rapidly reduced to the corresponding saturated esters in high yields, including minor amounts of the isopropyl esters resulting from partial transesterification (entries 1 and 3). Interestingly, transesterification could be completely suppressed for ethyl 6-heptenoate when the reaction was performed at room temperature (entry 2). The transfer hydrogenation of 4-allyl-2-methoxyphenol was, however, rather slow, though complete conversion into the expected product was reached after prolonged heating (entry 4). The electron-rich aromatics 3,4-dimethoxystyrene and isoosafrole were also nicely reduced in high isolated yields (entries 5 and 6). Good results were obtained for allylic alcohols, with either a monosubstituted or geminal carbon–carbon double bond (entries 7 and 8). In these cases, we did not observe any isomerisation to the corresponding carbonyl compounds. It is well known that transition-metal catalysts, some of which are also used in catalytic hydrogenation, can induce this type of isomerisation.18 In particular, the competition between hydrogenation and isomerisation of allylic alcohols over different supported palladium catalysts, including Pd/C, has been often described.19 It is noteworthy, that even the monoterpene (+)-linalool, which contains both a mono- and a tri-substituted carbon–carbon double bond, was transformed into the saturated tertiary alcohol 3,7-dimethyloctan-3-ol (tetrahydrolinalool) in moderate yield and longer reaction time (entry 9). Apparently, this transformation is not so trivial, with most methods showing a preferential reduction of the terminal carbon–carbon double bond.20

The reduction of allyl benzyl ether and N-allylcyclohexylamine deserves a comment aside. In both cases, the desired products were obtained in short reaction times and quantitative yields (Table 3, entries 10 and 11). Furthermore, no deallylation products were detected despite the known ability of nickel(0) to catalyse the allyl group cleavage in ethers21 and amines.22 In addition, removal of the benzyl group in allyl benzyl ether by hydrogenolysis was prevented (entry 10). This result is very interesting if we take into account that benzyl ethers can undergo hydrogenolysis, under the same standard conditions used for the catalytic hydrogenation of olefins (e.g., H2–Pd/C, EtOH).23 In order to know whether this special behaviour was particular for the NiNPs, a short comparative study was conducted with different nickel catalysts (Scheme 2). Raney nickel did not alter the starting material, whereas Ni(O-i-Pr)2 afforded benzyl n-propyl ether in moderate yield. According to the authors, in the latter case, the substrate underwent both partial hydrogenolysis and carbon–carbon double bond migration.24 Therefore, the NiNPs were shown to be superior to Raney nickel, which besides being the most universal and commercially available nickel catalyst, we must not ignore some of its inherent disadvantages, namely: (a) the difficulty in calculating the dosage (it is usually measured as a suspension rather than weighed); (b) ferromagnetic properties that preclude the use of magnetic stirring; (c) it is potentially hazardous (pyrophoric); and (d) it becomes inactive after prolonged storage, presumably because it loses hydrogen slowly.

The versatility of the NiNPs was demonstrated in the synthesis of brittonin A, a natural dihydrostilbene isolated from Frullania brittoniae subsp. truncatofilia (Fischerdig musciicola).24 We have recently reported a novel synthesis of stilbenes, from benzyl alcohols as phosphorus ylide partners, through a one-pot Wittig-type olefination reaction promoted by nickel nanoparticles.25 Resveratrol, DMU-212, and analogues have been synthesised using this methodology.26 The precursor of the target molecule, dehydrobrittonin A, is a symmetrically-substituted highly poly-methoxylated stilbene that could be synthesised from only one starting material (Scheme 3). Thus, 3,4,5-trimethoxybenzyl alcohol served both as the precursor of the corresponding ylide and as its partner in the Wittig-type olefination. This reaction was shown to be slower, in comparison with the homologues with less methoxy substituents, leading to the expected stilbene in moderate yield as a mixture of diastereoisomers. Final hydrogen-transfer reduction of dehydrobrittonin A, catalysed by NiNPs, furnished brittonin A in quantitative conversion after 2 h and 95% isolated yield (Scheme 3).

We also studied the possibility of reutilisation of the NiNPs using trans-stilbene as the substrate. Thus, once the reaction was stopped, the NiNPs were decanted and the supernatant removed, followed by further addition of 2-propanol and the substrate. Table 4 shows that the NiNPs, in a 1:1 M ratio, could be reused over four consecutive cycles with a quantitative conversion into the reduced product. It was observed, however, that longer time was required in each cycle to reach a complete conversion. This progressive catalyst deactivation was more pronounced for a 1:5 NiNPs/substrate molar ratio, with an important decrease in the conversion being observed in the second cycle. The latter result
differences from that obtained in the transfer hydrogenation of carbonyl compounds, where the NiNPs could be reused over five consecutive cycles with a good performance.  

Concerning the reaction mechanism and based on deuterium labeling experiments, previously carried out for the transfer hydrogenation of carbonyl compounds with isopropanol, a similar dihydride-type mechanism could be invoked in this case, where the two hydrogen atoms of the donor become equivalent after being transferred to the metal to give the dihydride (Scheme 4). It must be clarified that dihydride species refer in this case to those resulting from the transfer of the two hydrogen atoms of the donor to the surface of the metal.

Scheme 4. Proposed dihydride-type mechanism for the transfer hydrogenation of olefins with isopropanol catalysed by NiNPs.

3. Conclusion

We have demonstrated, for the first time, that nickel nanoparticles can effectively catalyse the heterogeneous transfer hydrogenation of olefins using 2-propanol as the hydrogen donor. A variety of non-functionalised and functionalised olefins have been reduced in high yields. The process has been shown to be highly chemoselective for substrates, which are prone to undergo isomerisation or hydrogenolysis. Moreover, the NiNPs-catalysed transfer hydrogenation, in combination with a previous NiNPs-promoted Wittig-type olefination, has been applied to the synthesis of the natural dihydrosimpletine brittonin A. The transfer hydrogenation methodology presented herein is, in general, superior to others involving nickel catalysts and can be considered as an interesting alternative to other reduction methods involving noble-metal catalysts, including catalytic hydrogenation.

4. Experimental

4.1. General

THF was directly used without any purification (Acros, 99.9%). Anhydrous nickel(II) chloride (Aldrich, 98%), lithium powder (MERCK AG, L), and 2-propanol (Panreac, Acros, >99.5%) were commercially available. All the starting materials were commercially available of the best grade (Aldrich, Acros, Alfa Aesar) and were used without further purification. NMR spectra were recorded on 300 and 400 spectrometers (300 and 400 MHz for 1H NMR, and 75 and 100 MHz for 13C NMR, respectively) using CDCl3 as solvent and TMS as internal standard; chemical shifts are given in δ (ppm) and coupling constants (J) in Hz. Mass spectra (El) were obtained at 70 eV, fragment ions in m/z with relative intensities (%) in parenthesis. The purity of volatile compounds and the chromatographic analyses (GLC) were determined with an instrument equipped with a flame ionisation detector and a 30 m capillary column (0.32 mm diameter, 0.25 μm film thickness), using nitrogen (2 mL/min) as carrier gas, Ṫinjector=275°C, Ṫcolumn=60°C (3 min) and 60–270°C (15°C/min); retention times (tR) are given under these conditions. Thin layer chromatography was carried out on TLC plastic sheets with silica gel 60 F254 (Merck). All products in Tables 2 and 3 were characterised by comparison of their physical and spectroscopic properties with those of commercially available samples:


4.2. General procedure for the NiNPs-catalysed transfer hydrogenation of olefins

The NiNPs suspension was freshly prepared by adding nickel(II) chloride (130 mg, 1 mmol) over a suspension of lithium (14 mg, 2 mmol) and DTBB (13 mg, 0.05 mmol) in dry THF (2 mL) at room temperature under argon. The reaction mixture, which was initially dark blue, changed to black indicating that nickel(0) nanoparticles were formed. After 10 min, i-ProH (5 mL) and the corresponding alkene (5 mmol) were consecutively added. The reaction mixture was warmed up to 76°C and monitored by GLC–MS until total or steady conversion of the starting material. The resulting suspension was diluted with diethyl ether (20 mL), filtered through a pad containing Celite and the filtrate was dried over MgSO4. The residue obtained after removal of the solvent (15 Torr) was pure enough or was purified by column chromatography (silica gel, hexane or hexane/EtOAc) to give the corresponding pure alkane.

4.2.1. 1-n-Butylbenzene (Table 2, entry 2). Colourless oil; tR 7.07: Rf 0.35 (hexane/EtOAc 95:5); δ1H 0.92 (3H, t, J=5.3, CH3); 1.32–1.38 (2H, m, CH2CH3); 1.55–1.63 (2H, m, CH2CH2CH3); 2.59 (2H, t, J=7.5, ArCH2); 7.13–7.27 (5H, m, 5×ArH); δ13C (CH3) 19.2, 22.3, 33.6, 35.6 (3×CH2), 125.5, 128.1, 128.3 (ArCH), 142.8 (ArC); m/z 134 (M+3, 3%), 92 (55), 91 (100), 65 (12).

4.2.2. 1,2-Diphenylethane (Table 2, entry 5). White solid; mp 51–53°C (hexane); tR 11.81: Rf 0.47 (hexane); δ1H 2.87 (4H, s, 2×CH2); 7.10–7.24 (10H, m, 10×ArH); δ13C 37.8 (2×CH2); 125.8, 128.2, 128.3 (10×ArCH), 141.6 (2×ArC); m/z 182 (M+3, 30%), 91 (100), 65 (18).

4.2.3. 1,1-Diphenylethane (Table 2, entry 6). Colourless oil; tR 11.56: Rf 0.50 (hexane/EtOAc 95:5); δ1H 1.59 (3H, d, J=7.3, CH3); 4.09 (1H, q, J=7.3, CH2CH3); 7.05–7.24 (10H, m, 10×ArH); δ13C (CH3) 21.8 (CH3), 44.7 (CH2); 125.3, 127.5, 128.2 (10×ArCH), 146.2 (2×ArC); m/z 182 (M+3, 36%), 168 (14), 167 (100), 165 (32), 152 (17), 77 (10).

4.2.4. Ethyl heptanoate (Table 3, entry 2). Colourless oil; tR 7.51: Rf 0.15 (hexane/EtOAc 95:5); δ1H 0.88 [3H, t, J=6.8, (CH2)2CH2]; 1.22–1.36 [9H, (CH3)2CH2], OCH2CH2, 1.59–1.63 (2H, m, CH3CH2CO); 2.26 (2H, t, J=7.8, CH2CH2CO), 4.12 (2H, q, J=7.1, OCH2CH2); δ13C 13.7, 13.8 (2×CH2); 22.2, 24.9, 28.7, 31.3, 34.4, 60.1 (6×CH2), 173.8 (CO); m/z 134 (M+3, 3%), 92 (55), 91 (100), 65 (12).
4.2.12. Benzyl n-propyl ether (Table 3, entry 10).

4.2.14. 1,2-Bis(3,4,5-trimethoxyphenyl)ethane (brittonin A)24. White solid; mp 142–143 °C (hexane); τ; 19.68; Rf 0.53 (hexane/EtOAc 7:3); δ 2.85 (4H, s, 2-CH2), 3.83 (18H, s, 6-CH3), 6.34 (4H, s, 4-ArH) δ 38.4 (2-CH3), 56.0 (6-CH3), 105.3 (4-ArCH), 136.1 (2-ArC), 137.3, 153.0 (6-ArCO); m/z 362 (M+ 32), 181 (100).

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Appendix. Supplementary data


References and notes


19. The complete characterisation of the NNPs has been recently submitted to an specialised catalysis journal.

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19. For a review on palladium-catalysed reactions of alcohols, including the isomerisation of unsaturated alcohols, see Muzart, J. Tetrahedron 2005, 61, 9423–9463.


