The $NiCl_2$–Li-Arene (cat.) Combination as Reducing System, Part 8**

Catalytic Hydrogenation of Organic Compounds Using the $NiCl_2$–Li-Naphthalene (cat.) Combination

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Catalytic hydrogenation is one of the most frequently applied reactions in organic synthesis which allows the reduction of many functional groups often with high control on the chemo-, regio-, and stereoselectivity.[1] In general, heterogeneous catalytic hydrogenation[2] is preferred due to the mild reaction conditions mostly required and to the easy separation of the catalyst. Among the many catalysts available, nickel catalysts[3] are universal and widely used both in the laboratory and in industry. They can be found in a supported form (nickel on kieselguhr,[3] alumina,[4] or graphite[5]), as a nickel-aluminum alloy powder,[6] or as obtained by reduction of nickel salts such as nickel aluminides and nickel borides,[7] as nickel precipitated from nickel chloride and zinc,[8] or as the Nic catalysts [NaH–NaOR–Ni(II) salts], which generate nickel hydride species.[9] However, Raney nickel is probably by far the most widely used nickel catalyst because of its high activity, being able to reduce practically any function.[3,10] Its main disadvantages are (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. On the other hand, in the last years we have developed a reduction methodology based on the use of dihydrated nickel(II) chloride, lithium, and a catalytic amount of an arene, which showed to be very efficient in the reduction of a wide variety of organic substrates such as alkenes,[11a] alkynes,[11b] carbonyl compounds and imines,[11c] organic halides,[11d] sulfonates, aromatic and heteroaromatic compounds,[11e] hydrazines, azo compounds, azoxy compounds, *N*-oxides,[11f] and nitrones.[11g] The main advantages of this methodology are: (a) the source of hydrogen is the water contained in the nickel salt; (b) the grade of hydrogenation can be controlled by the stoichiometry of the reaction; and (c) deuterated products are easily obtained by utilizing a nickel salt containing two molecules of deuterium oxide instead of water.

However, stoichiometric amounts of the nickel salt are needed in order to get good reaction conversions. For that reason we thought about the possibility of carrying out a hydrogenation reaction involving external molecular hydrogen and very reactive catalytic nickel(0), which could be prepared from anhydrous nickel(II) chloride, lithium, and a catalytic amount of naphthalene.

For the above purpose we prepared a solid mixture composed of nickel(II) chloride, lithium powder, and a catalytic amount of naphthalene in the molar ratio 1 : 5 : 0.05, respectively. Some preliminary experiments revealed that 20 mol % of nickel led to partial reduction of the substrates, and long reaction times were needed in some cases to complete the reaction, whereas *ca.* 40 mol % of nickel had an ideal behavior in most of the starting materials studied. Thus, the reaction of the above mixture (40 mol % Ni) with a variety of organic substrates in THF at room temperature, and under an atmosphere of molecular hydrogen (1 atm), led to the corresponding reduced products in moderate to excellent yields (Table 1).

** For Part 7, see Ref. [11g]

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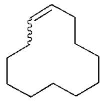
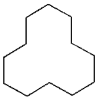
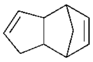
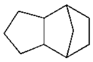
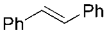
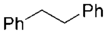
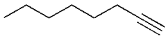
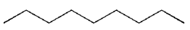
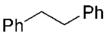
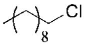
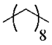
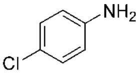
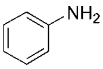
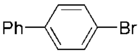
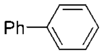
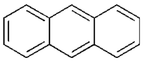
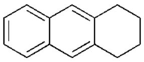
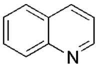
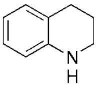
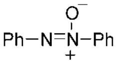
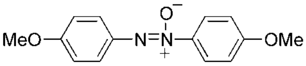
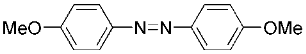
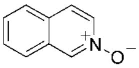
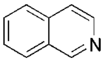
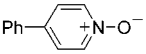
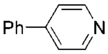
Table 1. Hydrogenation of organic compounds **1–7**

Entry	Starting Material	(No.)	Reaction time (h)	Product[a]	Yield (%)[b]
1		(**1a**)	1		95
2		(**1b**)	3		95
3		(**1c**)	1		96
4		(**2a**)	4		80[c]
5		(**2b**)	12		97[c]
6	$Ph—\equiv—Ph$	(**2c**)	2		96
7		(**3a**)	2		68[d]
8		(**3b**)	12		50[d]
9		(**3c**)	2		84
10		(**4a**)	2		68[d,e]
11		(**4b**)	12		98
12	$PhNHNH_2$	(**5a**)	1	$PhNH_2$	88
13	$PhNMeNH_2$	(**5b**)	1	PhNHMe	98
14	 $Ph-N=\overset{O^-}{\underset{+}{N}}-Ph$	(**6a**)	4	Ph–N=N–Ph	58
15		(**6b**)	12		57
16		(**7a**)	1		60
17		(**7b**)	1		67

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[a] All products were >95% pure (GLC).

[b] Isolated yield of the reaction crude after filtration and evaporation of solvents, unless otherwise is stated.

[c] GLC yield.

[d] Isolated yield after column chromatography (silica gel, hexane or hexane/diethyl ether).

[e] 12% yield of 9,10-dihydroanthacene was obtained as by-product.

This methodology was initially applied to the hydrogenation of olefins such as cyclododecene (**1a**), dicyclopentadiene (**1b**), and stilbene (**1c**), giving the expected reduced products in very high yields (Table 1, entries 1–3). A representative group of alkynes including terminal (**2a**), internal (**2b**), and conjugated alkynes (**2c**) were also transformed into the corresponding alkanes (Table 1, entries 4–6). This methodology allowed the halogen-hydrogen exchange with organic halides such as *n*-decyl chloride (**3a**), 4-chloroaniline (**3b**), and 4-bromobiphenyl (**3c**) (Table 1, entries 7–9). As regards aromatic compounds, it is worthy of note that the hydrogenation of anthracene (**4a**) under the above mentioned conditions furnished mainly 1,2,3,4-tetrahydroanthracene (Table 1, entry 10), whereas using the combination $NiCl_2 \cdot 2\,H_2O$/Li/DTBB (cat.),[11e] 9,10-dihydroanthracene was the only reaction product. Quinoline (**4b**) was converted efficiently into 1,2,3,4-tetrahydroisoquinoline (Table 1, entry 11).

The hydrogenation of nitrogen-nitrogen bonds was also achieved in short reaction times and good yields. Thus, phenylhydrazine (**5 a**) and 1-methyl-1-phenylhydrazine (**5 b**) were reduced to aniline and *N*-methylaniline, respectively (Table 1, entries 12 and 13). Finally, this methodology found application in deoxygenation reactions of azoxy compounds and *N*-oxides. Thus, starting from azoxybenzene (**6 a**) and 4,4′-dimethoxyazoxybenzene (**6 b**) the corresponding azo compounds were obtained (Table 1, entries 14 and 15, respectively), and the *N*-oxides isoquinoline *N*-oxide (**7 a**) and 4-phenylpyridine *N*-oxide (**7 b**) were transformed into the expected heteroaromatic compounds (Table 1, entries 16 and 17).

Other substrates such as ketones, imines and azo compounds remained unaltered or very low conversion was observed under the above described conditions.

The nickel(0) prepared in the mentioned manner was very finally divided, standing as a suspension even after several days, and proved to be highly reactive as any attempt to support it failed, resulting in deactivation. In general, the reactivity of this catalyst is comparable to that of Raney nickel as regards the hydrogenation of alkenes,[12] alkynes,[12] and hydrazines[13] which is also accomplished under soft reaction conditions. However, the reduction of aromatic compounds,[12] alkyl chlorides,[14] azoxy compounds,[15] and *N*-oxides[16] by Raney nickel does not take place or harsh reaction conditions are required. Our catalyst also proved to be superior to the nickel boride obtained with the $NiCl_2$/$NaBH_4$/DMF combination in the reduction of alkyl chlorides,[7b] and softer reaction conditions were required in the hydrogenation of aromatic and heteroaromatic compounds in comparison with other nickel catalysts (H_2/Ni/EtOH, $NiCl_2$/Zn/MeOH).[17] Better behavior of our catalyst was observed in the reduction of carbon-carbon double and triple bonds in comparison with the nickel-aluminum alloy, the latter being used in large excess in a basic medium and which only affects these functions when they are benzylic or conjugated with a carbonyl group.[6a] Finally, and in order to establish a comparison of our catalyst with the widely used palladium on charcoal, the hydrogenation of anthracene to furnish 1,2,3,4-tetrahydroanthracene was carried out in 2 h at room temperature with our nickel catalyst (Table 1, entry 10), whereas hydrogenation on Pd/C required the use of tetralin as solvent in a sealed tube at 340 °C.[18]

In this paper we have described the catalytic hydrogenation of a series of organic compounds by using a system composed of $NiCl_2$-Li-naphthalene (cat.). This combination, which generates a very reactive nickel, has been applied to the catalytic hydrogenation of a series of organic compounds such as alkenes, alkynes, organic halides, aromatic compounds, hydrazines, azoxy compounds, and *N*-oxides, under very mild reaction conditions (room temperature and atmospheric pressure). In general, this catalyst showed a reactivity superior to other nickel catalysts and, compared to Raney nickel, its behaviour was similar in the reduction of alkenes, alkynes, and hydrazines, but better results were obtained in the reduction of aromatic compounds, alkyl chlorides, azoxy compounds and *N*-oxides. Further work on the chemical nature of the catalyst will be carried out in the near future.

Experimental Section

General Methods

For general information see Ref. [11d] All starting materials (except compounds **6 a**, **6 b**, and **7 a**) were commercially available (Aldrich, Fluka) of the best grade and were used without further purification. For the preparation of compounds **6 a**, **6 b**, and **7 a**, see Ref. [11f] All products gave satisfactory physical, chromatographic, and spectroscopic data by comparison with authentic samples which were commercially available or previously prepared by us following other methodologies.[11]

Preparation of the Catalytic Mixture

The catalytic mixture was composed of lithium powder (175 mg, 25 mmol), anhydrous nickel(II) chloride (650 mg, 5.0 mmol), and ground naphthalene (32 mg, 0.25 mmol), which was always kept under nitrogen.

Hydrogenation of Compounds 1–7. General Procedure

The catalytic mixture (75 mg, 40 mol % Ni) was introduced into a Schlenck tube together with THF (3 mL) and the starting material (1 mmol) under a hydrogen atmosphere (1 atm) at room temperature. The reaction mixture, which was initially green, changed to black indicating the formation of Ni(0). The course of the reaction was followed by GLC and/or TLC and after the reaction time specified in Table 1, the resulting black suspension was diluted with diethyl ether (20 mL) and filtered through a pad containing silica gel and celite (*ca.* 3 : 1). After drying the filtrate over anhydrous Na_2SO_4, it was evaporated (15 torr) and the resulting residue analyzed without any purification or purified by column chromatography (silica gel, hexane or hexane/diethyl ether) (see footnotes in Table 1).

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[12] Ref. [3], Chapter 6.

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[14] Ref. [3], p. 81.

[15] Ref. [3], p. 134.

[16] Ref. [3], p. 131.

[17] Ref. [3], pp. 72–73.

[18] Ref. [3], p. 66.