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Highly Stereoselective Semihydrogenation of Alkynes Promoted by Nickel(0) Nanoparticles

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Abstract: A new method for the highly stereoselective *cis*-semihydrogenation of internal alkynes is described based on *in situ* generated Ni(0) nanoparticles and molecular hydrogen. This reduction system also allows the semihydrogenation of terminal alkynes.

Keywords: (*Z*)-alkenes; alkynes; *cis*-hydrogenation; nanoparticles; nickel; stereoselectivity

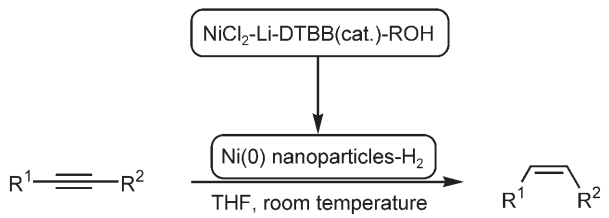
The semihydrogenation of the carbon-carbon triple bond is a particularly valuable reaction in synthetic organic chemistry. The difficulty to control the stereochemistry and to minimise the formation of over-reduced products make it a challenging transformation. In the last decades, different general methods have been developed for this purpose and applied depending on the stereochemistry desired for the final product, including: (a) heterogeneous catalytic hydrogenation,[1] (b) homogeneous catalytic hydrogenation,[2] and (c) non-catalytic chemical methods[3a] (e.g., reduction by diimide,[3b] dissolving metals,[3c, d] low-valent metal species,[3e] hydroalumination,[3f] or metal hydride-transition metal halide combinations[3g]).

Concerning the *cis* semireduction of alkynes and that of terminal alkynes, Lindlar catalyst,[4] trialkylammonium formates under palladium catalysis,[5] complex reducing agents of the type NaH-NaOR-MX_n,[6] and dispersed nickel on graphite,[7] are some of the formerly utilised reducing systems, but they do not always lead to an optimum selectivity. In fact, partial isomerisation of the (*Z*)-alkene to the (*E*)-alkene, shift of the double bond, over-reduction to the alkane, and problems with reproducibility were observed, especially with the Lindlar catalyst. In the more recent literature, the higher selectivities achieved with a montmorillonite-supported complex,[8] nickel boride or palladium catalysts on borohydride exchange resin,[9] a homogeneous palladium(0) catalyst,[10] palladium on pumice,[11] or using a variant of Lindlar's catalyst[12] are noteworthy. At any rate, most of the above-mentioned methods are not general but are rather applied to a specific type of substrate. Therefore, any new and efficient method for the semihydrogenation of alkynes is welcome.

In the recent years we have applied the system composed of $NiCl_2 \cdot 2\,H_2O$-Li-arene(cat.) to the reduction of a wide range of functional groups.[13] As regards the reduction of alkynes, a variety of substrates could be completely reduced to the corresponding alkanes, whereas the semihydrogenation reaction could be only controlled in a few cases without a general product stereochemistry.[14] On the other hand, we have recently discovered that very fine nickel(0) nanoparticles with diameters of 2.5 ± 1.5 nm can be prepared by reduction of anhydrous nickel(II) chloride with lithium powder and a catalytic amount of DTBB (4,4′-di-*tert*-butylbiphenyl) in THF at room temperature.[15]

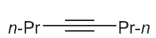
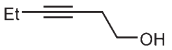
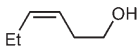
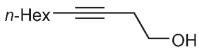
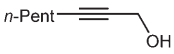
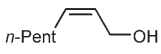
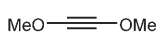
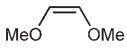
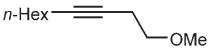
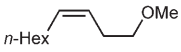
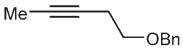
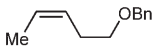
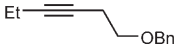
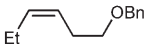
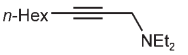
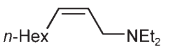
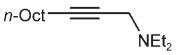
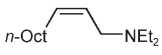
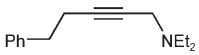
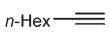
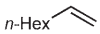
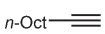
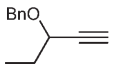
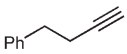
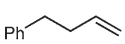
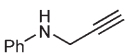
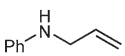
We report herein a new and efficient methodology for the stereoselective *cis*-semihydrogenation of alkynes, under the promotion of highly reactive nickel(0) nanoparticles generated from the reducing system $NiCl_2$-Li-DTBB(cat.)-ROH. This methodology has also found application in the semihydrogenation of terminal alkynes.

The roles of the different components of the reducing system mentioned above are as follows: (a) nickel(II) chloride is the source of Ni(0) nanoparticles, (b) lithium has a double role, the reduction of Ni(II) to Ni(0) and the *in situ* generation of molecular hydrogen by reaction with the alcohol, (c) DTBB is used in catalytic amounts and acts as an electron carrier from lithium to nickel(II)



Scheme 1.

Table 1. Selective semihydrogenation of internal and terminal alkynes.

Entry	Starting alkyne	t [h][a]	Product	Conversion [%][b]	Yield [%][c]
1		2		100	99[d]
2		4		100	98[d]
3		3		100	95[d]
4		8		100	83[d]
5		4		100	62
6		24		77	65[e] (96[d])
7		4[f]		84	97[d]
8		2		92	85
9		8		100	73
10		2		100	79
11		7		83	90
12		8		100	87
13		7		100	94
14		24[g]		100	85[d]
15		24[g]		100	85[d]
16		7[g]		79	74
17		24		87	87[d]
18		24[g]		100	79

[a] Reaction carried out at room temperature with EtOH as the hydrogen source, unless otherwise stated.
[b] Conversion determined by analytical GLC.
[c] Isolated yield of the olefin after column chromatography [silica gel (entries 1–10 and 14–18) or neutral alumina (entries 11–13), hexane or hexane/EtOAc], unless otherwise stated. For conversions lower than 100% the corresponding yield refers to the amount of starting material converted.
[d] Yield determined using analytical GLC and *n*-dodecane as an internal standard.
[e] $Z/E = 93:7$.
[f] Reaction performed at 0 °C.
[g] *i*-PrOH was used as the hydrogen source.

chloride, and (d) ROH is the source of hydrogen, the most effective alcohols being EtOH for internal alkynes and *i*-PrOH for terminal alkynes. One of the main advantages of this methodology is that the handling of external molecular hydrogen is avoided since it is generated *in situ* in the reaction flask.

The reducing system was applied to a wide range of internal and terminal alkynes with a high selectivity and under very mild reaction conditions (Scheme 1 and Table 1). Concerning the semihydrogenation of internal alkynes (Table 1), symmetrical dialkyl-substituted alkynes (entries 1 and 2) as well as cyclooctyne (entry 3) were reduced to the corresponding alkenes with excellent conversions and yields and with exclusive *cis*-stereochemistry. Several hydroxyalkyl-substituted internal alkynes were also successfully converted into the corresponding *cis* olefins (entries 4–6). It is noteworthy that even the more labile and isomerisation-prone oct-2-en-1-ol was obtained in a 93:7 *Z*/*E* diastereomeric ratio without any trace of the isomerised by-product octanal (entry 6). Alkynes bearing an alkoxy moiety (entries 8–10) were nicely semireduced, the reaction conditions being compatible with the presence of the benzyloxy group, which did not undergo hydrogenolysis. Furthermore, several propargylic amines could be also transformed into the corresponding *cis* allylic amines with high conversions and isolated yields (entries 11–13).

The above methodology also found application in the generally less studied and more difficult to control semihydrogenation of terminal alkynes. Thus, a variety of terminal alkynes bearing alkyl, alkoxyalkyl, and arylaminoalkyl substituents were reduced to the corresponding terminal alkenes in good yields albeit with variable amounts of the over-reduced alkanes (10–15%) (entries 14–18). It is worthy of note that also in this case the benzyloxy group remained untouched under the reaction conditions (entry 16).

In summary, a new, mild and simple methodology for the efficient stereoselective semihydrogenation of alkynes has been developed based on both *in situ* generated Ni(0) nanoparticles and hydrogen. Further research on the application of the herein reported reducing system to the selective reduction of olefins and dienes is under way. The use of a polymer-supported arene as electron carrier as well as a version of the reaction involving substoichiometric amounts of Ni(0) are also under study.

Experimental Section

General Remarks

Alkynes in entries 1, 2, 4–7, and 14–17 (Table 1) were commercially available. Alkynes in entries 8–10 and 18 were obtained by standard alkylation reactions from the starting alcohols and aniline, respectively. Cyclooctyne (entry 3) and the diethylaminoalkynes (entries 11–13) were prepared following literature procedures of L. Brandsma [*Synthesis of Acetylenes, Allenes and Cumulenes: Methods and Techniques*, Elsevier, 2004, pp. 215 and 2708, respectively].

General Procedure for the Semihydrogenation of Alkynes

Anhydrous $NiCl_2$ (130 mg, 1 mmol) was added to a preformed blue suspension of lithium powder (28 mg, 4 mmol) and DTBB (13 mg, 0.05 mmol, 2.5 mol %) in THF (5 mL) at room temperature. The resulting mixture was stirred until formation of a black suspension (*ca.* 10 min), thus indicating the formation of Ni(0) nanoparticles. The reaction mixture was diluted with THF (15 mL), followed by the addition of EtOH (0.12 mL, 2 mmol) or *i*-PrOH (0.15 mL, 2 mmol) and the alkyne (1 mmol). Filtration through a pad containing silica gel and celite (*ca.* 3:1), followed by drying with anhydrous Na_2SO_4, and solvent removal under vacuum (15 Torr), provided a crude reaction product that was purified by column chromatography (silica gel or neutral alumina, hexane or hexane/EtOAc, see footnote[c] in Table 1).

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