Asymmetric reduction and hydrogenation over heterogenous catalysts prepared by reacting nickel-boride with norephedrine

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Abstract

The reduction of acetophenone with borane–THF over heterogeneous catalysts prepared by reacting nickel-boride with $(1R,2S)$-$(-)$-norephedrine, afforded (R)-$(+)$-1-phenylethanol with high enantioselectivity (ee = 90%). The catalysts can be recycled two times with little or no loss of performance. The excellent enantioselective properties resulted from the formation of 1,3,2-oxazaborolidine which is strongly anchored at the surface of the nickel-boride. Used for the hydrogenation of acetophenone, 4-methylpentan-2-one and isophorone, the catalyst hydrogenated with a slight predominance of the S configuration. The ee was poor but it remained constant when the catalyst was reused. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

Two enantioselective heterogenous systems: Ni/tartrate/NaBr [1] and cinchona-Pt/Al$_2$O$_3$ [2–6] catalyse highly enantioselective hydrogenation of β-ketoesters and α-ketoesters, respectively. In both cases, the stereochemical control is achieved by adding a chiral modifier to the metal surface and only certain types of substrate are suited. There is a general consent that tartaric acid is chemically bonded to nickel and that during hydrogenation the chiral molecule does not leave the metal surface. In

the case of hydrogenation of α-ketoesters over cinchona-Pt/Al$_2$O$_3$, the aromatic π-system of the quinoline ring serves as a binding site for the catalyst surface, and the enantioselectivity is determined mainly by the interaction of the quinuclidine N-atom with the substrate [7–10].

The borane reduction of ketones catalysed by 1,3,2-oxazaborolidine is a very efficient homogeneous process for the preparation of secondary alcohols with high optical yields. Our goal is to anchor a 1,3,2-oxazaborolidine to a metal surface, hoping that interactions between this metal surface, the heterocycle and the prochiral ketone might induce enantioselective hydrogenation. The oxazaborolidine ring can be prepared by reacting a β-amino alcohol either

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with borane [11] or with a substituted boronic acid [12]. Water is formed in the second procedure and has to be eliminated to prevent hydrolysis of the heterocycle. Therefore, we decided to explore the reaction of a β-amino alcohol with a nickel-boride. The black solid thus obtained has been reacted with $(1R,2S)$-$(-)$-2-amino-1-phenylpropan-1-ol, norephedrine, and used in the reduction of acetophenone with borane–THF complex. This nickel-boride bound β-amino alcohol has also been used for the hydrogenation of 4-methylpentan-2-one, acetophenone and isophorone.

2. Experimental

2.1. Materials

Nickel iodide ($NiI_2 \cdot 6H_2O$) (Alfa) was dried in a desiccator for 48 h at room temperature, under vacuum over zeolite 4 Å freshly dehydrated at 600 K. Lithium borohydride 2.0 M solution in tetrahydrofuran (packaged under nitrogen) (Aldrich) 4-methylpentan-2-one (99.5%, HPLC grade) (Aldrich) norephedrine (Aldrich) isophorone (97%) (Aldrich) acetophenone (Aldrich) were used as received.

THF (Carlo Erba) was distilled under nitrogen immediately prior to use from sodium ketyl of benzophenone; cyclohexane (99.5%) (Aldrich) was refluxed for 2 h with Raney nickel and distilled under nitrogen.

2.2. Preparation of NiB_2

Reactions were carried out in an oven dried three-necked round bottom flask equipped with a magnetic stirrer and connected through a condenser to a vacuum line. The flask was charged with anhydrous NiI_2 (2.813 g, 9 mmol). The flask was evacuated and backfilled with nitrogen three times and a nitrogen flow was maintained during the reaction. Dry oxygen-free THF (80 ml) was syringed in, stirring at room temperature dissolving partially the NiI_2. A solu-

tion of lithium borohydride (9 ml, 18 mmol) was then added: gas evolution was observed immediately together with the decoloration of the dark solution and the precipitation of a black solid. After 10 min, the black suspension was heated to reflux during 2 h. After cooling down to room temperature, the solvent was removed by decantation through a transfer tube by means of a pressure differential. THF (80 ml) was syringed into the flask and the mixture stirred while refluxing for half an hour. After cooling down and allowing to settle, the THF was removed. This washing of the catalyst was repeated twice to eliminate lithium iodide.

2.3. NiB_2 treated with NaOH

An oxygen-free solution of sodium hydroxide (2.0 M, 70 ml) was added to NiB_2 (9 mmol), an immediate and vigourous gas evolution was observed. After 10 min, the black suspension was heated to reflux for 2 h. After cooling down, the aqueous solution was removed by decantation, the catalyst was washed twice with water and three times with THF.

2.4. Characterizations

The overall composition of each catalyst was determined by chemical analysis of the samples dissolved in nitric acid.

The total surface areas were measured by nitrogen adsorption at the temperature of liquid nitrogen (BET method). Before measuring the total surface, the catalyst was desorbed at 413 K for 4 h under high vacuum.

The nickel surface area was determined from hydrodesulfurization of 3-methylthiophene in the liquid phase. The stoichiometry of the reaction was taken as $S/Ni = 1/2$ [13]. The reaction was performed at 363 K under a hydrogen pressure of 1.1 MPa, using 0.3–0.6 g of the catalyst and 1.85 mmol of 3-methylthiophene in 150 ml of cyclohexane. After 2 h, which is sufficient for complete reactive adsorption of 3-methylthiophene on the catalyst surface, the

amount of 3-methylthiophene remaining in the reaction mixture was determined by gas chromatography with a (20%) Hallcomid on Chromosorb W column and *n*-octane as internal standard.

Infrared spectra were obtained with a Nicolet impact 400 FTIR spectrometer in the range $400–4000$ cm^{-1}. The samples of NiB_2 were diluted with KBr (1:25).

2.5. Reaction of NiB$_2$ with norephedrine: preparation of NiB$_{2-x}$(oxaza)$_x$

Norephedrine (0.9 mmol in 10 ml THF) was added to the stirred suspension of NiB_2 (9 mmol) in THF (80 ml). After 12 h at room temperature and 4 h at reflux, the THF was decanted and concentrated to 5 ml. Analysis of the condensate by t.l.c. showed that no amino alcohol remained. Furthermore, repeating the reaction using a graduated tube previously filled with mineral oil placed over the open end of a delivery tube showed that 0.45 mmol of hydrogen was formed at room temperature. Heating of the reaction mixture for 8 h at 55°C afforded the evolution of the same amount of hydrogen (0.45 mmol). Thus, the 0.9 mmol of amino alcohol reacted with boron and the catalyst is referred to as NiB_{2-x}(oxaza)$_x$, where x is the ratio amino alcohol/boron and oxaza stands for

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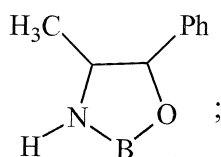
the reduction of acetophenone by borane affords evidence for the formation of an oxazaborolidine (vide supra).

2.6. Reduction of acetophenone using borane–THF and NiB$_{2-0.05}$(oxaza)$_{0.05}$

A total of 1.05 ml of borane–THF (1 M) was added to the stirred suspension of $NiB_{2-0.05}$(oxaza)$_{0.05}$ (15 mmol) in 100 ml of THF at room temperature under nitrogen. After 30 min, the mixture was treated with acetophenone (1.5 mmol) and stirring was continued at room temperature until the reaction was complete (g.l.c. analysis, usually 2–2.5 h). The solids were allowed to settle and the liquid phase was removed through a transfer tube by means of a pressure differential, the catalyst being left in the flask for reuse. The liquid phase was diluted with 2 M HCl and extracted with ethyl acetate, which was then washed with saturated aqueous NaCl, dried, and evaporated. The enantiomeric purity of the product was determined by capillary GC with a chiral column (hydrodex-β-cyclodextrin, 25 m × 0.25 mm (Machery–Nagel)).

2.7. Hydrogenation conditions

The hydrogenation of 4-methylpentan-2-one, acetophenone and of isophorone upon the prepared catalyst, using cyclohexane as solvent, was carried out in a 250-ml static reactor, under constant hydrogen pressure (0.9 MPa), with a stirring speed of 660 rpm at 298 K (isophorone) and at 333 K (4-methylpentan-2-one and acetophenone). Before introduction of the substrate, the reactor containing a suspension of the catalyst in cyclohexane (140 ml) was purged with a flow of hydrogen. The catalyst (9 mmol of Ni) was pretreated at room temperature for 1 h at a pressure of 0.9 MPa. Temperature was then raised to 298 or 333 K and the substrate (80 mmol) was introduced.

The end of the reaction (conversion $\geq 98\%$) was controlled by gas chromatographic analysis of samples withdrawn from the reaction mixture. After cooling down and settling, the reactor was depressurized, the liquid phase was removed through a transfer tube by means of a pressure differential, leaving catalyst behind for reuse. After removal of cyclohexane by evaporation, the solution was distilled under reduced pressure. This distillation gave 4-methylpentan-2-ol, 1-phenylethanol and dihydroisophorone with a chemical purity of 99.5%, 94% and 98%, respectively.

2.8. Determination of enantiomeric excess (ee)

The enantiomeric excesses were determined from measurements of optical rotation (Perkin Elmer 241 polarimeter).

$$ee\,(\%) = \frac{[\alpha]_D^{20} \text{ of hydrogenated product}}{[\alpha]_D^{20} \text{ of pure enantiomer}} \times 100$$

The specific optical rotations used were: (S)-4-methylpentan-2-ol $[\alpha]_D^{20} = +20.5°$ (neat), (S)-dihydroisophorone $[\alpha]_D^{20} = +29°$ (neat), (S)-1-phenylethanol $[\alpha]_D^{20} = -42°$ (neat). (1R,2S)-(−)-norephedrine $[\alpha]_D^{20} = -47°$ (C = 7, 1 N HCl).

3. Results and discussion

3.1. Evidence for the formation of nickel-boride: NiB₂

The bulk composition of the nickel-borides prepared according to Brown and Brown [14–16], by reducing nickel salts with $NaBH_4$ either in water or in 95% ethyl alcohol, is Ni_2B. The surface of these solids which has been characterized by Okamoto et al. [17] and Deng et al. [18] is relatively complex. From the XPS spectra, it appeared that the nickel metal is partially oxidized and that two kinds of boron species are present, one is assigned to boron interacting with nickel, the other one is assigned to oxidized boron (BO_2). The ratio of these two kinds of boron depends on the preparation procedure, this ratio is difficult to control and we believe that only boron interacting with nickel would act an anchor. Thus, we have decided to choose another method of preparation.

It has been reported by Stewart and Schaeffer [19] that the reduction of cobalt bromide with $LiBH_4$, in dry ether under oxygen-free conditions, affords a black pyrophoric material exhibiting chemical behavior typical of the elements. For example, boron reacts with dry methanol to give stoichiometrically methyl bo-

rate and hydrogen. Recently, the difference between nonaqueous and aqueous reduction of Co^{2+} by $NaBH_4$ has been pointed out by Glavee et al. [20–22]; in aqueous media, the primary product is Co_2B, in nonaqueous media the primary product is Co, which catalyses the decomposition of diborane to boron and hydrogen affording ultra fine particles, with the bulk composition being CoB_2 as was observed by Schaeffer.

The reduction of nickel iodide with lithium borohydride in oxygen-free dry THF, gives a black precipitate containing 2 mol of boron for each mole of nickel (Table 1, Eq. (1))

$$NiI_2 + 2LiBH_4 \xrightarrow[N_2]{\text{THF anhydrous}} NiB_2(s) + 2LiI + 4H_2 \qquad (1)$$
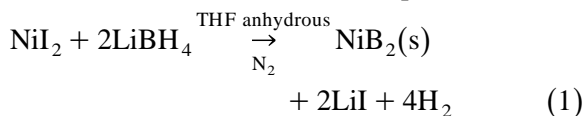
NiB_2 presents a very large BET surface area (120 m²/g) in comparison with the metal surface area (5 m²/g). These results show that the surface of the nanoscale particles is mainly occupied by boron atoms. The large increase of the nickel surface after a treatment with sodium hydroxide (Table 1) sustains this assertion and gives evidence for an intimate mixture of boron and nickel.

The IR data of NiB_2 are interpreted by comparison with those of bidentate mononuclear MBH_4 complex. For such complex

$$M\underset{H_b}{\overset{H_b}{<}}B\underset{H_t}{\overset{H_t}{<}},$$
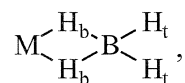
the terminal hydrogen–boron stretching frequency (ν_{B-H_t}) and the bridge stretching frequency (ν_{B-H_b}) are usually observed between

Table 1
Physical properties of the catalyst prepared by reduction of NiI_2 with $LiBH_4$

Catalyst	Ni/B atomic ratio**	S_{BET} (m²/g)	S_{Ni} (m²/g)
NiB₂	0.5	120	5
NiB₂*	4	80	80

*After treatment with sodium hydroxyde solution.
**The atomic ratio: NiB was determined by chemical analysis of the samples dissolved in nitric acid.

2400–2600 and 1300–1500 cm^{-1}, respectively [23]. Furthermore, a strong doublet, 50–80 cm^{-1} splitting is observed when one boron atom is bonded to a hydrogen terminal pair, whereas the spectrum exhibits only one frequency when a single terminal hydrogen is attached to the boron atom [24].

We observed a medium band at 2500 cm^{-1} (assigned to $B-H_t$) and a strong broad band centred at around 1350 cm^{-1}

$$Ni{\Large\langle}\genfrac{}{}{0pt}{}{H}{H}{\Large\rangle}B$$
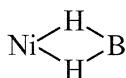
(bridge stretching). From the band intensities, one can estimate that the terminal hydrogen is often missing on the bridge structure:

$$Ni{\Large\langle}\genfrac{}{}{0pt}{}{H_b}{H_b}{\Large\rangle}B-H_t \; .$$
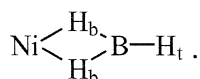
Though the bulk composition was NiB_2 (Table 1), no boron was detected by STEM analysis, however, two kinds of boron (169 and 179 eV) were found by Auger spectroscopy. The first one (169 eV) could be assigned to boron linked to nickel, the second one being elementary boron. Before the STEM analysis, the catalyst NiB_2 has been desorbed at 385 K for one night under high vacuum, thus, during the desorption and according to the other physico-chemical observations, the catalyst is decomposed and boron is pumped away.

3.2. Enantioselective borane reduction of acetophenone: evidence for the formation of $NiB_{2-x}(oxaza)_x$

The reduction of acetophenone has been carried out with 0.7:1 molar ratio of borane and norephedrine, i.e, with reaction conditions leading to poor enantioselectivity, the amount of borane being too low to form the oxazaborolidine and to reduce the ketone [25]. As shown in Table 2 the (R)-$(+)$-1-phenylethanol was obtained in excellent optical yield.

The oxazaborolidine ring has never before been prepared by reacting an amino alcohol with boron [27]; the close agreement observed in the borane reductions of acetophenone (homogeneous and heterogeneous, Table 2) clearly indicates, however, the formation of an oxazaborolidine in the reaction of norephedrine with nickel-boride.

The amino alcohol is strongly bound to the nickel-boride nanoparticles, since by t.l.c. no traces of amino alcohol could be detected in the liquid phase after reduction. Furthermore, the catalyst can be recycled two times with little or no loss of performance. Our catalyst affords higher enantiomeric excesses in the reduction of acetophenone than polymer-bound oxazaborolidine catalysts prepared with $(1R,2S)$-$(-)$-norephedrine [26], i.e., 90% as to compare with 74%.
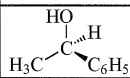
3.3. Hydrogenation over NiB_2, $NiB_{2-x}(oxaza)_x$ and $Ni(oxaza)_x$ catalysts

3.3.1. Hydrogenation of 4-methylpentan-2-one

(a) Over NiB_2. The hydrogenation was rather slow and 30 h were necessary for total conversion. The NMR spectra (^{1}H and [11]B) of the hydrogenated products showed that 4-methyl-

Table 2
Enantioselectivity in the reduction of acetophenone by BH_3 and the nickel-oxazaborolidine catalyst and reuse of this catalyst

Alcohol	1st reduction ee (%)	2nd reduction ee (%)	3rd reduction ee (%)
HO$\underset{H_3C}{\overset{}{\diagdown}}$$\overset{|}{\underset{C}{\diagdown}}$$\overset{\text{,,,}H}{\underset{C_6H_5}{}}$	92 86*	90	90

* Using 30 mol% of catalyst prepared by reacting $(1R,2S)$-$(-)$-2-amino-1-phenylpropanol with phenylboronic acid [26].

pentan-2-ol and the corresponding borate were obtained.

A reuse of the catalyst exhibited a different behaviour: the hydrogenation of the same amount of ketone in the same conditions was completed in 1 h instead of 30 h and the alcohol was the only product.

The low catalytic activity of NiB_2, in the hydrogenation of 4-methylpentan-2-one compared to its activity when it is reused, is in accordance with a large concentration of boron atoms at the surface, these atoms being progressively removed from the surface as borate by reacting with the alcohol formed.

(b) Over $NiB_{2-x}(oxaza)_x$, $x = 0.05$. The activity of this catalyst was the same of that of NiB_2, i.e., 30 h were necessary for completion of the reaction. The borate was the major product. After distillation under reduced pressure, 4-methylpentan-2-ol (12 mmol) with a purity of 99.5% was obtained with 1% ee. Similarly, the boron atoms of the $NiB_{2-x}(oxaza)_x$ are removed during the hydrogenation of 4-methylpentan-2-one, thus, reused these catalysts are referred to as $Ni(oxaza)_x$. As observed with NiB_2, $Ni(oxaza)_x$ presented a higher activity upon reuse: the ketone (80 mmol) was reduced in 1.5 h. After distillation, the (*S*) alcohol was isolated in 1% ee.

3.3.2. Hydrogenation over $Ni(oxaza)_{0.05}$

The ee observed in hydrogenation over $Ni(oxaza)_{0.05}$ catalyst is low, however, the following sequence of reactions diminishes strongly the interference of side products and artefacts. A catalyst prepared with $(1R,2S)$-$(-)$-norephedrine hydrogenates 4-methylpentan-2-one leading to the alcohol of predominantly (S)-$(+)$ configuration (ee = 1% determined from optical rotation) reused it hydrogenates acetophenone leading to the alcohol (S)-$(-)$ (ee = 1% from optical rotation and capillary g.c. with a chiral column); in a third utilization dihydroisophorone (S)-$(+)$ (ee = 2% from optical rotation) predominates in the hydrogenation of isophorone.

In this later case, the coordination of the ketone oxygen to the boron atom of the oxazaborolidine induces the enantioselective hydrogenation of the C=C bond. Thus, we are of the opinion that the binding of the oxazaborolidine atom at the more sterically accessible electron pair of the ketone oxygen atom, occurs as it is proposed in homogeneous reduction. But the next step of which the enantioselectivity depends on, i.e., the face selective hydride transfer via a six-membered transition state is of course impossible, the hydrogen atom which instead arises from the surface is not well suited, and the ee is very poor. Thus, as shown by the reduction with borane THF complex, norephedrine reacts with elementary boron, but the resulting oxazaborolidine cannot efficiently induce the enantioselective hydrogenation of ketone.

4. Conclusion

Nanoparticles of nickel-boride (NiB_2) have been prepared by reducing nickel iodide with lithium borohydride, in anhydrous oxygen-free THF. The hydroxy group and the amino-group of norephedrine react with boron atoms, evolving 1 mol of hydrogen for each mole of amino alcohol to afford a chiral oxazaborolidine strongly anchored at the surface of the particles. The reduction of acetophenone using borane–THF as reducing agent in the presence of 1 equivalent of nickel-boride bound oxazaborolidine affords 1-phenylethanol with excellent ee. The oxazaborolidine is strongly bound to the particles since the catalyst can be recycled at least two times with no loss of performance. The catalyst hydrogenates 4-methylpentan-2-one, acetophenone, isophorone into 4-methylpentan-2-ol, 1-phenylethanol, dihydroisophorone respectively in any case the *S* configuration predominates slightly. The ee is poor but as observed for the reduction it is constant when the catalyst is reused. In our hands, the catalytic hydrogenation over an oxazaborolidine boron-

bound to nickel particles cannot be useful in enantioselective synthesis of alcohol.

Acknowledgements

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