Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 1971–1973

TETRAHEDRON:
ASYMMETRY

Reaction of a chiral oxygen–sulfur paired bidentate ligand with nickel and iron boride: asymmetric borane reduction of ketones

K. Molvinger and J. Court*

LEDSS, CNRS (UMR 5616) et Université J. Fourier, BP53, 38041 Grenoble, France

Received 24 July 2001; accepted 9 August 2001

Abstract—An α-thio alcohol derived from camphor is anchored to nickel boride provided the nickel surface atoms have been passivated. The resulting heterogeneous catalyst affords moderate enantioselectivity in the reduction of acetophenone. © 2001 Elsevier Science Ltd. All rights reserved.

Synthesising optically active secondary alcohols has become a great challenge in organic chemistry. In homogeneous medium, oxazaborolidines[1] are used as chiral inductors for the borane reduction of ketones with excellent enantiomeric excess. After solvolysis two difficulties are encountered: (i) the purification of the product and (ii) the recovery of the catalyst precursor. These two problems have been solved by the heterogenization of the system. Oxazaborolidines have been anchored to a metallic surface (NiB_2)[2] by reacting an amino alcohol with nickel boride nanoparticles.[2,3] The results are as good as those in homogeneous systems with the advantages of easier separation (by decantation) and the option of immediate re-use of the catalyst after the reduction.

It has been reported that the bidentate oxygen–sulfur ligand (1*R*,2*S*,3*R*)-3-mercaptocamphan-2-ol catalyzes the homogeneous asymmetric borane reduction of ketones,[4] a chiral boride–ketone complex was formed and a second borane molecule was coordinated to the ligand oxygen atom.

In order to test the potential of the readily available nickel boride for heterogenization of enantioselective homogeneous catalysts, we attempted to form a Ni-supported oxathiaborolidine. Herein, we describe the results when (1*R*,2*S*,3*R*)-3-mercaptocamphan-2-ol[4] is reacted with nickel boride. We obtained low e.e. in the borane reduction of acetophenone, which we attributed to the competition of surface nickel atoms with boron atoms for the thiol function disfavouring the formation of the *S–B–O* ring. In order to test this explanation and with the aim of preparing oxathiaborolidine, we prepared iron boride particles.

In previous papers,[2,3] we showed that a Ni-supported oxazaborolidine was formed by reacting an amino alcohol with elemental boron in amorphous NiB_2. In most cases, the amino alcohols we used were commercial. In order to form an oxathiaborolidine, we first synthesized the chiral thio alcohol, (1*R*,2*S*,3*R*)-3-mercaptocamphan-2-ol.[5,6]

NiB_2 was prepared by reducing nickel chloride with lithium borohydride (Eq. (1)).[7] Previously,[2,3] we used nickel iodide (from dehydration of $NiI_2{\cdot}6H_2O$) for the preparation of nickel boride particles. $NiI_2{\cdot}6H_2O$ is no longer commercially available, so we reduced nickel chloride (from dehydration of $NiCl_2{\cdot}6H_2O$) instead. The procedure is analogous[2,3] but it is more difficult to remove the water from nickel chloride and it remains as the dihydrate.[8]

$$NiCl_2 + 2LiBH_4 \xrightarrow[N_2]{\text{anh. THF}} Ni + B_2H_6 + 2LiCl + H_2 \qquad (1)$$

$$B_2H_6 \xrightarrow[Ni,\ N_2]{\text{THF anh.}} 2B + 3H_2$$

The thio alcohol (1 mmol in 10 mL THF) was reacted with NiB_2 (10 mmol in 80 mL THF) applying the same procedure to that used for a β-amino alcohol. We measured the volume of hydrogen evolved during the

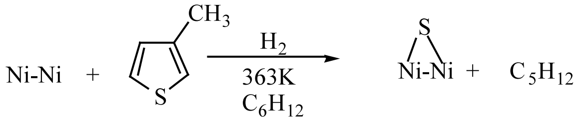
---

* Corresponding author. Fax: (33) 4 76 51 42 51; e-mail: jean.court@ujf-grenoble.fr

0957-4166/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0957-4166(01)00357-3

reaction and found that half an equivalent of hydrogen gas was released at room temperature, which we attributed to the reaction of the hydroxyl group as observed previously in the same reaction of a β-amino alcohol. Since it has been reported[4] that with chiral oxygen–sulfur bidentate ligands, maximum e.e. levels were always obtained when the reaction temperature was maintained at around 323 K, the suspension was heated and maintained at this temperature. More than half an equivalent of hydrogen was produced, which showed that the addition of the thiol function to a boron atom was not the only reaction of the thio alcohol ligand. The poor e.e. values observed in the reduction of acetophenone with the resulting heterogeneous catalyst (Table 1, entry 2), as compared with the value seen under homogeneous conditions (Table 1, entry 1), argued against an efficient cyclisation of the thio alcohol on the particle surface. Although the surface area of nickel in the nickel boride was low,[3] we assumed that the surface nickel atoms could compete with boron for the thiol function, as shown in Fig. 1. We have IR spectroscopic evidence for the hydrogen bridge structure,[3] the addition of the thiol function to nickel atoms might break a hydrogen link and could explain hydrogen production greater than that expected by analogy with the amino alcohol reaction.

To test this assumption, we decided to poison the nickel surface before adding the thio alcohol. Passivation of the nickel surface was carried out by hydrodesulfurization of 3-methylthiophene, a quantitative procedure[9] in which 3-methylthiophene reacted rapidly with nickel, according to Eq. (2).



(2)

Poisoning the nickel had a beneficial effect on the enantioselectivity (Table 1, compare entries 2 and 3) but the e.e. value remained lower than that observed under homogeneous conditions. In our opinion the moderate e.e. values resulted mainly from the rigidity of the chiral molecule, which has difficulty attaining the requisite conformation required to react with the same surface boron atom and form the oxathiaborolidine ring. The solid surface has a positive effect with 2-amino-1,2-diphenylethanol and norephedrine, since the observed e.e.s were higher in the heterogeneous reduction than under homogeneous conditions;[10] with MerCO[4] it seemed to be the opposite.[11] Similar difficulties were encountered in the formation of the

Table 1. Enantioselectivity in the reduction of acetophenone by borane, *N*-*N*-diethylaniline complex and oxathiaborolidine catalyst[13]

	Catalyst	E.e. (%) 1st reduction	E.e. (%) 2nd reduction
1	MerCO[a4]	87[4] (92[b])	
2	NiB_2 + MerCO[a]	7	2
3	NiB_2 + MerCO[a] + thiophene	31.5	24
4	FeB_2 + MerCO[a]	3.5	0
5	NiB_2 + CBS[c]	73	13

[a] (1*R*,2*S*,3*R*)-3-Mercaptocamphan-2-ol.

[b] Our experiment with the MerCO sample used for the reaction with NiB_2 and FeB_2.

[c] CBS: (*S*)-2-diphenylhydroxymethylpyrrolidine.

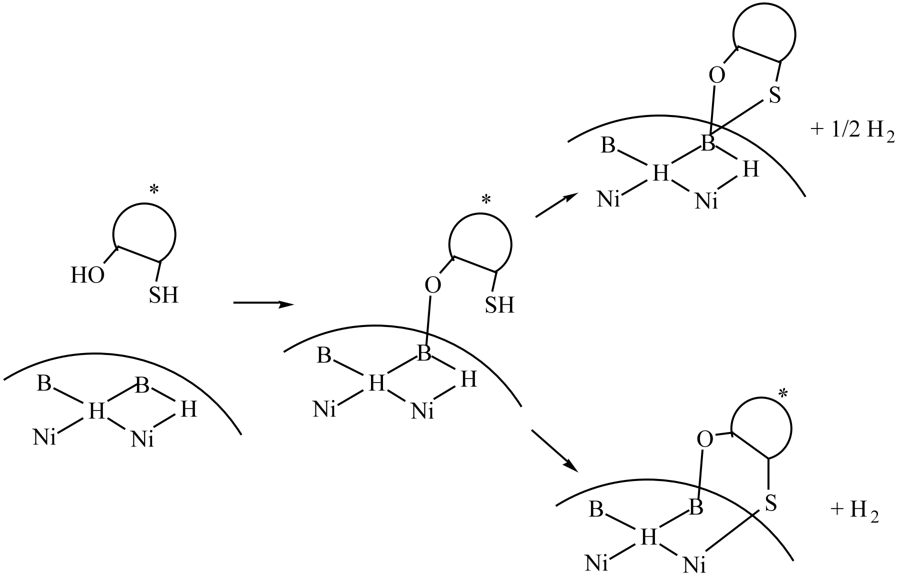


Figure 1.

oxazaborolidine ring from (*S*)-2-diphenylhydroxymethylpyrrolidine and nickel boride, since this was the most efficient catalyst for the homogeneous reduction of ketone with borane. The NiB_2/CBS system gave product with only moderate e.e. in the first use, and an unusual enantioselectivity fall when re-used (Table 1, entry 5). The low e.e. observed with the catalyst prepared by reacting MerCO with iron boride[12] was unexpected (Table 1, entry 4). Iron being less reactive towards sulfur compounds than nickel, competition with boron for the thiol function does not explain these results. This unexpectedly low enantioselectivity led us to investigate the reaction between iron boride and 2-amino-1,2-diphenylethanol. We obtained an iron supported oxazaborolidine, which gave the same enantioselectivity in the first reduction of acetophenone as $NiB_{2\text{-}0.1}(oxaza)_{0.1}$, i.e. 96% e.e., however, we obtained 88% e.e. when the catalyst was re-used instead of 95% e.e. with the nickel one. We attribute this difference to a higher boron lability in iron boride than in nickel boride.

In summary, the reaction of (1*R*,2*S*,3*R*)-3-mercaptocamphan-2-ol with nickel boride affords oxathiaborolidine anchored to the nanoparticles of nickel when the nickel surface atoms have been passivated. However, the rigidity of the chiral molecule prevents total heterocyclisation and moderate e.e. values were observed in the reduction of acetophenone.

References

1. Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **1992**, *3*, 1475.
2. Molvinger, K.; Lopez, M.; Court, J. *Tetrahedron Lett.* **1999**, *40*, 8375.
3. Molvinger, K.; Lopez, M.; Court, J. *J. Mol. Catal.* **1999**, *150*, 267.
4. Young, T. K.; Lee, D. S. *Tetrahedron: Asymmetry* **1999**, *10*, 405.
5. Lee, D. S.; Hung, S. M.; Lai, M. C.; Chu, H. Y.; Yang, T. K. *Org. Prep. Proc. Int.* **1993**, *25*, 673.
6. We note that Yang et al. do not mention the need for an acidic solution in the third step. In fact, we obtained a thiolate which remains in the aqueous phase if the medium is not strongly acidic.
7. A solution of lithium borohydride (18 mmol) was added to a suspension of anhydrous $NiCl_2$ (9 mmol) in dry, oxygen-free THF (100 mL). $NiCl_2 \cdot 6H_2O$ was first dried in a dessiccator for 24 h at room temperature under vacuum over zeolite 4 Å freshly dehydrated at 600 K, and then heated to 500 K in vacuo. Gas evolution was observed immediately with decolorisation of the dark solution and precipitation of a black solid. After stirring the mixture for 2 h, the catalyst was washed three times with THF to eliminate lithium chloride.
8. $NiCl_2 \cdot 2H_2O$ was heated at 493 K under 1 Pa for 3 h.
9. Sané, S.; Bonnier, J. M.; Damon, J. P.; Masson, J. *Appl. Catal.* **1984**, *9*, 69.
10. Molvinger, K.; Lopez, M.; Court, J. *Tetrahedron: Asymmetry* **2000**, *11*, 2263.
11. In an attempt to improve the heterocyclisation, after passivation of the nickel and addition of the thio alcohol, the reaction mixture was stirred at 363 K for 12 h. After three washings the usual procedure afforded 1-phenylethanol with low enantiomeric purity (e.e. = 7.5%).
12. A solution of lithium borohydride (18 mmol) was added to a suspension of anhydrous $FeCl_2$ (9 mmol) in dry, oxygen-free THF (100 mL). $FeCl_2 \cdot 4H_2O$ was first dried in a dessiccator for 24 h at room temperature under vacuum over zeolite (4 Å freshly dehydrated at 600 K, and then heated to 500 K under vacuum). Gas evolution was very slow, the iron chloride was totally dissolved, after 1 h a black solid was obtained. After stirring the mixture for 12 h, the catalyst was washed three times with THF to remove lithium chloride.
13. To $FeB_{2\text{-}0.1}(oxathia)_{0.1}$ or $NiB_{2\text{-}0.1}(oxathia)_{0.1}$ (10 mmol) in suspension in THF (10 mL) was added borane-*N*,*N*-diethylaniline complex (2.45 mL, 13 mmol). After 20 min, a solution of acetophenone (10 mmol) in THF (10 mL) was slowly added (1 h). After the end of the addition (30 min), the reaction mixture was removed by decantation, stirred with methanol (20 mL) for 20 min and treated with aqueous HCl (1 M, 8 mL) then extracted with ether. (The catalyst being left in the flask for re-use.) The ethereal solution was washed with aqueous HCl (1 M), extracted with ether, 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 (Macherey–Nagel)) and from measurements of optical rotation (Perkin–Elmer 241 polarimeter). We used $NiB_{2\text{-}0.1}(oxathia)_{0.1}$ by analogy with $NiB_{2\text{-}}0.1(oxaza)_{0.1}$ even though the heterocyclisation partially failed.