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Enantioselective borane reduction of ketones with oxazaborolidines boron-bound to nickel boride nanoparticles

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Abstract

A variety of substituted acetophenones can be reduced with high enantioselectivity by using borane and the heterogeneous catalyst derived from the reaction of (1*S*,2*R*)-(+)-2-amino-1,2-diphenylethanol with nickel–boride nanoparticles.

Keywords: enantioselective reduction; heterogeneous catalysts; oxazaborolidine; chiral alcohol; borane.

Chiral 1,3,2-oxazaborolidines are highly effective homogeneous catalysts for the enantioselective reduction of ketones to chiral secondary alcohols by borane.[1] Since separation of the alcohol product from the chiral amino alcohol (catalyst precursor) can be difficult,[2] polymer bound β-amino alcohols[3,4] and polymer supported boron-bound oxazaborolidines[5,6] have been described. The latter catalysts offer a great advantage over the homogeneous ones in that they can be recovered by simple filtration and then reused. However, the ketone before complexation must first diffuse into the polymer, thus the solvent used must swell the crosslinked polymer beads in order to increase accessibility to the catalytic sites. After reduction and hydrolysis, the product removal from the polymeric matrix can be difficult. We report herein that anchoring an optically active β-amino alcohol to nickel boride, prepared by lithium borohydride reduction of nickel iodide in anhydrous THF,[7] affords a heterogeneous catalyst for efficient, enantioselective reduction of ketones. The nickel boride oxazaborolidine catalyst was thus prepared in two steps (Scheme 1).

The reaction of (1*S*,2*R*)-(+)-2-amino-1,2-diphenylethanol with nickel boride produces 1 equivalent of hydrogen gas,[8] the hydroxyl group reacting first with a boron atom[9] and an oxazaborolidine anchored at the nickel surface.[10] The reduction of a variety of acetophenones using borane–THF as the reducing agent in the presence of 1 equivalent of nickel–boride bound oxazaborolidine was found to proceed efficiently in THF at room temperature. The enantiomeric excess observed for the first utilization of the catalyst and on reuse is given in Table 1. Also included in Table 1, for the purpose of comparison, is the result obtained by Quallich et al.[11] in the reduction of acetophenone using a catalyst prepared by reacting the

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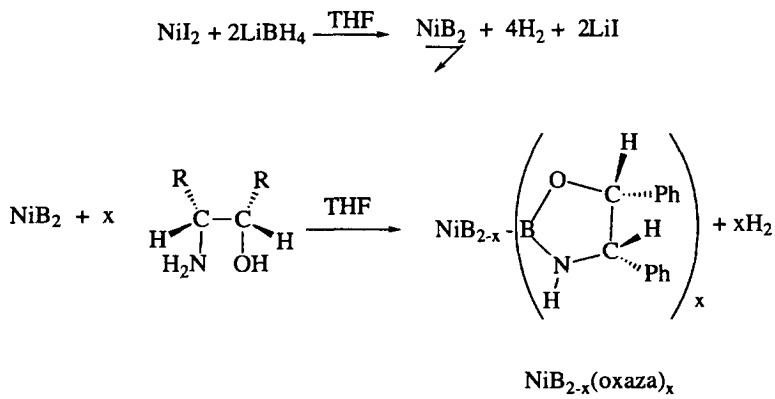
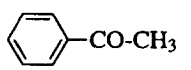
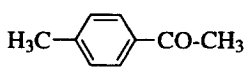
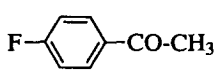
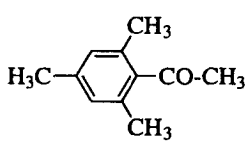


Scheme 1.

Table 1
Enantioselectivity in the reduction of acetophenone and substituted acetophenones by BH_3 and the nickel-oxazaborolidine catalyst and reuse of this catalyst. The reduction led to the alcohol of predominantly *S* configuration

ketones	1st reduction ee (%)	2nd reduction ee (%)	3rd reduction ee (%)	4th reduction ee (%)
	94 (92)*	91	91	90
	95	93	91	90
	92	91	91	92
	78			

* using 5 mol % of catalyst prepared by reacting (1*S*,2*R*)-(+)-2-amino-1,2-diphenylethanol with trimethylboroxine.

same amino alcohol with trimethylboroxine. The oxazaborolidine ring has never before been prepared by reacting an amino alcohol with boron;[1] the close agreement of the enantioselectivities observed in the borane reductions of acetophenone (homogeneous and heterogeneous) cleary indicates, however, the formation of an oxazaborolidine in our work.

Examination of the data obtained with acetophenone and with *para*-substituted acetophenones shows that the level of enantioselectivity is essentially insensitive to substitution in this position. The reduction of 2,4,6-trimethylacetophenone is much slower than the reduction of the monosubstituted compounds: 6 h are necessary to reach the completion of the reaction instead of 1 h. This should favor the uncatalyzed reaction. Addition of the ketone very slowly to the catalyst and borane would undoubtedly have given better results[12] than those obtained.[13]

The oxazaborolidine is strongly bound to the nickel boride nanoparticles, since by TLC no traces of the amino alcohol could be detected in the liquid phase after reduction. Furthermore, the catalyst can be recycled at least three times with little or no loss of performance, the ee obtained after four uses still being 90% or higher (Table 1). Our catalyst affords higher enantiomeric excesses than polymer-bound oxazaborolidine catalysts prepared with (1*R*,2*S*)-norephedrine[5] and does not lose its enantioselective properties after two uses, as do polymeric catalysts prepared with (*S*)-α,α-diphenyl-2-pyrrolidinemethanol.[6] Furthermore, the catalyst precursor, NiB_2, can be readily prepared in one step and gives only hydrogen on reaction with the β-amino-alcohol, in contrast the synthesis of polystyrene boronic acid from polystyrene is long and on reaction with the β-aminoalcohol water is generated, which must be totally removed. Finally, the handling of our catalyst is easier, the mechanical strength of metallic particles being higher than that of crosslinked polystyrene beads.

In summary, nanoparticles of nickel boride (NiB_2) have been prepared by reducing nickel iodide with lithium borohydride in anhydrous, oxygen-free THF. The hydroxyl group and the amino group of (1*S*,2*R*)-(+)-2-amino-1,2-diphenylethanol react with boron to generate 1 mol of hydrogen for 1 mol of amino alcohol and afford an oxazaborolidine which is strongly anchored at the surface of the particles. The borane-complexed oxazaborolidine reduces a variety of substituted acetophenones with high enantioselectivity. The heterogeneous catalyst can be recycled at least three times with little or no loss of performance. We believe that this catalyst offers several advantages over related systems and should find application.

Acknowledgements

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8. Half an equivalent was formed at room temperature which we attribute to the reaction of the hydroxyl group and half an equivalent was produced on refluxing which we attribute to the reaction of the amino group, well positioned for reacting with the same boron atom.
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