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New chiral phosphorus catalysts derived from (*S*)-binaphthol for highly enantioselective reduction of acetophenone by borane

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Abstract

New chiral (+)-2,2′-*O*,*O*-(1,1′-binaphthyl)-dioxo-*N*,*N*-diethylphospholidine **1** and its borane complex **3** were prepared from (*S*)-binaphthol and their use as catalysts in enantioselective borane reductions of prochiral acetophenone were investigated. Enantiomeric excesses of up to 98.5% have been obtained using 6 mol% of **1** at room temperature and using 6 mol% of **3** at 100°C. © 1999 Elsevier Science Ltd. All rights reserved.

The asymmetric borane reduction of prochiral ketones to enantiomerically enriched alcohols is a pivotal transformation in synthetic organic chemistry.[1] Many asymmetric catalysts have been developed for this asymmetric reaction. Oxazaborolidines strongly catalyze the reduction reaction and provide alcohols with excellent enantioselectivity.[2] Phosphinamide containing a N–P=O unit, which has been reported by Wills,[3] and tricoordinated phosphorus borane complexes, reported by Buono,[4] are efficient catalysts for the asymmetric reduction of ketones by borane. In addition, other researchers have reported related catalysts that also give modest or excellent results.[5] In this paper, we describe an optimized catalyst **1** and a procedure for its use in asymmetric carbonyl reduction by borane. To the best of our knowledge, these kinds of trivalent phosphorus compounds have rarely been utilized as chiral catalysts in the asymmetric reduction of ketones. Chiral nonracemic tricoordinated phosphorus borane complex **3** was also investigated.

Chiral (+)-2,2′-*O*,*O*-(1,1′-binaphthyl)-dioxo-*N*,*N*-diethylphospholidine **1** (Scheme 1) was derived from (*S*)-binaphthol and triethylaminophosphorus [triethylaminophosphorus was heated under reflux with (*S*)-binaphthol until no further diethylamine could be detected in the nitrogen stream from the reaction (**1**: $[\alpha]_D$ +473.8 (c=0.34, chloroform); m.p. 205–220°C; prepared in 90% yield)]. Compound **1** contains a stereogenic trivalent phosphorus atom which can donate a lone pair of electrons and the C_2 symmetry for the whole molecule, so it can efficiently catalyze the borane reduction and get the higher enantiomeric excesses of up to 98.5%.

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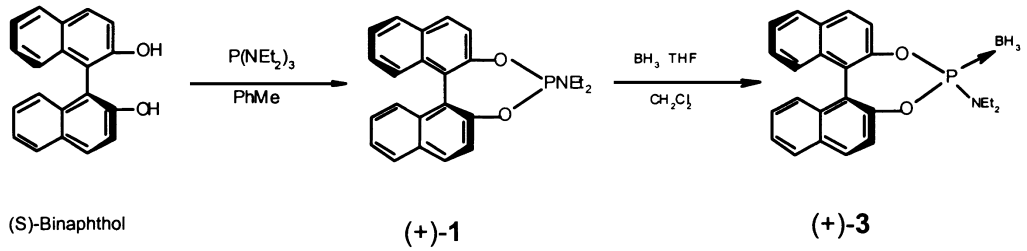


(S)-Binaphthol (+)-1 (+)-3

Scheme 1.

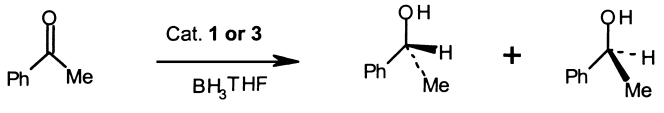
Table 1
Enantioselective synthesis of **2** using chiral catalyst **1**[6] (Scheme 2)

Entry	Cat.(mol%)	Temp(°C)	$[\alpha]_D$(c=1.0 MeOH, 25°C)[a]	Yield(%)	E.e.(%)[b]	E.e.(%)[c]
1	6	25	+44.6	95	>99	98.5
2	4	25	+40.95	90	92	91.3
3	2	25	+35.6	90	80	79.5

a: determined by Perkin-Elemer 241MC Polarimeter
b: based on the maximum $[\alpha]_D$ -45.5 (C 3, MeOH, 25°C).[7] The major configuration of **2** is R.
c: determined using Hewlett Packard 6890A chromatograph with a SGE Cydec-B as chiral column and n-hexane as eluant.

The use of a catalytic amount (6 mol%) of **1** in the enantioselective borane reduction of acetophenone led to phenethyl alcohol with 98.5% enantiomeric excess (Table 1, entry 1). As the catalytic amount increases (from 2 mol% to 6 mol%), the e.e. increases (from 79.5% to 98.5%). Table 1 shows that compound **1** dramatically increases the reaction rate and asymmetric induction is very high.

We also prepared the tricoordinated phosphorus complex **3** from **1** (Scheme 1) [compound **1** and 1 equiv. of borane, reflux, 3 h, under nitrogen (**3**: $[\alpha]_D$ +470 (c=0.40, chloroform); m.p. 144–146°C; prepared in 98% yield)], as the chiral catalyst for the borane reduction of acetophenone (Scheme 2).



R- **2** S- **2**

Scheme 2.

Table 2 shows that compound **3** dramatically increases the reaction rate and the asymmetric induction is very high. Furthermore, it shows the effect of temperature. The enantiomeric excess of **2** was higher (98.4%) at elevated temperatures (Table 2, entry 3) than that (81.1%) at room temperature (Table 2, entry 1).

With the same catalytic amount (6 mol%) and the same reaction temperature (25°C), the enantiomeric

Table 2
Enantioselective synthesis of **2** using chiral catalyst **3**[6] (Scheme 2)

Entry	Cat.(mol%)	Temp(°C)	$[\alpha]_D$(c=1.0 MeOH, 25°C)[a]	Yield(%)	E.e.(%)[b]	E.e.(%)[c]
1	6	25	+36	90	81	81.1
2	6	50	+43.2	93	97	96.1
3	6	100	+44.5	94	>99	98.4

a: determined by Perkin-Elemer 241MC Polarimeter
b: based on the maximum $[\alpha]_D$ -45.5 (C 3, MeOH, 25°C).[7] The major configuration of **2** is R.
c: determined using Hewlett Packard 6890A chromatograph with a SGE Cydec-B as chiral column and n-hexane as eluant.

excess of **2** using catalyst **1** (Table 1, entry 1, 98.5%) was higher than that using catalyst **3** (Table 2, entry 1, 81.1%).

We suggested that the efficient catalytic activity and asymmetric induction of **1** and **3** could result from the rigid C_2 symmetry of the binaphthol unit and its ability to donate a lone pair of electrons.

As described, new chiral nonracemic compounds **1** and **3**[8] derived from (*S*)-binaphthol are highly enantioselective catalysts for the asymmetric reduction of acetophenone by borane. Further investigation of the catalytic ability and the asymmetric induction in the enantioselective reductions of prochiral ketones are still in progress and our findings will be reported in due course.

Acknowledgements

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6. Typical reduction experiment (Table 1, entry 1): 1 M BH_3·THF (3 ml) was added to a toluene solution (5 ml) of acetophenone (0.3 g, 2.5 mmol) and catalyst **1** (0.06 g, 0.15 mmol) under nitrogen steam at room temperature. The mixture was then stirred for 1 h and 5 ml 2N hydrochloric acid was then added to the solution. The oil extract was dried (Na_2SO_4), then the solution was evaporated under the reduced pressure. The residue was purified by distillation (98~99°C/20 mmHg). (*R*)-(+)-**2** with e.e. 98.5% was obtained in 95% yield.
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8. All new compounds were characterized by NMR (^1H, ^{31}P), IR and elemental analysis.