

Asymmetric Addition of Diethylzinc to Aromatic Aldehydes Using Enantiomerically Pure Hydroxymethyl Oxazoline Ligands

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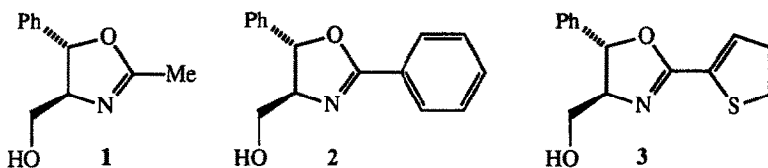
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Abstract: The addition of diethylzinc to aromatic aldehydes in the presence of catalytic amounts of enantiomerically pure hydroxymethyl oxazolines affords the corresponding secondary alcohols with modest levels of asymmetric induction.

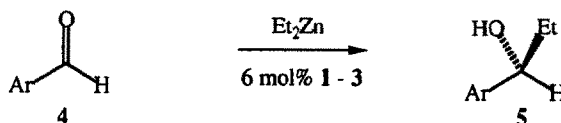
Enantiomerically pure oxazolines have been successfully employed as ligands for rhodium catalysed hydrosilylation,¹ copper catalysed cyclopropanation,² catalytic Diels Alder reaction,³ and palladium catalysed allylic substitution.⁴

We wish to report the use of the hydroxymethyl oxazolines **1** - **3** as catalysts for the asymmetric addition of diethylzinc to aromatic aldehydes.⁵ The oxazolines are readily prepared in one step from (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol and the corresponding nitrile or imidate ester hydrochloride, according to known procedures.^{6, 7}



In 1974, Meyers reported that moderate levels of enantioselectivity could be induced in the reaction of Grignard reagents with aldehydes in the presence of the oxazoline **1**.⁸ More recently, Jansen and Feringa have used oxazoline **1** as one of many ligands which impart asymmetric induction in the zinc chloride catalysed conjugate addition of Grignard reagents to cyclohexenone.⁹ As far as we are aware, the use of hydroxymethyl oxazolines as catalysts for asymmetric addition of diethylzinc to aromatic aldehydes has not been reported previously.

Initial experiments are encouraging, as summarised in the table, modest levels of asymmetric induction have been obtained in the reaction of diethylzinc with aromatic aldehydes **4**, in the presence of catalytic amounts of the ligands **1** - **3**. Reactions were run in hexane at 20 °C, using a 2:1 ratio of diethylzinc to aldehyde. In each case the (*S*)-(-)-enantiomer of 1-arylpropanol **5** was obtained in excess, as determined by comparison of the optical rotation with literature data.¹⁰



<i>Catalyst</i>	<i>Substrate: Ar</i>	<i>Yield (%)</i>	<i>Enantiomeric Excess (%)^a</i>
1	C ₆ H ₅ -	60	50
1	2-MeOC ₆ H ₄ -	86	67
1	4-MeOC ₆ H ₄ -	75	58
2	C ₆ H ₅ -	65	57
2 ^b	C ₆ H ₅ -	48	47
2	2-MeOC ₆ H ₄ -	78	59
2	4-MeOC ₆ H ₄ -	86	25
3	C ₆ H ₅ -	93	57
3	4-MeOC ₆ H ₄ -	71	49

^a Enantiomeric excess was determined by chiral hplc using a Chiralcel OB column, and by optical rotation¹⁰

^b The amount of catalyst was reduced from 6 mol% to 2 mol%

In conclusion, we have demonstrated that the use of enantiomerically pure oxazolines as catalysts for the addition of diethylzinc to aromatic aldehydes affords asymmetric induction (up to 67% ee). We are currently investigating further ligands containing hydroxy and oxazoline moieties in an effort to improve the enantioselectivities by changing the topology of the ligands.

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