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Enantioselective Addition of Diethylzinc to Benzaldehyde by Catalysts of Chiral Heterocyclic Ligands

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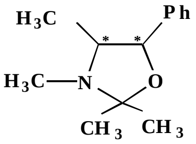
Abstract: Several kinds of chiral heterocyclic ligands without hydroxyl group have been synthesized and used as catalysts for the asymmetric addition of diethylzinc to benzaldehyde. These ligands promoted the formation of (*S*)-1-phenylpropanols in good yields and medium to good enantioselectivities (50 ~ 86 % ee.) .

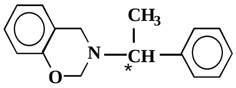
Keywords: Chiral heterocyclic ligands, hydroxyl group, asymmetric catalysis, enantioselectivity.

The enantioselective addition of diethylzinc reagents to prochiral carbonyl group has been achieved principally by catalytical amount of chiral β-amino alcohols which have proven to be highly effective catalysts[1]. A hydroxyl group has been regarded to be necessary for the chiral ligand to form a zinc alkoxide as the catalytic species[2]. We wish to report herein on the ethylation of benzaldehyde with diethylzinc promoted by several kinds of oxazolidine and thiazolidine derivatives which do not contain hydroxyl group. Four kinds chiral heterocyclic ligands we used are listed as follows:

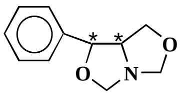
Chiral oxazolidine derivatives $\mathbf{L_1}$ was synthesized from (1*R*,2*S*)-(-)-ephedrine.



$\mathbf{L_1}$

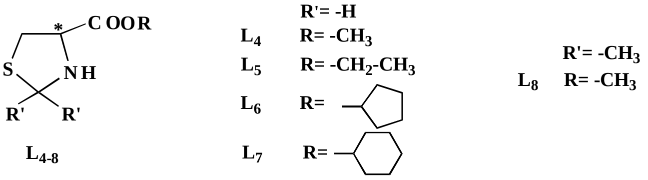


$\mathbf{L_2}$



$\mathbf{L_3}$

We synthesized (*R*)-3-(α-phenyl ethyl)-3,4-dihydro-2H-benzo[e][1,3]oxazine $\mathbf{L_2}$ from (*R*)-α-phenylethylamine. The compounds (4*R*,5*S*)-1-aza-3,7-dioxabicyclic[3.3.0]-6-phenyl octanes $\mathbf{L_3}$ was prepared from (1*R*,2*S*)-1-phenyl-2-amino-1,3-propanyldiol and formaldehyde. The ester derivatives of [1,3]-thiazolidine-4-carboxylic acid $\mathbf{L_4}$-$\mathbf{L_8}$ were synthesized from L-cysteine.



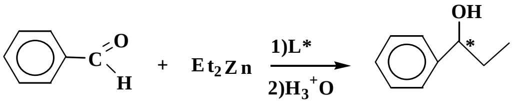


Table 1 Enantioselective addition of diethylzinc to benzaldehyde by catalysis with chiral ligands

Entry	Ligand	T(℃)	mol%	t(h)	Yield(%)	$[\alpha]_D^{24}$	Config.	%ee
1	**L1**	15	8	36	68	+23.5	R	51
2	**L2**	18	8	48	41	-19.2	S	41
3	**L3**	18	8	24	51	-19.4	S	41
4	**L4**	15	8	24	100	-28.9	S	62
5	**L4**	20	8	24	90	-31.2	S	66
6	**L5**	20	11	48	56	-29.6	S	63
7	**L6**	20	8	24	79	-35.6	S	76
8	**L6**	20	16	24	87	-38.0	S	80
9	**L7**	20	8	48	50	-34.0	S	72
10	**L7**	20	12	48	60	-32.0	S	68
11	**L7**	20	16	48	92	-40.2	S	86
12	**L8**	18	8	24	50	-14.5	S	31

Based on the reported value of $[\alpha]_D$ and 'H-NMR spectrum (*S*)-1-phenyl propanols in the presence of a shift reagent Eu(tfc)$_3$ (400HzNMR, ARX). Reported value for (*S*)-1-phenylpropanol in 99%ee. is $[\alpha]_D^{20}$-47 (C = 2.25,hexane) (according to the result of Aldrich Co.)

Enantioselective addition of diethylzinc to benzaldehyde (1 mol) in the presence of catalytic amounts (0.08-0.16 mol) of chiral ligands **L$_{1\text{-}8}$** was carried out generally in toluene-hexane(1:1) at room temperature, using 2.4 mol of diethylzinc for 24-48 h. Even though the exact mechanism of catalysis by the heterocyclic ligands containing no hydroxyl is not yet clear, the above described observations are encouraging in searching for new chiral promoters which were easily prepared for catalytic enantioselective synthesis.

References

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