

## Chiral Ligands from *Abrine*. 4. Heterocycle-Containing 1,2,3,4-Tetrahydro- $\beta$ -Carboline Methyl Ester Used for Catalysis of Enantioselective Addition of Diethylzinc to Benzaldehyde

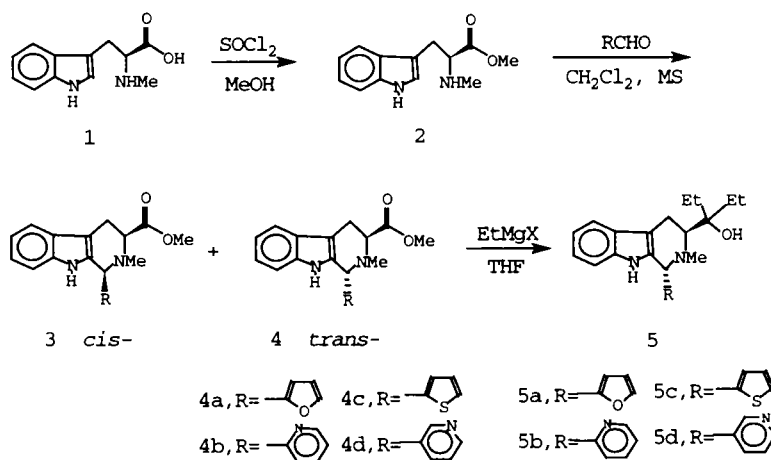
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**Abstract:** Four 1,2,3,4-tetrahydro- $\beta$ -carboline amino acid esters with a heterocycle at the C-1 position were used as chiral ligands in the enantioselective addition reactions. The different positions of the heteroatoms gave different effects, and medium but opposite enantioselectivity was recorded.

**Keywords:** Enantioselective addition; diethylzinc; 1,2,3,4-tetrahydro- $\beta$ -carboline ester.

The  $\beta$ -Amino alcohol plays a very important role in catalytic enantioselective addition<sup>1</sup>. Our former study focussed on 1,2,3,4-tetrahydro- $\beta$ -carboline (high enantioselectivity of up to 97.5%ee)<sup>2</sup>. Here, we first report that four 1,2,3,4-tetrahydro- $\beta$ -carboline amino acid esters with a heterocycle at the C-1 position were used as chiral ligands in the enantioselective addition of diethylzinc to benzaldehyde (**Table1**, entry 1–4), and a moderate degree of enantioselectivity was observed.



Scheme 1

1,2,3,4-Tetrahydro- $\beta$ -carboline amino acids esters were readily available by the Pictet-Spengler reaction<sup>3</sup> (**Scheme 1**). To compare the differences in corresponding alcohols, the Grignard addition products were examined in common addition reactions (**Scheme 2**, **Table 1**, entry 5–8).

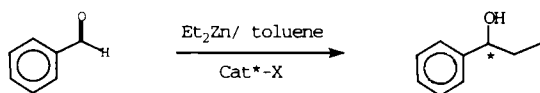
**Table 1.** The addition of  $\text{Et}_2\text{Zn}$  to  $\text{PhCHO}$  in the presence of chiral ligands

entry	Cat*-X <sup>1</sup>	Yield (%) <sup>2</sup>	Configuration	Ee (%) <sup>3</sup>
1	4a	83.0	S	15.8
2	4b	74.2	R	38.7
3	4c	70.2	S	17.7
4	4d	32.1	S	5.8
5	5a	57.3	R	5.3
6	5b	64.3	R	32.3
7	5c	70.6	R	39.9
8	5d	39.2	R	0.23

(1) The molar amounts of 4a to 4d was 10% of benzaldehyde's; 5a to 5d was 5%.

(2) Based on the isolated product.

(3) Determined with chiralcel OD column and eluted with iso-propanol and hexane (4.5:95.5) at a flow rate of 1 ml/min.



**Scheme 2**

It was strange that the conversion of the configuration of 1-phenyl-1-propanol was catalyzed by the esters (entry 1,3, and 4). The reasons could be due to the lone pair electrons of O, the p- $\pi$  conjugation of S atoms, the  $\pi$ - $\pi$  conjugation of N, or the ring size. The low enantioselectivity of entry 4 and 8 might be attributed to the N-atom at the 3'-position, which does not form the transition state easily.

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