Supporting Information

The Effects of Solvent on Switchable Stereoselectivity:
Copper-Catalyzed Asymmetric Conjugate Addition Using
$D_2$-Symmetric Biphenyl Phosphoramidite Ligand

Han Yu, Fang Xie, Zhenni Ma, Yangang Liu and Wanbin Zhang*

School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University,
800 Dongchuan Road, Shanghai 200240, P. R. China

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1. General Experimental Conditions

All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen. Toluene, PhCF₃, DMF, THF, Et₂O, DIPE, MTBE, and dichloromethane were dried according to published procedures. Commercially available reagents were used without further purification. All reactions were performed under a nitrogen atmosphere, and the workup was carried out in air unless otherwise stated.

NMR spectra were recorded on a Varian MERCURY plus-400 spectrometer. The chemical shifts were reported in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Coupling constants are reported in Hz and refer to apparent peak multiplicities. Optical rotations were measured with a SPSI SGW-1 polarimeter. All ee values were determined by HPLC using a Daicel Chiralcel OJ-H or AD-H column.

2. General Procedure for Preparation of the Substrates

To a solution of 2.2 g of NaOH in 20 mL of H₂O and 43 mmol of aromatic ketone in 12 mL ethanol at 0 °C was gradually added 1 equiv of aromatic aldehyde (43 mmol). The mixture was then allowed to warm to room temperature and stirred for 4 h, after which a precipitate of the product formed. The product was collected by suction filtration on a Buchner funnel and washed repeatedly with cold water in order to remove all traces of sodium hydroxide. Recrystallization of the product from ethanol afforded enones 1a-n. All spectroscopic data of enones 1a-n are in good agreement with reported literature data.¹

3. General Procedure for Copper-Catalyzed Enantioselective Conjugate Addition

A flame dried Schlenk tube was charged with Cu(OAc)₂·H₂O (1.0 mg, 0.005 mmol) and trans-L₂ (7.8 mg, 0.01 mmol) under a N₂ atmosphere, and the mixture was dissolved in dry toluene (1.5 mL). The solution was stirred at 25 °C for 30 min and then cooled to -50 °C. Et₂Zn (0.75 mmol, 0.75 mL of 1 M hexane solution) was added dropwise to the above solution. The colour of the solution gradually turned to light yellow after 5 min at -50 °C. The substrate 1a (0.50 mmol dissolved in 1.0 mL dry toluene) was then added dropwise. The mixture was stirred at -50 °C for 16 h before quenching with aqueous saturated NH₄Cl. The layers were separated and the aqueous layer was extracted with ethyl acetate (5 mL×2). The combined organic extracts were dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give the addition product. The enantiomeric excess of the product was determined by chiral HPLC.

References

4. Screening of trans-L3-5\textsuperscript{a} 

$$\begin{array}{cccc}
\text{Entry} & \text{L} & \text{Solvent} & \text{Yield (%)\textsuperscript{b}} & \text{Ee (%)\textsuperscript{c}} \\
1 & \text{trans-L3} & \text{Toluene} & 95 & 82 (R) \\
2 & \text{trans-L3} & \text{THF} & 95 & 75 (S) \\
3 & \text{trans-L4} & \text{Toluene} & 94 & 73 (R) \\
4 & \text{trans-L4} & \text{THF} & 96 & 61 (S) \\
5 & \text{trans-L5} & \text{Toluene} & 91 & 65 (R) \\
6 & \text{trans-L5} & \text{THF} & 93 & 53 (S) \\
\end{array}$$

\textsuperscript{a}1 mol% Cu salt, 2 mol% trans-L, 1.5 eq. ZnEt\textsubscript{2}. \textsuperscript{b}Yield of the isolated product. \textsuperscript{c}Determined by HPLC, Chiralcel AD-H column. The absolute configuration was determined by comparison with literature data.
5. NMR Charts of New Compounds

$^1$H NMR of 2b

$^{13}$C NMR of 2b

$^1$H NMR of 2h
$^{13}$C NMR of 2h

$^1$H NMR of 2i

$^{13}$C NMR of 2i
6. HPLC Date of Copper-Catalyzed Conjugate Addition Products

HPLC data of 2a, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2b, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2c, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2d, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2e, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2f, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2g, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2h, racemic sample

Toluene as solvent

THF as solvent

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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HPLC data of 2i, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2j, racemic sample

**Toluene as solvent**

**THF as solvent**

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Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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HPLC data of 2k, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2l, racemic sample

**Toluene as solvent**

**THF as solvent**
HPLC data of 2m, racemic sample

Toluene as solvent

THF as solvent
HPLC data of 2n, racemic sample

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Toluene as solvent

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**THF as solvent**