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PAPER

The effects of solvent on switchable stereoselectivity: copper-catalyzed asymmetric conjugate additions using D_2-symmetric biphenyl phosphoramidite ligands†

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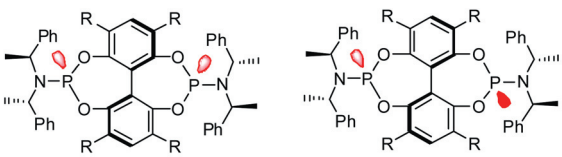
A highly enantioselective copper-catalyzed conjugate addition of diethylzinc to acyclic aromatic enones was developed with phosphoramidite ligands bearing a D_2-symmetric biphenyl backbone. This type of reaction demonstrated that toluene and THF solvents can completely reverse the absolute configuration of the products, thus simplifying the process of accessing either enantiomer (*S*: 92% ee, 94% yield; *R*: 99% ee, 96% yield).

Introduction

Catalytic asymmetric syntheses of both enantiomers of a chiral compound are of significant interest to the chemical community.[1] Commonly, in a catalytic asymmetric protocol, both isomers of a chiral ligand are required to access each enantiomer of chiral compounds. Alternatives include using different central metals in the presence of an identical ligand[2] or changing reaction parameters (temperature, additives, and solvents *etc.*).[3,4]

A number of effective chiral ligand systems have been developed for Cu-catalyzed enantioselective addition reactions of diethylzinc to structurally diverse enones.[5–8] Among the successful chiral ligands, BINOL-,[5] TADDOL-,[6] and BIPOL-derived phosphoramidites[7] have shown remarkable enantioselectivities in the reactions of diethylzinc to enones. Very recently, our group reported new types of biphenyl phosphoramidite ligands **L1–5** (Fig. 1) containing a D_2-symmetric backbone. These ligands demonstrated excellent activity and selectivity in Cu-catalyzed asymmetric 1,4-addition reactions of diethylzinc to α,β-unsaturated ketones and nitroalkenes. Their excellent chiral environment and their ability to be easily modified at the 3,3′,5,5′-position of the biphenyl backbone, makes them excellent ligands.[9] Interestingly, we found that the substituents at the 3,3′,5,5′-position of the biphenyl backbone of the ligands have a dramatic effect on the stereocontrol in Cu-catalyzed asymmetric 1,4-addition reactions.[9c,d]

In addition, Cu-catalyzed asymmetric additions to acyclic aromatic α,β-unsaturated enones such as chalcone, can provide valuable compounds for use as intermediates or building blocks in organic chemistry.[10] To explore the behaviour of the phosphoramidite ligands with a D_2-symmetric biphenyl backbone, the ligands were used in asymmetric conjugate additions of deithylzinc to α,β-unsaturated acyclic aromatic enones. Both enantiomeric products were obtained by changing reaction parameters, a method of which has not been significantly reported.[3]



cis-(*S*,*S*,*aR*,*S*,*S*)-**Ln** (**n=1**, **2**) *trans*-(*S*,*S*,*aR*,*S*,*S*)-**Ln** (**n=1**, **2**, **3**, **4**, **5**)

n=1, R=H; **n=2**, R=Me; **n=3**, R=Et; **n=4**, R=Ph; **n=5**, R=Br.

Fig. 1 Phosphoramidite ligands with a D_2-symmetric biphenyl backbone.

Results and discussion

Trans-**L2** provided excellent enantioselectivities for the asymmetric conjugate addition of diethylzinc to α,β-unsaturated carbonyl substrates and nitroalkenes.[9a–c] The conjugate addition of diethylzinc to chalcone **1a** was performed in the presence of 2 mol% of *trans*-**L2** and 1 mol% of copper salt in toluene, at a temperature of −40 °C (Table 1). $Cu(OAc)_2{\cdot}H_2O$ was found to be the most suitable catalyst precursor because of its high reactivity and enantioselectivity (entries 1–10). With $Cu(OAc)_2{\cdot}H_2O$ as the catalyst precursor and *trans*-**L2** as the ligand, we investigated the solvent effect (entries 10–16) and discovered that toluene provided the most promising results. When Et_2O, methyl *t*-butyl ether (MTBE) or diisopropyl ether (DIPE) were used as

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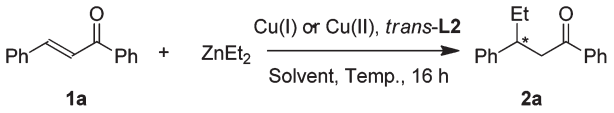
Table 1 Screening of reaction conditions[a]

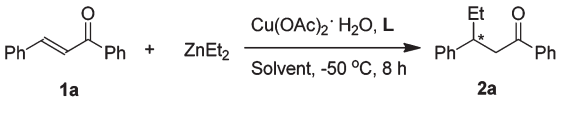


1a 2a

Entry	Cu salt	Solvent	T (°C)	Yield[b] (%)	ee[c] (%)
1	Cu(I)$(MeCN)_4PF_6$	Toluene	−40	96	68 (*R*)
2	Cu(II)$(OTf)_2$	Toluene	−40	95	78 (*R*)
3	Cu(II)$(acac)_2$	Toluene	−40	98	65 (*R*)
4	Cu(II)Br_2	Toluene	−40	95	53 (*R*)
5	Cu(II)$ClO_4{\cdot}6H_2O$	Toluene	−40	93	79 (*R*)
6	Cu(I)$(MeCN)_4BF_4$	Toluene	−40	90	76 (*R*)
7	Cu(I)$(MeCN)_4PF_6$	Toluene	−40	91	73 (*R*)
8	Cu(I)TC	Toluene	−40	99	67 (*R*)
9	Cu(I)(C_6H_6)OTf	Toluene	−40	94	66 (*R*)
10	Cu(II)$(OAc)_2{\cdot}H_2O$	Toluene	−40	96	92 (*R*)
11	Cu(II)$(OAc)_2{\cdot}H_2O$	$PhCF_3$	−40	95	73 (*R*)
12	Cu(II)$(OAc)_2{\cdot}H_2O$	Et_2O	−40	99	39 (*R*)
13	Cu(II)$(OAc)_2{\cdot}H_2O$	MTBE	−40	97	42 (*R*)
14	Cu(II)$(OAc)_2{\cdot}H_2O$	DIPE	−40	97	43 (*R*)
15	Cu(II)$(OAc)_2{\cdot}H_2O$	DCM	−40	93	70 (*R*)
16	Cu(II)$(OAc)_2{\cdot}H_2O$	THF	−40	96	81 (*S*)
17	Cu(II)$(OAc)_2{\cdot}H_2O$	THF	−30	97	75 (*S*)
18	Cu(II)$(OAc)_2{\cdot}H_2O$	THF	−50	95	92 (*S*)
19	Cu(II)$(OAc)_2{\cdot}H_2O$	THF	−60	93	91 (*S*)
20[d]	Cu(II)$(OAc)_2{\cdot}H_2O$	THF	−78	93	82 (*S*)
21[e]	Cu(II)$(OAc)_2{\cdot}H_2O$	Toluene	−30	98	81 (*R*)
22	Cu(II)$(OAc)_2{\cdot}H_2O$	Toluene	−50	96	99 (*R*)
23[d]	Cu(II)$(OAc)_2{\cdot}H_2O$	Toluene	−78	92	83 (*R*)

[a] 1 mol% Cu salt, 2 mol% *trans*-**L2**, 1.5 eq. $ZnEt_2$. [b] Yield of the isolated product. [c] Determined by HPLC, Chiralcel AD-H column. The absolute configuration was determined by comparison with literature data. [d] The reaction was stirred for 20 h. [e] The reaction was stirred for 12 h.

Table 2 Screening of ligands[a]



1a 2a

Entry	L	Solvent	Yield[b] (%)	ee[c] (%)
1	*cis*-**L1**	Toluene	92	77 (*R*)
2	*cis*-**L1**	THF	91	52 (*R*)
3	*trans*-**L1**	Toluene	93	79 (*R*)
4	*trans*-**L1**	THF	94	57 (*R*)
5	*cis*-**L2**	Toluene	96	93 (*R*)
6	*cis*-**L2**	THF	93	86 (*S*)
7	*trans*-**L2**	Toluene	96	99 (*R*)
8	*trans*-**L2**	THF	92	92 (*S*)

[a] 1 mol% Cu salt, 2 mol% **L**, 1.5 eq. $ZnEt_2$. [b] Yield of the isolated product. [c] Determined by HPLC, Chiralcel AD-H column. The absolute configuration was determined by comparison with literature data.

the reaction solvent, excellent reactivity but low enantioselectivities for the conjugate addition reactions were obtained (Table 1, entries 12–14). To our surprise, when THF was employed as the reaction solvent, the other enantiomer was obtained in excellent yield and enantioselectivity (entry 16), most probably due to THF's strong coordinating ability. These results indicated that the ether solvent possessed appropriate coordinating ability to be involved in the catalytic cycle, acting as a hemilabile ligand and altering the structure of the catalyst.

Since both enantiomers could be obtained by using toluene and THF as solvents, different temperatures were screened to optimize the reaction conditions. Reducing the reaction temperature from −30 °C to −50 °C provided excellent yields and increased enantioselectivity (entries 18 and 22). The highest enantioselectivity was observed at −50 °C in both toluene and THF. Furthermore, decreasing the temperature to −78 °C resulted in a slight decrease in yield, and an obvious drop in enantioselectivity in toluene or THF at this temperature (entries 20 and 23).

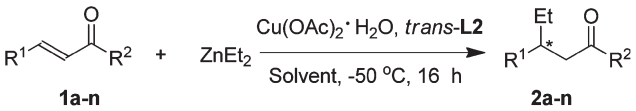
Encouraged by the results described above, reactions involving several phosphoramidite ligands containing a D_2-symmetric biphenyl backbone were investigated to identify the most efficient ligand for use in toluene and THF (Table 2).

Ligand screening revealed that the phosphoramidite ligands **L1–2** in Fig. 1 were effective for this transformation (91–96% yield, *R*-**2a**: 52–99% ee, *S*-**2a**: 86–92%). Both *cis*- and *trans*-**L1** lacking substituents at the 3,3′,5,5′-position, gave *R* configuration products (entries 1–4). Substituents at the 3,3′,5,5′-position of the biphenyl backbone of the ligands showed significant influence on catalysis. No matter whether the 3,3′,5,5′-position contained substituents or not, both *cis*- and *trans*-**L** provided *R* configuration product when using toluene as the solvent. *Trans*-**L** gave higher enantioselectivity compared to its *cis*-**L** counterpart (entries 1, 3, 5 and 7), and up to 99% ee was obtained with methyl-substituted *trans*-**L2** (entries 1, 3, 5 and 7). When THF was used as the reaction solvent, ligands *cis*-**L2** and *trans*-**L2**, containing substituents on the biphenyl backbone, all provided *S* configuration product (entries 6 and 8). Up to 92% ee was obtained with methyl-substituted *trans*-**L2** (entry 8). *Trans*-**L3–5** were also examined, however no improvement was observed with these ligands (ESI†).

With toluene and THF used as a reversal solvent pair, we expected to induce the formation of both absolute configurations in the products. A wide range of aromatic enones were examined to investigate substrate scope and the reversal in stereoselectivity (Table 3).

To our delight, a complete switch in stereoselectivity was observed for all of the substrates. The introduction of a methyl group at the *ortho*-, *meta*- and *para*-position on the phenyl ring R^1 or R^2 of substrate **1**, led to a drop in enantioselectivity when using both solvents, which may be a result of steric hindrance (entries 1–4 and 8–10). When a methoxy group was introduced at the *para*-position of the phenyl ring R^1 or R^2, decreased enantioselectivity was observed with the exception of substrate **1e**, whose enantioselectivity was similar to that of substrate **1a** (entries 1, 5 and 11). Addition of an electron-withdrawing substituent (such as *para*-bromo group) to the phenyl ring R^1 or addition of a *para*-chloro group to the phenyl ring R^2, was detrimental to enantioselectivity when compared to substrates lacking substituted groups on the phenyl ring (entries 1, 6 and 12). Neither the electron-donating nor the electron-withdrawing groups at the *para*-position of the phenyl ring of R^1 or R^2 improved the enantioselectivity of this reaction. Furthermore, replacement of R^1 or R^2 with 2-naphthyl groups resulted in a decrease in enantioselectivity when the reaction was performed

Table 3 Substrate scope[a]



Entry	Substrate	R^1	R^2	Solvent	Yield[b] (%)	ee[c] (%)
1	**1a**	Ph	Ph	THF	94	92 (*S*)
				Toluene	96	99 (*R*)
2	**1b**	*o*-MeC_6H_4	Ph	THF	91	80 (*S*)
				Toluene	92	71 (*R*)
3	**1c**	*m*-MeC_6H_4	Ph	THF	92	78 (*S*)
				Toluene	94	85 (*R*)
4	**1d**	*p*-MeC_6H_4	Ph	THF	93	86 (*S*)
				Toluene	95	86 (*R*)
5	**1e**	*p*-$MeOC_6H_4$	Ph	THF	93	92 (*S*)
				Toluene	96	90 (*R*)
6	**1f**	*p*-BrC_6H_4	Ph	THF	95	86 (*S*)
				Toluene	96	96 (*R*)
7	**1g**	2-naphthyl	Ph	THF	90	87 (*S*)
				Toluene	92	91 (*R*)
8	**1h**	Ph	*o*-MeC_6H_4	THF	90	60 (*S*)
				Toluene	91	79 (*R*)
9	**1i**	Ph	*m*-MeC_6H_4	THF	92	90 (*S*)
				Toluene	93	75 (*R*)
10	**1j**	Ph	*p*-MeC_6H_4	THF	91	83 (*S*)
				Toluene	95	91 (*R*)
11	**1k**	Ph	*p*-$MeOC_6H_4$	THF	93	65 (*S*)
				Toluene	97	92 (*R*)
12	**1l**	Ph	*p*-ClC_6H_4	THF	92	81 (*S*)
				Toluene	93	92 (*R*)
13	**1m**	Ph	2-Naphthyl	THF	93	87 (*S*)
				Toluene	94	92 (*R*)
14[d]	**1n**	Ph	Me	THF	93	86 (*S*)
				Toluene	90	97 (*R*)

[a] 1 mol% Cu salt, 2 mol% *trans*-**L2**, 1.5 eq. $ZnEt_2$. [b] Yield of the isolated product. [c] Determined by HPLC, Chiralcel AD-H column. The absolute configuration was determined by comparison with literature data. [d] The ee value (toluene as solvent) is cited from our previous report for comparison.[9a]

in THF or toluene (entries 1, 7 and 13). The above results suggested that the effect of steric hindrance and the electron-donating/withdrawing properties of the *para*-position substituent on the phenyl ring R^1 or R^2, decreased enantioselectivity. We also performed the reaction using a typical acyclic enone, benzalacetone (**1n**). Using toluene and THF as a solvent pair, products were obtained with high enantioselectivities and reversed absolute configurations (entry 14).

In order to explain the reversal phenomenon, a stereochemical pathway has been proposed according to our experimental results (Fig. 2). As a copper ion coordinates to one phosphorus on the ligand,[11] the other phosphorus remains relatively far away from the reaction center. Both the *cis* and *trans* configurations of the ligands therefore have little effect on the absolute configuration of the products. The steric repulsion between the substituents at the 3,3′- or 5,5′-position of the biphenyl backbone with the aryl groups of the substrate or THF, may determine the stereochemical outcome of the 1,4-addition. For the transition states involving THF as a solvent in this reaction, the oxygen atom of THF coordinates with the zinc ion. Steric repulsion between the substituent at the 3,3′,5,5′-position of the biphenyl backbone of ligand **L2** and THF in **L2**-THF-TS2, is larger than that in **L2**-THF-TS1 between the substituent at the 3,3′,5,5′-position of the biphenyl backbone of ligand **L2** and the aryl group of the substrate. This leads to the 1,4-adduct with a *S* isomer configuration. However, when toluene is used as a solvent, there are no coordination effects. The steric repulsion between the aryl group of ligand **L2** and the aryl group of the substrate in transition state **L2**-TS2, is smaller than that between

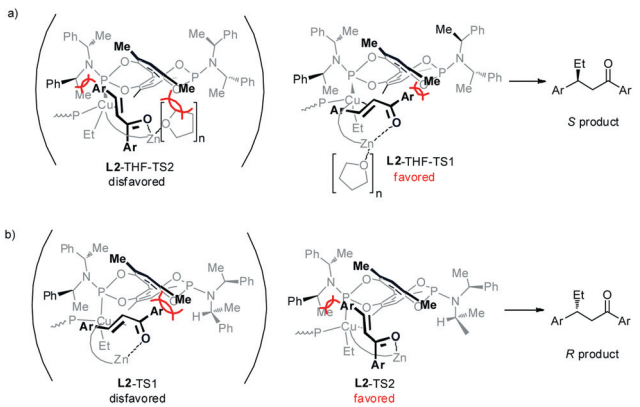


Fig. 2 Proposed stereochemical pathway showing the facial coordination of the copper atom with the enone substrate.

the substituent at the 3,3′,5,5′-position of the biphenyl backbone, and the aryl group of the substrate in **L2**-TS1. This leads to the 1,4-adduct with the *R* isomer configuration.

Conclusions

In summary, we have developed a highly enantioselective copper-catalyzed conjugate addition of diethylzinc to acyclic aromatic enones with phosphoramidite ligands bearing a D_2-symmetric biphenyl backbone. These types of reactions demonstrated that toluene and THF solvents can be used to completely reverse the absolute configuration of the products, thus simplifying the process of accessing either enantiomer (*S*: 92% ee, 94% yield; *R*: 99% ee, 96% yield).

Experimental section

General details

Commercially available reagents were used without further purification other than those described below. Substrates **1** were prepared according to modified methods of reported procedures.[10] All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen. Toluene, $PhCF_3$, DMF, THF, Et_2O, DIPE, MTBE, and dichloromethane were dried according to published procedures. Column chromatography was run on silica gel (100–200 mesh). ^1H NMR (400 MHz) spectra and ^{13}C NMR (100 MHz) spectra were obtained on a Varian MERCURY plus-400 spectrometer. HRMS was performed on a Micromass LCT TM at the Instrumental Analysis Center of Shanghai Jiao Tong University.

General procedures for conjugate addition

A flame dried Schlenk tube was charged with $Cu(OAc)_2{\cdot}H_2O$ 1.0 mg (0.005 mmol) and two equivalents of ligand (0.010 mmol) under nitrogen, and the mixture was dissolved in dry toluene (1.5 mL), resulting in a colorless solution. The solution was stirred at 25 °C for 2 h and then cooled to −50 °C. The substrate **1** (0.50 mmol dissolved in 1.0 mL dry toluene) was then added dropwise over 3 min. The solution was stirred for 5 min at −50 °C and gradually turned to light yellow. Diethylzinc (0.75 mmol, 0.75 mL of 1 M sol. in hexane) was added dropwise over 3 min. The reaction mixture was stirred at −50 °C for 16 h and monitored by TLC until full conversion of product was observed. The reaction mixture was quenched with aqueous saturated NH_4Cl and extracted with ethyl acetate (5 mL × 2). The organic extracts were combined, concentrated and the residue was purified by silica gel column chromatography to afford the product **2**. Enantiomeric excess was determined by chiral HPLC. Melting points of racemic product **2** was measured with SGW X-4 micro melting point apparatus.

1,3-Diphenylpentan-1-one (2a)[10]

A white solid, mp: 55–56 °C; using THF as solvent: *S*-**2a**, 92% ee, 94% yield; using toluene as solvent: *R*-**2a**, 99% ee, 96% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92–7.87 (m, 2H), 7.55–7.50 (m, 1H), 7.45–7.40 (m, 2H), 7.31–7.15 (m, 5H), 3.31–3.22 (m, 3H), 1.85–1.74 (m, 1H), 1.70–1.57 (m, 1H), 0.80 (t, J = 7.4 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 13.1 min, t_R = 15.1 min.

1-Phenyl-3-*o*-tolylpentan-1-one (2b)

A white solid, mp: 56–57 °C; using THF as solvent: *S*-**2b**, 80% ee, 91% yield; using toluene as solvent: *R*-**2b**, 71% ee, 92% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92–7.88 (m, 2H), 7.55–7.50 (m, 1H), 7.45–7.40 (m, 2H), 7.22–7.05 (m, 4H), 3.66–3.55 (m, 1H), 3.30–3.20 (m, 2H), 2.38 (s, 3H), 1.85–1.57 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 163.5, 145.0, 130.6, 128.5, 127.8, 126.4, 113.8, 55.7, 45.5, 43.4, 29.5, 12.3. HRMS calcd for $C_{17}H_{19}O$ $[M + Na]^+$ 253.1592, found 253.1599. ESI-MS: 253. HPLC conditions: Chiralcel OJ-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 14.4 min, t_R = 16.8 min.

1-Phenyl-3-*m*-tolylpentan-1-one (2c)[10]

A white solid, mp: 57–58 °C; using THF as solvent: *S*-**2c**, 78% ee, 92% yield; using toluene as solvent: *R*-**2c**, 85% ee, 94% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93–7.90 (m, 2H), 7.56–7.50 (m, 1H), 7.46–7.40 (m, 2H), 7.21–6.80 (m, 4H), 3.31–3.15 (m, 3H), 2.34 (s, 3H), 1.84–1.60 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 16.6 min, t_R = 18.2 min.

1-Phenyl-3-*p*-tolylpentan-1-one (2d)[10]

A white solid, mp: 59–60 °C; using THF as solvent: *S*-**2d**, 86% ee, 93% yield; using toluene as solvent: *R*-**2d**, 86% ee, 95% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93–7.88 (m, 2H), 7.56–7.51 (m, 1H), 7.46–7.40 (m, 2H), 7.16–7.05 (m, 4H), 3.30–3.15 (m, 3H), 2.34 (s, 3H), 1.84–1.60 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 18.0 min, t_R = 23.1 min.

3-(4-Methoxyphenyl)-1-phenylpentan-1-one (2e)[10]

A white solid, mp: 62–63 °C; using THF as solvent: *S*-**2e**, 92% ee, 93% yield; using toluene as solvent: *R*-**2e**, 90% ee, 96% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90–7.86 (m, 2H), 7.57–7.51 (m, 1H), 7.46–7.39 (m, 2H), 7.15–7.11 (m, 2H), 6.85–6.80 (m, 2H), 3.77 (s, 3H), 3.30–3.17 (m, 3H), 1.83–1.58 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 39.6 min, t_R = 65.3 min.

3-(4-Bromophenyl)-1-phenylpentan-1-one (2f)[10]

A white solid, mp: 65–66 °C; using THF as solvent: *S*-**2f**, 86% ee, 95% yield; using toluene as solvent: *R*-**2f**, 96% ee,

96% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93–7.88 (m, 2H), 7.55–7.50 (m, 1H), 7.45–7.39 (m, 4H), 7.13–7.08 (m, 2H), 3.26–3.18 (s, 3H), 1.82–1.70 (m, 1H), 1.66–1.54 (m, 1H), 0.79 (t, J = 7.2 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 25.3 min, t_R = 35.3 min.

3-(Naphthalen-2-yl)-1-phenylpentan-1-one (2g)[10]

A white solid, mp: 55–56 °C; using THF as solvent: *S*-**2g**, 87% ee, 90% yield; using toluene as solvent: *R*-**2g**, 91% ee, 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93–7.89 (m, 2H), 7.80–7.76 (m, 3H), 7.66 (s, 1H) 7.56–7.50 (m, 1H), 7.47–7.38 (m, 5H), 3.45–3.10 (m, 3H), 1.95–1.64 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 28.1 min, t_R = 38.9 min.

3-Phenyl-1-*o*-tolylpentan-1-one (2h)

A white solid, mp: 57–58 °C; using THF as solvent: *S*-**2h**, 60% ee, 90% yield; using toluene as solvent: *R*-**2h**, 79% ee, 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 1H), 7.35–7.14 (m, 8H), 3.21–3.12 (m, 3H), 2.27 (s, 3H), 1.82–1.56 (m, 2H), 0.81 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 144.5, 138.8, 137.7, 131.9, 131.1, 128.6, 128.2, 127.9, 126.5, 125.7, 48.8, 43.6, 29.6, 20.9, 12.3. HRMS calcd for $C_{17}H_{19}O$ [M + Na]$^+$ 253.1592, found 253.1586. ESI-MS: 253. HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 13.0 min, t_R = 16.5 min.

3-Phenyl-1-*m*-tolylpentan-1-one (2i)

A white solid, mp: 60–61 °C; using THF as solvent: *S*-**2i**, 90% ee, 92% yield; using toluene as solvent: *R*-**2i**, 75% ee, 93% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72–7.68 (m, 2H), 7.36–7.15 (m, 7H), 3.30–3.20 (m, 3H), 2.38 (s, 3H), 1.84–1.56 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.7, 145.1, 138.4, 137.5, 133.8, 128.8, 128.3, 127.8, 126.4, 125.4, 45.6, 43.2, 29.3, 21.5, 12.3. HRMS calcd for $C_{17}H_{19}O$ [M + Na]$^+$ 253.1592, found 253.1588. ESI-MS: 253. HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 15.6 min, t_R = 18.4 min.

3-Phenyl-1-*p*-tolylpentan-1-one (2j)[10]

A white solid, mp: 59–60 °C; using THF as solvent: *S*-**2j**, 83% ee, 91% yield; using toluene as solvent: *R*-**2j**, 91% ee, 95% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.0 Hz, 2H), 7.31–7.15 (m, 7H), 3.27–3.19 (m, 3H), 2.39 (s, 3H), 1.84–1.55 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 26.6 min, t_R = 35.2 min.

1-(4-Methoxyphenyl)-3-phenylpentan-1-one (2k)[10]

A white solid, mp: 60–62 °C; using THF as solvent: *S*-**2k**, 65% ee, 93% yield; using toluene as solvent: *R*-**2k**, 92% ee, 97% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.87 (d, J = 12 Hz, 2H), 7.31–7.14 (m, 5H), 6.92–6.87 (m, 2H), 3.85 (s, 3H), 3.26–3.17 (m, 3H), 1.82–1.56 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 57.2 min, t_R = 77.6 min.

1-(4-Chlorophenyl)-3-phenylpentan-1-one (2l)[10]

A white solid, mp: 65–67 °C; using THF as solvent: *S*-**2l**, 81% ee, 92% yield; using toulene as solvent: *R*-**2l**, 92% ee, 93% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.80 (m, 2H), 7.41–7.37 (m, 2H), 7.31–7.25 (m, 2H), 7.23–7.15 (m, 3H), 3.27–3.17 (m, 3H), 1.81–1.60 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 24.3 min, t_R = 29.1 min.

1-(Naphthalen-2-yl)-3-phenylpentan-1-one (2m)[10]

A white solid, mp: 58–60 °C; using THF as solvent: *S*-**2m**, 87% ee, 93% yield; using toluene as solvent: *R*-**2m**, 92% ee, 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.00 (d, J = 8.6, 1H), 7.95 (d, J = 8.0, 1H), 7.87 (d, J = 8.6, 2H), 7.60 (t, J = 7.9, 1H), 7.55 (t, J = 7.4, 1H), 7.34–7.28 (m, 5H), 3.42 (t, J = 6.9, 2H), 3.38–3.29 (m, 1H), 1.92–1.82 (m, 1H), 1.77–1.66 (m, 1H), 0.86 (t, J = 7.4, 3H). HPLC conditions: Chiralcel AD-H column, i-PrOH–hexane 2 : 98, flow rate: 1.0 mL min^{-1}, UV detection at 254 nm, t_s = 33.4 min, t_R = 41.6 min.

4-Phenylhexan-2-one (2n)[10]

Colorless oil; using THF as solvent: *S*-**2n**, 85% ee, 80% yield; using toulene as solvent: *R*-**2n**, 98% ee, 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7. 15 (m, 5H), 3.05–3.00 (m, 1H), 2.72 (d, J = 7.2 Hz, 2H), 2.03 (s, 3H), 1.69–1.58 (m, 2H), 0.78 (t, J = 7.4 Hz, 3H). GC, Supelco γ-DEX-120 column (30 m × 0.25 mm, ID): 115 °C; Retention time: t_s = 29 min, t_R = 30 min.

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