Tetrahedron: *Asymmetry* 25 (2014) 327–333

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Novel C_2-symmetric chiral *O,N,N,O*-tetradentate 2,2-bipyridyldiolpropane ligands: synthesis and application in asymmetric diethylzinc addition to aldehydes

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ARTICLE INFO

Article history:
Received 11 November 2013
Accepted 16 December 2013

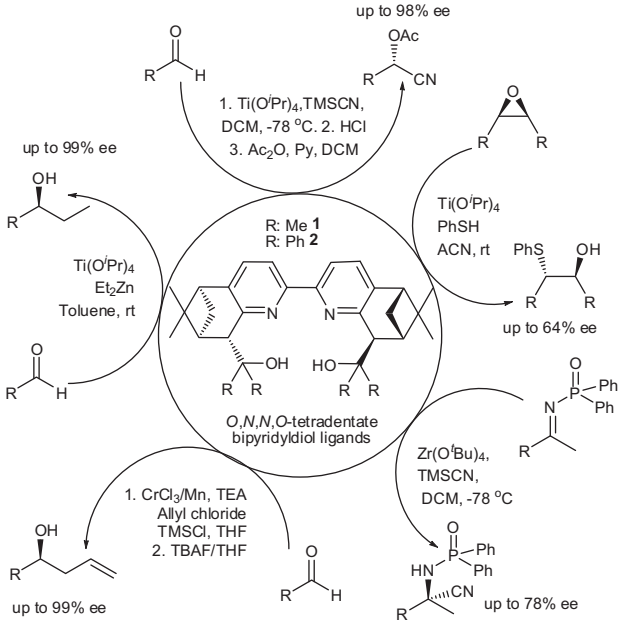
ABSTRACT

First synthesis of C_2-symmetric chiral *O,N,N,O*-tetradentate 2,2-bipyridyldiolpropane ligands is described. The Mukaiyama–Michael reaction was applied as an important reaction for the synthesis of 2,2-bipyridylpropane **9**. Among the ligands synthesized, ligand **11** exhibits excellent chiral induction (up to 97% ee) in diethylzinc addition to various aldehydes. The use of additional Lewis acid such as $Ti(O^iPr)_4$ in diethylzinc addition reaction is not required for the present catalytic system.

1. Introduction

Over the last three decades, numerous developments in the field of asymmetry synthesis made the synthesis of enantioenriched compounds easier.[1] Plenty of chiral ligands/catalysts have been applied for stereoselective reactions; they are mostly either available from natural sources or synthesized from naturally available chiral starting materials by chiral pool synthesis.[1] Although many catalytic systems are available for enantio/diastereoselective reactions, synthetic research is still in search of new catalysts for the advancement of the field. We have been studying the synthesis and application of *O,N,N,O*-tetradentate-bipyridyldiol ligands (Scheme 1) towards various stereoselective reactions.[2] These bipyridyldiol ligands are synthesized from α-pinene and provide moderate to excellent chiral induction for many asymmetric reactions especially in the case of Nozaki–Hiyama–Kishi allylation[2a] of aldehydes where the ligand **1** serves as one of the best ligands providing an excellent ee of homoallylic alcohols.

For the further advancement of catalytic activity of these bipyridyldiol ligands, its skeleton modification was considered.[3] Thus, we envisioned that the introduction of an additional carbon between the two pyridine rings in bipyridyl ligands **1** and **2** would change the ring size of the resulting metal complexes (Scheme 2) from 6,5,6-membered rings (a,b,c) to either 6,6,6-membered rings (d,e,f) with a tetravalent metal or 6,7,6-membered rings (g,h,i) with a bivalent metal. These possible metal complexes would have advantages of having less steric hindrance between the rings and would afford more stability and also the possibility of close proximity incoming substrates. It was considered that changes in the environment of bipyridyldiolmethane ligands would have the impact of stronger chiral induction in stereoselective reactions.



Scheme 1. Application of bipyridyldiol ligands in the asymmetric synthesis.

The asymmetric addition of diethylzinc to carbonyl compounds is a synthetically very useful reaction and it is a bench mark reaction for the assessment of the ability to transfer the inherent chirality of any catalyst to a prochiral carbonyl compound especially

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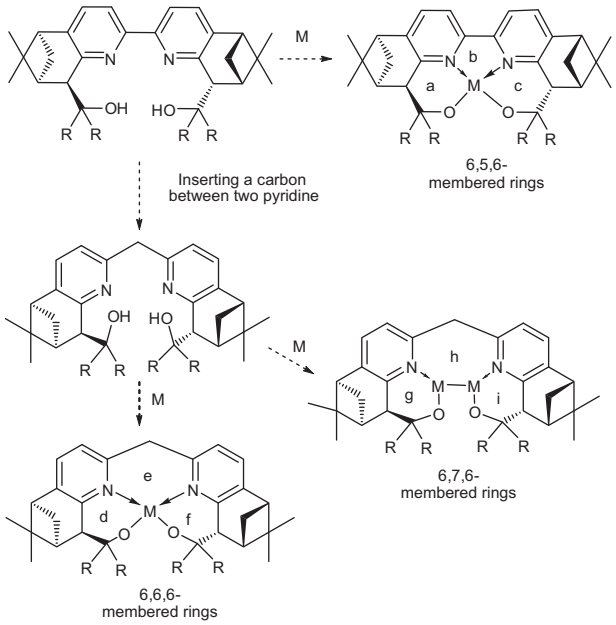
http://dx.doi.org/10.1016/j.tetasy.2013.12.020



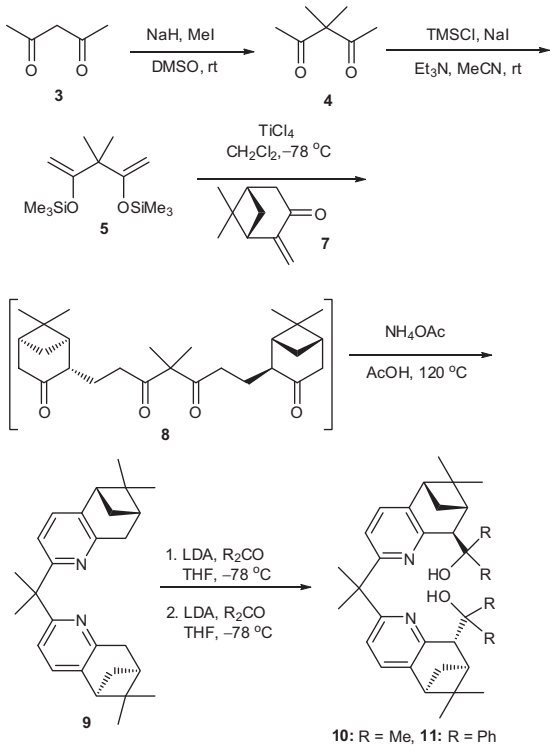
Scheme 2. Proposed model and possible metal complexes of the bipyridyldiolmethane ligands.

to aldehydes.[4,7] Herein, we report the synthesis of *O,N,N,O*-tetradentate bipyridyldiol methane type ligands and their application towards the enantioselective addition of diethylzinc to aldehydes.

2. Results and discussion

2.1. Synthesis of *O,N,N,O*-tetradentate 2,2-dipyridyldiolpropane ligands

The first target for the synthesis of 2,2-dipyridyldiolpropane ligands **10** and **11** was the preparation of 2,2-dipyridylpropane **9** (Scheme 3). Although the synthesis of **9** in low yield had been previously reported by Chelucci et al. as a double Michael addition of dilithium enolate of 3,3-dimethylpentane-2,4-dione **4** to pinocarvone **7** followed by azaanellation of bis(1,5-diketone) **8** with ammonium acetate and acetic acid,[3] in our hands, this procedure afforded **9** in very low yield (~5%). Thus 2,2-dipyridylpropane were to be synthesized by a new route that consists of the titanium mediated Mukaiyama–Michael reaction. The Mukaiyama–Michael reaction has been known for a long time for the synthesis of 1,5-diketones.[5] Our synthetic sequences for the synthesis of tetradentate ligands **10** and **11** commenced with the dimethylation of pentane-2,4-dione **3** with sodium hydride and methyl iodide in DMSO to give diketone **4** in good yield (62%).[6a] Then bis(trimethylsilyl enol ether) **5** was obtained in excellent yield (80%) by treatment of **4** with in situ generated trimethylsilyl iodide (from TMSCl/NaI) and triethylamine in acetonitrile at room temperature.[6b] The obtained silyl enol ether **5** was then subjected to $TiCl_4$ mediated Mukaiyama–Michael reaction with the α,β-unsaturated ketone, (−)-pinocarvone **7** that was prepared from a photooxygenation–elimination reaction of α-(+)-pinene **6** with singlet oxygen.[6c] The crude bis(1,5-diketone) **8** afforded by the Mukaiyama–Micheal reaction was next reacted with ammonium acetate and acetic acid at refluxing temperature to give azaanellated product, 2,2-dipyridylpropane **9** in 20% yield (two steps).[3] Although the overall yield of the Mukaiyama–Micheal and azaanellation reaction was low, it was consistent and reproducible in our hands. In addition to the spectroscopic data, X-ray crystallography of the product confirmed that the obtained product was 2,2-dipyridylpropane **9** (Fig. 1).



Scheme 3. Synthesis of *O,N,N,O*-tetradentate 2,2-dipyridyldiolpropane ligands.

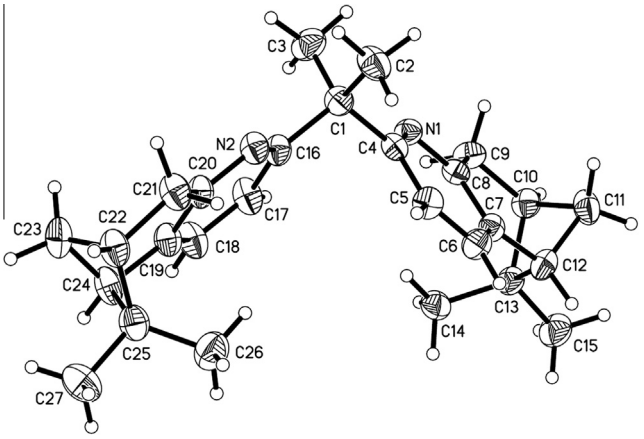


Figure 1. X-ray crystal structure of 2,2-dipyridylpropane **9** (hexagonal crystal system and P6(1) space group; CCDC number: 963556).

After having **9** in hand, its carbanion, generated by reaction with LDA, was reacted with ketones (with acetone for **10** or with benzophenone for **11**) and the same step was repeated once more to get the desired tetradentate diol ligands in moderate yields (36% of **10** and 34% of **11**, yield for two steps).[2e] Due to the bulky nature of the carbanion, this addition reactions to ketones did not go to completion, however similar results were found in the literature especially in the case of the synthesis of simple bipyridyldiols **1** and **2** where the steric hindrance is significant. Thus, an ample amount of 2,2-dipyridyldiolpropane ligands **10** and **11** were synthesized by the present synthetic route. The structure of the prepared ligands was confirmed by X-ray crystallography (Fig. 2).

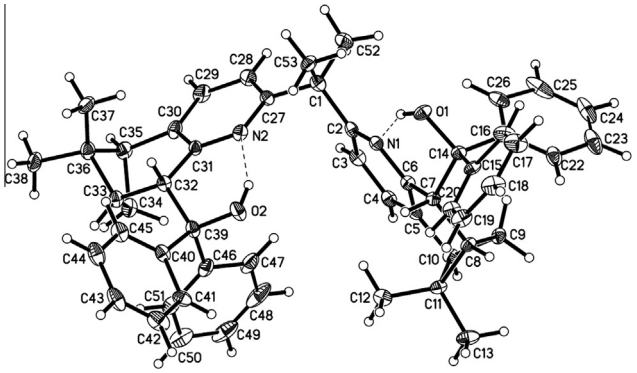


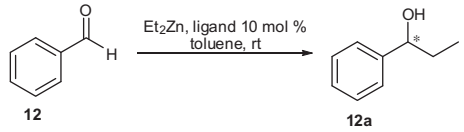
Figure 2. X-ray crystal structure of *O,N,N,O*-tetradentate ligand, 2,2-dipyridyldiolpropane **11** (monoclinic crystal system, P2(1) space group; CCDC number: 963355).

2.2. Optimization of reaction condition for diethylzinc addition to aldehydes

Application of the catalytic properties of ligands **10** and **11** were was then examined for the benchmark reaction of diethylzinc addition to benzaldehyde. The optimization of the reaction condition was started with the screening of ligands as shown in Table 1. At first, 10 mol % of ligand was treated with diethylzinc in toluene at room temperature, followed by the addition of benzaldehyde **12** to give the corresponding secondary alcohol **12a**. Although both ligands **10** (tetramethyl substituted 2,2-bipyridyldiolpropane), and **11** (tetraphenyl substituted 2,2-bipyridyldiolpropane) catalyze this model reaction to render **12a** in good yield, the selectivity varies drastically from one another, which wherein ligand **11** exhibits excellent ee (95%), however, ligand **10** shows very less ee (24%). Therefore, among the two ligands, **11** was chosen as a better catalyst and further possible reaction conditions using **11** were then optimized.

The results of screening of various solvents (Table 2, entries 1–5) for the **11** catalyzed diethylzinc addition to benzaldehyde shown that toluene is the optimal solvent for thi catalytic system. Further, the mol % of **11** was studied for the possible improvement in the enantioselectivity of **12a**. When the catalyst loading was reduced to 5 mol % (Table 2, entry 7), the selectivity and yield of the reaction were reduced very slightly (93% ee and 84% yield) as compared to the result of 10 mol % (95% ee and 88% yield, Table 2, entry 1). However, when the catalyst loading was reduced further with 1 mol % the ee and yield of the reaction at rt decreased (Table 2, entry 6; 34% ee and 46% yield). Conversely, the increase of mol % of **11** to **15** as well as to 20 mol % did not increase the ee rather it slightly increases the yield (Table 2, entries 8 and 9, respectively). Thus 10 mol % of ligand **11** was selected as an optimal catalyst loading for this reaction. Next, the reaction temperature was optimized.

Table 1
Screening of ligand[a]

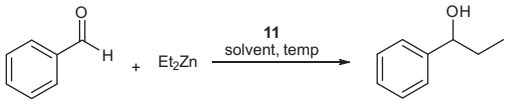


12 12a

Entry	Ligand	ee[b] (%)
1	**10**	24
2	**11**	95

[a] PhCHO/Et_2Zn/ligand ratio = 1:2:0.1.
[b] Ee checked by chiral HPLC using a Chiralcel OD-H column.

Table 2
Optimization of diethylzinc addition reaction catalyzed by **11**[a]



12 12a

Entry	**11** (mol %)	Solvent[b]	Temp (°C)	Time (h)	Yield[c] (%)	ee[d] (%)
1	10	Toluene	rt	24	88	95
2	10	CH_2Cl_2	rt	24	73	92
3	10	THF	rt	24	31	88
4	10	Ether	rt	24	85	94
5	10	Dioxane	rt	24	88	93
6	1	Toluene	rt	24	46	34
7	5	Toluene	rt	24	84	93
8	15	Toluene	rt	24	91	95
9	20	Toluene	rt	24	90	95
10	10	Toluene	0	57	82	96
11	10	Toluene	−20	57	84	97

[a] All reactions were carried under an argon atmosphere.
[b] All solvents were dried before use.
[c] The yields represents that of column purified compounds.
[d] Ee of the compounds measured by HPLC using a Chiralcel OD-H column.

When the reaction was conducted at −20 °C there was 2% ee improvement with little extended reaction time, however, when the temperature was further reduced there was no significant amplification in ee, thus −20 °C was selected as a suitable reaction temperature. Therefore the optimal reaction conditions were an addition of diethylzinc (2 equiv) to ligand **11** (10 mol %) in toluene (1 mL) at rt, stirred for 10 min, then cool to −20 °C followed by the addition of benzaldehyde (1 equiv) (Table 2, entry 11).

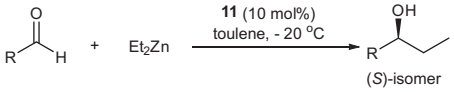
2.3. Scope of the ligand 11 catalyzed diethylzinc addition reaction

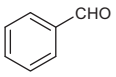
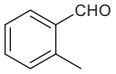
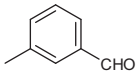
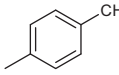
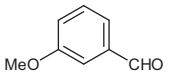
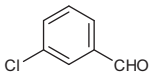
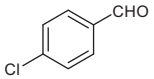
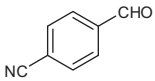
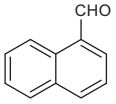
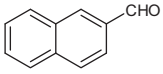
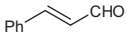
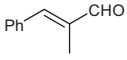
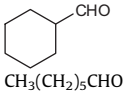
The catalytic property of **11** was then examined for various aromatic, polycyclic aromatic and aliphatic aldehydes (Table 3). All of these aldehydes provided excellent enantioselectivities (up to 97% ee) in moderate to excellent yields (up to 99%). In the case of tolualdehyde, the effect of the position of the substituent was tested (Table 3 entries 2–4); *ortho*-substitution showed a little more enantioselectivity (96% ee) compared to *meta* (93% ee) that showed slightly more selectivity than *para*-substitution (90% ee). Other substituents such as methoxy, chloro and cyano (Table 3 entries 5–8) were also checked and found to be suitable substituents of benzaldehyde for the present catalytic system. Polycyclic aromatic aldehyde such as 1- and 2-naphthaldehyde (**20** and **21**) were also found to afford the corresponding secondary alcohol **20a** and **21a** in excellent ee (97%). α,β-Unsaturated aldehydes (**22** and **23**) and aliphatic aldehydes (**24** and **25**) were also transformed into the corresponding diethylzinc addition product in high ee, however, the rate of reaction of these aldehydes were was slow, and therefore the yields obtained were only low to moderate.

3. Conclusion

Two novel chiral C_2-symmetric *O,N,N,O*-tetradentate 2,2-dipyridyldiolpropane ligands **10** and **11** were synthesized. 2,2-Dipyridylpropane **9** was synthesized for the first time using a Mukaiyama–Michael addition route. Among these ligands, the ligand **11** was found to be an effective catalyst for the diethylzinc addition to various aldehydes. The idea of insertion of an extra carbon to dipyridyldiol ligands **1** and **2** to modify the resulting metal complexes ring size had a decisive influence on the enantioselectivity of secondary alcohols obtained (up to 97% ee). The present catalytic system is a very useful addition to the existing catalytic

Table 3
Scope of **11** catalyzed diethylzinc addition to various aldehydes in 57 h[a]



Entry	Aldehyde[b]	Product/config.	Yield[c] (%)	ee[d] (%)
1	 **12**	**12a**/(*S*)	84	96
2	 **13**	**13a**/(*S*)	82	96[e]
3	 **14**	**14a**/(*S*)	95	93
4	 **15**	**15a**/(*S*)	63	90
5	 **16**	**16a**/(*S*)	69	93[e]
6	 **17**	**17a**/(*S*)	99	96
7	 **18**	**18a**/(*S*)	79	96
8	 **19**	**19a**/(*S*)	92	93[f]
9	 **20**	**20a**/(*S*)	86	97
10	 **21**	**21a**/(*S*)	90	97
11	 **22**	**22a**/(*S*)	63	85
12	 **23**	**23a**/(*S*)	52	90
13	 **24**	**24a**/(*S*)	15	86[g]
14	$CH_3(CH_2)_5CHO$ **25**	**25a**/(*S*)	15	83[g]

[a] Reagent ratio; aldehyde/Et_2Zn/ligand **11** = 1:2:0.1.
[b] All the aldehydes used as purchased except benzaldehyde which was freshly distilled.
[c] The yields represents that for column purified compounds.
[d] Ee of the compounds measured by HPLC using Chiralcel OD-H, OJ and Chiralpak AD columns.
[e] Ee was checked by HPLC on its acetate derivative prepared by reaction with Ac_2O and Py.
[f] Ee was checked on its benzoate derivative prepared by reaction with BzCl and Py.
[g] Ee was checked by ^{19}F NMR for its (*R*)-(+)-MTPA ester.

system for diethylzinc addition reaction to aldehyde. The application of these catalysts to other asymmetric reactions is under investigation.

4. Experimental

4.1. General

Unless otherwise mentioned, all the reactions were performed under an argon atmosphere in dried and freshly distilled solvent. The yields are of column chromatography purified material. The column chromatography was performed using 230–400 mesh neutral silica gels. The reported spectroscopic data are recorded on Bruker 300 and 400 NMR spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) relative to $CDCl_3$ (7.26 and 77.0 ppm), the coupling constants are reported in Hertz (Hz) and the multiplicities are indicated as br = broad, s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet. Infrared spectra were recorded using a Perkin Elmer FT/IR spectrometer. Enantiomeric excesses were determined on a Lab Alliance Series III high performance liquid chromatography (HPLC) with Chiracel OD-H, OJ and Chiralpak AD chiral columns. Optical rotations were measured on a JASCO P-1010 polarimeter at the indicated temperature with a sodium lamp (D line, 589 nm). (−)-Pinocarvone **7** and 3,3-dimethylpentane-2,4-dione **4** were synthesized according to literature procedures.

4.2. Synthesis of bis(trimethylsiyl enol ether) 5

To a stirred solution of 2,4-diketone **4** (12.0 g, 93.6 mmol) in acetonitrile (100 mL) under argon were added Et_3N (32.6 mL, 234.0 mmol), TMSCl (29.6 mL, 234.0 mmol), and NaI (35.0 g, 234.0 mmol) and stirred at room temperature for overnight. Then, it was diluted with hexane (100 mL) and the acetonitrile layer was extracted twice with hexane (2 × 100 mL). The combined organic layers were washed with a saturated $NaHCO_3$ solution (100 mL) and brine (100 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by vacuum distillation (60 °C at 1 mmHg) to afford **5** (21.3 g, 80%). ^1H NMR (400 MHz, $CDCl_3$, δ): 4.17 (s, 2H), 4.02 (s, 2H), 1.16 (s, 6H), 0.19 (s, 18H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 163.6, 88.0, 46.0, 24.9, 0.1. IR (KBr): 3125 (CH), 2964 (CH), 1254 (C–O) cm^{-1}. LRMS-FAB (*m*/*z*): 273 ($[M+H]^+$, 70), 147 (31), 73 (100). HRMS-FAB (*m*/*z*): $[M]^+$ calcd for $C_{13}H_{28}O_2Si_2$, 272.1628; found, 272.1625.

4.3. Synthesis of 2,2′-(propane-2,2-diyl)bis(6,6-dimethyl-5,6,7,8-tetrahydro-5,7-methanoquinoline) 9

To a DCM (73 mL) solution of $TiCl_4$ (9.0 mL, 80.7 mmol) were added a solution of (−)-pinocarvone **7** (11.0 g, 73.4 mmol) in DCM (73 mL) and solution of silyl enol ether (10.0 g, 36.7 mmol) in DCM (36 mL) at −78 °C under an argon atmosphere. After 4 h of stirring (TLC monitored), it was quenched with 10% K_2CO_3 (100 mL) and extracted three times with DCM. The combined DCM layer was washed with brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude bis(1,5-diketone) **8**.

To this crude product **8** were added acetic acid (184 mL) and ammonium acetate (45.7 g, 587.2 mmol) and refluxed for 12 h. The reaction was then cooled to 5 °C, basified with 4 M NaOH and extracted three times with ethyl acetate. The combined ethyl acetate was dried with $MgSO_4$, filtered, concentrated, and purified by column chromatography (5% EtOAc/hexane) to give product **9** (2.8 g, 20%). Mp: 160–161 °C. $[\alpha]_D^{20.7} = +79.3$ (*c* 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.03–7.01 (d, *J* = 7.8 Hz, 2H), 6.72–6.70 (d, *J* = 7.8 Hz, 2H), 3.06 (s, 4H), 2.69–2.62 (m, 4H), 2.35–2.33 (m, 2H), 1.77 (s, 6H), 1.38 (s, 6H), 1.29–1.26 (d, *J* = 9.2 Hz, 2H), 0.63 (s, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 165.1, 155.2, 138.3, 132.8, 117.8, 47.5, 46.1, 40.3, 39.4, 36.6, 31.9, 29.0, 26.0, 21.3. IR (KBr): 2973 (CH), 2921 (CH), 1573 (C=C), 1468 (C=C) cm^{-1}. LRMS-EI (*m*/*z*): 386 (M^+, 100), 371 (45), 343 (20). HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{27}H_{34}N_2$, 386.2720; found, 386.2719.

4.4. 2,2′-(2,2′-(Propane-2,2-diyl)bis(6,6-dimethyl-5,6,7,8-tetrahydro-5,7-methanoquinoline-8,2-diyl))bis(propan-2-ol) 10

At first, *n*-BuLi (0.69 mL, 1.1 mmol, 1.6 M in hexane) was added to diisopropylamine (0.16 mL, 1.15 mmol) in THF (5 mL) at ice bath

temperature to generate lithium diispropylamide (LDA). After 30 min of stirring, LDA solution was cooled to −78 °C and then a solution of 2,2-dipyridylpropane **9** (0.39 g, 1.00 mmol) in THF (2 mL) was added to the above solution. Immediate formation of a dark brown solution indicates carbanion formation. This was stirred for 2 h at the same temperature. Then acetone (0.17 mL, 4 mmol) in THF (10 mL) was added dropwise to the above dark brown solution. The resulting solution was left to stir overnight; during this time the temperature of the reaction slowly increased to room temperature. It was then quenched with water and extracted with EtOAc (3 × 30 mL) and the combined EtOAc layer was dried with $MgSO_4$, filtered and concentrated to obtain crude mono-acetone addition product of **9** which was dried under high vacuum and carried on for the next step without purification. The above reaction was once again repeated for mono-acetone addition product to give the desired product **10** (0.18 g, 36%, two steps). The low yield of **10** was noticed when the two reactions above were conducted as a one pot reaction where a second equivalent of LDA was generated separately and added to the mono-acetone addition product of **9** followed by acetone addition. $[\alpha]_D^{20.0} = -1.0$ (*c* 4.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.73 (s, 2H), 7.26–7.14 (d, *J* = 7.8 Hz, 2H), 6.93–6.91 (d, *J* = 7.8 Hz, 2H), 3.07 (s, 2H), 2.64–2.61 (t, *J* = 5.6 Hz, 2H), 2.47–2.43 (m, 2H), 2.23–2.20 (t, *J* = 5.6 Hz, 2H), 1.72 (s, 6H), 1.33 (s, 6H), 1.22–1.18 (m, 8H), 0.82 (s, 6H), 0.60 (s, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 162.9, 157.1, 139.9, 133.9, 117.9, 74.0, 52.5, 46.4, 46.1, 42.4, 42.0, 29.2, 29.0, 27.9, 27.1, 26.2, 21.1. IR (KBr): 3315 (O–H), 2974 (CH), 2941 (CH), 2889 (CH), 1575 (C=C), 1471 (C=C) cm^{-1}.

4.5. 2,2′-(Propane-2,2-diyl)bis(6,6-dimethyl-5,6,7,8-tetrahydro-5,7-methanoquinoline-8,2-diyl)bis(diphenylmethanol) 11

At first, *n*-BuLi (0.69 mL, 1.1 mmol, 1.6 M in hexane) was added to diisopropylamine (0.16 mL, 1.15 mmol) in THF (5 mL) at ice bath temperature to generate lithium diispropylamide (LDA). After 30 min of stirring, LDA solution was cooled to −78 °C and then a solution of 2,2-dipyridylpropane **9** (0.39 g, 1.00 mmol) and TMEDA (150 μL, 1.0 mmol) in THF (2 mL) was added to above solution. Immediate formation of a dark brown solution indicates carbanion formation. This was stirred for 2 h at the same temperature. Then solution of benzophenone (0.186 g, 1.0 mmol) in THF (10 mL) was added and stirred overnight at room temperature. Water was added to quench the reaction, which was extracted with EtOAc (3 × 30 mL) and the combined EtOAc layer was dried ($MgSO_4$) and concentrated to give the crude product of mono-benzophenone addition product which was purified by column chromatography using silica gel (230–400 mesh, 6% EtOAc/hexane) to obtain pure product (0.33 g, 58%). Mp: 140–141 °C. $[\alpha]_D^{22.5} = -221$ (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 10.07 (s, 1H), 7.36–7.33 (m, 4H), 7.29–7.26 (m, 1H), 7.16–7.14 (d, *J* = 7.7 Hz, 1H), 7.08–7.02 (m, 4H), 6.97–6.95 (m, 3H), 6.90–6.88 (d, *J* = 7.6 Hz, 1H), 4.35 (s, 1H), 3.11 (s, 2H), 2.75–2.72 (t, *J* = 5.4 Hz, 1H), 2.68–2.59 (m, 2H), 2.47–2.45 (t, *J* = 5.4 Hz, 1H), 2.37 (m, 2H), 2.04–1.98 (m, 1H), 1.89 (s, 3H), 1.88 (s, 3H), 1.40 (s, 3H), 1.37 (s, 3H), 1.33–1.31 (d, *J* = 9.4 Hz, 1H), 0.86 (s, 3H), 0.65 (s, 3H), −0.23 to −0.25 (d, *J* = 10.0 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 161.9, 156.4, 146.7, 145.8, 141.1, 134.4, 128.3, 128.1, 128.0, 127.0, 126.8, 126.2, 118.6, 81.9, 60.3, 47.7, 46.9, 45.4, 43.0, 41.4, 29.1, 28.0, 26.4, 21.3, 21.0, 14.2. IR (KBr): 3659 (O–H), 3058 (CH), 2974 (CH), 2928 (CH), 1574 (C=C), 1445 (C=C), 756 (CH aromatic) cm^{-1}. LRMS-FAB (*m*/*z*): 569 ([M+H]$^+$, 27), 551 (18), 491 (15). HRMS-FAB: [M]$^+$ calcd for $C_{40}H_{44}N_2O_1$, 568.3454; found, 568.3459.

The above reaction was repeated once again on the mono-benzophenone addition product (0.33 g) to obtain crude **11** which was purified by column chromatography (230–400 mesh, 5% EtOAc/hexane) to give pure ligand **11** (0.255 g, 58%; 34% (over two steps)). Mp: 178–179 °C. $[\alpha]_D^{22.1} = -303.2$ (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 10.05 (s, 2H), 7.38–7.35 (m, 8H), 7.31–7.29 (m, 2H), 7.22–7.20 (d, *J* = 7.8 Hz, 2H), 7.15–7.13 (d, *J* = 7.8 Hz, 2H), 7.00–6.97 (m, 2H), 6.93–6.91 (m, 4H), 6.87–6.83 (m, 4H), 4.41 (s, 2H), 2.63–2.62 (m, 2H), 2.55–2.53 (m, 2H), 2.11–2.06 (m, 2H), 2.01 (s, 6H), 1.40 (s, 6H), 0.88 (s, 6H), −0.12 to −0.14 (d, *J* = 10.0 Hz, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 161.9, 156.4, 146.7, 145.8, 141.1, 134.4, 128.3, 128.1, 128.0, 127.0, 126.8, 126.2, 118.6, 81.9, 47.7, 46.9, 45.4, 43.0, 41.4, 29.1, 28.0, 26.4, 21.3. IR (KBr): 3058 (CH), 2975 (CH), 1575 (C=C), 1444 (C=C), 754 (CH aromatic) cm^{-1}. LRMS-FAB (*m*/*z*): 751 ([M+H]$^+$, 8), 568 (20), 167 (100). HRMS-FAB: [M]$^+$ calcd for $C_{53}H_{54}N_2O_2$, 750.4185; found, 750.4193.

4.6. General procedure for 11 catalyzed diethylzinc addition to aldehydes

Under an argon atmosphere, diethylzinc (0.9 mL, 1.0 mmol, 1.1 M in toluene) was added dropwise into a solution of ligand **11** (37 mg, 0.05 mmol) in toluene (1 mL) at room temperature. After 10 min of stirring, the above solution was cooled to −20 °C and followed by the addition of an aldehyde (0.5 mmol). The resulting reaction mixture was stirred at the same temperature for 57 h then quenched with 1 M HCl and extracted three times with EtOAc. The combined EtOAc layer was dried over $MgSO_4$, filtered, concentrated to give a crude material and was purified by column chromatography (230–400 mesh silica gel) to obtain a pure product. The ee of this product was then checked by HPLC using Chiralcel OD-H/OJ/Chiralpak AD chiral columns. The ee of enantiomeric products that were not separable in the above mentioned chiral columns were checked via an acetate or benzoate derivative. The ee of the product obtained from aliphatic aldehydes were checked by ^{19}F NMR of its (*R*)-(+)-MTPA ester.

4.6.1. (*S*)-1-Phenyl-propan-1-ol 12a[7a–c,h–j,l,n]

Yield: 84%. $[\alpha]_D^{19.9} = -58.8$ (*c* 0.65, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.36–7.32 (m, 4H), 7.30–7.27 (m, 1H), 4.58–4.55 (t, *J* = 8.0 Hz, 1H), 2.24 (br, 1H), 1.85–1.71 (m, 2H), 0.94–0.90 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 144.6, 128.4, 127.5, 126.0, 76.0, 31.9, 10.2. IR (KBr): 3365 (O–H), 3029 (CH), 2964 (CH), 2933 (CH), 1492 (C=C), 700 (CH aromatic) cm^{-1}. Ee: 96% (Chiralcel OD-H, flow rate 0.25 mL/min, 10% IPA/hexane, 254 nm, t_r (*R*) = 23.35 min (2.16%), t_r (*S*) = 25.98 min (97.84%)).

4.6.2. (*S*)-1-*o*-Tolyl-propan-1-ol 13a[2a]

Yield: 82%. $[\alpha]_D^{21.1} = -64.3$ (*c* 1.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.47–7.45 (d, *J* = 8.0 Hz, 1H), 7.26–7.14 (m, 3H), 4.85–4.82 (t, *J* = 4.0 Hz, 1H), 2.35 (s, 3H), 2.18 (br, 1H), 1.78–1.72 (m, 2H), 1.00–0.97 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 142.8, 134.6, 130.3, 127.1, 126.2, 125.3, 71.9, 30.9, 19.1, 10.3. IR (KBr): 3368 (O–H), 3024 (CH), 2933 (CH), 2964 (CH), 2876 (CH), 1487 (C=C), 750 (CH aromatic) cm^{-1}. 1-o-Tolylpropyl acetate **13aa**: General procedure for acetylation: pyridine (2.5 equiv) was added into a solution of **13a** (1 equiv) in DCM at ice bath temperature under an argon atmosphere. To this acetic anhydride (2.2 equiv) was added drop wise and the resulting mixture was stirred at room temperature until TLC showed completion of the reaction. Then evaporation of the volatiles and purification by column chromatography yields **13aa**.[7o] $[\alpha]_D^{20.0} = -75.2$ (*c* 0.95, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.35–7.33 (dd, *J* = 7.3 and 2.1 Hz, 1H), 7.22–7.17 (m, 2H), 7.16–7.13 (m, 1H), 5.92–5.88 (m, 1H), 2.41 (s, 3H), 2.08 (s, 3H), 1.95–1.75 (m, 2H), 0.94–0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 170.5, 155.9, 139.2, 135.2, 130.3, 127.5, 126.1, 125.8, 108.9, 78.0, 74.0, 65.2, 30.6, 29.7, 28.9, 21.3, 19.3, 10.1. IR (KBr): 2923 (CH), 2851 (CH), 1736 (C=O), 1459 (C=C) cm^{-1}. Ee: 96% (Chiralcel OD-H, flow rate 0.25 mL/

min, 10% IPA/hexane, 254 nm, t_r (*R*) = 16.85 min (1.75%), t_r (*S*) = 16.85 min (98.25%)).

4.6.3. (*S*)-1-*m*-Tolyl-propan-1-ol 14a[7m,n]

Yield: 95%. $[\alpha]_D^{20.0} = -47.4$ (*c* 1.64, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.26–7.23 (m, 3H), 7.16–7.09 (m, 3H), 4.54–4.51 (t, *J* = 6.6 Hz, 1H), 2.38 (s, 1H), 2.35 (br, 1H), 1.85–1.72 (m, 2H), 0.94–0.91 (t, *J* = 7.4, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 144.6, 137.9, 128.3, 128.2, 126.7, 123.1, 76.0, 31.8, 21.4, 10.2. IR (KBr): 3370 (O–H), 3026 (CH), 2963 (CH), 2933 (CH), 2875 (CH), 1608 (C=C), 1456 (C=C), 703 (CH aromatic) cm^{-1}. Ee: 93% (Chiralcel OD-H, flow rate 0.25 mL/min, 10% IPA/hexane, 254 nm, t_r (*R*) = 20.84 min (3.36%), t_r (*S*) = 23.34 min (96.63%)).

4.6.4. (*S*)-1-*p*-Tolyl-propan-1-ol 15a[2a,7l,n]

Yield: 63%. $[\alpha]_D^{20.0} = -37.8$ (*c* 1.50, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.24–7.22 (d, *J* = 8.0 Hz, 2H), 7.18–7.16 (d, *J* = 8.1 Hz, 2H), 4.53–4.50 (t, *J* = 6.6 Hz, 1H), 2.51 (br, 1H), 2.38 (s, 1H), 1.85–1.70 (m, 2H), 0.94–0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 141.7, 137.0, 129.0, 126.0, 75.8, 31.8, 21.1, 10.2. IR (KBr): 3367 (O–H), 3020 (CH), 2963 (CH), 2931 (CH), 2875 (CH), 1455 (C=C), 816 (CH aromatic) cm^{-1}. Ee: 90% (Chiralpak AD, flow rate 0.20 mL/min, 10% IPA/hexane, 254 nm, t_r (*R*) = 30.06 min (4.86%), t_r (*S*) = 39.20 min (95.13%)).

4.6.5. (*S*)-1-(3-Methoxyphenyl)propan-1-ol 16a[7i,k]

Yield: 69%. $[\alpha]_D^{20.0} = -48$ (*c* 2.35, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.26–7.22 (t, *J* = 8.0 Hz, 1H), 6.89–6.88 (m, 3H), 6.81–6.78 (m, 1H), 4.54–4.51 (t, *J* = 6.6 Hz, 1H), 3.78 (s, 1H), 2.32 (br, 1H), 1.82–1.68 (m, 2H), 0.92–0.88 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 159.6, 146.4, 129.3, 118.3, 112.8, 111.4, 75.8, 55.1, 31.8, 10.1. IR (KBr): 3330 (O–H), 2963 (CH), 2935 (CH), 1586 (C=C), 1458 (C=C), 1262 (C–O), 783 (CH aromatic) cm^{-1}.

1-(3-Methoxyphenyl)propyl acetate ***16aa***:[7o] The **13aa** synthetic procedure was followed. $[\alpha]_D^{20.0} = -75.3$ (*c* 1.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.27–7.23 (d, *J* = 7.9 Hz, 1H), 6.92–6.90 (d, *J* = 7.8 Hz, 1H), 6.88–6.87 (t, *J* = 2.3 Hz, 1H), 6.83–6.80 (m, 1H), 5.66–5.63 (t, *J* = 6.8 Hz, 1H), 3.79 (s, 3H), 2.07 (s, 3H), 1.93–1.79 (m, 2H), 0.90–0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 170.3, 159.6, 142.2, 129.4, 118.8, 113.0, 112.3, 77.2, 55.1, 29.3, 21.2, 9.9. IR (KBr): 2969 (CH), 2879 (CH), 2837 (CH), 1733 (C=O), 1587 (C=C), 1239 (C–O), 782 (CH aromatic) cm^{-1}. Ee: 93% (Chiralcel OD-H, flow rate 0.25 mL/min, 10% IPA/hexane, 254 nm, t_r (*R*) = 18.86 min (3.30%), t_r (*S*) = 20.16 min (96.67%)).

4.6.6. (*S*)-1-(3-Chlorophenyl)propan-1-ol 17a[2a,7k,l]

Yield: 99%. $[\alpha]_D^{20.0} = -30.5$ (*c* 3.50, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.31–7.30 (m, 1H), 7.24–7.20 (m, 2H), 7.16–7.14 (m, 1H), 4.51–4.48 (t, *J* = 6.5 Hz, 1H), 2.67 (br, 1H), 1.76–1.66 (m, 2H), 0.89–0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 146.7, 134.2, 129.6, 127.5, 126.1, 124.1, 75.2, 31.8, 9.9. IR (KBr): 3365 (O–H), 3065 (CH), 2960 (CH), 2934 (CH), 2877 (CH), 1598 (C=C), 1575 (C=C), 783 (CH aromatic) cm^{-1}. Ee: 96% (Chiralpak AD, flow rate 0.50 mL/min, 10% IPA/hexane, 254 nm, t_r (*R*) = 21.90 min (1.82%), t_r (*S*) = 22.68 min (98.17%)).

4.6.7. (*S*)-1-(4-Chlorophenyl)propan-1-ol 18a[7a,b,i,l]

Yield: 79%. $[\alpha]_D^{20.0} = -34.8$ (*c* 3.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.31–7.28 (dd, J_1 = 6.5 Hz, J_2 = 2.0 Hz, 2H), 7.25–7.23 (dd, *J* = 6.5 and 1.7 Hz, 2H), 4.56–4.53 (t, *J* = 6.5 Hz, 1H), 2.13 (br, 1H), 1.80–1.66 (m, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 143.0, 133.0, 128.5, 127.3, 75.2, 31.9, 9.9. IR (KBr): 3360 (O–H), 2965 (CH), 2934 (CH), 2877 (CH), 1489 (C=C), 1092 (C–O), 824 (CH aromatic) cm^{-1}. Ee: 96% (Chiralpak AD, flow rate 0.50 mL/min, 10% IPA/hexane, 254 nm, t_r (*R*) = 25.62 min (1.84%), t_r (*S*) = 26.22 min (98.15%)).

4.6.8. (*S*)-4-(1-Hydroxypropyl)benzonitrile 19a[7e,g,j]

Yield: 92%. $[\alpha]_D^{20.0} = -39.9$ (*c* 3.40, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.54–7.52 (d, *J* = 6.7 Hz, 2H), 7.40–7.38 (d, *J* = 8.2 Hz, 2H), 4.61–4.58 (t, *J* = 6.3 Hz, 1H), 3.06 (br, 1H), 1.73–1.65 (m, 2H), 0.87–0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 150.3, 132.1, 126.6, 118.9, 110.6, 74.8, 31.9, 9.7. IR (KBr): 3435 (O–H), 2967 (CH), 2934 (CH), 2877 (CH), 2227 (CN), 1608 (C=C), 847 (CH aromatic) cm^{-1}. *1-(4-Cyanophenyl)propyl benzoate* ***19aa***: Pyridine (2.5 equiv) was added to a solution of **19a** (1 equiv) in DCM at ice bath temperature under an argon atmosphere. To this benzoyl chloride (2.2 equiv) was added dropwise and the resulting mixture was stirred at room temperature until TLC showed completion of the reaction. Then evaporation of the volatiles and purification by column chromatography yields **19aa**. $[\alpha]_D^{20.0} = +54.7$ (*c* 3.95, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 8.09–8.07 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.66–7.64 (d, *J* = 8.4 Hz, 2H), 7.61–7.57 (t, *J* = 7.5 Hz, 1H), 7.52–7.45 (m, 4H), 5.93–5.90 (t, *J* = 7.0 Hz, 1H), 2.10–1.92 (m, 2H), 1.00–0.97 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 165.7, 146.1, 133.3, 132.4, 129.9, 129.7, 128.5, 128.3, 127.0, 118.7, 111.7, 29.5, 9.8. IR (KBr): 3063 (CH), 2972 (CH), 2937 (CH), 2879 (CH), 2229 (CN), 1451 (C=C), 842 (CH aromatic) cm^{-1}. Ee: 93% (Chiralcel OJ, flow rate 0.50 mL/min, 10% IPA/hexane, 254 nm, t_r (*R*) = 33.01 min (3.67%), t_r (*S*) = 37.77 min (96.33%)).

4.6.9. (*S*)-1-(Naphthalen-1-yl)propan-1-ol 20a[7f,i,k–m]

Yield: 86%. $[\alpha]_D^{20.0} = -51.2$ (*c* 1.64, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 8.13–8.10 (t, *J* = 1.9 Hz, 1H), 7.90–7.87 (m, 1H), 7.80–7.78 (d, *J* = 8.1 Hz, 1H), 7.63–7.62 (d, *J* = 7.0 Hz, 1H), 7.54–7.46 (m, 3H), 5.39–5.36 (m, 1H), 2.20 (br, 1H), 2.06–1.89 (m, 2H), 1.05–1.01 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 140.2, 133.8, 130.5, 128.9, 127.9, 125.9, 125.5, 125.4, 123.3, 122.9, 72.5, 31.1, 10.5. IR (KBr): 3372 (O–H), 3059 (CH), 2931 (CH), 2964 (CH), 2932 (CH), 1510 (C=C), 1455 (C=C), 777 (CH aromatic) cm^{-1}. Ee: 97% (Chiralcel OD-H, flow rate 0.50 mL/min, 10% IPA/hexane, 210 nm, t_r (*S*) = 20.65 min (98.55%), t_r (*R*) = 34.02 min (1.44%)).

4.6.10. (*S*)-1-(Naphthalen-2-yl)propan-1-ol 21a[7b,h,j,k,n]

Yield: 90%. $[\alpha]_D^{20.0} = -37.3$ (*c* 3.65, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.86–7.82 (m, 3H), 7.76 (s, 1H), 7.52–7.46 (m, 3H), 4.75–4.72 (t, *J* = 6.5 Hz, 1H), 2.29 (br, 1H), 1.95–1.81 (m, 2H), 0.97–0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 142.0, 133.3, 133.0, 128.2, 127.9, 127.7, 126.1, 125.7, 124.7, 124.2, 76.1, 31.7, 10.1. IR (KBr): 3365 (O–H), 3305 (CH), 2964 (CH), 2932 (CH), 1601 (C=C), 1507 (C=C), 819 (CH aromatic) cm^{-1}. Ee: 97% (Chiralcel OD-H, flow rate 0.50 mL/min, 10% IPA/hexane, 210 nm, t_r (*S*) = 22.65 min (98.45%), t_r (*R*) = 25.56 min (1.54%)).

4.6.11. (*S*)-(*E*)-1-Phenylpent-1-en-3-ol 22a[7a,b,f,h–k,n]

Yield: 63%. $[\alpha]_D^{20.0} = -9.6$ (*c* 1.64, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.40–7.38 (d, *J* = 8.4 Hz, 2H), 7.34–7.30 (t, *J* = 7.2 Hz, 2H), 7.27–7.23 (m, 1H), 6.60–6.56 (d, *J* = 15.8 Hz, 1H), 6.25–6.19 (dd, *J* = 15.9, 6.7 Hz, 1H), 4.23–4.18 (m, 1H), 1.93 (br, 1H), 1.72–1.63 (m, 2H), 1.00–0.96 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 136.8, 132.3, 130.4, 128.6, 127.6, 126.4, 74.4, 30.2, 9.8. IR (KBr): 3365 (O–H), 3059 (CH), 2931 (CH), 2964 (CH), 1493 (C=C), 1450 (C=C), 747 (CH aromatic) cm^{-1}. Ee: 85% (Chiralcel OD-H, flow rate 0.50 mL/min, 10% IPA/hexane, 254 nm, t_r (*R*) = 23.09 min (7.61%), t_r (*S*) = 23.09 min (92.38%)).

4.6.12. (*S*)-(*E*)-2-Methyl-1-phenylpent-1-en-3-ol 23a[7k,n]

Yield: 52%. $[\alpha]_D^{20.0} = +30.5$ (*c* 1.65, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 7.37–7.29 (m, 4H), 7.24–7.22 (t, *J* = 5.8 Hz, 1H), 6.51 (s, 1H), 4.13–4.09 (t, *J* = 6.6 Hz, 1H), 2.16 (br, 1H), 1.88 (s, 3H), 1.73–1.66 (m, 2H), 0.99–0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 140.1, 137.7, 129.0, 128.1, 126.4, 125.9, 79.5, 27.9, 13.1, 10.1. IR (KBr): 3364 (O–H), 3081 (CH), 3024 (CH), 2962 (CH), 2875 (CH), 1600 (C=C), 1492 (C=C), 746 (CH aromatic) cm^{-1}. Ee: 90% (Chiralcel OD-H, flow rate 0.50 mL/min, 3% IPA/hexane, 254 nm, t_r (*R*) = 33.18 min (5.04%), t_r (*S*) = 36.22 min (94.95%)).

4.6.13. (*S*)-1-Cyclohexylpropan-1-ol 24a[7a,b,i,g]

Yield: 15%. $[\alpha]_D^{20.0} = -4.2$ (*c* 0.45, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 3.30–3.25 (m, 1H), 1.80–1.65 (m, 5H), 1.55–0.98 (m, 9H), 0.97–0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 77.5, 43.2, 29.3, 27.8, 26.8, 26.6, 26.4, 26.2, 10.2. IR (KBr): 3371 (O–H), 2925 (CH), 2852 (CH), 1449 (CH bend) cm^{-1}.

(2S)-1-Cyclohexylpropyl-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate ***24aa***:[7o] The enantiomeric excess of **24a** was determined by NMR for its (*R*)-(+)-MTPA ester (Mosher's ester). *General procedure for MTPA ester preparation:* A solution of **24a** (1 equiv), (*R*)-(+)-MTPA ((*R*)-2-methoxy-3,3,3-trifluoro-2-phenylpropanoic acid) (2 equiv), and DMPA (catalytic) in DCM was cooled with an ice bath. To this solution was added DCC (4 equiv) and stirred until TLC showed completion of reaction. Then this was diluted with hexane, filtered, concentrated, and purified by column chromatography (230–400 mesh silica gel, 50% EtOAc/hexane) to obtain **24aa**. ^1H NMR (400 MHz, $CDCl_3$, δ): 7.58–7.57 (m, 2H), 7.41–7.38 (m, 4H), 4.91–4.89 (m, 1H), 3.58–3.56 (m, 3H), 1.76–1.58 (m, 8H), 1.23–1.00 (m, 7H), 0.93–0.89 (t, *J* = 7.4 Hz, 2H), 0.81–0.78 (t, *J* = 7.4 Hz, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 129.4, 128.2, 127.4, 82.6, 55.7, 55.4, 40.2, 34.9, 28.6, 27.5, 26.3, 26.1, 26.0, 25.5, 24.7, 23.5, 9.8. IR (KBr): 3031 (CH), 3065 (CH), 2932 (CH), 2855 (CH), 1748 (C=O), 1256 (C–O), 716 (CH aromatic) cm^{-1}. Ee: 86% (ee was determined by ^{19}F NMR (376.49 MHz, $CDCl_3$, δ): −71.16 (*R*), −71.20 (*S*); integration ratio of *R*:*S* = 1.00:13.37).

4.6.14. (*S*)-Nonan-3-ol 25a[7a,b,d,i]

Yield: 15%. $[\alpha]_D^{20.0} = +3.5$ (*c* 0.55, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, δ): 3.52–3.47 (m, 1H), 1.51–1.27 (m, 13H), 0.93–0.89 (t, *J* = 7.4 Hz, 3H), 0.87–0.84 (m, 4H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 73.26, 36.9, 31.8, 30.1, 29.4, 25.6, 22.6, 14.0, 9.8. IR (KBr): 3348 (O–H), 2958 (CH), 2930 (CH), 2872 (CH), 1464 (C–O) cm^{-1}.

(2S)-Nonan-3-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate ***25aa***:[7d,o] The MTPA ester was made by following the same procedure as for **24aa**. ^1H NMR (400 MHz, $CDCl_3$, δ): 7.57–7.55 (m, 2H), 7.41–7.39 (m, 4H), 5.06–5.03 (m, 1H), 3.58–3.56 (m, 3H), 1.70–1.56 (m, 4H), 1.28–1.20 (m, 8H), 0.95–0.82 (m, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$, δ): 166.4, 132.6, 129.5, 128.3, 127.4, 78.8, 55.4, 33.0, 31.6, 29.0, 26.7, 24.8, 22.5, 14.0, 9.6. IR (KBr): 3065 (CH), 2932 (CH), 2857 (CH), 1744 (C=O), 1452 (C=C), 716 (CH aromatic) cm^{-1}. Ee: 83% (ee was determined by ^{19}F NMR (376.49 MHz, $CDCl_3$, δ): −71.27 (*R*), −71.35 (*S*); integration ratio of *R*:*S* = 1.00:11.05).

Acknowledgements

The authors thank Mr. Ping-Kuei Liao, at National Dong Hwa University, for his help in obtaining X-ray data, and the financial support from the National Science Council of the Republic of China (NSC 100-2113-M-259-006-MY3).

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