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Asymmetric 1,4-addition of diethylzinc to α,β-unsaturated enones catalyzed by chiral imino-thiophosphoramide ligands and copper(I)

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Abstract—In the presence of a catalytic amount of chiral imino-thiophosphoramide ligand **L7** (6 mol%) and Cu(I) salt (3 mol%), the asymmetric addition of diethylzinc to α,β-unsaturated carbonyl compounds could be achieved in good yields with moderate ees (up to 75% ee) at −20 °C in toluene. A novel chiral imino-thiophosphoramide ligand system for this asymmetric 1,4-addition reaction has been explored.

1. Introduction

The 1,4-conjugate addition of various organometallic reagents to α,β-unsaturated carbonyl compounds is an important process for C–C bond formation in organic synthesis.[1] Many chiral auxiliaries and stoichiometric reagents have been described recently, which promote enantioselective addition.[2] A prominent position in this rapidly expanding field is occupied by the copper catalyzed and chiral-ligand-accelerated 1,4-addition of organozinc reagents originally introduced and rendered practical by Alexakis, Feringa and Pfaltz.[3] In particular, chiral phosphoramidites,[4a–c] phosphites,[4d–i] phosphines,[4j] aminophosphanes,[4k–m] sulfonamides[4n,o] and peptide-based phosphines[4p] were used as ligands in the addition to cyclic enones with very good enantioselectivities. However, all-encompassing chiral ligands effective in the asymmetric conjugate addition of dialkylzincs to all of the five-, six- and seven-membered cyclic enones and acyclic enones has been less successful.[5,6] The development of new chiral ligands plays a pivotal role for overcoming this substrate limitation in asymmetric carbon–carbon bond forming reactions. Recently, we were interested in the synthesis of a novel type of air- and moisture-stable chiral thiophosphoramide ligands based on a series of chiral binaphthalenediamine (BINAM), (1*R*,2*R*)-(−)-1,2-cyclohexanediamine or (1*R*,2*R*)-(+)-1,2-diphenylethane-1,2-diamime[7,8] and the applications of these novel chiral ligands in asymmetric catalysis.[9]

Herein, we report the results of our novel chiral imino-thiophosphoramide ligands and one imino-selenophosphoramide ligand derived from (1*R*,2*R*)-(−)-1,2-cyclohexanediamine on the catalytic enantioselective 1,4-conjugate addition of diethylzinc to α,β-unsaturated enones. The method described here allows efficient, catalytic and moderately enantioselective functionalization of six and seven-membered cyclic enones. In addition, the chiral ligands can be easily recovered and reused in the same enantioselective addition without loss of efficiency and enantioselectivity, although this type of imino-thiophosphoramide ligands is not effective in the enantioselective addition of diethylzinc to five-membered cyclic enone and acyclic enones.

2. Results and discussion

The chiral imino-thiophosphoramide ligands **L1**–**L13** are readily synthesized from the reaction of (1*R*,2*R*)-(−)-1-*N*-diphenylthiophosphorylcyclohexane-1,2-diamine **1**[9] with arylaldehydes. In Scheme 1, we elucidated the reaction procedures for the preparation of chiral ligands **L1**–**L13**. In general, they can be synthesized by the reaction of **1** with various arylaldehydes in ethanol either at room temperature or under reflux (for sterically bulky arylaldehydes) for 4–5 h in moderate yields (Scheme 1). The novel chiral imino-selenophosphoramide ligand **L14** was synthesized in the similar way

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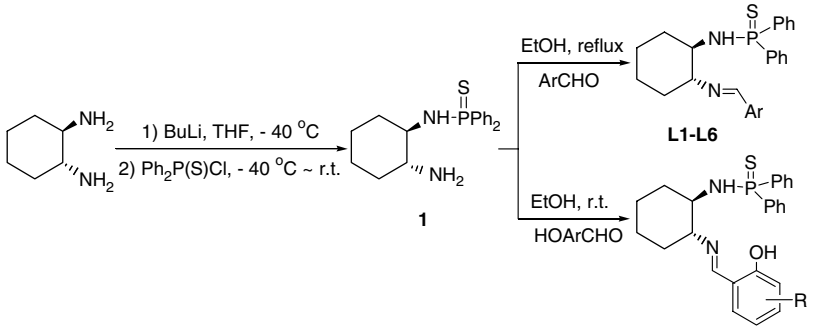
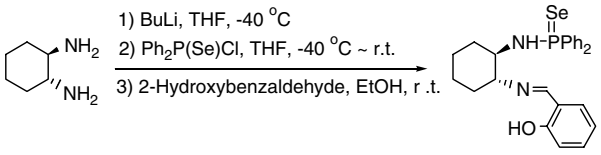


L1: Ar= C_6H_5 (62%)
L2: Ar= 2,3-$Cl_2C_6H_3$ (60%)
L3: Ar= 2,6-$Cl_2C_6H_3$ (60%)
L4: Ar= 2-Furyl (66%)
L5: Ar= 1-Naphthyl (55%)
L6: Ar= 2-Pyridyl (58%)

L7: Ar= 2-OHC_6H_4 (75%)
L8: Ar= 5-^{t}Bu-2-OHC_6H_3 (62%)
L9: Ar= 3,5-$^t Bu_2$-2-OHC_6H_2 (51%)
L10: Ar= 3,5-Cl_2-2-OHC_6H_2 (80%)
L11: Ar= 5-Br-2-OHC_6H_3 (54%)
L12: Ar= 2-OH-1-naphthyl (57%)
L13: Ar= 6-Me-2-OH-1-naphthyl (52%)

Scheme 1.

(Scheme 2). These chiral ligands **L1**–**L14** are air- and moisture-stable under ambient atmosphere (Schemes 1 and 2).



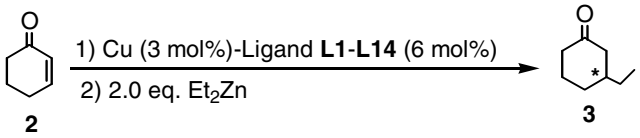
L14 (58%)

Scheme 2.

Using 2-cyclohexene-1-one **2** as the substrate and diethylzinc as the Michael addition reagent, we examined the 1,4-addition reaction in the presence of novel imino-thiophosphoramide ligands **L1**–**L3** and **L7**–**L10** with various copper salts in various solvents at different temperatures to develop the optimal reaction conditions. The results are summarized in Table 1 (entries 1–16). As can be seen from Table 1, **L2** and **L7** are the best chiral ligands for this enantioselective 1,4-addition reaction to give the product **3** with 62% ee in 97% yield and 65% ee in 95% yield in toluene at 20 °C for 2 h with the (*S*)-configuration, respectively (Table 1, entries 2 and 4). Chiral ligands **L1** and **L8** gave the addition product **3** in moderate ee as well (Table 1, entries 1 and 5). On the other hand, chiral ligands **L3**, **L9** and **L10** having dichloro- or di(*tert*-butyl) groups on the benzene ring of the arylaldehydes gave the 1,4-addition product **3** in 0 ~ lower ee (7–14% ee) with the (*S*)-configuration under the same conditions (Table 1, entries 3, 6 and 7). These results suggest that the substituents of aryl group in imino-thiophosphoramide ligands play an important role in chiral induction for asymmetric 1,4-addition reaction. Using **L7** as a ligand at 0 °C, a similar ee (64% ee) of **3** was achieved after 3 h in toluene (Table 1, entry 8). At lower temperature, **L7** is still active for this reaction. It was found that at −20 °C, the enantioselectivity of this reaction was increased to 75% ee for 6 h and at −40 °C, the enantioselectivity was slightly decreased to 72% ee for 10 h in toluene, respectively (Table 1, entries 8–10). The best reaction temperature for this reaction is −20 °C. The copper(I) salts such as $Cu(CH_3CN)_4ClO_4$ or $Cu(CH_3CN)_4BF_4$ showed higher catalytic activity and chiral induction ability than $CuOTf \cdot 1/2C_6H_6$ or $Cu(OTf)_2$ salt under the same conditions (Table 1, entries 11–13). The solvent effects have been also examined using **L7** as a chiral ligand at −20 °C under otherwise similar conditions. Toluene is the solvent of choice for this asymmetric addition reaction (Table 1, entries 14–16). Under the optimized reaction conditions, we next examined the remaining chiral ligands **L4**–**6** and **L11**–**14** in this reaction. The results are also summarized in Table 1 (Table 1, entries 17–23). We found that using **L11**–**L13** as the ligands in this reaction, the addition product **3** can be obtained in high yields in moderate ee (44% ee–65% ee), while, poor enantioselectivities were achieved in the presence of ligands **L5** and **L6** (Table 1, entries 17–22). The imino-selenophosphoramide ligand **L14**, which is very similar to ligand **L7** structurally, gave the addition product in 97% yield with 62% ee (Table 1, entry 23). The best reaction conditions are to carry out this reaction in toluene at −20 °C using $Cu(CH_3CN)_4ClO_4$ (3 mol %) as the catalyst precursor and **L7** (6 mol %) as the chiral ligand. This asymmetric addition reaction can be completed within 6 h under this reaction conditions. Moreover, this chiral ligand is quite stable and can be recovered in 96% yield after usual workup. The recovered ligand **L7** can be reused in this reaction without loss of catalytic ability or enantioselectivity (Table 1, entry 24).

Under the optimized reaction conditions, the 1,4-additions of diethylzinc to 2-cyclopentene-1-one and 2-cycloheptene-1-one have been also examined. It was found that for 2-cyclopentene-1-one, the corresponding 1,4-addition product **4** was obtained in moderate yield with 17% ee in the presence of ligand **L7** and with 22% ee in the presence of ligand **L12** and for 2-cycloheptene-1-

Table 1. The enantioselective 1,4-addition reaction of 2-cyclohexene-1-one with $ZnEt_2$ catalyzed by copper salt and chiral ligand



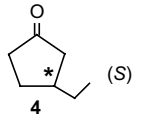
Entry	Copper salt	Ligand	Solv.	Temp. (°C)	Time (h)	Yield[a] (%)	Ee[b] (%)	Config.[c]
1	$Cu(MeCN)_4ClO_4$	**L1**	PhMe	20	2	97	55	*S*
2	$Cu(MeCN)_4ClO_4$	**L2**	PhMe	20	2	97	62	*S*
3	$Cu(MeCN)_4ClO_4$	**L3**	PhMe	20	2	97	0	—
4	$Cu(MeCN)_4ClO_4$	**L7**	PhMe	20	2	95	65	*S*
5	$Cu(MeCN)_4ClO_4$	**L8**	PhMe	20	2	92	46	*S*
6	$Cu(MeCN)_4ClO_4$	**L9**	PhMe	20	2	92	7	*S*
7	$Cu(MeCN)_4ClO_4$	**L10**	PhMe	20	2	90	14	*S*
8	$Cu(MeCN)_4ClO_4$	**L7**	PhMe	0	3	95	64	*S*
9	$Cu(MeCN)_4ClO_4$	**L7**	PhMe	−20	6	97	75	*S*
10	$Cu(MeCN)_4ClO_4$	**L7**	PhMe	−40	10	95	72	*S*
11	$CuOTf\cdot 1/2C_6H_6$	**L7**	PhMe	−20	6	95	68	*S*
12	$Cu(OTf)_2$	**L7**	PhMe	−20	6	95	69	*S*
13	$Cu(MeCN)_4BF_4$	**L7**	PhMe	−20	6	94	74	*S*
14	$Cu(MeCN)_4ClO_4$	**L7**	Et_2O	−20	6	92	71	*S*
15	$Cu(MeCN)_4ClO_4$	**L7**	THF	−20	6	95	8	*S*
16	$Cu(MeCN)_4ClO_4$	**L7**	CH_2CI_2	−20	6	95	70	*S*
17	$Cu(MeCN)_4ClO_4$	**L4**	PhMe	−20	6	92	64	*S*
18	$Cu(MeCN)_4ClO_4$	**L5**	PhMe	−20	6	94	7	*R*
19	$Cu(MeCN)_4ClO_4$	**L6**	PhMe	−20	6	95	20	*S*
20	$Cu(MeCN)_4ClO_4$	**L11**	PhMe	−20	6	97	62	*S*
21	$Cu(MeCN)_4ClO_4$	**L12**	PhMe	−20	6	98	57	*S*
22	$Cu(MeCN)_4ClO_4$	**L13**	PhMe	−20	6	95	44	*S*
23	$Cu(MeCN)_4ClO_4$	**L14**	PhMe	−20	6	97	62	*S*
24[d]	$Cu(MeCN)_4ClO_4$	**L7**	PhMe	−20	6	94	72	*S*

[a] Isolated yield.
[b] Determined by chiral GLC.
[c] Determined by the sign of the specific rotation.
[d] Recovered **L7** was used as a ligand in reaction.

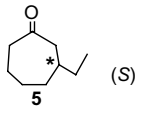
one, the corresponding 1,4-addition product **5** was obtained in high yield with moderate ee (52% ee) within 6 h, respectively (Scheme 3).

This catalytic enantioselective 1,4-addition reaction system has also been applied to acyclic enones, such as chalcone **6**. It was found that the reaction was complete within 24 h at room temperature in 97% yield with 8% ee in the presence of ligand **L1** and in moderate yield with 2% ee in the presence of ligands **L7** and **L12** (Scheme 4).

Although the real active species is not yet fully understood in this catalytic addition reaction, we believe that this series of imino-thiophosphoroamide ligands **L1**–**L13** and imino-selenophosphoramide ligand **L14** are bidentate ligands in this catalytic asymmetric reaction.[10]

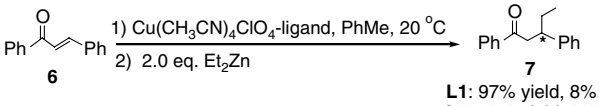


L7: -20 °C, 60%, 17% ee, 6 h.
L12: -20 °C, 71%, 22% ee, 6 h.



L7: -20 °C, 96%, 52% ee, 6 h.

Scheme 3.



L1: 97% yield, 8% ee.
L7: 70% yield, 2% ee.
L12: 50% yield, 2% ee.

Scheme 4.

This is because it is well known that the sulfur atom can strongly coordinate to the late transition metals[11] and the Cu(I) atom has a greater affinity for soft ligands (olefins, sulfur, phosphorus and selenium).[12] In addition, a nitrogen atom can coordinate to various transition metals such as Cu(I) and hydroxyl group in **L7** is also a precoordinative atom in this catalytic system. In order to verify this speculation, we attempted to get evidence from ^{31}P NMR and ^{13}C NMR spectroscopic measurements of **L7** in the absence or presence of Cu(I) salt. We found that the signal in the ^{31}P NMR spectrum was shifted upfield from +58.26 to +57.98 ppm along with the alteration of the peak shape after adding an equal molar amount of $Cu(CH_3CN)_4ClO_4$ into **L7** solution (Figs. 1 and 2). This result suggests that the sulfur atom on phosphorus may indeed coordinate to Cu(I). Moreover, the ^{13}C NMR spectrum gives us more detailed

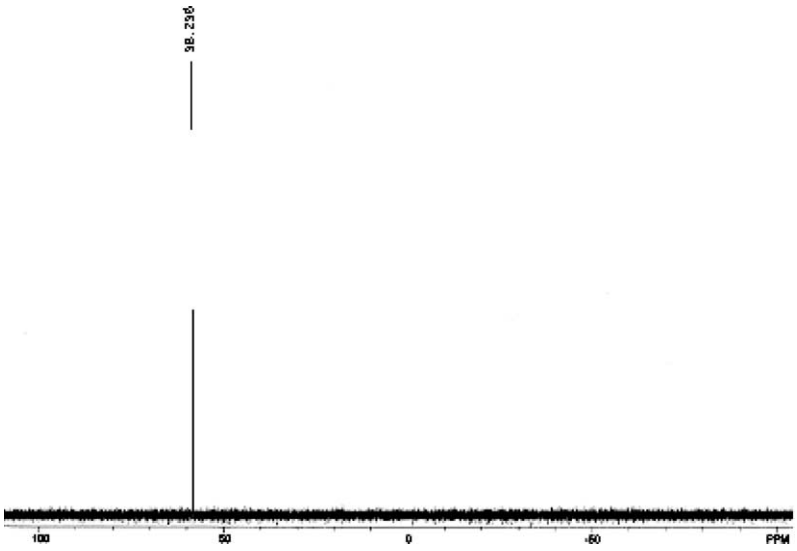


Figure 1. The ^{31}P NMR spectrum of ligand **L7**.

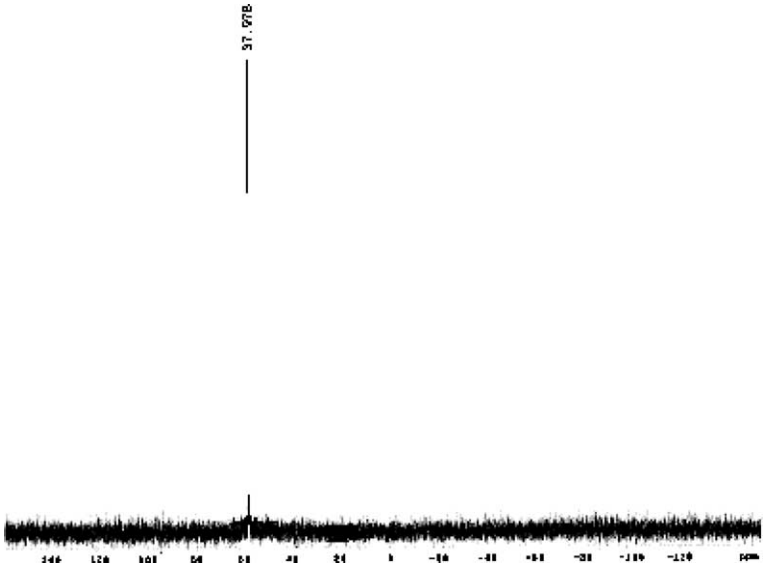


Figure 2. The ^{31}P NMR of spectrum ligand **L7** with $Cu(CH_3CN)_4ClO_4$.

information on the coordination of nitrogen atom. It was found that the signal the carbon atom (imino carbon) connected with the nitrogen atom in **L7** has a significant downfield shift from +164.57 to +196.64 ppm, while the aromatic carbon atom connected to hydroxy group showed a small downfield shift, from +161.07 to +161.58 ppm after adding the copper(I) into **L7** solution (Figs. 3 and 4). These observations indicate that the nitrogen atom in imino group may indeed coordinate to copper(I), but the hydroxyl group is not involved in the coordination to Cu(I) salt. Overall, we can conclude that our novel chiral imino-thiophosphoroamide ligand system might be an *S*,*N*-bidentate ligand system for copper(I) centre.

Since the phosphorus signal of **L7** showed only a small shift after addition of $Cu(CH_3CN)_4ClO_4$, this is not strong evidence to prove that the sulfur atom indeed coordinates to copper(I). In order to elucidate further that the heteroatom on phosphorus is crucial for this catalytic asymmetric reaction, the corresponding axially chiral phosphoramide ligand **L15** was prepared by similar procedures (Scheme 5). In addition, it was found that no enantioselectivity could be realized by this ligand under the same conditions (75% yield, 0% ee) (Scheme 6). This result may indicate that the S atom in ligand **L7** potentially coordinates to Cu(I).

3. Conclusion

We disclosed an efficient catalytic system for the enantioselective 1,4-conjugate addition of diethylzinc to α,β-unsaturated enones catalyzed by Cu(I) and novel chiral imino-thiophosphoroamide or imino-selenophosphoramide ligands, which are easily available, quite stable,

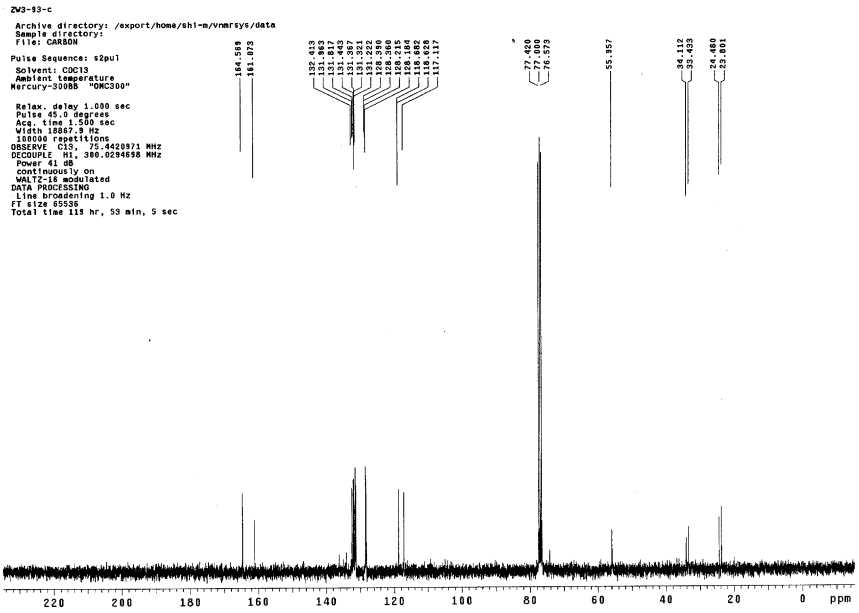


Figure 3. The ^{13}C NMR spectrum of ligand **L7**.

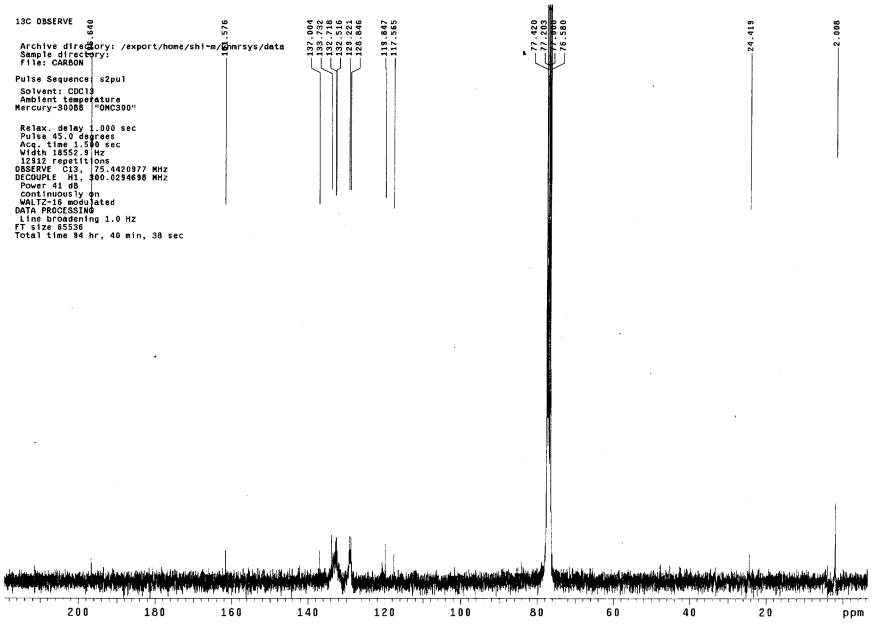
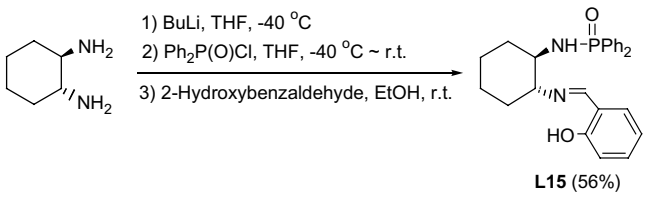
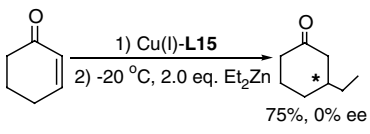


Figure 4. The ^{13}C NMR spectrum of ligand **L7** with $Cu(CH_3CN)_4ClO_4$.



Scheme 5.



Scheme 6.

recoverable and reusable in asymmetric catalysis. The catalytic system allows efficient, catalytic and moderately enantioselective functionalization of six- and seven-membered cyclic enones, although it is not effective for five-membered cyclic enone and acylic enones. We confirmed that this series of chiral imino-phosphoramide ligands are novel type of *S*,*N*-bidentate ligands

through ^{31}P NMR, ^{13}C NMR spectroscopic experiments and the comparative experiment using phosphoramide ligand **L15**. Efforts are underway to elucidate the mechanistic details of this catalytic system and to extend the scope of these novel chiral ligands in other asymmetric C–C bond forming transformations.

4. Experimental section

4.1. General remarks

All reactions were conducted in oven (135 °C) and flame-dried glassware under an inert atmosphere of dry argon or nitrogen. Toluene was distilled from sodium metal; dichloromethane was distilled from calcium hydride; diethyl ether, tetrahydrofuran and benzene were distilled from sodium metal/benzophenone ketyl. ^1H NMR, ^{13}C NMR and ^{31}P NMR spectra were recorded at 300, 75 and 121 MHz, respectively. Mass spectra were recorded by the EI method. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with silica gel coated plates. P-Arus reagent [prepared by dissolving *p*-anisaldehyde (10 mL), acetic acid (7.5 mL) and concentrated H_2SO_4 (25 mL) in 95% ethanol (500 mL)] was used for those substrates that do not have absorption in UV region. Flash column chromatography was carried out using 200–300 mesh silica gel at increased pressure. Enantiomeric ratios were determined by chiral GLC or HPLC analysis. The absolute configuration was assigned by comparison the optical rotation with those reported date.[13] Racemic products were synthesized according to the literatures.[14,15] Melting points are uncorrected.

4.2. Representative experimental procedure for the synthesis of chiral ligands L1–L6

A solution of (1*R*,2*R*)-(−)-*N*-diphenylthiophosphoryl-cyclohexane-1,2-diamine **1** (66 mg, 0.2 mmol) and benzaldehyde (51 μL, 0.2 mmol) in ethanol (5 mL) was refluxed for 4 h. After the reaction solution was cooled to room temperature, the solvent was removed under reduced pressure. The residue was recrystallized from dichloromethane and petroleum ether solution to give the product **L1** as a pale solid.

4.2.1. Ligand 1 (L1). A pale solid, yield 62%. Mp: 126–128 °C; $[\alpha]_D^{20} = -78.6$ (*c* 0.245, $CHCl_3$); IR (CH_2Cl_2) υ 2929, 1642, 1437, 1104, 638 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.13–1.35 (m, 3H, CH_2 and CH), 1.57–1.76 (m, 4H, $2CH_2$), 2.27–2.31 (m, 1H, NH), 2.44–2.49 (m, 1H, CH), 3.08–3.16 (m, 1H, CH), 3.38–3.47 (m, 1H, CH), 7.25–7.48 (m, 9H, Ar), 7.78–7.95 (m, 6H, Ar), 8.35 (s, 1H, CH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 57.77; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.23, 24.82, 33.50, 34.32, 56.53 (d, $J_{C-P} = 2.3$ Hz), 75.50 (d, $J_{C-P} = 9.5$ Hz), 128.17 (d, $J_{C-P} = 13.7$ Hz), 128.45 (d, $J_{C-P} = 22.8$ Hz), 128.98, 129.72, 130.76, 131.26 (d, $J_{C-P} = 2.5$ Hz), 131.30 (d, $J_{C-P} = 3.1$ Hz), 131.40 (d, $J_{C-P} = 11.2$ Hz), 131.99 (d, $J_{C-P} = 11.9$ Hz), 134.20 (d, $J_{C-P} = 101.9$ Hz), 135.83 (d, $J_{C-P} = 102.4$ Hz), 136.16, 160.55; EI (MS) *m*/*e* 418 (M^+, 12.12), 217 (41.27), 201 (100), 185 (57.22), 139 (32.71); Anal. Calcd for $C_{25}H_{27}N_2PS \cdot 1/2C_2H_5OH$: C, 70.72; H, 6.85; N, 6.34; found: C, 70.63; H, 6.64; N, 6.36%.

4.2.2. Ligand 2 (L2). A yellow solid, yield 60%. Mp: 172–173 °C; $[\alpha]_D^{20} = -25.4$ (*c* 1.225, $CHCl_3$); IR (CH_2Cl_2) υ 2929, 1437, 1104, 638 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.20–1.39 (m, 3H, CH_2 and CH), 1.64–1.77 (m, 4H, $2CH_2$), 2.24–2.28 (m, 1H, NH), 2.45–2.51 (m, 1H, CH), 3.14–3.22 (m, 1H, CH), 3.47–3.55 (m, 1H, CH), 7.18–7.56 (m, 8H, Ar), 7.79–7.98 (m, 5H, Ar), 8.73 (s, 1H, CH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 57.94; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.04, 24.82, 33.43, 34.40, 55.99 (d, $J_{C-P} = 1.4$ Hz), 75.83 (d, $J_{C-P} = 8.6$ Hz), 126.92, 127.30, 128.00 (d, $J_{C-P} = 13.2$ Hz), 128.24 (d, $J_{C-P} = 12.1$ Hz), 131.13 (d, $J_{C-P} = 3.3$ Hz), 131.26 (d, $J_{C-P} = 10.9$ Hz), 131.38 (d, $J_{C-P} = 2.4$ Hz), 131.74 (d, $J_{C-P} = 11.0$ Hz), 132.02, 133.09, 133.22, 134.31 (d, $J_{C-P} = 107.7$ Hz), 134.95, 135.83 (d, $J_{C-P} = 102.9$ Hz), 156.86; EI (MS) *m*/*e* 487 (M^+, 3.05), 269 (100), 217 (66.91), 139 (55.16), 96 (29.08); Anal. Calcd for $C_{25}H_{25}Cl_2N_2PS$: C, 61.60; H, 5.17; N, 5.75; found: C, 61.52; H, 5.13; N, 5.49%.

4.2.3. Ligand 3 (L3). A yellow solid, yield 60%. Mp: 140–141 °C; $[\alpha]_D^{20} = -72.6$ (*c* 0.67, $CHCl_3$); IR (CH_2Cl_2) υ 2929, 1437, 1104, 777, 638 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.20–1.38 (m, 3H, CH_2 and CH), 1.58–1.78 (m, 4H, $2CH_2$), 2.21–2.34 (m, 1H, NH), 2.80–2.81 (m, 1H, CH), 3.39–3.47 (m, 1H, CH), 3.52–3.63 (m, 1H, CH), 7.20–7.45 (m, 9H, Ar), 7.94–8.12 (m, 4H, Ar), 8.53 (s, 1H, CH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 57.10; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.19, 24.49, 32.14, 33.10, 57.21 (d, $J_{C-P} = 2.2$ Hz), 75.30 (d, $J_{C-P} = 10.1$ Hz), 128.12 (d, $J_{C-P} = 12.9$ Hz), 128.17 (d, $J_{C-P} = 12.5$ Hz), 128.44, 130.23, 131.31 (d, $J_{C-P} = 2.5$ Hz), 131.35 (d, $J_{C-P} = 2.7$ Hz), 131.50 (d, $J_{C-P} = 10.9$ Hz), 131.60 (d, $J_{C-P} = 10.7$ Hz), 133.03, 134.31, 134.75 (d, $J_{C-P} = 100.5$ Hz), 135.84 (d, $J_{C-P} = 104.0$ Hz), 157.62; EI (MS) *m*/*e* 487 (M^+, 2.31), 269 (100), 217 (50.98), 139 (40.34); Anal. Calcd for $C_{25}H_{25}Cl_2N_2PS$: C, 61.60; H, 5.17; N, 5.75; found: C, 61.36; H, 5.18; N, 5.62%.

4.2.4. Ligand 4 (L4). A brown solid, yield 66%. Mp: 177–178 °C; $[\alpha]_D^{20} = -9.6$ (*c* 0.3, $CHCl_3$); IR (CH_2Cl_2) υ 3054, 1437, 1265, 1105, 696 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.21–1.30 (m, 3H, CH_2 and CH), 1.66–1.78 (m, 4H, $2CH_2$), 2.25–2.29 (m, 1H, NH), 2.41–2.44 (m, 1H, CH), 3.07–3.15 (m, 1H, CH), 3.35–3.43 (m, 1H, CH), 6.53–6.55 (m, 1H, CH), 6.81 (d, $J = 3.0$ Hz, 1H, CH), 7.26–7.42 (m, 6H, Ar), 7.58–7.59 (m, 1H, Ar), 7.85–7.99 (m, 4H, Ar), 8.17 (s, 1H, CH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 57.58; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.15, 24.84, 33.53, 34.17,

56.66 (d, $J_{C-P} = 1.7$ Hz), 75.73 (d, $J_{C-P} = 8.6$ Hz), 111.73, 114.33, 128.12 (d, $J_{C-P} = 13.0$ Hz), 128.16 (d, $J_{C-P} = 12.3$ Hz), 131.27 (d, $J_{C-P} = 11.5$ Hz), 131.29 (d, $J_{C-P} = 2.9$ Hz), 131.33 (d, $J_{C-P} = 2.7$ Hz), 132.12 (d, $J_{C-P} = 11.1$ Hz), 133.92 (d, $J_{C-P} = 102.2$ Hz), 135.80 (d, $J_{C-P} = 102.5$ Hz), 144.82, 149.36, 151.52; EI (MS) m/e 408 (M^+, 14.46), 217 (46.19), 191 (100), 175 (45.71), 96 (38.54); Anal. Calcd for $C_{23}H_{25}N_2OPS$: C, 67.62; H, 6.17; N, 6.86; found: C, 67.42; H, 6.22; N, 6.65%.

4.2.5. Ligand 5 (L5). A yellow solid, yield 55%. Mp: 121–122 °C; $[\alpha]_D^{20} = -82.6$ (c 0.69, $CHCl_3$); IR (CH_2Cl_2) υ 3054, 1438, 1265, 1104 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.28–1.41 (m, 3H, CH_2 and CH), 1.69–1.85 (m, 4H, $2CH_2$), 2.33–2.37 (m, 1H, NH), 2.51–2.55 (m, 1H, CH), 3.18–3.26 (m, 1H, CH), 3.49–3.56 (m, 1H, CH), 7.07–7.97 (m, 16H, Ar), 8.99 (s, 1H, CH), 9.05 (d, $J = 7.5$ Hz, 1H, Ar); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 57.70; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.19, 24.81, 33.66, 34.18, 56.56 (d, $J_{C-P} = 2.0$ Hz), 76.63 (d, $J_{C-P} = 7.7$ Hz), 124.63, 125.14, 126.05, 127.18, 128.02 (d, $J_{C-P} = 13.1$ Hz), 128.08 (d, $J_{C-P} = 13.1$ Hz), 128.59, 129.30, 131.10 (d, $J_{C-P} = 3.1$ Hz), 131.16, 131.23 (d, $J_{C-P} = 3.0$ Hz), 131.26, 131.35 (d, $J_{C-P} = 11.3$ Hz), 131.90 (d, $J_{C-P} = 11.1$ Hz), 133.85, 133.93 (d, $J_{C-P} = 102.3$ Hz), 135.26, 135.72 (d, $J_{C-P} = 102.2$ Hz), 160.32; EI (MS) m/e 468 (M^+, 16.04), 251 (100), 235 (49.70), 217 (36.55), 139 (34.51); Anal. Calcd for $C_{29}H_{29}N_2PS$: C, 74.33; H, 6.24; N, 5.98; found: C, 74.05; H, 6.45; N, 5.76%.

4.2.6. Ligand 6 (L6). A brown solid, yield 58%. Mp: 167–168 °C; $[\alpha]_D^{20} = -75.8$ (c 0.33, $CHCl_3$); IR (CH_2Cl_2) υ 3054, 1437, 1265, 1105, 896 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.15–1.37 (m, 3H, CH_2 and CH), 1.52–1.79 (m, 4H, $2CH_2$), 2.31–2.35 (m, 1H, NH), 2.43–2.47 (m, 1H, CH), 3.15–3.23 (m, 1H, CH), 3.50–3.58 (m, 1H, CH), 7.17–7.23 (m, 2H, Ar), 7.30–7.42 (m, 6H, Ar), 7.74–7.91 (m, 4H, Ar), 8.01 (d, $J = 8.1$ Hz, 1H, Ar), 8.42 (s, 1H, CH), 8.67 (d, $J = 4.8$ Hz, 1H, Ar); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 57.95; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.10, 24.81, 33.40, 34.36, 56.15 (d, $J_{C-P} = 1.3$ Hz), 75.32 (d, $J_{C-P} = 8.9$ Hz), 121.49, 124.78, 128.01 (d, $J_{C-P} = 13.1$ Hz), 128.20 (d, $J_{C-P} = 12.9$ Hz), 131.11 (d, $J_{C-P} = 2.9$ Hz), 131.28 (d, $J_{C-P} = 11.2$ Hz), 131.31 (d, $J_{C-P} = 3.2$ Hz), 131.80 (d, $J_{C-P} = 11.3$ Hz), 134.45 (d, $J_{C-P} = 102.4$ Hz), 135.86 (d, $J_{C-P} = 102.0$ Hz), 136.49, 149.27, 154.46, 161.48; EI (MS) m/e 419 (M^+, 7.36), 217 (29.33), 202 (100), 139 (25.10); Anal. Calcd for $C_{24}H_{26}N_3PS$: C, 68.71; H, 6.25; N, 10.02; found: C, 68.44; H, 6.44; N, 10.02%.

4.3. The representative experimental procedure for the synthesis of ligands L7–L13

A solution of (1*R*,2*R*)-(−)-*N*-diphenylthiophosphoryl-cyclohexane-1,2-diamine **1** (66 mg, 0.2 mmol) and salicylaldehyde (22 μL, 0.2 mmol) in ethanol (5 mL) were stirred at room temperature for 4 h. The resulted precipitates were obtained by filtration to give the product **L7** as a yellow solid.

4.3.1. Ligand 7 (L7). A yellow solid, yield 75%. Mp: 155–156 °C; $[\alpha]_D^{20} = -146.4$ (c 0.7, $CHCl_3$); IR (CH_2Cl_2) υ 1628, 1435, 1140, 1094, 1063, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.30–1.35 (m, 3H, CH_2 and CH), 1.63–1.83 (m, 4H, $2CH_2$), 2.18–2.23 (m, 1H, NH), 2.54–2.55 (m, 1H, CH), 3.13–3.14 (m, 1H, CH), 3.34 (s, 1H, CH), 6.90–7.02 (m, 2H, Ar), 7.23–7.43 (m, 8H, Ar), 7.79–7.90 (m, 4H, Ar), 8.39 (s, 1H, CH), 13.18 (br, 1H, OH); ^{31}P NMR ($CDCl_3$, 121 MHz, 80% H_3PO_4) δ 58.26; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 23.88, 24.62, 33.57, 34.30, 55.01, 72.40 (d, $J_{C-P} = 8.3$ Hz), 116.57, 118.51, 118.71, 127.89 (d, $J_{C-P} = 12.5$ Hz), 128.16 (d, $J_{C-P} = 12.7$ Hz), 131.01 (d, $J_{C-P} = 3.7$ Hz), 131.06 (d, $J_{C-P} = 11.0$ Hz), 131.11 (d, $J_{C-P} = 11.9$ Hz), 131.27 (d, $J_{C-P} = 2.8$ Hz), 131.64, 132.28, 135.56 (d, $J_{C-P} = 102.3$ Hz), 136.64 (d, $J_{C-P} = 99.5$ Hz), 160.83, 165.24; EI (MS) m/e 434 (M^+, 14.82), 217 (100), 201 (29.21), 183 (28.12), 139 (50.20); Anal. Calcd for $C_{25}H_{27}N_2OPS$: C, 69.10; H, 6.26; N, 6.45; found: C, 68.99; H, 6.51; N, 6.40%.

4.3.2. Ligand 8 (L8). A yellow solid, yield 62%. Mp: 192–193 °C; $[\alpha]_D^{20} = -83.3$ (c 0.94, $CHCl_3$); IR (CH_2Cl_2) υ 2932, 1633, 1492, 1105, 693 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.25–1.38 (m, 12H, C_4H_9 and CH_2 and CH), 1.59–1.82 (m, 4H, $2CH_2$), 2.19–2.23 (m, 1H, NH), 2.52–2.53 (m, 1H, CH), 3.12–3.13 (m, 1H, CH), 3.31–3.34 (m, 1H, CH), 6.95 (d, $J = 9.0$ Hz, 1H, Ar), 7.26–7.42 (m, 8H, Ar), 7.81–7.90 (m, 4H, Ar), 8.40 (s, 1H, CH), 12.92 (br, 1H, OH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 58.17; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 23.78, 24.46, 31.46, 33.44, 33.95, 34.00, 55.99, 74.25 (d, $J_{C-P} = 7.8$ Hz), 116.56, 117.89, 127.68, 128.21 (d, $J_{C-P} = 12.4$ Hz), 128.25 (d, $J_{C-P} = 12.8$ Hz), 129.69, 131.29 (d, $J_{C-P} = 10.8$ Hz), 131.37 (d, $J_{C-P} = 2.6$ Hz), 131.41 (d, $J_{C-P} = 2.6$ Hz), 131.87 (d, $J_{C-P} = 10.8$ Hz), 133.34 (d, $J_{C-P} = 102.1$ Hz), 135.51 (d, $J_{C-P} = 102.3$ Hz), 141.27, 158.66, 164.97; EI (MS) m/e 490 (M^+, 22.61), 273 (100), 257 (51.97), 242 (40.02), 217 (58.04), 139 (40.11); Anal. Calcd for $C_{29}H_{35}N_2OPS$: C, 70.99; H, 7.19; N, 5.71; found: C, 71.01; H, 7.38; N, 5.57%.

4.3.3. Ligand 9 (L9). A yellow solid, yield 51%. Mp: 198–199 °C; $[\alpha]_D^{20} = -84.8$ (c 0.35, $CHCl_3$); IR (CH_2Cl_2) υ 2952, 1437, 1105, 717 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.20–1.30 (m, 3H, CH_2 and CH), 1.48 (s, 9H, C_4H_9), 1.57 (s, 9H, C_4H_9), 1.63–1.74 (m, 3H, CH_2 and CH), 1.83–2.24 (m, 1H, NH), 2.54–2.57 (m, 1H, CH), 3.10–3.15 (m, 1H, CH), 3.28–3.31 (m, 1H, CH), 3.71–3.75 (m, 1H, CH), 7.11 (d, $J = 2.4$ Hz, 1H, Ar), 7.23–7.43 (m, 7H, Ar), 7.83–7.94 (m, 4H, Ar), 8.40 (s, 1H, CH), 13.55 (br, 1H, OH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 58.11; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 18.42, 23.97, 24.53, 29.49, 31.55, 33.53, 34.16, 35.07, 56.26 (d, $J_{C-P} = 2.0$ Hz), 74.07 (d, $J_{C-P} = 8.9$ Hz), 117.77, 125.92, 127.08, 128.24 (d, $J_{C-P} = 13.0$ Hz), 128.28 (d, $J_{C-P} = 12.8$ Hz), 131.42 (d,

$J_{C-P} = 1.8$ Hz), 131.46 (d, $J_{C-P} = 2.0$ Hz), 131.48 (d, $J_{C-P} = 10.9$ Hz), 131.96 (d, $J_{C-P} = 11.0$ Hz), 133.31 (d, $J_{C-P} = 102.1$ Hz), 135.48 (d, $J_{C-P} = 103.2$ Hz), 136.71, 140.12, 158.01, 165.79; EI (MS) m/e 546 (M^+, 34.04), 329 (80.24), 313 (100), 217 (80.02), 139 (34.35); Anal. Calcd for $C_{33}H_{43}N_2OPS \cdot C_2H_5OH$: C, 70.91; H, 8.33; N, 4.73; found: C, 70.73; H, 8.05; N, 4.70%.

4.3.4. Ligand 10 (L10). A yellow solid, yield 80%. Mp: 205–206 °C; $[\alpha]_D^{20} = -182.5$ (c 0.62, $CHCl_3$); IR (CH_2Cl_2) υ 2928, 1633, 1436, 1104, 714 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.27–1.43 (m, 3H, CH_2 and CH), 1.68–1.87 (m, 4H, $2CH_2$), 2.29–2.34 (m, 1H, NH), 2.45–2.48 (m, 1H, CH), 3.29–3.31 (m, 1H, CH), 3.33–3.39 (m, 1H, CH), 7.11 (d, $J = 2.4$ Hz, 1H, Ar), 7.24–7.46 (m, 7H, Ar), 7.74–7.82 (m, 4H, Ar), 8.24 (s, 1H, CH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 58.62; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 23.53, 24.34, 32.83, 33.84, 55.50, 72.23 (d, $J_{C-P} = 7.1$ Hz), 118.94, 121.91, 123.20, 128.18 (d, $J_{C-P} = 12.5$ Hz), 128.38 (d, $J_{C-P} = 12.8$ Hz), 128.97, 131.07 (d, $J_{C-P} = 11.1$ Hz), 131.49 (d, $J_{C-P} = 3.7$ Hz), 131.59 (d, $J_{C-P} = 2.5$ Hz), 131.63 (d, $J_{C-P} = 10.9$ Hz), 132.29, 133.26 (d, $J_{C-P} = 103.1$ Hz), 135.27 (d, $J_{C-P} = 102.0$ Hz), 157.65, 162.95; EI (MS) m/e 503 (M^+, 4.92), 285 (100), 217 (75.23), 139 (54.05); Anal. Calcd for $C_{25}H_{25}Cl_2N_2OPS$: C, 59.65; H, 5.01; N, 5.56; found: C, 59.73; H, 4.90; N, 5.41%.

4.3.5. Ligand 11 (L11). A yellow solid, yield 54%. Mp: 229–230 °C; $[\alpha]_D^{20} = -84.9$ (c 0.34, $CHCl_3$); IR (CH_2Cl_2) υ 3733, 3055, 1438, 869 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.22–1.38 (m, 3H, CH_2 and CH), 1.62–1.87 (m, 4H, $2CH_2$), 2.19–2.23 (m, 1H, NH), 2.47–2.51 (m, 1H, CH), 3.11–3.16 (m, 1H, CH), 3.41–3.42 (m, 1H, CH), 6.88 (d, $J = 9.0$ Hz, 1H, Ar), 7.24–7.44 (m, 8H, Ar), 7.74–7.85 (m, 4H, Ar), 8.26 (s, 1H, CH), 13.13 (br, 1H, OH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 58.46; ^{13}C NMR (DMSO-d_6, 75 MHz, TMS) δ 24.33, 25.17, 33.93, 34.82, 55.33, 72.81 (d, $J_{C-P} = 8.4$ Hz), 109.40, 119.59, 120.80, 128.28 (d, $J_{C-P} = 12.2$ Hz), 128.64 (d, $J_{C-P} = 12.6$ Hz), 131.36 (d, $J_{C-P} = 3.9$ Hz), 131.44 (d, $J_{C-P} = 10.8$ Hz), 131.46 (d, $J_{C-P} = 11.2$ Hz), 131.70 (d, $J_{C-P} = 3.1$ Hz), 133.87, 135.07, 136.22 (d, $J_{C-P} = 102.8$ Hz), 137.44 (d, $J_{C-P} = 99.5$ Hz), 160.74, 164.31; EI (MS) m/e 514 (M^++1, 18.46), 512 (M^+−1, 17.75), 297 (100), 295 (97.17), 217 (99.53), 139 (67.60); Anal. Calcd for $C_{25}H_{26}BrN_2OPS$: C, 58.48; H, 5.10; N, 5.46; found: C, 58.30; H, 5.33; N, 5.20%.

4.3.6. Ligand 12 (L12). A yellow solid, yield 57%. Mp: 232–233 °C; $[\alpha]_D^{20} = -171.6$ (c 0.44, $CHCl_3$); IR (CH_2Cl_2) υ 2928, 1623, 1538, 1104 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.32–1.48 (m, 4H, CH_2), 1.67–1.79 (m, 2H, CH_2), 2.07–2.11 (m, 1H, NH), 2.43–2.47 (m, 1H, CH), 2.57–2.62 (m, 1H, CH), 3.02–3.28 (m, 1H, CH), 3.04–3.44 (m, 1H, CH), 6.98 (d, $J = 9.3$ Hz, 1H, Ar), 7.13–7.34 (m, 8H, Ar), 7.45–7.48 (m, 1H, Ar), 7.65–7.98 (m, 6H, Ar), 8.93 (s, 1H, CH), 14.45 (br, 1H, OH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 58.46; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.03, 24.43, 32.55, 34.03, 56.44, 67.94 (d, $J_{C-P} = 8.9$ Hz), 106.68, 118.16, 122.79, 124.38, 126.41, 128.09 (d, $J_{C-P} = 17.4$ Hz), 128.24, 128.31 (d, $J_{C-P} = 16.1$ Hz), 128.37, 129.23, 131.20 (d, $J_{C-P} = 10.9$ Hz), 131.50 (d, $J_{C-P} = 2.5$ Hz), 131.50 (d, $J_{C-P} = 2.5$ Hz), 131.86 (d, $J_{C-P} = 11.0$ Hz), 133.02 (d, $J_{C-P} = 105.0$ Hz), 135.04 (d, $J_{C-P} = 102.3$ Hz), 137.08, 157.68, 174.98; EI (MS) m/e 484 (M^+, 35.91), 267 (56.35), 251 (100), 234 (48.18), 217 (64.27), 139 (46.16); Anal. Calcd for $C_{29}H_{29}N_2OPS$: C, 71.88%; H, 6.03%; N, 5.78%; found: C, 71.77%; H, 6.08%; N, 5.70%.

4.3.7. Ligand 13 (L13). A yellow solid, yield 52%. Mp: 166–167 °C; $[\alpha]_D^{20} = -56.8$ (c 0.29, $CHCl_3$); IR (CH_2Cl_2) υ 2925, 1620, 1506, 1275 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.24–1.80 (m, 6H, CH_2), 2.06–2.12 (m, 1H, NH), 2.36–2.45 (m, 1H, CH), 2.51 (s, 3H, Me), 2.62–2.66 (m, 1H, CH), 3.20–3.29 (m, 1H, CH), 3.37–3.41 (m, 1H, CH), 6.92 (d, $J = 9.0$ Hz, 1H, Ar), 7.12–7.25 (m, 5H, Ar), 7.32–7.35 (m, 2H, Ar), 7.56 (d, $J = 8.1$ Hz, 1H, Ar), 7.70 (d, $J = 9.3$ Hz, 1H, Ar), 7.75 (s, 1H, Ar), 7.78–7.90 (m, 4H, Ar), 8.93 (s, 1H, CH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 58.54; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 22.10, 24.09, 24.47, 32.65, 34.14, 55.37 (d, $J_{C-P} = 3.5$ Hz), 67.82 (d, $J_{C-P} = 8.0$ Hz), 106.36, 118.04, 123.28, 124.41, 124.49, 128.19 (d, $J_{C-P} = 13.4$ Hz), 128.30 (d, $J_{C-P} = 13.1$ Hz), 129.06, 131.20 (d, $J_{C-P} = 12.7$ Hz), 131.45 (d, $J_{C-P} = 1.9$ Hz), 131.47 (d, $J_{C-P} = 1.1$ Hz), 131.86 (d, $J_{C-P} = 11.5$ Hz), 132.97 (d, $J_{C-P} = 109.6$ Hz), 133.88, 135.00 (d, $J_{C-P} = 101.8$ Hz), 136.94, 137.80, 157.71, 175.16; EI (MS) m/e 498 (M^+, 2.79), 217 (29.18), 183 (20.19), 139 (17.79), 97 (31.82), 57 (100); Anal. Calcd for $C_{30}H_{31}N_2OPS \cdot 1/3EtOH$: C, 71.66%; H, 6.47%; N, 5.45%; found: C, 71.74%; H, 6.26%; N, 5.44%.

4.4. The synthesis of ligand 14 (L14)

This ligand was synthesized in the similar method as that described for the preparation of ligand 7 (**L7**).

4.4.1. Ligand 14 (L14). A yellow solid, yield 58%. Mp: 171–172 °C; $[\alpha]_D^{20} = -146$ (c 0.24, $CHCl_3$); IR (CH_2Cl_2) υ 3054, 1629, 1421, 1265, 895 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.24–1.34 (m, 3H, CH_2 and CH), 1.63–1.88 (m, 4H, CH_2), 2.17–2.21 (m, 1H, NH), 2.48–2.51 (m, 1H, CH), 3.13–3.21 (m, 1H, CH), 3.37–3.43 (m, 1H, CH), 6.91 (dt, $J = 7.5$, 0.9 Hz, 1H, Ar), 6.99 (d, $J = 9.0$ Hz, 1H, Ar), 7.22–7.42 (m, 7H, Ar), 7.78–7.87 (m, 5H, Ar), 8.39 (s, 1H, CH), 13.06 (br, 1H, OH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 54.90; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 23.73, 24.35, 33.39, 33.68, 56.64 (d, $J_{C-P} = 1.4$ Hz), 73.89 (d, $J_{C-P} = 8.2$ Hz), 117.03, 118.56, 118.64, 128.17 (d, $J_{C-P} = 12.8$ Hz), 128.22 (d, $J_{C-P} = 12.9$ Hz), 131.32, 131.45 (d, $J_{C-P} = 11.6$ Hz), 131.46 (d, $J_{C-P} = 2.0$ Hz), 131.52 (d,

$J_{C-P} = 1.6$ Hz), 131.97 (d, $J_{C-P} = 11.6$ Hz), 132.34, 133.16 (d, $J_{C-P} = 91.2$ Hz), 135.06 (d, $J_{C-P} = 91.7$ Hz), 161.01, 164.82; EI (MS) m/e 481 (M^+, 3.37), 401 (14.95), 217 (100), 201 (26.97); Anal. Calcd for $C_{25}H_{27}N_2OPSe$: C, 62.37; H, 5.65; N, 5.82; found: C, 62.15; H, 5.75; N, 5.63%.

4.5. The synthesis of ligand 15 (L15)

This ligand was synthesized in the similar method as that described for the preparation of ligand 7 (**L7**).

4.5.1. Ligand 15 (L15). A yellow solid, yield 56%. Mp: 215–216 °C; $[\alpha]_D^{20} = -59.3$ (c 0.4, $CHCl_3$); IR (CH_2Cl_2) υ 3175, 1631, 1437, 1280, 1185, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.25–1.73 (m, 7H, CH_2 and CH), 1.72–1.73 (m, 1H, CH), 2.43–2.49 (m, 1H, CH), 2.57–2.63 (m, 1H, CH), 3.06–3.09 (m, 1H, NH), 6.96 (t, $J = 7.5$ Hz, 1H, Ar), 7.05 (d, $J = 7.8$ Hz, 1H, Ar), 7.27–7.46 (m, 8H, Ar), 7.68–7.82 (m, 4H, Ar), 8.45 (s, 1H, CH), 13.19 (br, 1H, OH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85% H_3PO_4) δ 23.62; ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.12, 24.99, 33.76, 35.64, 55.83 (d, $J_{C-P} = 1.9$ Hz), 75.01 (d, $J_{C-P} = 9.2$ Hz), 117.40, 118.93, 119.02, 128.63 (d, $J_{C-P} = 10.9$ Hz), 128.80 (d, $J_{C-P} = 10.1$ Hz), 131.48 (d, $J_{C-P} = 130.3$ Hz), 131.58, 131.83 (d, $J_{C-P} = 9.2$ Hz), 131.93 (d, $J_{C-P} = 2.7$ Hz), 132.01 (d, $J_{C-P} = 3.0$ Hz), 132.73, 132.87 (d, $J_{C-P} = 9.4$ Hz), 133.89 (d, $J_{C-P} = 126.5$ Hz), 161.34, 164.78; EI (MS) m/e 418 (M^+, 15.43), 216 (39.11), 201 (100), 142 (23.97); ESI (HRMS) for $C_{25}H_{27}O_2NaN_2P$: 441.17007; found: 441.17024.

4.6. General procedure for the Cu(I)-catalyzed 1,4-conjugate addition

A solution of $Cu(CH_3CN)_4ClO_4$ (5.0 mg, 0.015 mmol) and **L7** (13.0 mg, 0.03 mmol) in dry toluene (3 mL) was stirred for 1 h at room temperature under an argon atmosphere. Then, 2-cyclohexene-1-one **2** (48 μL, 0.5 mmol) was added into the reaction mixture and the solution was stirred for a further 10 min. Et_2Zn (1.2 mL, 1.0 mmol, 0.87 M solution in hexane) was added dropwise within 30 s. The resulting mixture was stirred at −20 °C for 6 h. The reaction was quenched by addition of saturated ammonium chloride aqueous solution (4.0 mL). After extraction with ether (3 × 5.0 mL), the combined organic layers were dried over anhydrous $MgSO_4$. The residue obtained upon removal of volatiles in vacuo was purified by a flash column chromatography on silica gel (eluent: pentane/ether = 30/1) to afford (*S*)-(−)-ethylcyclohexanone **3** (61 mg, 97%) as a colourless oil. And ligand **7** was recovered in 96% yield.

(*S*)-(−)-3-Ethylcyclohexanone **3** (Table 1, entry 9). 61 mg, 97% yield, 75% ee. ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.90 (t, $J = 7.6$ Hz, Me), 1.44–1.25 (m, 3H), 1.58–1.70 (m, 2H), 1.85–2.10 (m, 3H), 2.20–2.46 (m, 3H); $[\alpha]_D^{20} = -10.3$ (c 2.9, $CHCl_3$) for 75% ee; Chiraldex G-BP column, 20 m × 0.25 mm, 50 °C (2 min), 50–112 °C, 5 °C/min, 112 °C (2 min) 10.0 psi N_2, $t_R = 12.503$ min, $t_S = 12.620$ min.

(*S*)-(−)-3-Ethylcyclopentanone **4** (Scheme 3). 40 mg, 71% yield. ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.95 (t, $J = 7.5$ Hz, Me), 1.41–1.58 (m, 3H), 1.75–1.85 (m, 1H), 2.10–2.44 (m, 5H); $[\alpha]_D^{20} = -9.7$ (c 0.1, $CHCl_3$) for 22% ee; Rt-βDEXcst™, 30 m × 0.25 mm, 70 °C (20 min), 70–115 °C, 1 °C/min, 115 °C (10 min), 8.4 psi N_2, $t_S = 59.488$ min, $t_R = 60.235$ min.

(*S*)-(−)-3-Ethylcycloheptanone **5** (Scheme 3). 68 mg, 96% yield. ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.91 (t, $J = 7.5$ Hz, Me), 1.25–1.45 (m, 4H), 1.51–1.70 (m, 2H), 1.80–1.95 (m, 3H), 2.35–2.52 (m, 4H); $[\alpha]_D^{20} = -13.2$ (c 2.1, $CHCl_3$) for 52% ee; Chiraldex G-BP column, 20 m × 0.25 mm, 90 °C (30 min), 8.0 psi N_2, $t_S = 9.618$ min, $t_R = 10.138$ min.

(*S*)-(+)-1,3-Diphenylpentan-1-one **7** (Scheme 4). 115 mg, 97%. ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.80 (t, $J = 7.5$ Hz, Me), 1.61–1.82 (m, 2H), 3.20–3.29 (m, 3H), 7.16–7.31 (m, 5H), 7.40–7.45 (m, 2H), 7.50–7.56 (m, 1H), 7.89–7.92 (m, 2H); $[\alpha]_D^{20} = +0.4$ (c 2.8, EtOH) for 8% ee; Chiralpak AD, hexane/*i*-PrOH = 95/5, 0.7 mL/min, $t_S = 9.426$ min, $t_R = 11.081$ min.

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