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Chiral C_1-symmetric diaminothiophosphoramide–Cu(I) catalyzed asymmetric addition of diethylzinc to *N*-sulfonylimines

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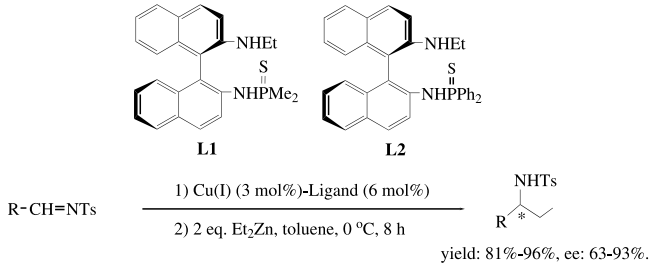
Abstract—In the presence of a catalytic amount of chiral diaminothiophosphoramide **L7** (6 mol%) and Cu(I) (3 mol%), the asymmetric addition of diethylzinc to *N*-sulfonylimines could be achieved in good yields with moderate to good e.e. (50–74% e.e.) at 0°C in toluene. A novel chiral diaminothiophosphoramide ligand system for this asymmetric addition reaction has been explored.

1. Introduction

The efficient and catalytic asymmetric synthesis of amines is one of the most promising methodologies in homogeneous catalysis.[1] Enantioselective addition of organometallic reagents to C=N of imines is a convenient route to obtain optically active amines.[2] This approach has especially been used in chiral amine ligand-catalyzed asymmetric addition of alkyllithium;[3] chiral amino alcohol ligands,[4] copper–amidophosphines,[5] and Zr-peptide-based chiral ligand-catalyzed asymmetric addition of organozinc;[6] chiral allylpalladium-catalyzed allylation by allylstannane,[7] and rhodium–monophosphine-catalyzed arylation by arylstannane[8] with very good enantioselectivities. Recently, we have been interested in the syntheses and applications of novel chiral ligands based on the axially chiral binaphthalenediamine (BINAM)[9,10] and found that in the presence of a catalytic amount of chiral binaphthylthiophosphoramide **L1** or **L2** (6 mol%) and Cu(I) (3 mol%), the asymmetric addition of diethylzinc to *N*-sulfonylimines could be achieved in good yields with moderate to high e.e. (63–93% e.e.) at 0°C in toluene (Scheme 1).[11] In order to expand this novel type of chiral thiophosphoramide ligand to other systems, we decide to utilize homochiral 1,2-cyclohexanediamine or 1,2-diphenylethylenediamine as a chiral source to prepare their corresponding thiophosphoramide ligands and utilize them in asymmetric catalysis. Herein, we wish to report the synthesis of novel homochiral C_1-symmetric diaminothiophosphoramide ligands **L3**–**L7** derived from chiral 1,2-cyclohexanediamine and 1,2-diphenylethylenediamine and the results of our studies on the catalytic enantioselective addition of diethylzinc to *N*-sulfonylimines by means of these novel chiral ligands.



Scheme 1.

2. Results and discussion

These chiral ligands **L3**–**L7** were easily obtained from (1*R*,2*R*)-(−)-1,2-cyclohexanediamine **1** and (1*R*,2*R*)-(+)-1,2-diphenylethane-1,2-diamine **2**.[12] The procedures for their preparation are outlined in Schemes 2–5. The chiral ligand **L3** can be easily synthesized through lithiation of the relevant diamine with butyllithium followed by phosphorylation with diphenylthiophos-

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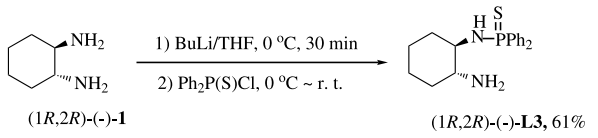
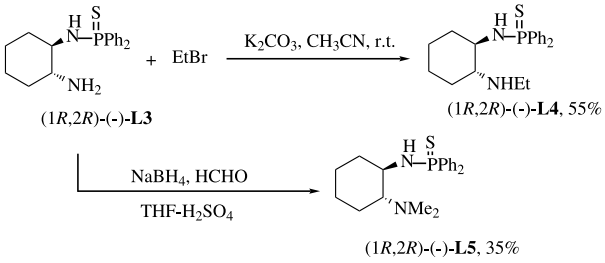
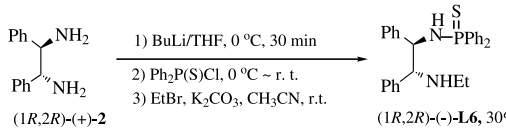


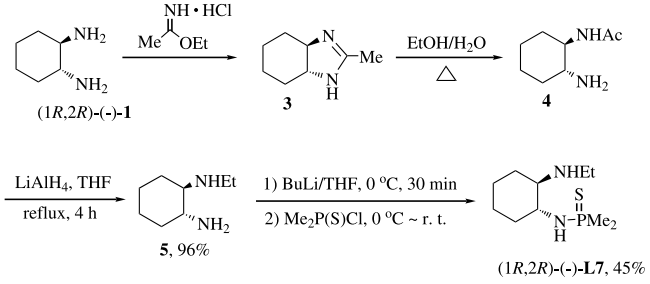
Scheme 2.



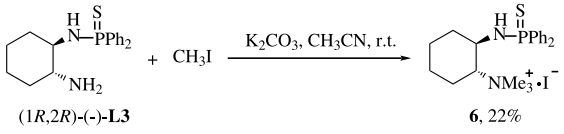
Scheme 3.



Scheme 4.



Scheme 5.



Scheme 6.

phoryl chloride in THF in good yield (Scheme 2). The *N*-substituted diphenylthiophsophoramide ligands **L4** and **L5** were synthesized in moderate yields by further reaction of **L3** with ethyl bromide and potassium carbonate in acetonitrile and treatment of **L3** with $NaBH_4$/HC(O)H in acidic THF solution, respectively (Scheme 3). The chiral ligand **L6** can be similarly synthesized through lithiation, phosphorylation and ethylation of the relevant diamine (Scheme 4). The preparation of *N*-substituted dimethylthiophsophoramide ligand **L7** is shown in Scheme 5 according to the reported procedure.[13] Namely, the condensation of (1*R*,2*R*)-(−)-1,2-cyclohexanediamine **1** with the Pinner salt derived from acetonitrile conveniently provided the corresponding imidazoline **3**. After refluxing a solution of **3** in neutral ethanol–water mixture for 20 h, *N*-monoacylated (1*R*,2*R*)-(−)-1,2-cyclohexanediamine **4** was produced in good yield (Scheme 5). The *N*-monoethylated (1*R*,2*R*)-(−)-1,2-cyclohexanediamine **5** was obtained by reduction of **4** with $LiAlH_4$ which was further treated with butyllithium and then by phosphorylation with dimethylthiophosphoryl chloride in THF to give the homochiral ligand **L7** in moderate yield (Scheme 5). We found that these homochiral ligands **L3**–**L7** are stable to ambient air and moisture and can be reused in this asymmetric reaction. We also found that if using methyl iodide as the alkylation reagent to modify **L3**, the reaction afforded the ammonium iodide **6** rather than the desired C_1-symmetric ligand (Scheme 6). The structure of compound **6** was determined by X-ray diffraction (Fig. 1).[14]

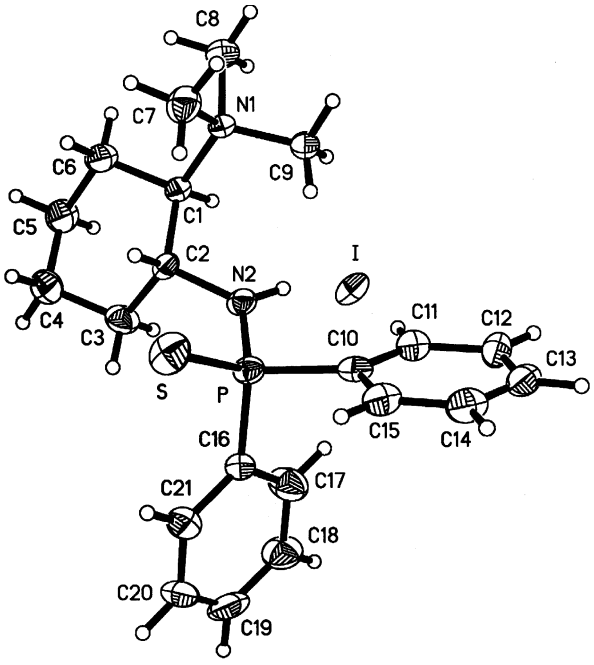
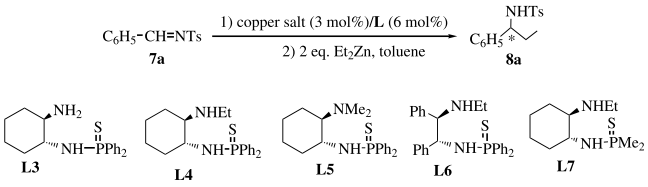


Figure 1. The ORTEP draw of ammonium iodide **6**.

Using *N*-(benzylidene)-*p*-methylbenzenesulfonamide (*N*-sulfonylimine) **7a** as the substrate and diethylzinc as the nucleophilic addition reagent, we examined this asymmetric addition using the obtained C_1-symmetric homochiral thiophosphoramide ligands **L3**–**L7** under various reaction conditions to develop the optimal reaction conditions. The results are summarized in Table 1. In an early study, an examination of the temperature profile of $Cu(CH_3CN)_4ClO_4$/**L4**-catalyzed asymmetric addition of diethylzinc to *N*-sulfonylimines was performed. We found that reaction temperature had a great influence on the yield and enantioselectivity of the addition product **8a**. At room temperature, the reaction was completed within 12 h and the desired ethylation product **8a** was given in 73% yield (56% e.e.) (Table 1, entry 1). Lowering the reaction temperature to 0°C, the yield of the addition product **8a** was increased to 84% with 65% e.e. (Table 1, entry 2). When the reaction was

Table 1. The asymmetric addition reaction of diethylzinc to *N*-sulfonylimine **7a** catalyzed by copper salt and chiral ligands **L3–7**



Entry	Copper salt	Ligand	Solvent	Temp. (°C)	Time (h)	Yield[a] (%)	E.e.[b] (%)
1	$Cu(MeCN)_4ClO_4$	**L4**	$PhCH_3$	12	12	73	56
2	$Cu(MeCN)_4ClO_4$	**L4**	$PhCH_3$	0	13	84	65
3	$Cu(MeCN)_4ClO_4$	**L4**	$PhCH_3$	−20	36	52	67
4	$Cu(MeCN)_4BF_4$	**L4**	$PhCH_3$	0	21	82	53
5	$CuOTf{\cdot}1/2C_6H_6$	**L4**	$PhCH_3$	0	15	66	64
6	$Cu(OTf)_2$	**L4**	$PhCH_3$	0	28	56	60
7	$Cu(MeCN)_4ClO_4$	**L4**	Et_2O	0	10	89	65
8	$Cu(MeCN)_4ClO_4$	**L4**	THF	0	24	35	47
9	$Cu(MeCN)_4ClO_4$	**L4**	CH_2Cl_2	0	24	31	31
10[c]	$Cu(MeCN)_4ClO_4$	**L4**	$PhCH_3$	0	13	72	56
11	$Cu(MeCN)_4ClO_4$	**L4**	$PhCH_3$	0	60	46	39
12	$Cu(MeCN)_4ClO_4$	**L4**	$PhCH_3$	0	60	64	40
13	$Cu(MeCN)_4ClO_4$	**L4**	$PhCH_3$	0	13	92	68
14	$Cu(MeCN)_4ClO_4$	**L4**	$PhCH_3$	0	48	58	39
15	$Cu(MeCN)_4ClO_4$	**L4**[d]	$PhCH_3$	0	13	83	57

[a] Isolated yields.
[b] Determined by chiral HPLC.
[c] $LiClO_4$ was added as additive.
[d] Recovered ligand was used.

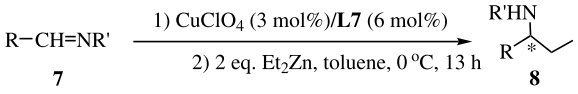
carried out at −20°C, the reaction was sluggish and the achieved e.e. of **8a** was slightly increased to 67% (Table 1, entry 3). Thus, the best reaction temperature is 0°C. The catalytic activity of $Cu(CH_3CN)_4ClO_4$ (84% yield, 65% e.e.) was similar as another copper salts $CuOTf{\cdot}1/2C_6H_6$ (66% yield, 64% e.e.), but better than other copper salts such as, $Cu(CH_3CN)_4BF_4$ (82% yield, 53% e.e.) and $Cu(OTf)_2$ (56% yield, 60% e.e.) (Table 1, entries 4–6). The solvent effects were examined by use of $Cu(CH_3CN)_4ClO_4$/**L4** catalytic system. We found that toluene and Et_2O are the solvent of choice (Table 1, entries 1, 7–9).

By screening chiral ligands **L3–7**, we found that **L7** was the best chiral ligand for this enantioselective addition reaction, which gave the addition product in 68% e.e. and 92% yield at 0°C under the same conditions (Table 1, entries 11–14). It should be noted that chiral ligand **L5** having an *N*,*N*-dimethyl group gave the addition product **8a** in 64% yield with 40% e.e. under the same conditions (Table 1, entry 12) and the *N*-unsubstituted chiral ligand **L3** gave the addition product **8a** only in moderate yield and e.e. as well (Table 1, entry 11). These results suggested that the substituent on the amino group in the diamine structure played a very important role in asymmetric induction in this addition reaction. The homochiral C_1-symmetric ligand **L6** derived from (1*R*,2*R*)-(+)-1,2-diphenylethane-1,2-diamime **2** furnished the addition product **8a** in 58% yield and 39% e.e. under the same conditions (Table 1, entry 14). Ligand **L4** can be easily recovered from the reaction mixture in 70–80% yield through silica gel column chromatography after usual workup, and can be reused in this asymmetric reaction in similar yield and with slightly lower enantioselectivity (Table 1, entry 15). The best reaction conditions are using $Cu(CH_3CN)_4ClO_4$ (3 mol%) as a catalyst precursor and **L7** (6 mol%) as a chiral ligand in toluene at 0°C.

We next examined the asymmetric addition reaction of diethylzinc to a variety of *N*-sulfonylimines **7** under the optimized reaction conditions. The results are summarized in Table 2. As can be seen from Table 2, good yields (69–99%) and moderate to good enantioselectivities (50–74% e.e.) could be achieved for various aromatic *N*-sulfonylimines **7** having either electron-donating groups or electron-withdrawing groups on the benzene ring (Table 2, entries 1–8 and 10). Although these results are not comparable with the best literature value hitherto reported for the asymmetric addition of diethylzinc to *N*-sulfonylimines,[5a] this is still a case for exploring a novel ligand system for the enentioselective addition of organozinc to C=N double bond. For the methanesulfonylimine **7i**, 99% yield (63% e.e.) also could be realized (Table 2, entry 9).

Although the real active species is not yet fully understood in this catalytic addition reaction, we believe that this family of chiral C_1-symmetric thiophosphoramides **L3–L7** are bidentate ligands in this catalytic asymmetric reaction because it is well known that sulfur atoms can coordinate strongly to late transition metals.[15] In order

Table 2. The asymmetric addition of diethylzinc to various *N*-sulfonylimines **7** in the presence of Cu(I) (3 mol%) and **L7** (6 mol%)



Entry	R	R′	Imine	Yield[a] (%)	E.e.[b] (%)	$[\alpha]_D^{20}$ (*c* in $CHCl_3$)
1	C_6H_5	Ts	**7a**	**8a**, 92	68	−35.6 (3.17)[c]
2	*p*-MeC_6H_4	Ts	**7b**	**8b**, 84	63	−30.6 (0.85)
3	*m*-MeC_6H_4	Ts	**7c**	**8c**, 67	50	−23.3 (2.55)
4	*p*-$MeOC_6H_4$	Ts	**7d**	**8d**, 76	74	38.5 (0.85)
5	*p*-ClC_6H_4	Ts	**7e**	**8e**, 74	74	−43.4 (1.88)
6	*m*-ClC_6H_4	Ts	**7f**	**8f**, 69	53	−28.0 (2.80)
7	*p*-$CF_3C_6H_4$	Ts	**7g**	**8g**, 71	64	−25.1 (3.15)
8	*m*-FC_6H_4	Ts	**7h**	**8h**, 82	57	−24.6 (3.15)
9	C_6H_5	Ms	**7i**	**8i**, 99	63	−22.5 (3.10)
10	*i*-Me_2CH	Ts	**7j**	**8j**, 82	61	−4.1 (2.85)

[a] Isolated yields.
[b] Determined by chiral HPLC.
[c] The absolute configuration of **8a** was assigned to *S* by comparing the specific rotation with the reported data.[5]

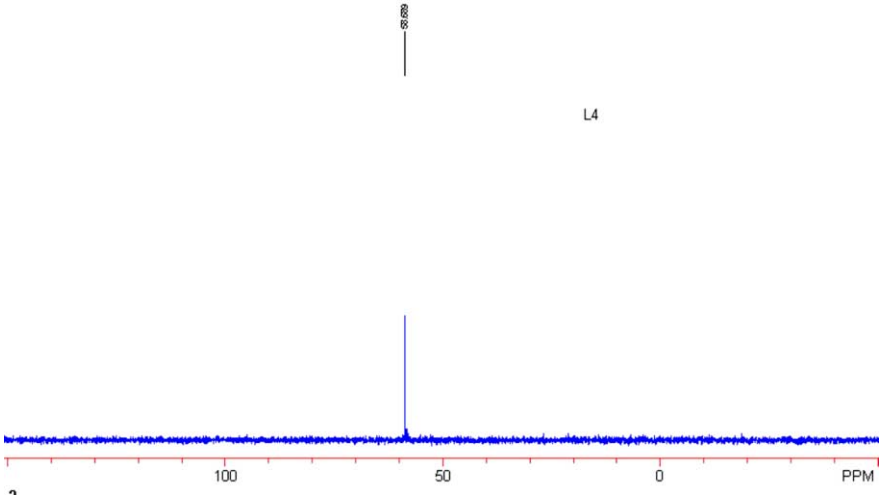


Figure 2. The ^{31}P NMR spectrum of **L4**.

to provide evidence for the coordination of nitrogen and sulfur atom in **L4** to Cu(I), the ^{31}P NMR studies of a 1:1 mixture of **L4** and $Cu(CH_3CN)_4ClO_4$ in $CDCl_3$ at room temperature were carried out. In the absence of $Cu(CH_3CN)_4ClO_4$, the signal of the phosphorous connected to the sulfur atom in **L4** appeared at δ 58.69 (Fig. 2), while it appeared a new signal at δ 61.45 in **L4** in the presence of $Cu(CH_3CN)_4ClO_4$ (Fig. 3). Moreover, in our previous work, we have proved that the N atom in this type of C_1-symmetric thiophsophoramide ligand system indeed coordinated to Cu metal center.[11] Those results may partially indicate that Cu(I) can be potentially coordinated by both the S and N atoms in ligand **L4**.

3. Conclusion

In conclusion, we have synthesized a new family of chiral diaminothiophosphoramides derived from (1*R*,2*R*)-(−)-1,2-cyclohexanediamine and (1*R*,2*R*)-(+)-1,2-diphenylethane-1,2-diamime, which are readily available, very stable and recoverable, and have applied them to the copper-catalyzed asymmetric addition of diethylzinc to *N*-sulfonylimines **7** in high yields and with moderate to good enantioselectivities. 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

4.1. General remarks

All reactions were conducted in an 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

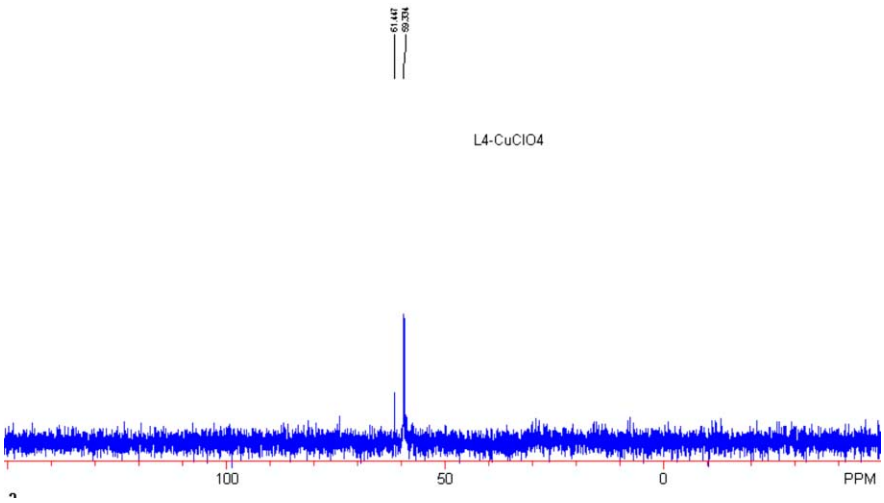


Figure 3. The ^{31}P NMR spectrum of the mixture of **L4** and $Cu(CH_3CN)_4ClO_4$.

hydride; diethyl ether, tetrahydrofuran and benzene were distilled from sodium metal/benzophenone ketyl. ^1H, ^{13}C and ^{31}P NMR spectra were recorded at 300, 75 and 121 MHz, respectively. Mass spectra were recorded by the EI method. All of the solid compounds reported in this paper gave satisfactory CHN microanalyses or HRMS analyses. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with silica gel coated plates. Enantiomeric ratios were determined by HPLC, using a chiralpak AS column, a chiralpak AD column or a chiralcel OD column with hexane and *i*-PrOH as solvents. Melting points are uncorrected.

4.2. Materials

N-Arylidene-*p*-methylbenzenesulfonamides **7a**–**7h** and aliphatic *N*-tosylated imine **7j**,[16] *N*-benzylidenemethylsulfonamide **7i**[17] were prepared by the reported synthetic methods. The physical and spectroscopic data of **7a**–**j** are in consistent with those reported in the literature.[16,17]

4.3. Representative experimental procedure for the synthesis of ligands L3–7

4.3.1. Chiral ligand L3. To a solution of (1*R*,2*R*)-(−)-1,2-cyclohexanediamine **1** (1.37 g, 12 mmol) in THF (10.0 mL) was added dropwise *n*-butyllithium (8.13 mL, 13.0 mmol, 1.6 M solution in hexane) at 0°C over 30 min, and the reaction mixture was stirred for 1 h at the same temperature. Then, diphenylthiophosphinic chloride (3.28 g, 13.0 mmol) in 5.0 mL of THF was added dropwise and the reaction solution was slowly warmed to rt. A saturated aqueous sodium bicarbonate was added to quench the reaction and exacted twice with dichloromethane. The organic layer was dries over anhydrous $MgSO_4$ and evaporated under reduced pressure. The residue was purified by an alumina column chromatography (eluent: dichloromethane/methanol = 80/1) to give the ligand **L3** as an amber solid (2.4 g, 61%). Mp: 60–62°C; $[\alpha]_D^{20} = -22.8$ (*c* 0.072, $CHCl_3$); IR (CH_2Cl_2) *v* 2925, 2854, 1669, 1437, 1105, 638 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.07–1.25 (m, 4H, CH_2), 1.62–1.67 (m, 2H, CH_2), 1.91–2.00 (m, 2H, CH_2), 2.35–2.46 (m, 1H, CH), 2.92–2.99 (m, 1H, CH), 3.10–3.14 (m, 2H, NH_2), 3.38 (dd, $J = 6.9$, 7.2 Hz, 1H, NH), 7.42–7.49 (m, 6H, Ar), 7.88–7.96 (m, 2H, Ar), 8.02–8.09 (m, 2H, Ar); ^{31}P NMR ($CDCl_3$, 121 MHz, 85%H_3PO_4) δ +59.24; ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 29.36, 30.44, 34.28, 35.44, 56.02 (d, $J_{C-P} = 6.6$ Hz), 58.05 (d, $J_{C-P} = 2.5$ Hz), 128.01 (d, $J_{C-P} = 13.2$ Hz), 128.23 (d, $J_{C-P} = 12.3$ Hz), 130.84 (d, $J_{C-P} = 11.0$ Hz), 131.27 (d, $J_{C-P} = 1.7$ Hz), 131.30 (d, $J_{C-P} = 3.3$ Hz), 131.70 (d, $J_{C-P} = 11.4$ Hz), 135.01 (d, $J_{C-P} = 101.8$ Hz), 135.12 (d, $J_{C-P} = 101.8$ Hz); MS (EI) *m*/*z* 331 (M^++1, 0.70), 234 (24.19), 217 (57.97), 139 (35.67), 97 (100); HRMS (EI) calcd for $C_{18}H_{23}N_2PS$ requires: 330.13196; found: 330.12854.

4.3.2. Chiral ligand L4. To a solution of ligand **L3** (3.3 g, 10 mmol) in CH_3CN (25 ml) was added potassium carbonate (2.76 g, 20 mmol) and bromoethane (5.0 ml, 66 mmol), then the reaction mixture was stirred at rt for 24 h. The mixture was washed by 10% brine, extracted twice with dichloromethane, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by an alumina column chromatography (eluent: ethyl acetate) to give the chiral ligand **L4** as an amber oil (1.97 g, 55%). It can be easily recovered from the reaction mixture in 70–80% yield through silica gel column chromatography after usual workup. $[\alpha]_D^{20} = -53.5$ (*c* 0.095, $CHCl_3$); IR (CH_2Cl_2) *v* 3247, 2930, 2856, 1437, 751, 638 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.16 (t, $J = 8.7$ Hz, 3H, CH_3), 1.53–1.55 (m, 2H, CH_2), 1.68–1.73 (m, 2H, CH_2), 1.83–1.88 (m, 2H, CH_2), 2.10–2.13 (m, 2H, CH_2), 2.34 (br, 1H, NH), 2.49–2.58 (m, 2H, CH_2), 2.82–2.88 (m, 1H, CH), 3.15–3.20 (m, 1H, CH), 4.04 (br, 1H, NH), 7.39–7.47 (m, 6H, Ar), 7.86–7.94 (m, 2H, Ar), 8.02–8.10 (m, 2H, Ar); ^{31}P NMR ($CDCl_3$, 121 MHz, 85%H_3PO_4) δ +58.69; ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 15.26, 24.37, 24.66, 30.88, 33.80, 39.96, 55.12 (d, $J_{C-P} = 2.0$ Hz), 61.28 (d, $J_{C-P} = 8.7$ Hz), 127.81 (d, $J_{C-P} = 12.4$ Hz),

128.08 (d, $J_{C-P}=12.5$ Hz), 130.45 (d, $J_{C-P}=10.7$ Hz), 131.03 (d, $J_{C-P}=2.9$ Hz), 131.10 (d, $J_{C-P}=3.2$ Hz), 131.59 (d, $J_{C-P}=11.3$ Hz), 135.24 (d, $J_{C-P}=103.3$ Hz), 135.46 (d, $J_{C-P}=100.5$ Hz); MS (EI) m/z 359 (M^++1, 0.59), 331 (1.14), 217 (90.32), 139 (55.20), 97 (100); HRMS (EI) calcd for $C_{20}H_{27}N_2PS$ requires: 358.16325; found: 358.16111.

4.3.3. Chiral ligand L5. A solution of ligand **L3** (264 mg, 0.8 mmol) in THF (10 mL) and $NaBH_4$ (302 mg, 8.0 mmol) were simultaneously added to a stirred solution of 20% H_2SO_4 (1.0 mL) and 40% formaldehyde aqueous solution (1.0 mL, 12.0 mmol) in THF (20 mL) with ice-cooling over a period of 15 min, the mixture was stirred for an additional hour and then 1.0 M NaOH was added until pH>7. After extraction with ethyl acetate, the combined organic layers were dried over anhydrous $MgSO_4$. The residue obtained upon evaporation was purified by a silica gel column chromatography (eluent: ethyl acetate/petroleum = 1/2) to afford the ligand **L6** as a colorless oil (99 mg, 35%). $[\alpha]_D^{20}=-31.1$ (c 2.2, $CHCl_3$); IR (CH_2Cl_2) ν 2932, 2859, 1437, 1104, 638 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.95–1.08 (m, 2H, CH_2), 1.16–1.18 (m, 2H, CH_2), 1.43–1.48 (m, 2H, CH_2), 1.75–1.82 (m, 2H, CH_2), 2.23 (s, 6H, CH_3), 2.29–2.36 (m, 1H, CH) 3.28–3.41 (m, 1H, CH), 4.45 (br, 1H, NH), 7.39–7.48 (m, 6H, Ar), 7.78–7.86 (m, 2H, Ar), 8.09–8.17 (m, 2H, Ar); ^{31}P NMR ($CDCl_3$, 121 MHz, 85%H_3PO_4) δ +58.81; ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 20.56, 24.32, 25.22, 33.84, 39.60, 52.51 (d, $J_{C-P}=2.4$ Hz), 67.11 (d, $J_{C-P}=10.1$ Hz), 127.86 (d, $J_{C-P}=13.0$ Hz), 128.29 (d, $J_{C-P}=12.7$ Hz), 130.30 (d, $J_{C-P}=11.0$ Hz), 131.05 (d, $J_{C-P}=2.9$ Hz), 131.19 (d, $J_{C-P}=3.8$ Hz), 132.09 (d, $J_{C-P}=10.9$ Hz), 135.62 (d, $J_{C-P}=105.2$ Hz), 136.13 (d, $J_{C-P}=98.9$ Hz); MS (EI) m/z 358 (M^+, 3.59), 217 (20.97), 141 (45.69), 125 (100), 96 (30.36); HRMS(EI) calcd for $C_{20}H_{27}N_2PS$ requires: 358.16325; found: 358.16281.

4.3.4. Chiral ligand L6. This compound was prepared by the same method as that described above for the preparation of ligand **L3** and **L4** using (1*R*,2*R*)-(+)-1,2-diphenylethane-1,2-diamime **2** as a starting material. After purification, it was given as a light yellow solid, yield 30%. Mp: 135–137°C; $[\alpha]_D^{20}=-7.1$ (c 1.55, $CHCl_3$); IR (CH_2Cl_2) ν 3028, 1437, 1106, 1063, 644 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.84–0.88 (m, 1H, CH), 1.00 (t, $J=7.0$ Hz, 3H, CH_3), 1.42–1.43 (m, 1H, CH), 2.31–2.54 (m, 2H, CH_2), 3.86 (d, $J=7.6$ Hz, 1H, NH), 4.49–4.55 (m, 1H, NH), 6.91–7.46 (m, 16H, Ar), 7.61–7.68 (m, 2H, Ar), 7.79–7.86 (m, 2H, Ar); ^{31}P NMR ($CDCl_3$, 121 MHz, 85%H_3PO_4) δ +65.97; ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 15.13, 41.19, 60.86 (d, $J_{C-P}=1.8$ Hz), 68.15 (d, $J_{C-P}=8.4$ Hz), 126.74, 127.50, 127.57 (d, $J_{C-P}=13.1$ Hz), 127.83 (d, $J_{C-P}=2.9$ Hz), 127.97 (d, $J_{C-P}=1.5$ Hz), 128.05, 128.24, 130.96, 131.10, 131.44 (d, $J_{C-P}=11.9$ Hz), 132.00 (d, $J_{C-P}=11.1$ Hz), 132.44 (d, $J_{C-P}=2.7$ Hz), 133.06 (d, $J_{C-P}=118.0$ Hz), 133.33 (d, $J_{C-P}=113.6$ Hz), 140.25 (d, $J_{C-P}=2.1$ Hz), 141.63 (d, $J_{C-P}=6.5$ Hz); MS (EI) m/z 457 (M^++1, 0.50), 217 (17.02), 134 (100); HRMS(EI) calcd for $C_{28}H_{29}N_2PS$ requires: 456.1789; found: 456.1761.

4.3.5. Compound 5. To a stirred suspension of $LiAlH_4$ (456 mg, 12.0 mmol) in 20.0 mL of anhydrous THF was added dropwise a solution of monoacetylated diamine **4**[12] (312 mg, 2.0 mmol) in 10.0 mL of THF. The mixture was heated under reflux for 4 h. After reaction, the reaction mixture was cooled in an ice-bath and the remaining hydride was carefully quenched by dropwise addition of water (5.0 mL) and then 10% NaOH (5.0 mL). A white precipitate was filtered off and thoroughly washed with ethyl acetate. The combined filtrate and ethyl acetate washings were washed with brine and dried over anhydrous $MgSO_4$. After the solvents were evaporated under reduced pressure, product **5** was given in 272 mg, 96% as an amber oil. $[\alpha]_D^{20}=-75.3$ (c 0.36, $CHCl_3$); IR (CH_2Cl_2) ν 1449, 1265, 1120, 739, 704 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.76–1.27 (m, 11H, CH_2 and CH_3), 1.54–1.66 (m, 2H, NH_2), 1.88–2.06 (m, 2H, CH_2), 2.24–2.32 (m, 1H, NH), 2.37–2.46 (m, 1H, CH) 2.67–2.76 (m, 1H, CH); MS (EI) m/z 142 (M^+, 22.80), 126 (15.86), 110 (10.13), 97 (35.82), 84 (99.89), 56 (100).

4.3.6. Chiral ligand L7. This compound was prepared by the same method as that described above for the preparation of ligand **L4**. An amber solid, 45% yield. Mp: 64–65°C; $[\alpha]_D^{20}=-138.4$ (c 0.6, $CHCl_3$); IR (CH_2Cl_2) ν 2930, 2856, 1450, 1105, 942, 728 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.09 (t, $J=7.2$ Hz, 3H, CH_3), 1.18–1.35 (m, 6H, CH_2), 1.65 (br, 1H, NH), 1.72–1.76 (m, 2H, CH_2), 1.81 (d, $J=0.9$ Hz, 3H, CH_3), 1.85 (d, $J=1.2$ Hz, 3H, CH_3), 2.11–2.20 (m, 2H, CH_2), 2.43–2.50 (m, 1H, CH), 2.69 (br, 1H, NH), 2.76–2.82 (m, 1H, CH); ^{31}P NMR ($CDCl_3$, 121 MHz, 85%H_3PO_4) δ +60.59; ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 15.30, 23.42 (d, $J_{C-P}=67.7$ Hz), 24.46, 24.51 (d, $J_{C-P}=71.3$ Hz), 24.86, 30.80, 34.85, 40.60, 56.16 (d, $J_{C-P}=3.2$ Hz), 61.91 (d, $J_{C-P}=7.9$ Hz); MS (EI) m/z 234 (M^+, 0.88), 205 (0.92), 141 (8.09), 125 (100), 93 (28.72); HRMS(EI) calcd for $C_{10}H_{23}N_2PS$ requires: 234.13196, found: 234.13320.

4.3.7. Compound 6. To a solution of ligand **L3** (330 mg, 1 mmol) in CH_3CN (10 ml) was added potassium carbonate (2.76 g, 20 mmol) and methyl iodide (0.62 ml, 10 mmol), then the reaction mixture was stirred at rt for 24 h. The mixture was washed by 10% brine, extracted twice with dichloromethane, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by an alumina column chromatography (eluent: ethyl acetate/methol = 50/1) to give the compound **6** as a colorless solid (103 mg, 22%). Mp: 214–215°C; IR (CH_2Cl_2) ν 3445, 3142, 2938, 1436, 637 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.10–1.15 (m, 1H, CH_2), 1.35–1.65 (m, 4H, CH_2), 1.81–1.86 (m, 1H, CH_2), 2.05–2.13 (m, 1H, CH_2), 2.29–2.33 (m, 1H, CH_2), 3.38 (s, 9H, CH_3), 4.26–4.34 (m, 1H, CH), 4.77–4.85 (m, 1H, CH), 6.01–6.06 (m, 1H, Ar), 7.39–7.48 (m, 6H, Ar), 8.04–8.14 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 121 MHz, 85%H_3PO_4) δ +58.73; MS (EI) m/z 358 (M^+–142, 2.68), 217 (15.06), 141 (27.42), 125 (100). Anal. calcd for: $C_{21}H_{30}N_2PSI$ requires C, 50.40%; H, 6.04%; N, 5.60%. Found: C, 50.68%; H, 5.95%; N, 5.46%.

4.4. General procedure for the synthesis of the racemic products which were used for the chiral HPLC analysis

Under argon atmosphere, to a solution of *N*-(*m*-fluorobenzylidene)-*p*-methylbenzenesulfonamide **7h** (139 mg, 0.5 mmol) in THF (4.0 mL) was added dropwise ethylmagnesium bromide (1.5 mL, 1.5 mmol, 1.0 M in THF) at 0°C. The reaction mixture was stirred for 10 h at the same temperature, and then 1.0N HCl (5.0 mL) was added. After extraction with ethyl acetate, the combined organic layers were dried over $MgSO_4$. The residue obtained upon removal of volatiles in vacuo was purified by column chromatography on silica gel (eluent: petroleum/ethyl acetate = 10/1) to afford the racemic product **8h** (140 mg, 91%) as a colorless solid.

The other racemates **8a**–**j** were synthesized in the same manner as that described above.

4.5. General procedure for the Cu-catalyzed addition of diethylzinc to sulfonylimine

A solution of $Cu(CHCN)_4ClO_4$ (5.0 mg, 0.015 mmol) and ligand **L7** (7.0 mg, 0.03 mmol) in dry toluene (3.0 mL) was stirred for 1 h at rt under an argon atmosphere. *N*-(Benzylidene)-*p*-methylbenzenesulfonamide **7a** (129 mg, 0.5 mmol) was added and the solution was stirred for a further 10 min, then Et_2Zn (1 mL, 1 mmol, 1.0 M solution in hexane) was added dropwise within 30 seconds at 0°C. The resulting mixture was stirred for about 13 h at the same temperature, 1.0 M HCl (4.0 mL) was added. After extraction with ethyl acetate (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 column chromatography on silica gel (eluent: petroleum/ethyl acetate = 10/1) to afford the addition product (127 mg, 92%) as a colorless solid.

4.6. (*S*)-(−)-4-Methyl-*N*-(1-phenylpropyl)benzenesulfonamide 8a (entry 1 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.79 (t, J = 7.2 Hz, 3H, Me), 1.69–1.82 (m, 2H, CH_2), 2.36 (s, 3H, Me), 4.15–4.22 (m, 1H, CH), 4.73 (br, 1H, NH), 6.99–7.02 (m, 2H, Ar), 7.10–7.18 (m, 5H, Ar), 7.53 (d, J = 6.3 Hz, 2H, Ar); $[\alpha]_D^{20} = -35.6$ (c 3.17, $CHCl_3$) for 68% e.e.; Chiralpak AS, hexane/*i*-PrOH = 75/25, 0.7 mL/min, $t_{major} = 15.050$ min, $t_{minor} = 20.414$ min.

4.7. (−)-4-Methyl-*N*-(1-tolylpropyl)benzenesulfonamide 8b (entry 2 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.77 (t, J = 7.5 Hz, 3H, Me), 1.65–1.86 (m, 2H, CH_2), 2.27 (s, 3H, Me), 2.37 (s, 3H, Me), 4.07–4.17 (m, 1H, CH), 4.72 (br, 1H, NH), 6.88 (d, J = 8.4 Hz, 2H, Ar), 6.97 (d, J = 8.1 Hz, 2H, Ar), 7.12 (d, J = 8.1 Hz, 2H, Ar), 7.54 (d, J = 8.4 Hz, 2H, Ar); $[\alpha]_D^{20} = -30.6$ (c 0.85, $CHCl_3$) for 63% e.e.; Chiralpak AS, hexane/*i*-PrOH = 75/25, 0.7 mL/min, $t_{minor} = 13.737$ min, $t_{major} = 17.710$ min.

4.8. (−)-4-Methyl-*N*-(1-*m*-tolylpropyl)benzenesulfonamide 8c (entry 3 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.79 (t, J = 7.5 Hz, 3H, Me), 1.61–1.85 (m, 2H, CH_2), 2.18 (s, 3H, Me), 2.36 (s, 3H, Me), 4.08–4.17 (m, 1H, CH), 4.90 (br, 1H, NH), 6.70 (s, 1H, Ar), 6.82 (d, J = 7.8 Hz, 1H, Ar), 6.94 (d, J = 8.1 Hz, 1H, Ar), 7.03–7.12 (m, 3H, Ar), 7.53 (d, J = 8.4 Hz, 2H, Ar); $[\alpha]_D^{20} = -23.3$ (c 2.55, $CHCl_3$) for 49% e.e.; Chiralpak AD, hexane/*i*-PrOH = 85/15, 0.7 mL/min, $t_{minor} = 12.200$ min, $t_{major} = 17.533$ min.

4.9. (−)-4-Methyl-*N*-[1-(4-methoxyphenyl)propyl]benzenesulfonamide 8d (entry 4 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.77 (t, J = 7.8 Hz, 3H, Me), 1.63–1.86 (m, 2H, CH_2), 2.37 (s, 3H, Me), 3.75 (s, 3H, Me), 4.09–4.16 (m, 1H, CH), 4.67 (br, 1H, NH), 6.69 (d, J = 11.4 Hz, 2H, Ar), 6.92 (d, J = 11.4 Hz, 2H, Ar), 7.13 (d, J = 8.7 Hz, 2H, Ar), 7.54 (d, J = 8.7 Hz, 2H, Ar); $[\alpha]_D^{20} = -38.5$ (c 0.85, $CHCl_3$) for 74% e.e.; Chiralpak AS, hexane/*i*-PrOH = 75/25, 0.7 mL/min, $t_{minor} = 20.260$ min, $t_{major} = 28.473$ min.

4.10. (−)-4-Methyl-*N*-[1-(4-chlorophenyl)propyl]benzenesulfonamide 8e (entry 5 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.78 (t, J = 7.5 Hz, 3H, Me), 1.63–1.82 (m, 2H, CH_2), 2.38 (s, 3H, Me), 4.14–4.21 (m, 1H, CH), 5.01 (br, 1H, NH), 6.96 (d, J = 9.0 Hz, 2H, Ar), 7.09–7.14 (m, 4H, Ar), 7.51 (d, J = 9.0 Hz, 2H, Ar); $[\alpha]_D^{20} = -43.4$ (c 1.88, $CHCl_3$) for 74% e.e.; Chiralpak AS, hexane/*i*-PrOH = 75/25, 0.7 mL/min, $t_{minor} = 12.243$ min, $t_{major} = 18.990$ min.

4.11. (−)-4-Methyl-*N*-[1-(3-chlorophenyl)propyl]benzenesulfonamide 8f (entry 6 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.80 (t, J = 7.2 Hz, 3H, Me), 1.60–1.80 (m, 2H, CH_2), 2.37 (s, 3H, Me), 4.14–4.21 (m, 1H, CH), 4.87 (br, 1H, NH), 6.86 (s, 1H, Ar), 6.92–6.96 (m, 1H, Ar), 7.09–7.14 (m, 4H, Ar), 7.51 (d, J = 7.2 Hz, 2H, Ar); $[\alpha]_D^{20} = -28.0$ (c 2.8, $CHCl_3$) for 53% e.e.; Chiralpak AD, hexane/*i*-PrOH = 85/15, 0.7 mL/min, $t_{minor} = 11.470$ min, $t_{major} = 12.477$ min.

4.12. (−)-4-Methyl-*N*-(1-(4-trifluoromethylphenyl)propyl)-benzenesulfonamide 8g (entry 7 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.82 (t, J = 7.5 Hz, 3H, Me), 1.64–1.83 (m, 2H, CH_2), 2.33 (s, 3H, Me), 4.24–4.31 (m, 1H, CH), 5.08 (br, 1H, NH), 7.06 (d, J = 7.8 Hz, 2H, Ar), 7.11 (d, J = 8.1 Hz, 2H, Ar), 7.36 (d, J = 8.4 Hz, 2H, Ar), 7.46 (d, J = 8.4 Hz, 2H, Ar); $[\alpha]_D^{20} = -25.1$ (c 3.15, $CHCl_3$) for 64% e.e., Chiralcel OD, hexane/*i*-PrOH = 9/1, 0.7 mL/min, $t_{minor} = 14.848$ min, $t_{major} = 17.621$ min.

4.13. (−)-4-Methyl-*N*-[1-(3-fluorophenyl)propyl]-benzenesulfonamide 8h (entry 8 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.79 (t, $J=7.2$ Hz, 3H, Me), 1.63–1.80 (m, 2H, CH_2), 2.36 (s, 3H, Me), 4.16–4.23 (m, 1H, CH), 4.95 (br, 1H, NH), 6.65–6.69 (m, 1H, Ar), 6.80–6.86 (m, 2H, Ar), 7.09–7.17 (m, 3H, Ar), 7.54 (d, $J=8.1$ Hz, 2H, Ar); $[\alpha]_D^{20}=-24.6$ (c 3.15, $CHCl_3$) for 57% e.e.; Chiralcel OD, hexane/*i*-PrOH = 9/1, 0.7 mL/min, $t_{minor}=14.946$ min, $t_{major}=18.921$ min.

4.14. (−)-*N*-(1-Phenylpropyl)methanesulfonamide 8i (entry 9 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.91 (t, $J=7.5$ Hz, 3H, Me), 1.77–1.91 (m, 2H, CH_2), 2.56 (s, 3H, Me), 4.32–4.39 (m, 1H, CH), 4.86 (br, 1H, NH), 7.27–7.41 (m, 5H, Ar); $[\alpha]_D^{20}=-22.5$ (c 3.1, $CHCl_3$) for 63% e.e.; Chiralpak AS, hexane/*i*-PrOH = 75/25, 0.7 mL/min, $t_{minor}=12.578$ min, $t_{major}=13.716$ min.

4.15. (−)-4-Methyl-*N*-(1-ethyl-2-methylpropyl)benzenesulfonamide 8j (entry 10 in Table 2)

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.69–0.89 (m, 9H, 3Me), 1.22–1.29 (m, 1H, CH), 1.37–1.47 (m, 1H, CH), 1.71–1.77 (m, 1H, CH), 2.42 (s, 3H, Me), 2.99–3.04 (m, 1H, CH), 4.35 (br, 1H, NH), 7.28 (d, $J=9.0$ Hz, 2H, Ar), 7.77 (d, $J=8.7$ Hz, 2H, Ar); $[\alpha]_D^{20}=-4.1$ (c 2.85, $CHCl_3$) for 61% e.e.; Chiralpak AD, hexane/*i*-PrOH = 85/15, 0.7 mL/min, $t_{major}=10.177$ min, $t_{minor}=11.517$ min.

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14. $C_{21}H_{30}N_2PSI$, formula weight: 500.40, temperature: 293(2) K, crystal system, space group: monoclinic, $P2(1)$, unit cell dimensions: $a=8.9294(8)$ Å, $b=8.7601(8)$ Å, $c=14.5754(13)$ Å, $\alpha=90°$, $\beta=91.826(2)°$, $\gamma=90°$, $V=1139.54(18)$ Å^3, $Z_{value}=2$, $D_{calcd}=1.458$ g/cm^3, $F_{000}=508$, crystal size: 0.470×0.255×0.168 mm, data/restraints/parameters = 4643/2/246, final R indices [$I>2\sigma(I)$]: $R_1=0.0423$, $wR_2=0.1018$, R indices (all data): $R_1=0.0501$; $wR_2=0.1333$. Its crystal structure has been deposited at the Cambridge Crystallographic Data Center and has been allocated the deposition number: CCDC 217719.
15. For selected X-rays of Cu complexes coordinated by S, N ligands, see: (a) Knotter, D. M.; Grove, D. M.; Smeets, W. J. J.; Spek, A. L.; van Koten, G. *J. Am. Chem. Soc.* **1992**, *114*, 3400–3410; (b) Brubaker, G. R.; Brown, J. N.; Yoo, M. K.; Kutchan, T. M.; Mottel, E. A. *Inorg. Chem.* **1979**, *18*, 299–302.
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