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N-Phosphano nitrogen-containing five-membered aromatic chiral α-sulfoxides as new chiral ligands in asymmetric palladium-catalyzed allylic alkylation: stereoelectronic effects of the substituents on the aromatic rings

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Abstract—New chiral ligands, *N*-diphenylphosphano nitrogen-containing five-membered aromatic compounds bearing chiral sulfinyl groups as the sole chiral source has been developed. The structure of a palladium intermediate derived from the new chiral sulfoxide ligand was determined as a palladium complex with a five-membered chelate ring formed by coordination of the phosphano group and the sulfinyl sulfur atom involved. The stereoelectronic effects of substituents on the aromatic rings are discussed.

1. Introduction

Catalytic asymmetric synthesis has attracted much attention in recent years for the efficient preparation of optically active compounds,[1] particularly for a facile entry to chiral biologically active compounds and chiral pharmaceuticals. A number of asymmetric synthetic methodologies for carbon–carbon bond formation have been developed,[2] and various types of chiral ligands for the catalytic asymmetric synthesis have been devised so far, by utilizing chiral amines, amides, alcohols, phophines, biaryls with axial chirality, and so on.[3] However, hitherto few precedents of chiral sulfoxide ligands have appeared.[4]

Quite recently, we have developed novel several chiral sulfoxide ligands which are useful for transition metal-catalyzed asymmetric carbon–carbon bond formation.[5]

For further development of new chiral ligands possessing chiral sulfinyl groups as sole chiral sources, we have utilized phosphanoamino groups as other coordination sites besides chiral sulfinyl groups. In these cases, the formation of several chelates **1a**–**d** will be possible by coordination of nitrogen or phosphano groups in the phosphanoamines and sulfur or oxygen atoms in the chiral sulfoxides to metal catalysts. In the protocol of our plan, we employed pyrrole or indole skeletons as main frameworks of ligands for the conformational fixation, in which chiral sulfinyl groups were incorporated at the 2 or 7 positions, resultantly providing five- or six-membered chelates **2** and **3** by coordination of phosphano groups. We will discuss sterically and, or electronically the effects of substituents introduced on the skeletons (Scheme 1).

On these lines, we have developed novel chiral sulfoxide ligands consisting of *N*-phosphano nitrogen-containing five-membered aromatics, and demonstrate the usefulness of the ligands in terms of reactivity of the catalysts with the ligands and the resultant enantioselectivity.

2. Results and discussion

2.1. Synthesis of chiral pyrrolyl and indolyl sulfoxide ligands

Novel chiral *N*-phosphanopyrrolyl and -indolyl aryl sulfoxides were prepared as follows. α-Sulfinylation of *N*-*t*-butoxycarbonylpyrroles **4a**,**b**[6] and indoles **8a**–**d** with (−)-menthyl (*S*)-*p*-toluene-, 1-naphthalene-,[7] or 2-methoxy-1-naphthalenesulfinates[8] (**5a**–**c**) was carried out at −78 °C in THF for 24 h using lithium diisopropylamide to give the corresponding α-sulfinylated pyrroles (*S*)-**6a**–**d**

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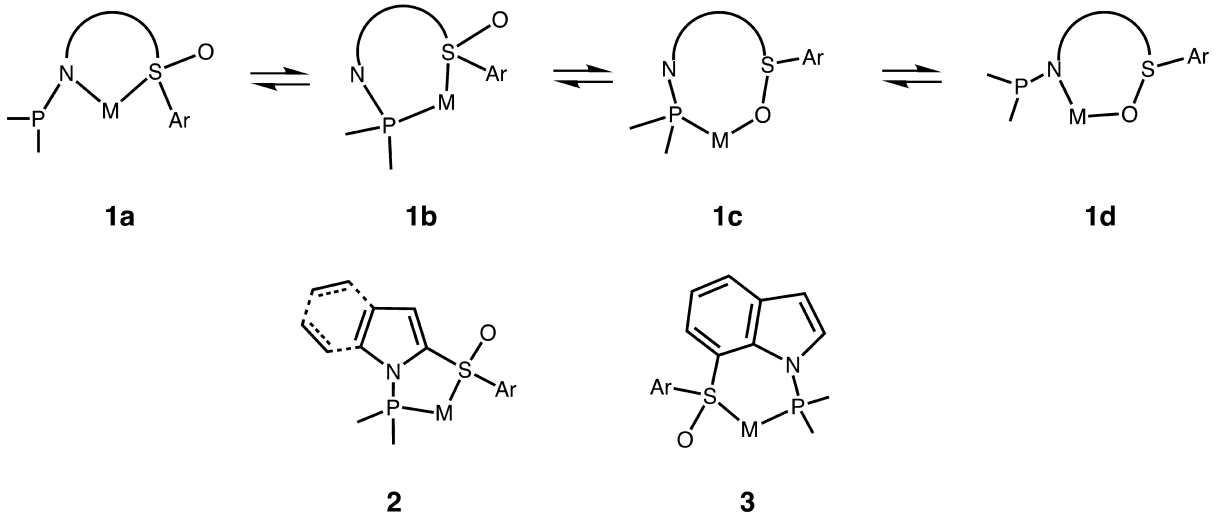


Scheme 1.

and indoles (*S*)-**9a**–**e**. Upon treatment with *n*-butyllithium followed by the reaction with chlorodiphenylphosphane, (*S*)-**6a**–**d** and (*S*)-**9a**–**e** were converted into (*S*)-**7a**–**d** and (*S*)-**10a**–**e**, respectively.

Sulfinylation of 7-bromoindole (**11**)[9] (derived from 2-bromonitrobenzene upon treatment with vinylmagnesium bromide) with (*Ss*)-**5c** using *n*-butyllithium followed by *N*-phosphanation of (*R*)-**12** with chlorodiphenylphosphane gave (*R*)-**13** (Scheme 2).

2.2. Palladium-catalyzed asymmetric reactions with chiral sulfoxide ligands

The effects of the new chiral sulfoxide ligands thus obtained were studied in the palladium-catalyzed asymmetric alkylation of (±)-**14** with dimethyl malonate. The reactions of (±)-**14** with sodium dimethyl malonate (generated by treating with sodium hydride) were carried out in THF at −78 °C in the presence of [PdCl(π-allyl)]$_2$ (0.03 equiv.) and a chiral ligand (*S*)-**7a**–**c** (0.06 equiv.) to give (*S*)-**15** with moderate e.e. Incorporation of a methoxy group at the C_2 position of the naphthalene ring in the sulfoxide provided high enantioselectivity of (*S*)-**15**, presumably due to steric effects of the methoxy substituent. The highest e.e. (74 and 83%) of (*S*)-**15** was obtained with (*S*)-**7c** at −45 and −78 °C, respectively, although in a little lower chemical yield (Scheme 3).

The replacement of the pyrrole skeleton in (*S*)-**7** with an indolyl function ((*S*)-**10**) in the chiral sulfoxide ligands provided a similar stereochemical result. The reaction of (±)-**14** with sodium malonate in THF at 0, −20, or −45 °C using (*S*)-**10a** gave (*S*)-**15** with 56, 60, or 73% e.e., respectively, in high yield (81–92%); similarly the reaction in DME at the same temperature afforded (*S*)-**15** with 59, 65, or 73% e.e., respectively, in high yield (83–94%).

Unambiguous effects of electron-donating groups on the pyrrole and indole rings of the chiral ligands were observed, resulting in remarkable improvement of the reactivity of the catalysts with the ligands and the resultant enantioselectivity. Introduction of two methyl groups at the 3- and 5-positions of the pyrrole ring in (*S*)-**7c** improved dramatically the chemical yield and the e.e. of the products; the palladium-catalyzed reaction of (±)-**14** with sodium malonate using (*S*)-**7d** as a ligand in THF at −20, −45, or −78 °C for 2, 7, or 20 h gave (*S*)-**15** with 65, 80, or 83% e.e. in excellent yields (97 and 96%), respectively, although in a little lower chemical yield (32%) at −78 °C.

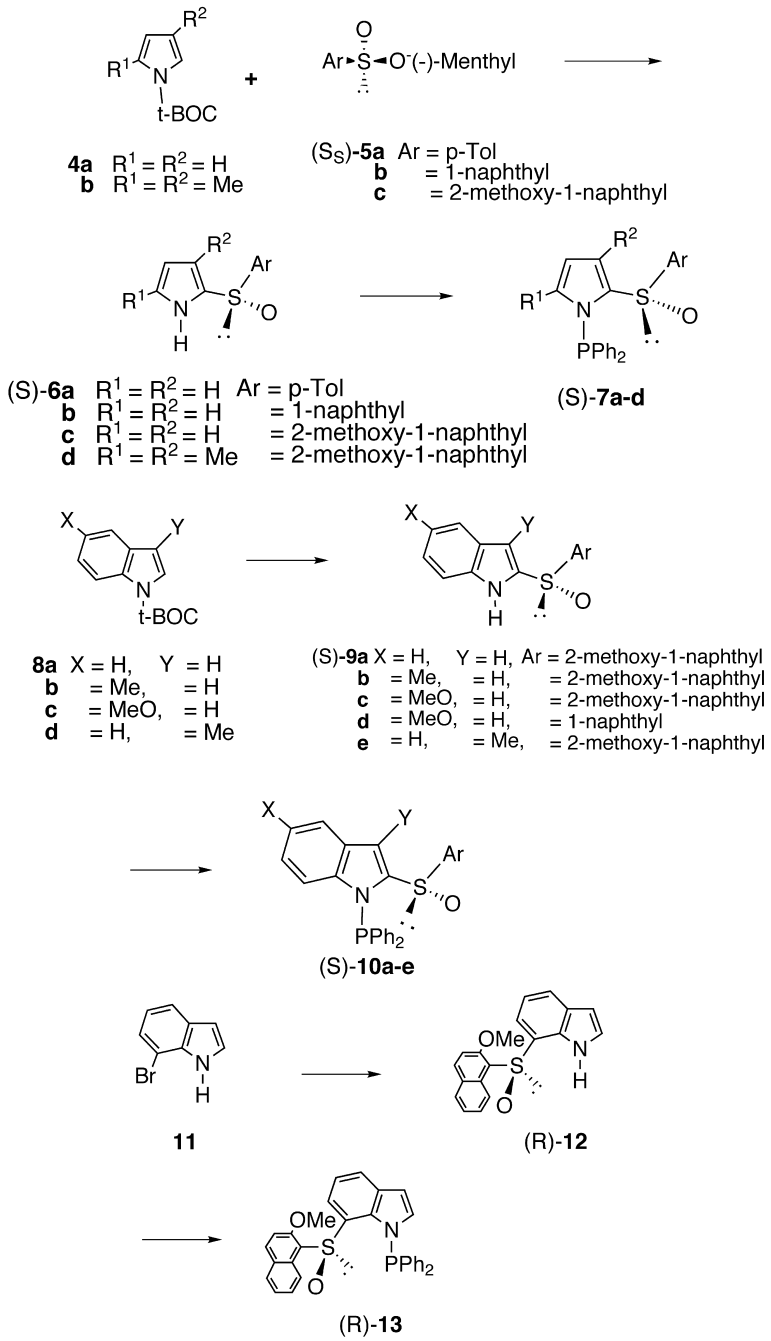
In the case of indole systems the substituents at the 5-positions of the indole rings in **10a**,**b** were marginally effective for the reactivity. Introduction of electron-donating groups (methoxy group) at the 5-positions of the indoles improved electronically the reactivity to provide slightly higher chemical yield (87–90%) with a little lower enantioselectivity, as shown in Table 1, in comparison with those by (*S*)-**10a**. Introduction of a methyl group at the C_5 position, however, was not so effective in achieving high efficiency in terms of the chemical yield and the enantioselectivity, providing a slightly lower chemical yield of (*S*)-**15** with slightly lower e.e.

Introduction of a methyl group at the 3-position of the indole ring ((*S*)-**10e**) provided the highest enantioselectivity (93%) of (*S*)-**15**, presumably owing to the steric control in the conformational equilibrium of the vicinal chiral sulfinyl group.

Interestingly, the existence of a methoxy group on the naphthalene ring in the sulfinyl groups of (*S*)-**10c** was also highly effective in achieving high enantioselectivity and chemical yield, in contrast with those by (*S*)-**10d**.

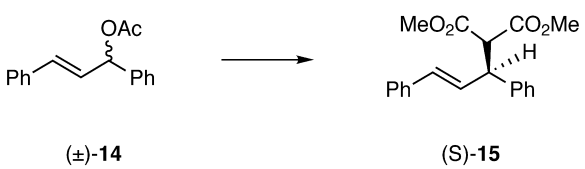
Use of another indolyl sulfoxide (*R*)-**13** as a ligand provided (*S*)-**15** in 76% yield with a slightly lower enantioselectivity, as listed in Table 1.

The molecular structure of the chiral sulfoxide ligand ((*S*)-**10a**)-palladium [$PdCl_2{\cdot}(CH_3CN)_2$] complex was determined as a five-membered chelate **16** formed by

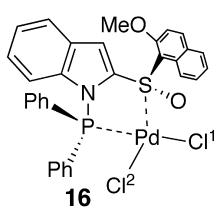


Scheme 2.

coordination of the sulfinyl sulfur atom and the phosphano group to the palladium catalyst, as shown in Figure 1, by the X-ray crystallographic analysis. In comparison with a palladium complex of (*S*)-2-(diphenylphosphano)phenyl 2-methoxy-1-naphthyl sulfoxide reported by us previously,[5f] the molecular structure indicates that the bond lengths



Scheme 3.



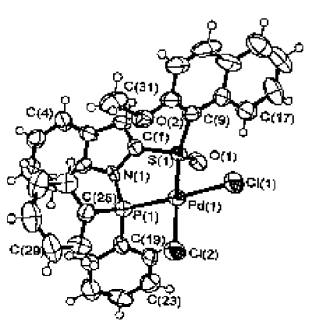


Figure 1. Crystallographic data (ORTEP drawing) for (S)-16. Selected bond distance (Å) and angles (deg): Pd(1)–S(1) 2.229(4), Pd(1)–P(1) 2.222(4), Pd(1)–Cl(1) 2.338(4) Pd(1)–Cl(2) 2.299(4), N(1)–P(1) 1.716(12), S(1)–C(1) 1.716(12) S(1)–Pd(1)–P(1) 88.85(14), S(1)–Pd(1)–Cl(1) 89.42(14).

Table 1. Palladium-catalyzed asymmetric alkylations of **14** using chiral ligands (*S*)-**7**, (*S*)-**10**, and (*R*)-**13**[a]

Ligand	Solvent	Reaction temp. (°C)	Reaction time (*h*)	Yield (%) of (*S*)-**15**	e.e. (%) of (*S*)-**15**[b]
(*S*)-**7a**	THF	0	3	76	17
	THF	−20	24	72	24
(*S*)-**7b**	THF	−20	8	89	29
(*S*)-**7c**	THF	0	1	70	45
	THF	−20	4	78	53
	THF	−40	8	40	74
	THF	−78	23	7	83
	DME	0	2	68	40
	DME	−20	7	53	55
(*S*)-**7d**	THF	−20	2	97	65
	THF	−45	7	96	80
	THF	−78	20	32	83
(*S*)-**10a**	THF	0	80	92	56
	THF	−20	4	92	60
	THF	−45	21	81	73
	DME	0	80	94	59
	DME	−20	4	91	65
	DME	−45	21	83	73
(*S*)-**10b**	THF	0	13	91	52
	THF	−20	13	81	55
	THF	−45	21	43	65
	DME	0	13	79	56
	DME	−20	13	72	61
	DME	−45	21	61	65
(*S*)-**10c**	THF	−20	2	90	57
	THF	−45	8	87	61
(*S*)-**10d**	THF	0	3	88	31
	THF	−20	14	57	32
	THF	−45	14	29	36
	DME	0	3	82	37
	DME	−20	14	45	36
	DME	−45	18	32	48
(*S*)-**10e**	THF	−20	10	93	74
	THF	−45	16	83	82
	THF	−78	24	68	93
(*R*)-**13**	THF	−20	2	93	32
	THF	−45	16	76	41

[a] The reactions of **14** with carbanion of dimethyl malonate (generated by treating with NaH (2.0 equiv.) were carried out in THF or DME in the presence of $[PdCl(\pi\text{-allyl})]_2$ (0.03 equiv.) and a chiral ligand (*S*)-**7**, (*S*)-**10**, or (*R*)-**13** (0.06 equiv.).
[b] The enantiomeric excess (e.e.) of (*S*)-**15** was determined by the HPLC analysis with Chiralpak AD.

between the nitrogen-phosphane and the sulfur-aromatic carbon atoms are slightly shorter, and the Pd–Cl[1] bond length is a little longer, compared with the Pd–Cl[2] bond, owing to the electronic (π-accepting) effects of the phosphorus atom; however, the bond angles between the Pd–P–N and the Pd–S–C are very similar to those in the 2-(diphenylphosphano)phenyl sulfoxide–palladium complex.

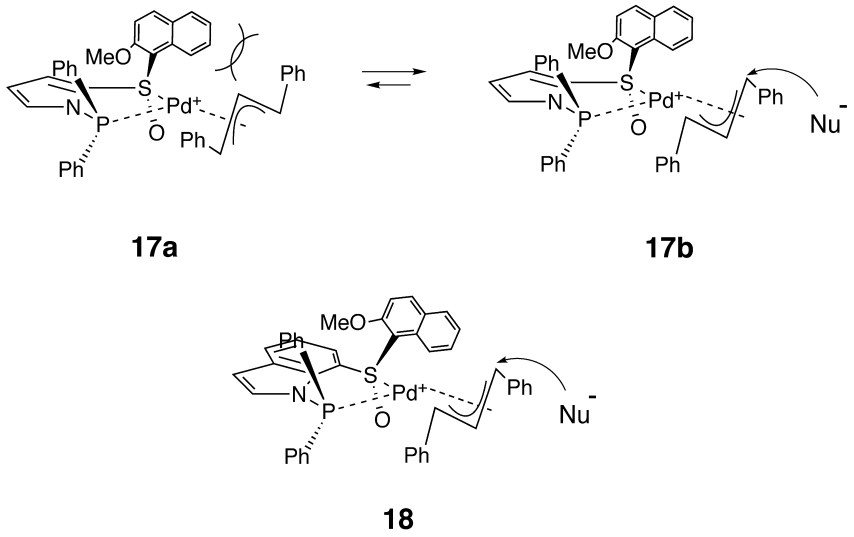
2.3. The mechanism for the asymmetric induction with chiral *N*-phosphano pyrrolyl and indolyl sulfoxides as chiral ligands

The mechanism of the asymmetric induction in these asymmetric alkylations with new chiral ligands is rationalized on the basis of the stereochemical results and the molecular structure of the intermediary palladium complex as follows. In the conformational equilibrium of π-allylpalladium complexes derived from the intermediary palladium-chiral ligand complexes, an M-typed π-allyl intermediate **17b** is sterically preferred to W-typed **17a** because of the existence of steric interference between the aryl substituent on the sulfinyl group and the phenyl of the γ-allyl system in **17a**. The nucleophile (the carbanion of dimethyl malonate) attacks the γ-carbon in the allyl terminus of **17b** *trans* to the better π-accepting atom, which is the phosphano group in the present case, giving (*S*)-**15**. The remarkable increase in enantioselectivity by the 2-methoxy-1-naphthyl sulfoxide (*S*)-**7c** and (*S*)-**10c** over that by (*S*)-**7b** and (*S*)-**10d** is rationalized presumably by the planar fixation of the conformation of the aromatic carbon–sulfur bond in the intermediate ascribed to the dipole–dipole repulsion between the sulfinyl S–O bond and the methoxy group.

A six-membered palladium complex **18** formed by coordination of the sulfinyl sulfur atom and the phosphano group in (*R*)-**13** provided slightly lower enantioselectivity in the allylic alkylations, presumably due to the less effective steric environment involved in the complex (Scheme 4).

3. Conclusion

Thus, evidently it should be concluded that these novel chiral sulfoxide ligands developed by us are very useful as chiral ligands in palladium-catalyzed asymmetric



Scheme 4.

alkylation, and the introduction of the electron-donating substituents on the aromatic rings enables us to improve remarkably the reactivity of the intermediary complexes and the enantioselectivity by the stereoelectronic effects. Our present work is one of the most useful asymmetric synthetic methods with high efficiency using chiral sulfoxides as the sole chiral sources in the ligands, involving studies on the stereoelectronic effects of the substituents on the pyrrole and indole skeletons and the structural determination of an intermediary palladium complex with a chiral β-phosphano sulfoxide.

4. Experimental

4.1. General

Infrared (IR) spectra were obtained in the indicated state with a JASCO DR-81 Fourier-Transform IR spectrometer. NMR spectra were determined in the indicated solvent with a JOEL EX-270 (^{1}H NMR; 270 MHz) high-resolution NMR spectrometer; chemical shifts are given in ppm from tetramethylsilane as an internal standard. Splitting patterns are designated as s, singlet; d, doublet; dd, doublet of doublets; m, multiplet. Mass spectra were taken on a JOEL JMS-DX 303/JMA-DA 5000 system. High performance liquid chromatography (HPLC) was performed with a Tosoh UV-8010 CCPM (column: Dicel Chiralpak AD (hexane/*i*-PrOH 20:1), 0.5 ml/min, 254 nm). Optical rotations were measured at 24 °C with a JASCO DIP-370 polarimeter. X-ray diffraction analysis was carried out on a Rigaku RAXIS-IV diffractometer. Flash column chromatography was performed with Merck Silica gel 60 (230–400 mesh). Thin layer or thick layer plates (preparative TLC) were made of Merck Silica gel 60PF-254 activated by drying at 140 °C for 3.5 h.

4.1.1. (*S*)-2-Pyrrolyl *p*-tolyl sulfoxide (6a). A 100 ml two-necked flask equipped with a septum inlet and magnetic stirring bar was flushed with argon, and maintained under a positive pressure of argon. A solution of diisopropylamine (607 mg, 6.0 mmol) in THF (10 ml) was added to the flask. A 1.56 M butyllithium solution in hexane (4.0 ml, 6.0 mmol) was added to the above solution at −78 °C and the mixture was stirred at the same temperature for 30 min. A solution of *tert*-butyl 1-pyrrolecarboxylate (**4a**) (1.0 g, 6.0 mmol) in THF (5 ml) was added to the above solution. After the mixture had been stirred at −78 °C for 1.5 h, a solution of (−)-menthyl (*S*)-*p*-toluenesulfinate (**5a**) (883 mg, 3.0 mmol) in THF (10 ml) was added and the reaction mixture was further stirred at −78 °C for 24 h.

The reaction solution was diluted with ether, quenched with a saturated aqueous NH_4Cl, and washed with a saturated aqueous NaCl. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residual oil was subjected to flash column chromatography (ethyl acetate–hexane 1:1) to give (*S*)-**6a** (369 mg, 60% yield).[6]

The sulfinylations of *tert*-butyl 2,4-dimethyl-1-pyrrolecarboxylate (**4b**), *tert*-butyl 1-indolecarboxylate (**8a**), *tert*-butyl 5-methyl-1-indolecarboxylate (**8b**), *tert*-butyl 5-methoxy-1-indolecarboxylate (**8c**), *tert*-butyl 3-methyl-1-indolecarboxylate (**8d**) with (*Ss*)-**5a**, (−)-menthyl (*S*)-1-naphthalenesulfinate (**5b**) or (−)-menthyl (*S*)-2-methoxy-1-naphthalenesulfinate (**5c**) were carried out in the same way as described above to give (*S*)-2-pyrrolyl 1-naphthyl sulfoxide (**6b**), (*S*)-2-pyrrolyl 2-methoxy-1-naphthyl sulfoxide (**6c**), (*S*)-3,5-dimethyl-2-pyrrolyl 2-methoxy-1-naphthyl sulfoxide (**6d**), (*S*)-2-indolyl 2-methoxy-1-naphthyl sulfoxide (**9a**), (*S*)-5-methyl-2-indolyl 2-methoxy-1-naphthyl sulfoxide (**9b**), (*S*)-5-methoxy-2-indolyl 2-methoxy-1-naphthyl sulfoxide (**9c**), (*S*)-5-methoxy-2-indolyl 1-naphthyl sulfoxide (**9d**), and (*S*)-3-methyl-2-indolyl 2-methoxy-1-naphthyl sulfoxide (**9e**), respectively.

4.1.2. Compound (*S*)-6b. Yield 47%. $[\alpha]_D$ +472.4° (c=0.3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3227, 3020, 1418, (pyrrole), 1016 (sulfoxide). ^{1}H NMR (270 MHz, $CDCl_3$) δ: 6.16–6.19 (1H, m, Ar-H), 6.65–6.68 (1H, m, Ar-H), 6.82–6.86 (1H, m, Ar-H), 7.45–8.01 (6H, m, Ar-H), 8.35 (1H, dd, J=1.2,

6.1 Hz, Ar-H), 8.92 (1H, s, NH). MS *m/z* 241 (M^+). Exact mass determination: 241.0558 (calcd for $C_{14}H_{11}NOS$: 241.0561).

4.1.3. Compound (*S*)-6c. Yield 37%. $[\alpha]_D$ +86.5° (*c*=2.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3447, 3018, 1431, (pyrrole), 1026 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 4.07 (3H, s, $-OCH_3$), 6.15–6.18 (1H, m, Ar-H), 6.39–6.42 (1H, m, Ar-H), 6.94–6.97 (1H, m, Ar-H), 7.25–7.57 (3H, m, Ar-H), 7.79–7.98 (2H, m, Ar-H), 8.80 (1H, dd, *J*=0.9, 7.7 Hz, Ar-H), 9.95 (1H, s, NH). MS *m/z* 271 (M^+). Exact mass determination: 271.0693 (calcd for $C_{15}H_{13}NO_2S$: 271.1669).

4.1.4. Compound (*S*)-6d. Yield 29%. $[\alpha]_D$ +46.1° (*c*=1.0, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3443, 3018, 1431, (pyrrole), 1022 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 2.18 (3H, s, CH_3), 2.25 (3H, s, CH_3), 4.14 (3H, s, $-OCH_3$), 5.72 (1H, d, *J*=2.8 Hz, Ar-H), 7.31–7.95 (5H, m, Ar-H), 8.77 (1H, dd, *J*=0.8, 7.7 Hz, Ar-H), 8.9 (1H, s, NH). MS *m/z* 299 (M^+). Exact mass determination: 299.0961 (calcd for $C_{20}H_{17}NO_2S$: 299.0980).

4.1.5. Compound (*S*)-9a. Yield 41%. $[\alpha]_D$ +245.2° (*c*=1.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3441, 3016, 1508, 1467 (indole), 1024 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 4.04 (3H, s, $-OCH_3$), 6.58 (1H, dd, *J*=0.9, 1.1 Hz, Ar-H), 7.04–7.63 (7H, m, Ar-H), 7.81–8.02 (2H, m, Ar-H), 8.78–8.81 (1H, m, Ar-H), 9.43 (1H, s, NH). MS *m/z* 321 (M^+). Exact mass determination: 321.0780 (calcd for $C_{19}H_{15}NO_2S$: 321.0824).

4.1.6. Compound (*S*)-9b. Yield 50%. $[\alpha]_D$ +40.3° (*c*=2.53, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3211, 3011, 2943, 1431 (indole), 1022 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 2.38 (3H, s, CH_3), 4.04 (3H, s, $-OCH_3$), 6.49–6.50 (1H, dd, *J*=0.8, 0.8 Hz, Ar-H), 7.06 (1H, d, *J*=1.2 Hz, Ar-H), 7.26–8.02 (7H, m, Ar-H), 8.80 (1H, d, *J*=1.2 Hz, Ar-H), 9.32 (1H, s, NH). MS *m/z* 335 (M^+). Exact mass determination: 335.0978 (calcd for $C_{20}H_{17}NO_2S$: 355.0980).

4.1.7. Compound (*S*)-9c. Yield 35%. $[\alpha]_D$ +149.5° (*c*=0.9, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3443, 3018, 1508, 1467 (indole), 1026 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 3.77 (3H, s, $-OCH_3$), 4.02 (3H, s, $-OCH_3$), 6.49 (1H, dd, *J*=0.8, 1.3 Hz, Ar-H), 6.85–6.94 (1H, m, Ar-H), 7.23–8.05 (7H, m, Ar-H), 8.78–8.81 (1H, m, Ar-H), 9.45 (1H, s, NH). MS *m/z*: 331 (M^+). Exact mass determination: 351.0957 (calcd for $C_{20}H_{17}NO_3S$: 351.0929).

4.1.8. Compound (*S*)-9d. Yield 65%. $[\alpha]_D$ +22.9° (*c*=2.09, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3011, 2856, 1508, 1448 (indole), 1020 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 3.78 (3H, s, $-OCH_3$), 6.84–6.89 (2H, m, Ar-H), 6.89–6.96 (1H, d, *J*=17.5 Hz, Ar-H), 7.15–7.19 (1H, d, *J*=8.9 Hz, Ar-H), 7.50–8.08 (6H, m, Ar-H), 8.35–8.38 (1H, dd, *J*=1.2, 1.2 Hz, Ar-H), 8.61 (1H, s, NH). MS *m/z*: 321 (M^+). Exact mass determination: 321.0820 (calcd for $C_{19}H_{15}NO_2S$: 321.0823).

4.1.9. Compound (*S*)-9e. Yield 4.6%. $[\alpha]_D$ +51.6° (*c*=0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1504, 1448 (indole), 1020 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 2.32 (3H, s, $-CH_3$), 4.05 (3H, s, $-OCH_3$), 7.05–7.62 (7H, m, Ar-H), 7.80 (1H, d, *J*=8.2 Hz, Ar-H), 7.98 (1H, d, *J*=9.0 Hz, Ar-H), 8.86 (1H, d, *J*=8.0 Hz, Ar-H), 9.11 (1H, s, NH). MS *m/z* 335 (M^+). Exact mass determination: 335.0961 (calcd for $C_{20}H_{17}NO_2S$: 335.0980).

4.1.10. (*S*)-*N*-(Diphenylphosphano)-2-pyrrolyl *p*-tolyl sulfoxide (7a). A 25 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar was flushed with argon, and maintained under a positive pressure of argon.

A solution of **6a** (369 mg, 1.80 mmol) in THF (10 ml) was added to the flask. A 1.56 M butyllithium solution in hexane (1.3 ml, 1.98 mmol) was added at −78 °C to the above solution and the mixture was stirred at the same temperature for 45 min. A solution of chlorodiphenylphosphane ($ClPPh_2$) (477 mg, 2.16 mmol) in THF (5 ml) was added to the above solution. After the mixture was stirred at the same temperature for 2 h, the reaction solution was diluted with ether and filtered through celite. The filtrate was concentrated in vacuo. The crude product was subjected to flash column chromatography (ethyl acetate–hexane 2:3) to give (*S*)-**7a** (48 mg, 64% yield).

The phosphanations of (*S*)-**6b**–**d**, (*S*)-**9a**–**d**, or (*R*)-**12** were carried out in the same way as described above to give (*S*)-*N*-(diphenylphosphano)-2-pyrrolyl 1-naphthyl sulfoxide (**7b**), (*S*)-*N*-(diphenylphosphano)-2-pyrrolyl 2-methoxy-1-naphthyl sulfoxide (**7c**), (*S*)-3,5-dimethyl-*N*-(diphenylphosphano)-2-pyrrolyl 2-methoxy-1-naphthyl sulfoxide (**7d**), (*S*)-*N*-(diphenylphosphano)-2-indolyl 2-methoxy-1-naphthyl sulfoxide (**10a**), (*S*)-*N*-(diphenylphosphano)-5-methyl-2-indolyl 2-methoxy-1-naphthyl sulfoxide (**10b**), (*S*)-*N*-(diphenylphosphano)-5-methoxy-2-indolyl 2-methoxy-1-naphthyl sulfoxide (**10c**), (*S*)-*N*-(diphenylphosphano)-5-methoxy-2-indolyl 1-naphthyl sulfoxide (**10d**), (*S*)-*N*-(diphenylphosphano)-3-methyl-2-indolyl 2-methoxy-1-naphthyl sulfoxide (**10e**), and (*R*)-*N*-(diphenylphosphano)-7-indolyl 2-methoxy-1-naphthyl sulfoxide (**13**), respectively.

4.1.11. Compound (*S*)-7a. $[\alpha]_D$ +41.4° (*c*=1.3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3460, 3053, 1435, (pyrrole), 1045 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 2.32 (3H, s, CH_3), 6.25–6.28 (1H, m, Ar-H), 6.53–6.56 (1H, m, Ar-H), 6.61–6.64 (1H, m, Ar-H), 7.09–7.51 (14H, m, Ar-H). MS *m/z* 389 (M^+). Exact mass determination: 389.1024 (calcd for $C_{23}H_{20}NOPS$: 389.1003).

4.1.12. Compound (*S*)-7b. Yield 61%. $[\alpha]_D$ +272.4° (*c*=0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3437, 3057, 1435, (pyrrole), 1043 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 6.11–6.16 (2H, m, Ar-H), 6.61–6.63 (1H, m, Ar-H), 7.16–7.70 (14H, m, Ar-H), 7.83 (1H, d, *J*=8.1 Hz, Ar-H), 7.92 (1H, d, *J*=8.1 Hz, Ar-H), 8.40 (1H, d, *J*=7.3 Hz, Ar-H). MS *m/z* 425 (M^+). Exact mass determination: 425.0986 (calcd for $C_{26}H_{20}NOPS$: 425.1003).

4.1.13. Compound (*S*)-7c. Yield 60%. $[\alpha]_D$ +79.7° (*c*=1.3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3422, 3059, 1435, (pyrrole), 1026 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 3.74 (3H, s, $-OCH_3$), 6.23–6.26 (1H, m, Ar-H), 6.54–6.57 (1H, m, Ar-H), 6.61–6.64 (1H, m, Ar-H), 6.86–7.81 (15H, m, Ar-H), 9.08 (1H, d, *J*=8.7 Hz, Ar-H). MS *m/z* 455 (M^+).

Exact mass determination: 455.1138 (calcd for $C_{27}H_{22}NO_2PS$: 455.1109).

4.1.14. Compound (*S*)-7d. Yield 46%. $[\alpha]_D$ +118.9° (c=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3620, 3020, 1425, (pyrrole), 1032 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 2.18 (3H, s, CH_3), 2.23 (3H, s, CH_3), 3.71 (3H, s, $-OCH_3$), 5.90 (1H, s, Ar-H), 6.78–7.66 (15H, m, Ar-H), 9.28–9.31 (1H, m, Ar-H). MS m/z 483 (M^+). Exact mass determination: 483.1425 (calcd for $C_{29}H_{26}NO_2PS$: 483.1422).

4.1.15. Compound (*S*)-10a. Yield 59%. $[\alpha]_D$ +209.6° (c=0.9, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3439, 3009, 1508, 1467 (indole), 1026 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 4.01 (3H, s, $-OCH_3$), 6.57–8.02 (20H, m, Ar-H), 8.80 (1H, d, J=9.5 Hz, Ar-H). MS m/z 505 (M^+). Exact mass determination: 505.1302 (calcd for $C_{31}H_{24}NO_2PS$: 505.1266).

4.1.16. Compound (*S*)-10b. Yield 55%. $[\alpha]_D$ −55.6° (c=2.05, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400, 3053, 2928, 1508, 1467 (indole), 1026 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 2.33 (3H, s, CH_3), 3.77 (3H, s, –OMe), 6.44–6.47 (1H, d, J=8.7 Hz, Ar-H), 6.62–7.70 (18H, m, Ar-H), 8.90 (1H, d, J=8.7 Hz, Ar-H). MS m/z 519 (M^+). Exact mass determination: 519.1411 (calcd for $C_{32}H_{26}NO_2PS$: 519.1422).

4.1.17. Compound (*S*)-10c. Yield 52%. $[\alpha]_D$ +244.6° (c=0.8, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 3018, 1510, 1431 (indole), 1035 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 3.76 (3H, s, $-OCH_3$), 3.78 (3H, s, –OMe), 6.46 (2H, d, J=1.5 Hz, Ar-H), 6.64–7.70 (17H, m, Ar-H), 8.91–8.94 (1H, d, J=8.7 Hz, Ar-H). MS m/z 535 (M^+). Exact mass determination: 535.1380 (calcd for $C_{32}H_{26}NO_2PS$: 535.1371).

4.1.18. Compound (*S*)-10d. Yield 58%. $[\alpha]_D$ +104.65° (c=2.06, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3055, 3001, 2831, 1431 (indole), 1033 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 3.72 (3H, s, $-OCH_3$), 6.55–6.56 (1H, d, J=2.5 Hz, Ar-H), 6.62 (1H, d, J=0.5 Hz, Ar-H), 6.76 (1H, d, J=1.8 Hz, Ar-H), 6.94 (1H, d, J=2.1 Hz, Ar-H), 7.02–7.90 (16H, m, Ar-H), 8.12–8.15 (1H, d, J=8.4 Hz, Ar-H). MS m/z 505 (M^+). Exact mass determination: 505.1198 (calcd for $C_{31}H_{24}NO_2PS$: 505.1265).

4.1.19. Compound (*S*)-10e. Yield 17%. $[\alpha]_D$ +66.6° (c=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3177, 2959, 1506, 1450 (indole), 1020 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 2.29 (3H, s, CH_3), 3.94 (3H, s, CH_3), 7.08–7.63 (13H, m, Ar-H), 7.79–7.98 (6H, m, Ar-H), 8.85 (1H, d, J=8.9 Hz, Ar-H). MS m/z 519 (M^+). Exact mass determination: 519.1420 (calcd for $C_{32}H_{26}NO_2PS$: 519.1422).

4.1.20. Compound 13. Yield 58%. $[\alpha]_D$ +9.0° (c=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3412, 2988, 1506, 1433 (indole), 1024 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 3.26 (3H, s, $-OCH_3$), 6.18–6.25 (2H, m, Ar-H), 6.63–7.72 (17H, m, Ar-H), 8.31 (1H, dd, J=1.0, 6.8 Hz, Ar-H), 8.90–8.94 (1H, m, Ar-H). MS m/z 505 (M^+). Exact mass determination: 505.1412 (calcd for $C_{31}H_{24}NO_2PS$: 505.1266).

4.1.21. (*R*)-7-Indolyl 2-methoxy-1-naphthyl sulfoxide (12). A 50 ml two-necked flask equipped with a septum inlet and magnetic stirring bar was flushed with argon, and maintained under positive pressure of argon. A solution of 7-bromoindole (11)[9] (294 mg, 1.5 mmol) in THF (10 ml) was added at −78 °C to the flask. A 1.56 M *n*-butyllithium solution in hexane (2.0 ml, 3.0 mmol) was added to the above solution and the mixture was warmed to 0 °C during 3 h. A solution of (−)-menthyl sulfinate, (*Ss*)-**2c**, (360 mg, 1.0 mmol), in THF (5 ml) was added. After the mixture was stirred at 0 °C for 24 h, the reaction was quenched with a saturated aqueous NH_4Cl, and the mixture was diluted with ether. The solution was washed with a saturated aqueous NH_4Cl and a saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was subjected to flash column chromatography (ethyl acetate–hexane 1:1) to give **12** (308 mg, 64% yield).

4.1.22. Compound 12. $[\alpha]_D$ +486.4° (c=0.9, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3427, 3018, 1508, 1431 (indole), 1022 (sulfoxide). ^1H NMR (270 MHz, $CDCl_3$) δ: 3.85 (3H, s, $-OCH_3$), 6.56–6.58 (1H, m, Ar-H), 6.86–7.99 (9H, m, Ar-H), 8.77 (1H, d, J=8.7 Hz, Ar-H), 10.19 (1H, s, NH). MS m/z 321 (M^+). Exact mass determination: 321.0862 (calcd for $C_{20}H_{17}NO_2S$: 321.0824).

4.2. Palladium-catalyzed asymmetric nucleophilic substitution reactions of 1,3-diphenyl-2-propenyl acetate (14) with chiral *N*-(diphenylphosphino) sulfoxide ligands. General procedure

A 25 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar, and containing sodium hydride (60% oil dispersion, 37 mg, 0.912 mmol), was flushed with argon, and maintained under a positive pressure of argon. A solution of dimethyl malonate (120 mg, 0.912 mmol) in THF (2.5 ml) was added at 0 °C to the above flask and stirred for 15 min. Another 25 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar, and containing di-μ-chlorobis (π-allyl) dipalladium $[PdCl(CH_2{=}CHCH_2)]_2$ (5 mg, 0.014 mmol) and chiral *N*-(diphenylphosphano) sulfoxide ligands (0.028 mmol) was flushed with argon, and maintained under a positive pressure of argon. A solution of (±)-1,3-diphenyl-2-propenyl acetate (**14**) (115 mg, 0.456 mmol) in THF (1 ml) was added at room temperature to the above solution, and the mixture was stirred at room temperature for 30 min. The solution was added to the above solution including sodium dimethyl malonate, and the reaction mixture was stirred under the conditions listed in Table 1. The reaction solution was diluted with ether, and the solution was washed with a saturated aqueous NH_4Cl and a saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was subjected to preparative TLC (ether–hexane 1:4) to give optically active diethyl (1,3-diphenyl-2-propenyl) propanedioate (**15**).[10] The e.e. of product was determined by HPLC analysis with Chiralpak AD (*i*-PrOH–hexane 1:20, flow rate 0.5 ml/min, retention time; 28 min (*R*), 38 min (*S*)). The results are summarized in Table 1.

4.3. Structure determination of Pd-(*S*)-10a complex (16) by X-ray diffraction

A reaction mixture of (*S*)-**10a** (30 mg, 0.06 mmol) and

$PdCl_2{\cdot}(CH_3CN)_2$ (18 mg, 0.06 mmol) in EtOH (3 ml) was stirred at room temperature for 15 min. The yellowish precipitates (16 mg, 40% yield) were collected and recrystallized from CH_2Cl_2–hexane.

A palladium complex (**16**) with (*S*)-**9a** was obtained as yellow prisms.

Diffraction intensities were collected from a crystal of dimensions 0.30×0.15×0.10 mm on a Rigaku AFC-7 FOS four-circle diffractometer. Of the total 2852 unique reflections (complete for $2\theta<136.1°$, 1895 satisfied the criterion $F>3\sigma$ (F) and only these were used in the solution and refinement of the structure. Crystal data $C_{13}H_{24}NO_2SCl_2PPd$, M=682.88, orthorhombic, space group $P2_12_12_1$, a=13.263 (7), b=17.366 (8), c=12.090 (6) Å, V=2784.7 (2) Å^3, Z=4, Dc=1.629 g cm^{-3}, $F(000)$=1376, Cu Kα X-radiation (graphite monochromator), λ=1.54178 Å.

Lists of atomic parameters, bond length, and bond angles have been deposited to the Cambridge Crystallographic Data Centre.

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