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Asymmetric Allylic Alkylation and Hydrogenation with Transition Metal Complexes of Diphosphite Ligands Based on (1*S*,2*S*)-*Trans*-1,2-cyclohexanediol

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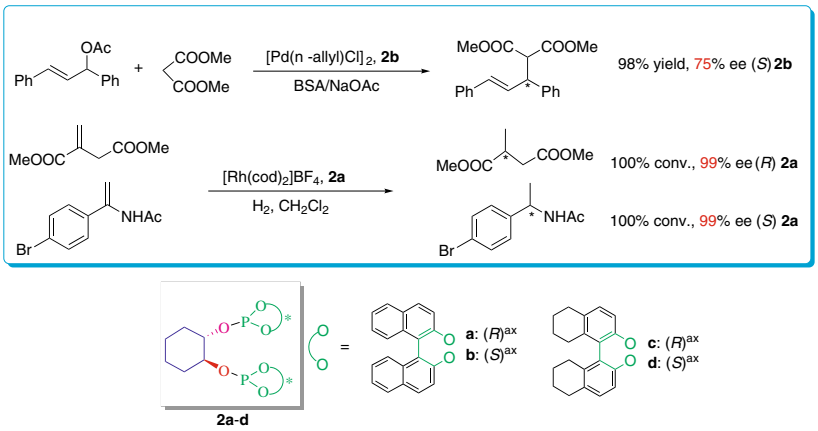
Abstract The preparation of new palladium complexes *in situ* that were composed of a series of chiral diphosphite ligands, which were derived from (1*S*,2*S*)-*trans*-1,2-cyclohexanediol, have been described. It was found that (1*S*,2*S*)-bis[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphite-cyclohexanediol was the suitable ligand in the Pd-catalyzed allylic alkylation, and up to 75% ee for (*E*)-dimethyl 2-(1,3-diphenylallyl)malonate was obtained. In compared with the results of the asymmetric allylic alkylation, (1*S*,2*S*)-bis[(*R*)-1,1′-binaphthyl-2,2′-diyl] phosphite-cyclohexanediol was proved to be the most efficient ligand in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate and enamides with up to 99% ee. The stereochemically matched combinations between the diol skeleton and diaryl moieties of the ligands were essential for inducing high enantioselectivities in the two transformations. It was found that the sense of the enantiodiscrimination of the products was mainly determined by the configuration of the binaphthyl phosphite moieties.

Graphical Abstract



Keywords Phosphite ligands · Allylic alkylation · Hydrogenation · Cyclohexanediol

1 1 Introduction

One of the main aims in organic synthesis is the catalytic enantioselective formation of C–C bonds [1, 2]. In this respect, the Pd-catalyzed asymmetric allylic alkylation with several stabilized nucleophiles and the Rh-catalyzed

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asymmetric hydrogenation are two kinds of efficient and versatile methods [3–9]. Up to now, many kinds of chiral ligands, especially mixed bidentate donor ligands, such as P-P,[10–13] P-N,[14–21] P-S,[22–24] P–O ligands,[25, 26] have been synthesized, and successfully applied in these transformations. In recent years, owing to their synthetic availability, high resistance to oxidation, and their low cost,[27] more and more attention has been devoted to phosphite ligands for these reactions and achieved magnificent results [28–30]. In spite of huge achievements in this field, however, further research is still needed to develop the new catalytic systems which can catalyze a wide range of substrates with good activity and good enantioselectivity.

In our previous work, we synthesized bidentatephosphite ligands **1a–d** (Fig. 1) using (1*R*,2*R*)-*trans*-1,2-cyclohexanediol **3** as the diol skeleton. These ligands were successfully employed in the Rh-catalyzed asymmetric hydrogenation of α,β-unsaturated carboxylic acid derivatives and enamides with up to 99% ee [31]. The correct assembly of central chirality in the scaffold and axial chirality of the biaryl phosphite moieties was very important for achieving higher enantioselectivity in this reaction. Ligands **2a–b** (Fig. 1) were synthesized by changing the configuration of the chiral diol skeleton, and applied them in the Cu-catalyzed asymmetric conjugate addition, good catalytic activity and enantioselectivity was received when complex **2b**/CuTc was used as the catalyst [32]. Considering the backbone and the biaryl phosphite moiety flexibility of ligands **1a-d** and **2a-b** play an important role in affecting the activity and enantioselectivity of the transformations,[32–35] we wondered whether the ligands **2a-b** would be suitable for the Pd-catalyzed asymmetric allylic alkylation.

In order to enrich the types of phosphite ligands, ligands **2c** and **2d** (Fig. 1), which derived from (1*S*,2*S*)-*trans*-1,2-cyclohexanediol, were also synthesized. To our delight, ligand **2b** gave excellent yields (up to 98%) and good enantioselectivities (ee up to 75%) in a CH_2Cl_2/THF mixture (v/v,1:1) using catalytic precursor [Pd(π-allyl)Cl]$_2$ and NaOAc as a base. At the same time, ligands **2a-d** were applied in the Rh-catalyzed asymmetric hydrogenation. Fortunately, 99% ee for dimethyl itaconate and *N*-(1-(4-bromophenyl)vinyl)acetamide were obtained when **2a**/[Rh(cod)$_2$]BF_4 were used as the catalyst.

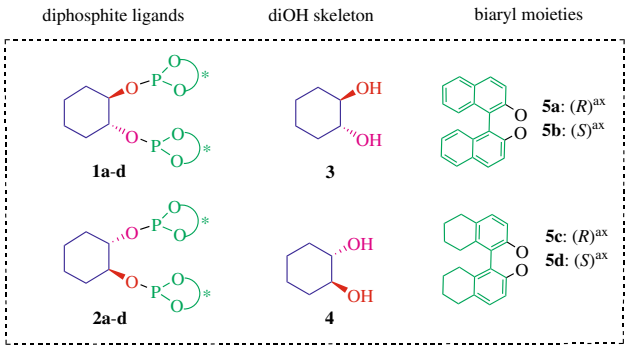


Fig. 1 The diphosphite ligands derived from (1*R*,2*R*)-*trans*-1,2-cyclohexanediol and (1*S*,2*S*)-*trans*-1,2-cyclohexanediol

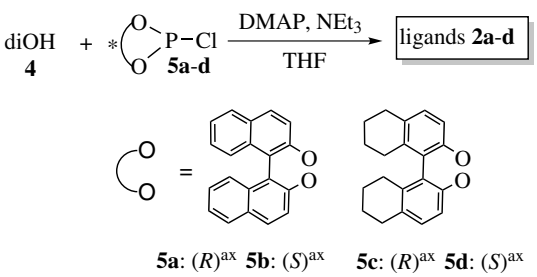
2 Materials and Methods

2.1 General Procedures

NMR spectra were recorded on Bruker 300 MHz or Bruker 400 MHz spectrometers. ^{1}H and ^{13}C NMR spectra were reported in parts per million (ppm) with TMS (δ=0.00 ppm) as an internal standard. ^{31}P NMR spectra were reported in ppm with 85% H_3PO_4 as an external reference. Proton chemical shifts (δ) and coupling constants (J) were reported in ppm and Hz, respectively. Spin multiplicities were given as s (singlet), d (doublet), t (triplet) and m (multiplet). HRMS were recorded on a Bruker microTOF-QII mass instrument. All non-aqueous reactions and manipulations were performed under an N_2 atmosphere with standard Schlenk techniques. Reactions were monitored by thin layer chromatography (TLC, silica gel GF254 plates). Column chromatography separations were conducted on silica gel (200–300 mesh). Reagents NEt_3, THF, Et_2O, hexane, 1,4-dioxane and toluene were distilled with Na and benzophenone as an indicator. CH_3CN and CH_2Cl_2 were dried over CaH_2 before use. H_8-Binaphthol was prepared according to a literature procedure [36]. All the other chemicals were obtained commercially and used without further purification.

2.2 Synthesis of Diphosphites 2a–d

As shown in Scheme 1, bidentatephosphite ligands **2c** and **2d** were synthesized stereospecifically in one step from (1*S*,2*S*)-*trans*-1,2-cyclohexanediol, and 2,2′-dihydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl



Scheme 1 The synthesis of diphosphite ligands **2c** and **2d** based on (1*S*,2*S*)-*trans*-1,2-cyclohexanediol

phosphochloridites **5c**-**d**, by starting from 2,2′-dihydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthol. Diphosphite ligands **2a**-**b** were synthesized stereospecifically according to the literature procedures,[33] and their ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, and HRMS were consistent with the expectation for them. All of the ligands were stable during the purification of neutral silica gel under a nitrogen atmosphere with reasonable yields.

2.2.1 *(1S,2S)-bis[(R)-1,1′-H_8-binaphthyl-2,2′-diyl] phosphite-cyclohexanediol* ***2c***

To a 100 mL Schlenk flask equipped with a condenser were added 1.0 g of (*R*)-H_8-binaphthol, 20 mL of toluene, and 12 mL of PCl_3. Under a nitrogen atmosphere the mixture was refluxed for 20 h. After removal of the excess PCl_3 and toluene, the residue was dissolved in 20 mL of toluene, and then was transferred to another Schlenk flask, and toluene was removed in vacuo to obtain the compound (*R*)-1,1′- H_8-binaphthyl-2,2′-diyl-chlorophosphite **5c** as a white powder, which was used directly in the following step without further purification. To a stirred solution of compound **4** (77.5 mg, 0.67 mmol), compound **5c** (529.9 mg, 1.48 mmol), and 4-dimethylaminopyridine (DMAP) (17.4 mg, 0.15 mmol) in THF (10 mL) at −15 °C, NEt_3 (0.32 mL) was slowly added using a syringe over 2 min., and the solution was stirred for 0.5 h at −15 °C. The mixture was then stirred at room temperature for 1 h. THF was distilled off in vacuo, and then toluene (20 mL) was added. The solid was removed by filtration through a pad of silica gel, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (R_f = 0.47, *n*-hexane:toluene = 1:1), and furnished ligand **2c** as a white foamy solid (231.1 mg, 45% yield). $[\alpha]_D^{20}$ = −137 (*c* 0.12, CH_2Cl_2); Mp 95–96 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.13 (d, *J* = 8.0 Hz, 2H, Ar), 7.06 (d, *J* = 8.0 Hz, 2H, Ar), 6.98 (d, *J* = 8.0 Hz, 2H, Ar), 6.85 (d, *J* = 8.2 Hz, 2H, Ar), 4.05 (s, 2H, CH), 2.86–2.70 (m, 8H, CH_2), 2.69–2.56 (m, 4H, CH_2), 2.13 (ddd, *J* = 28.0, 16.8, 8.2 Hz, 6H, CH_2), 1.81–1.68 (m, 12H, CH_2), 1.63 (s, 2H, CH_2), 1.58–1.30 (m, 8H, CH_2) ppm. ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.95, 145.45, 136.93, 134.64, 133.46, 129.50, 129.04, 127.39, 119.01, 118.70, 76.80, 76.60, 32.41, 28.49, 27.35, 27.22, 23.04, 22.13, 22.04, 22.02, 21.91 ppm. ^{31}P NMR (162 MHz, DMSO-d_6) δ 144.99 ppm. HRMS (ESI^+): calcd for $C_{46}H_{50}NaO_6P_2$ $[M+Na]^+$783.2975; found: 783.2947.

2.2.2 *(1S,2S)-bis[(S)-1,1′-H_8-binaphthyl-2,2′-diyl] phosphite-cyclohexanediol* ***2d***

(*S*)-1,1′-H_8-Binaphthyl-2,2′-diyl-chlorophosphite **5d** was synthesized by the same procedure as that of **5c**, and was used directly without further purification. Treatment of compound **4** (77.6 mg, 0.67 mmol), **5d** (530.1 mg, 1.48 mmol), and DMAP (17.8 mg, 0.15 mmol) as described for the synthesis of ligand **2c** afforded ligand **2d**, which was purified by flash chromatography (R_f = 0.44, *n*-hexane:toluene = 1:1) to produce a white solid (211.8 mg, 42% yield). $[\alpha]_D^{20}$ = +147 (*c* 0.13, CH_2Cl_2); Mp 109–110 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.12 (s, 2H, Ar), 7.05 (dd, *J* = 17.6, 8.2 Hz, 4H, Ar), 6.88 (d, *J* = 7.4 Hz, 2H, Ar), 4.15 (s, 2H, CH), 2.76 (s, 8H, CH_2), 2.58 (s, 4 H, CH_2), 2.10 (d, *J* = 10.6 Hz, 6H, CH_2), 1.71 (s, 16H, CH_2), 1.46 (s, 6H, CH_2) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.27, 145.77, 137.25, 134.96, 133.78, 129.82, 129.36, 127.71, 119.33, 119.02, 77.12, 76.92, 32.73, 28.81, 27.67, 27.54, 23.36, 22.45, 22.36, 22.34, 22.23 ppm. ^{31}P NMR (161 MHz, DMSO-d_6) δ 142.59 ppm. HRMS (ESI^+): calcd for $C_{46}H_{50}NaO_6P_2$ $[M+Na]^+$783.2975; found: 783.2965.

2.3 Representative Procedure for the Pd-Catalyzed Allylic Alkylation of 1,3-Diphenyl-2-propenyl acetate 6a

To a flame dried Schlenk tube, $[Pd(\pi\text{-allyl})Cl]_2$ (0.9 mg, 0.0025 mmol) and ligand **2a** (3.7 mg, 0.005 mmol) were added under nitrogen, followed by addition of mixed solvent (CH_2Cl_2/THF = 1:1) 2 mL. The solution was stirred at 40 °C for 0.5 h. Then 1,3-diphenyl-2-propenyl acetate **6a** (0.083 mmol) was added, and the mixture was stirred for 10 min before the addition of nucleophile (0.25 mmol), BSA (0.062 mL, 0.25 mmol), and anhydrous NaOAc (8.2 mg, 0.10 mmol). After being stirred for 12 h at room temperature, water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). And the combined organic phase was dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by flash chromatography using petroleum ether/EtOAc 20:1 (v/v) as eluant to afford the desired product. The enantiomeric excess of the products were determined by HPLC analysis with a Chiralpak AD-H column (0.46 × 25 cm).

2.4 Representative Procedure for the Rh-Catalyzed Asymmetric Hydrogenation

After stirring a solution of $[Rh(cod)_2]BF_4$ (0.0025 mmol) and ligand **2a** (0.00275 mmol) in degassed CH_2Cl_2 (1 mL) at room temperature for 1 h, a solution of the corresponding substrate (0.25 mmol) in degassed CH_2Cl_2 (2 mL) was added. The mixture was transferred via syringe into a stainless autoclave that had been previously purged with argon. The hydrogenation was carried out in the autoclave at room temperature for 6 h. After releasing H_2, the reaction mixture was passed through a short silica gel column to remove the catalyst. After evaporation of the solvent under reduced

pressure, the residue was purified by flash chromatography on silica gel. The data on conversion and enantiomeric excess of the product were determined by GC with a gamma-DEX 225 column (30 m × 0.25 mm × 0.25 μm film thickness) CP-Chirasil-DEX CB column (25 m × 0.25 mm × 0.25 μm film thickness) or AT FFAP (30 m × 0.25 mm × 0.25 μm film thickness). The absolute configuration was determined by comparison with authentic samples [37].

3 Results and Discussion

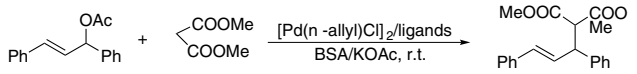
3.1 Pd-catalyzed Asymmetric Allylic Alkylation

We first examined the effects of ligands **2a–d** on the reaction. The transformation was proceeded smoothly in the presence of $[Pd(\pi\text{-allyl})Cl]_2$ (0.0025 mmol), ligand (0.005 mmol), *N,O*-bis-(trimethylsilyl)acetamide (BSA, 0.25 mmol), and a catalytic amount of KOAc as base in CH_2Cl_2 at room temperature for 24 h. The results were summarized in Table 1. 52% yield and 22% ee (*R*) were obtained when using **2a**/$[Pd(\pi\text{-allyl})Cl]_2$ as the catalyst (Table 1, entry 1). Ligand **2b**, which bore (*S*)-binaphthyl moieties in comparison with ligand **2a**, gave 65% yield and 29% ee (*S*) (Table 1, entry 2). Ligand **2c** gave 43% yield and 13% ee (*R*) for the product **8a** (Table 1, entry 3), in contrast, the configuration of the H_8-binaphthyl moiety was opposite to that of **2c** and gave 18% ee (*S*) (Table 1, entry 4) when ligand **2d** was used. Based on the data of the yields and enantioselectivities, ligand **2b** was screened as the most efficient ligand. Moreover, it was found that the sense of enantioselectivity was mainly determined by the configuration of the binaphthyl or H_8-binaphthyl moiety of ligands **2a–d**, and an (*R*)-binaphthyl fragment gives an (*R*)-product, and conversely an (*S*)-product for an (*S*)-binaphthyl.

Using the catalyst prepared *in situ* from $[Pd(\pi\text{-allyl})Cl]_2$ and ligand **2b**, the AAA of substrate **6a** and dimethyl malonate **7a** with a variety of solvents was investigated, and a profound solvent effect on the reaction was observed. Enantioselectivities 34% ee (*S*) and 37% ee (*S*) were obtained in CH_3CN and Et_2O, respectively (Table 1, entries 5–6). 52% yield and 43% (*S*) ee were obtained when using THF as the solvent (Table 1, entry 7). Toluene was proven to be the unbeneficial solvent for this transformation (Table 1, entry 8). In order to further improve the yield and enantioselectivity, we attempted to use mixed solvents in this reaction. The yield increased from 65 to 85% and up to 61% ee (*S*) was received, when 2 mL of THF was added into 2 mL of CH_2Cl_2 (Table 1, entry 9).

Palladium catalyst precursors, such as $[Pd_2(dba)_3]\cdot CHCl_3$, $Pd(TFA)_2$, $Pd(OAc)_2$, and so on, were examined (Table 2, entries 1–5). Similar results were received when $[Pd_2(dba)_3]\cdot CHCl_3$ and $Pd(CH_3CN)_2Cl_2$

Table 1 The effect of ligand structures and solvents on the enantioselectivity for the allylic alkylation of (*E*)-1,3-diphenyl-2-propenyl acetate **6a** with dimethyl malonate **7a**



6a **7a** **8a**

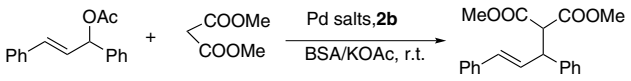
Entry	Ligands	Solvent	Yield[a](%)	%ee[b] (conf.)
1	**2a**	CH_2Cl_2	52	22 (*R*)
2	**2b**	CH_2Cl_2	65	29(*S*)
3	**2c**	CH_2Cl_2	43	13 (*R*)
4	**2d**	CH_2Cl_2	56	18 (*S*)
5	**2b**	CH_3CN	95	34 (*S*)
6	**2b**	Et_2O	30	37 (*S*)
7	**2b**	THF	52	43 (*S*)
8	**2b**	Toluene	n.d	n.d
9	**2b**	CH_2Cl_2/THF	85	61 (*S*)
10	**2b**	CH_2Cl_2/CH_3CN	84	28 (*S*)
11	**2b**	THF/CH_3CN	91	30 (*S*)

Reaction conditions: $[Pd(\pi\text{-allyl})Cl]_2$ (0.0025 mmol), ligand (0.005 mmol), compound **6a** (0.083 mmol), compound **7a** (0.25 mmol), BSA (0.25 mmol), KOAc (0.1 mmol), solvent (4 mL), 25 °C, 24 h

[a]Isolated yield

[b]The enantiomeric excess of compound **8a** was determined by HPLC analysis (column Chiralpak AD-H 0.46 × 25 cm). The absolute configuration of **8a** was determined by comparison with authentic sample

Table 2 Screening of Pd salts in asymmetric allylic alkylation



6a **7a** **8a**

Entry	Pd salts	L/Pd	Yield[a](%)	%ee[b] (conf.)
1	$[Pd_2(dba)_3]\cdot CHCl_3$	1.0	62	32 (*S*)
2	$Pd(TFA)_2$	1.0	61	42 (*S*)
3	$Pd(OAc)_2$	1.0	48	28 (*S*)
4	$Pd(acac)_2$	1.0	n.d	n.d
5	$Pd(CH_3CN)_2Cl_2$	1.0	65	33 (*S*)
6	$[Pd(\pi\text{-allyl})Cl]_2$	0.5	71	40 (*S*)
7	$[Pd(\pi\text{-allyl})Cl]_2$	2.0	75	47 (*S*)

Reaction conditions: Pd salts (0.0025 mmol), ligand (0.0025-0.01 mmol), compound **6a** (0.083 mmol), compound **7a** (0.25 mmol), BSA (0.25 mmol), KOAc (0.1 mmol), solvents CH_2Cl_2/THF (4 mL,v/v), 25 °C, 12 h

[a]Isolated yield

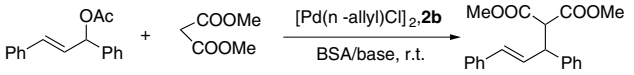
[b]The enantiomeric excess and the absolute configuration of the products were determined using the same conditions as noted in Table 1

were used as the precursors (Table 2, entries 1 *vs*. 5). The activity obtained with $Pd(TFA)_2$ was lower than $[Pd_2(dba)_3]\cdot CHCl_3$, but the enantiomeric excess was higher (Table 2, entry 2 *vs*. 1). Both low activity and enantioselectivity were gained when $Pd(OAc)_2$ was used (Table 2, entry 3). No product was even detected in this reaction when using $Pd(acac)_2$ instead of $[Pd(\pi\text{-allyl})Cl]_2$ (Table 2, entry 4). Based the above results, $[Pd(\pi\text{-allyl})Cl]_2$ was proven to be the most suitable catalyst precursor. Then the effects of ligand-to-palladium ratio on the catalytic activities and enantioselevtivities of the transformation were investigated. The results showed that reducing or increasing the loading of ligand had a detrimental effect on the reaction (Table 2, entries 6–7). High enantioselectivity (61% ee) was obtained when the loading of ligand was 1.0 equiv (Table 1, entry 13). The trade-off between activities and enantioselectivities was optimum with $[Pd(\pi\text{-allyl})Cl]_2$ and a ligand-to-palladium ratio of 1:1.

Next, the role of bases in allylic alkylation of compound **6a** and **7a** was probed, and the results were summarized in Table 3. High yield but poor ee were obtained when potassium bicarbonate was used (Table 3, entry 1). Potassium carbonate or caesium carbonate, instead of potassium bicarbonate gave (*S*)-**8a** in 61 and 76% yields with 43 and 42% ee, respectively (Table 3, entries 2–3). Using lithium carbonate as the base, the reaction gave a higher enantioselectivity (51%) as compared to caesium carbonate (Table 3, entry 4). Similar enantioselectivities were received when lithium acetate and cesium acetate were used in this reaction (Table 3, entries 5–6). Up to 75% ee was obtained when sodium acetate was used as the base (Table 3, entry 7). These results indicated that base had an important influence on the ee values. Considering the yield and ee value, NaOAc among the bases screened was found as the most befitting base in conjunction with *N,O*-bis-(trimethylsilyl)acetamide. By lowering the reaction temperature from 25 to −10 °C, the ee values of product **8a** decreased from 75 to 70%, and the yield significantly decreased (Table 3, entries 7–9).

Then, the scope of alkylation substrate and malonates was explored in the Pd-catalyzed AAA, and the results were collected in Table 4. Several substituted aromatic allylic acetates, containing either electron-donating groups

Table 3 Screening of bases in asymmetric allylic alkylation



6a **7a** **8a**

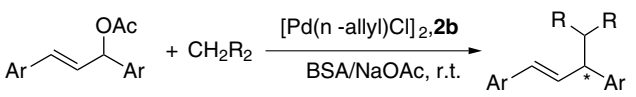
Entry	Base	T (°C)	Yield[a] (%)	%ee[b] (conf.)
1	$KHCO_3$	25	82	30 (*S*)
2	K_2CO_3	25	61	43 (*S*)
3	Cs_2CO_3	25	76	42 (*S*)
4	Li_2CO_3	25	87	51 (*S*)
5	LiOAc	25	79	40 (*S*)
6	CsOAc	25	86	41 (*S*)
7	NaOAc	25	98	75 (*S*)
8	NaOAc	0	90	74 (*S*)
9	NaOAc	−10	82	70 (*S*)

Reaction conditions: $[Pd(\pi\text{-allyl})Cl]_2$ (0.0025 mmol), ligand **2b** (0.005 mmol), compound **6a** (0.083 mmol), compound **7a** (0.25 mmol), BSA (0.25 mmol), base (0.1 mmol), CH_2Cl_2/THF (4 mL,v/v), -10-25 °C, 12 h

[a]Isolated yield

[b]The enantiomeric excess and the absolute configuration of the products were determined using the same conditions as noted in Table 1

Table 4 Scope of substrates for Pd-catalyzed asymmetric allylic alkylation



6 **7** **8**

Entry	Ar	R	Product	Yield[a](%)	%ee[b] (conf.)
1	Ph	COOEt	**8b**	97	53 (*S*)
2	Ph	COOBn	**8c**	99	42 (*S*)
3	2-BrC_6H_4	COOMe	**8d**	68	29 (*S*)
4	2-BrC_6H_4	COOEt	**8e**	86	21 (*S*)
5	2-BrC_6H_4	COOBn	**8 f**	99	33 (*S*)
6	3-BrC_6H_4	COOMe	**8 g**	68	48 (*S*)
7	3-BrC_6H_4	COOEt	**8h**	98	63 (*S*)
8	3-BrC_6H_4	COOBn	**8i**	99	53 (*S*)
9	4-BrC_6H_4	COOMe	**8j**	64	56 (*S*)
10	4-BrC_6H_4	COOEt	**8k**	98	60 (*S*)
11	4-BrC_6H_4	COOBn	**8l**	99	48 (*S*)
12	2-MeC_6H_4	COOMe	**8 m**	37	4 (*S*)
13	2-MeC_6H_4	COOEt	**8n**	72	4 (*S*)
14	2-MeC_6H_4	COOBn	**8o**	61	2 (*S*)
15	3-MeC_6H_4	COOMe	**8p**	51	48 (*S*)
16	3-MeC_6H_4	COOEt	**8q**	99	60 (*S*)
17	3-MeC_6H_4	COOBn	**8r**	99	52 (*S*)
18	4-MeC_6H_4	COOMe	**8 s**	64	53 (*S*)
19	4-MeC_6H_4	COOEt	**8t**	99	62 (*S*)
20	4-MeC_6H_4	COOBn	**8u**	99	40 (*S*)

Reaction conditions: $[Pd(\pi\text{-allyl})Cl]_2$ (0.0025 mmol), ligand **2b** (0.005 mmol), compound **6** (0.083 mmol), compound **7** (0.25 mmol), BSA (0.25 mmol), NaOAc (0.1 mmol), CH_2Cl_2/THF (4 mL,v/v), 25 °C, 12 h

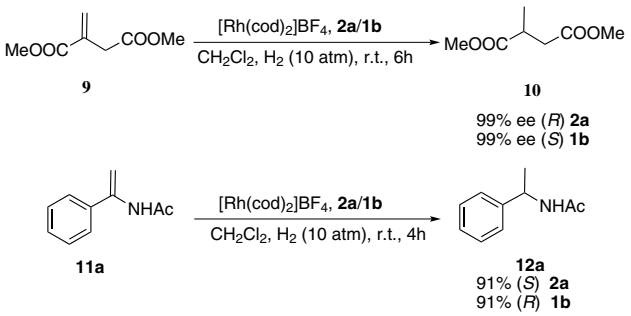
[a]Isolated yield

[b]The enantiomeric excess and the absolute configuration of the products were determined using the same conditions as noted in Table 1

or electron-withdrawing groups at the *ortho*-, *meta*- or *para*-position of the phenyl ring, were subjected to the optimal set of reaction conditions. Moderate to good ees were received when the electron-withdrawing groups at the *meta*- or*para*-position of the phenyl ring. (Table 4, entries 6–11 *vs*. 3–5). It was demonstrated that the nucleophile have a significant impact on the reaction outcome. Compared with dimethyl and dibenzyl malonate, when diethyl malonate was used as the nucleophile, better ee values were received (Table 4, entries 7, 10 vs. 6, 8, 9, 11). The same trend was also observed when the electron-donating groups groups at the *meta*- or *para*-position of the phenyl ring (Table 4, entries 12–20). The results also suggested that the electronic property of the substrate did not have a significant impact on the reaction outcome when the substituent group at the *meta*- and *para*-posotion of the pheny ring (Table 4, entries 6–11 *vs*. 15–20). And excellent yields and good enantioselectivities were obtained when using diethyl malonate as the nucleophile (Table 4, entries 7, 10, 16, 19).

3.2 Rh-catalyzed asymmetric hydrogenation

It is noted that, for ligands **2a**, (*R*)-BINOL was matched cooperatively to the corresponding (1*S*,2*S*)-*trans*-1,2-cyclohexanediol skeleton, while for ligands **1b**, (*S*)-BINOL and (1*R*,2*R*)-*trans*-1,2-cyclohexanediol were matched in Rh-catalyzed asymmetric hydrogenation (Scheme 2). This result was different from our previous conclusion in the asymmetric allylic alkylation.



Scheme 2 Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate **9** and *N*-(1-phenylvinyl)acetamide **11a**

Ligand **2a** proved to be effective for the hydrogenation of *N*-(1-phenylvinyl)acetamide **11a** (Scheme 2). The same ee values but the opposite configuration for the product **12a** was received when **1b**/$[Rh(cod)_2]BF_4$ was used as the catalyst [31].

The Rh-catalyzed asymmetric hydrogenation of other enamides (**11b, 11c, 11e** and **11f**), which were not examined in our previous work,[31] were assessed. As shown in Fig. 2, the hydrogenation appeared to be insensitive to the position of the substituent on the phenyl ring. Moreover, the enantioselectivity was also obviously affected by the presence of either electron-donating or electron-withdrawing groups on the phenyl ring. Therefore, high enantioselectivity was obtained by introducing the electron-withdrawing groups at the *para* positions of the aryl group. To our delight, up to 99% ee was obtained when using **11h** as the substrate. This is another successful case for substrate **11h** that ever reported with phosphite ligands [38–41]. The stereochemically matched combinations of (1*S*,2*S*)-*trans*-1,2-cyclohexanediol backbone and (*R*)-binaphthyl in the ligand **2a** and (1*R*,2*R*)-*trans*-1,2-cyclohexanediol backbone and (*S*)-binaphthyl in the ligand **1b**, were essential for inducing high enantioselectivity. It is worth noting that, unlike aromatic allylic acetates and dimethyl itaconate, an (*R*)-binaphthyl fragment gives an (*S*)-product and conversely an (*R*)-product for an (*S*)-binaphthyl when enamide was used as the substrate.

4 Conclusion

In summary, the newly catalytic systems, which were readily constituted from a catalytic precursor $[Pd(\pi\text{-allyl})Cl]_2$ and ligands **2a**-**d**, were successfully developed in the allylic alkylation with up to 75% ee. The matched combination

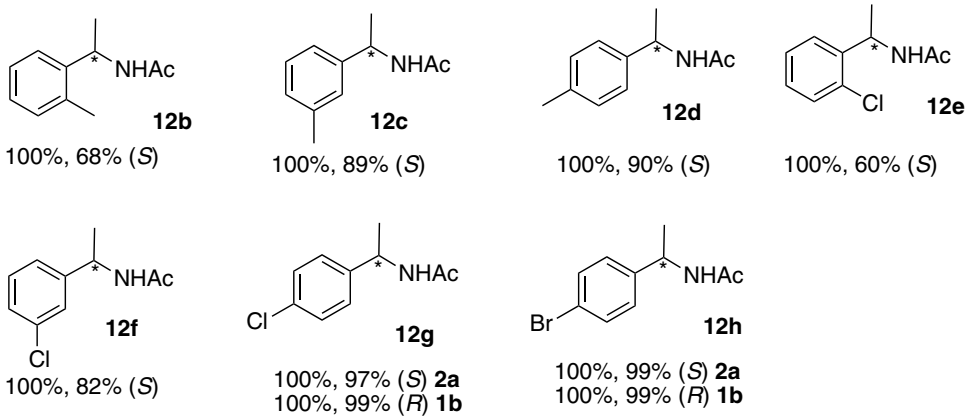


Fig. 2 Selected results for the asymmetric Rh-catalyzed hydrogenation of substrates **11b**–**h** using $[Rh(cod)_2]BF_4$/**2a** catalytic system

of the chirality at C-1 and C-2 centers of (1*S*,2*S*)-*trans*-1,2-cyclohexanediol backbone and (*S*)-binaphthyl moieties was fundamental to obtain higher enantioselectivity and activity using ligand **2b**. The $[Rh(cod)_2]BF_4$/ ligands **1b** and **2a** complexes respectively were found to be effective in the asymmetric hydrogenation of dimethyl itaconate and enamides, reaching up to 99% ee for dimethyl 2-methylsuccinate and *N*-(1-(4-bromophenyl)ethyl)acetamide under the optimal conditions. It is noted that ligand **1b** is enantiomer of ligand **2a**, and for ligands **1b**, (*S*)-BINOL and (1*R*,2*R*)-*trans*-1,2-cyclohexanediol were matched, and (*R*)-BINOL was matched cooperatively to the corresponding (1*S*,2*S*)-*trans*-1,2-cyclohexanediol skeleton for ligands **2a**. Moreover, the sense of the enantiodiscrimination of the products was mainly determined by the configuration of the binaphthyl phosphite moieties. Additional studies highlighting the potential of these ligands in other asymmetric reactions are currently underway.

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