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Kinetic resolution of allylic esters in palladium-catalyzed asymmetric allylic alkylations using C–N bond axially chiral aminophosphine ligands

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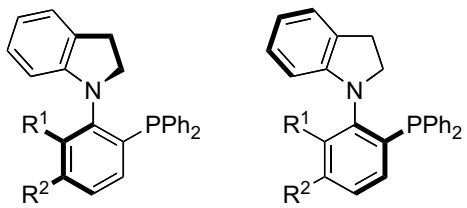
ABSTRACT

Chiral allylic esters, such as (*R*)-1,3-diphenyl-2-propenyl acetate (*R*)-**2a**, were synthesized by kinetic resolution in a palladium-catalyzed asymmetric allylic alkylation using *N*-aryl indoline type C–N bond axially chiral aminophosphines (*S*)-**1** as ligands.

1. Introduction

In recent years, palladium-catalyzed allylic alkylation has been extended to catalytic asymmetric synthesis as a versatile C–C bond forming tool.[1] Among the many chiral ligands designed for this reaction, chiral P,N-ligands have played an important role owing to their steric and electronic asymmetry,[2,3] such as PHOX ligands,[4] binaphthyl-based ligands,[5] and the QUINAP-type ligand.[6] We recently reported a palladium-catalyzed asymmetric allylic alkylation using chiral phosphinohydrazones,[7] pyrrolidinyl-containing chiral aminophosphines,[8] and *N*-aryl indoline type C–N bond axially chiral aminophosphines.[9]

Although the usual synthetic target is the product from a nucleophilic addition, several reports have recently appeared documenting the kinetic resolution of allylic acetates and carbonates over the course of these reactions.[10] Herein, we report the synthesis of chiral allylic esters by the kinetic resolution of racemic allylic esters in palladium-catalyzed asymmetric allylic alkylation using *N*-aryl indoline type C–N bond axially chiral aminophosphines **1**.



(*S*)-**1** (*R*)-**1**

a: $R^1 = CH_2OAc$, $R^2 = H$
b: $R^1 = Me$, $R^2 = H$
c: $R^1 = CF_3$, $R^2 = H$
d: R^1-R^2 = -$(CH)_4$-

2. Results and discussion

Although we had already reported the synthesis of chiral **3a** by palladium-catalyzed asymmetric allylic alkylation of racemic 1,3-diphenyl-2-propenyl acetate (±)-**2a** using chiral aminophosphines **1a**–**d** for 24 h,[9a] we investigated the kinetic resolution of the starting material in this reaction. At first, we examined the palladium-catalyzed asymmetric allylic alkylation of racemic 1,3-diphenyl-2-propenyl acetate (±)-**2a** with 3.0 equiv of dimethyl malonate (DMM) using chiral aminophosphines (*S*)-**1a** in THF for 4 h at 25 °C (Table 1, entry 1). In this case, the reaction conversion was 19% and the chiral unreacted allylic acetate (*R*)-**2a** was recovered in 17% ee with the corresponding product (*R*)-**3a** (89% ee). A difference in the rate of reaction for the two enantiomers of the starting material was observed. The (*S*)-enantiomer of **2a** reacted significantly faster than the (*R*)-enantiomer. Next, we investigated the ability of ligands (*S*)-**1b**–**d** (entries 3, 5, and 6). Using aminophosphine ligand (*S*)-**1c**, the reaction proceeded in 52% conversion while the unreacted chiral allylic acetate (*R*)-**2a** was recovered in 69% ee. In this case, the selectivity factor (*S* value) was 8.9 (entry 5). Conversely, (*S*)-**1b** and **1d** were not effective ligands for this kinetic resolution (entries 3 and 6). We investigated the effect of reaction time in this kinetic resolution using aminophosphine ligand (*S*)-**1b** (entries 2–4). The reaction conversion and ee of **2a** were increased with longer reaction times. On the other hand, the *S* value decreased while the ee of product **3a** increased. When the reaction conversion reached 94%, product (*R*)-**3a** was obtained in 86% ee and the unreacted acetate (*R*)-**2a** was recovered in 98% ee, although the *S* value was low (entry 4). Next, the effect of the amount of nucleophile was investigated (entry 5 vs 7). The reaction with 0.6 equiv of DMM gave (*R*)-**3a** in good enantioselectivity (97% ee) with 52% conversion after 8 h. In this case, the *S* value was 11.7 and the enantioselectivity of unreacted acetate (*R*)-**2a** was 75% ee. The concentration of reaction solvent was also investigated (entries 7, 8, and 10). The diluted reaction conditions caused the reaction rate to slow and *S* value to increase. Changing the amount of catalyst to 4 mol %, the reactivity and *S* value were decreased (entry 8 vs

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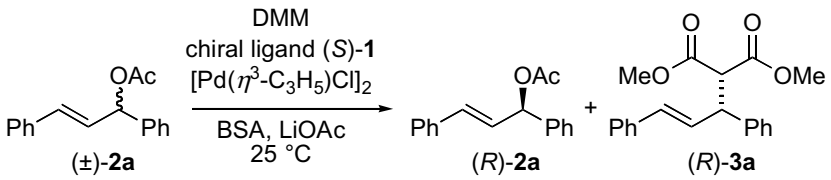
Table 1
Kinetic resolution in palladium-catalyzed asymmetric allylic alkylation using (*S*)-**1**[a]



Entry	Ligand	Time (h)	DMM (equiv)	Solv.	Concn (M)	Conv[b] (%)	ee of (*R*)-**2a**[c] (%)	ee of (*R*)-**3a**[c] (%)	*S*[d]
1	(*S*)-**1a**	4	3.0	THF	0.5	19	17	89	7.2
2	(*S*)-**1b**	2	3.0	THF	0.5	26	20	73	4.3
3	(*S*)-**1b**	4	3.0	THF	0.5	76	79	83	3.5
4	(*S*)-**1b**	6	3.0	THF	0.5	94	98	86	3.2
5	(*S*)-**1c**	4	3.0	THF	0.5	52	69	94	8.9
6	(*S*)-**1d**	4	3.0	THF	0.5	23	9	55	2.0
7	(*S*)-**1c**	8	0.6	THF	0.5	52	75	97	11.7
8	(*S*)-**1c**	18	0.6	THF	0.25	54	82	96	13.5
9[e]	(*S*)-**1c**	24	0.6	THF	0.25	17	16	86	11.3
10	(*S*)-**1c**	24	0.6	THF	0.125	37	48	94	15.8
11	(*S*)-**1c**	18	0.6	Et_2O	0.25	60	96	86	17.2
12	(*S*)-**1c**	18	0.6	DCM	0.25	60	98	93	21.4
13	(*S*)-**1c**	18	0.6	$PhCF_3$	0.25	56	89	91	16.1
14	(*S*)-**1c**	18	0.6	PhMe	0.25	54	92	95	23.9
15[f]	(*S*)-**1c**	18	0.6	PhMe	0.25	Trace	—	—	—
16[g]	(*S*)-**1c**	18	0.6	PhMe	0.25	Trace	—	—	—
17[h]	(*S*)-**1c**	18	0.6	PhMe	0.25	55	81	89	12.7
18[i]	(*S*)-**1c**	48	0.6	PhMe	0.25	22	27	96	107
19	(*S*)-**1c**	40	0.65	PhMe	0.25	60	95(37)[j]	95(59)[k]	14.8
20	(*S*)-**1c**	40	0.7	THF	0.25	71	99(24)[j]	94(66)[k]	11.2

[a] The reactions were carried out in various solvents at 25 °C with DMM and BSA (3.0 equiv), in the presence of LiOAc (2 mol %) and ligand (*S*)-**1** (10 mol %) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (5 mol %).
[b] Determined by ^1H NMR.
[c] Determined by HPLC analysis using a chiral column (Daicel CHIRALCEL® OD-H).
[d] $S = \ln[(1 - C/100)(1 - ee/100)]/\ln[(1 - C/100)(1 + ee/100)]$ (*C* = conversion; ee = ee of **2a**).
[e] This reaction was carried out using 4 mol % of ligand (*S*)-**1c** and 2 mol % of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$.
[f] This reaction was carried out using 5 mol % of $[IrCl(C_8H_{12})]_2$ instead of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$.
[g] This reaction was carried out using 10 mol % of $(C_7H_8)Mo(CO)_3$ instead of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$.
[h] This reaction was carried out at 35 °C.
[i] This reaction was carried out at 5 °C.
[j] Values in parentheses are isolated yields of **2a**.
[k] Values in parentheses are isolated yields of **3a**.

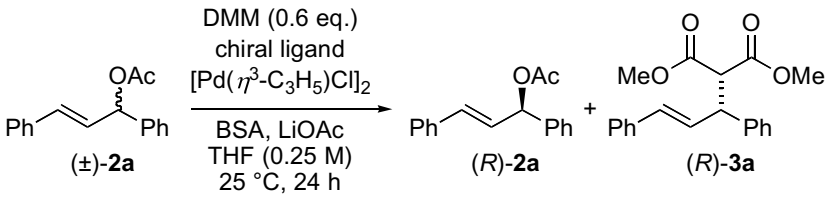
9). We examined the effect of reaction solvents using chiral aminophosphines (*S*)-**1c** for 18 h at 25 °C (entries 8, 11–14). When the reaction was carried out in diethyl ether instead of THF, the *S* value was increased to 17.2, but the enantioselectivity of (*R*)-**3a** decreased to 86% ee (entry 11). When PhMe was used as a solvent, the reaction conversion was 56% and the chiral unreacted allylic acetate (*R*)-**2a** was recovered in 92% ee (*S* value = 23.9) with the corresponding product (*R*)-**3a** in 95% ee. We investigated the kinetic resolution in iridium and molybdenum-catalyzed asymmetric allylic alkylation. Unfortunately neither reaction proceeded (entries 15 and 16). We also investigated the effect of reaction temperature. The reaction conversion was increased slightly to 35 °C, but the *S* value and the enantioselectivity of (*R*)-**3a** decreased (entry 14 vs 17). On the other hand, the reaction was carried out at 5 °C, and the reaction rate was very slow (entry 18). Using 0.65 equiv of dimethyl malonate in PhMe, the reaction gave 59% of (*R*)-**3a** in 95% ee and 37% of unreacted (*R*)-**2a** in good enantioselectivity (95% ee) for 40 h (entry 19). Furthermore, when using 0.7 equiv of dimethyl malonate in THF, unreacted acetate (*R*)-**2a** was obtained in 24% with high enantioselectivity (99% ee) (entry 20).

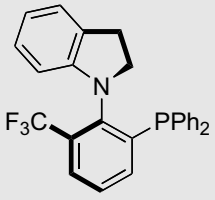
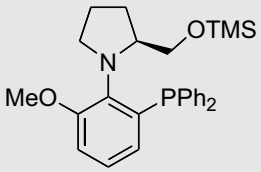
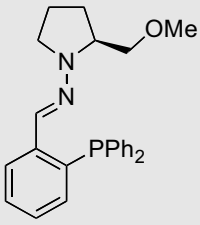
Under the reaction conditions of 4 mol % of catalyst in THF (Table 1, entry 9), we examined the kinetic resolution of (±)-**2a** in the palladium-catalyzed asymmetric allylic alkylation using pyrrolidinyl-containing chiral aminophosphine (*S*)-**4**[8] and chiral phosphinohydrazone (*S*)-**5**[7] instead of (*S*)-**1c**. As shown in Table 2, chiral hydrazone (*S*)-**5** was a slightly effective ligand for kinetic resolution (*S* value = 3.8) (entry 3), but the selectivity was low when using (*S*)-**4** as a ligand (entry 2).

We next attempted the reaction of various allylic esters such as racemic 1,3-diphenyl-2-propenyl pivalate (±)-**2b**[11] and benzoate (±)-**2c**[12] with DMM and acetate (±)-**2a** with diethyl malonate in PhMe for 18 h at 25 °C (Table 3). As shown in entries 2 and 3, the unreacted chiral pivalate (*R*)-**2b** and benzoate (*R*)-**2c**[10a] were recovered with moderate enantioselectivities, and the corresponding products (*R*)-**3** were obtained with good enantioselectivity. The reaction with diethyl malonate gave (*R*)-**3b** in good enantioselectivity (94% ee) at 53% conversion. In this case, the *S* value was 13.8 while the enantioselectivity of unreacted acetate (*R*)-**2a** was 78% ee.

Finally, we suggested the plausible asymmetric induction process of the kinetic resolution in palladium-catalyzed asymmetric allylic alkylation of (±)-**2a** with DMM using chiral aminophosphines (*S*)-**1c** as shown in Scheme 1. There are two candidates, **A** and **B**, which are considerable reaction intermediates formed from palladium complex with chiral ligands (*S*)-**1c**. According to the result, (*S*)-**2a** reacted with the chiral palladium complex significantly faster than (*R*)-**2a**. Thus, **C** was easily formed from **A** due to the steric hindrance of the phenyl rings between the allylic substrate and the ligand. In addition, the nucleophilic attack to **C** occurs predominantly at the allyl terminus, *trans* to the better π–acceptor (P > N).[13] As a result, the (*R*)-product **3a** was obtained mainly from (*S*)-**2a**, while (*R*)-**2a** was recovered in this reaction using the chiral aminophosphine (*S*)-**1c** as a ligand.

Table 2
The kinetic resolution in palladium-catalyzed asymmetric allylic alkylation using various chiral ligands[a]



Entry	Ligand	Conv.[b] (%)	ee of (*R*)-**2a**[c] (%)	ee of (*R*)-**3a**[c] (%)	*S*[d]
1	 (*S*)-**1c**	17	16	86	11.3
2	 (*S*)-**4**	58	2.6	−89	1.1
3	 (*S*)-**5**	29	21	74	3.8

[a] The reactions were carried with DMM (0.6 equiv) and BSA (3.0 equiv), in the presence of LiOAc (2 mol %) and ligand (*S*)-**1** (4 mol %) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2 mol %) in THF (0.25 M) at 25 °C for 24 h.
[b] Determined by ^1H NMR.
[c] Determined by HPLC analysis using a chiral column (Daicel CHIRALCEL® OD-H).
[d] $S = \ln[(1 - C/100)(1 - ee/100)]/\ln[(1 - C/100)(1 + ee/100)]$ (C = conversion; ee = ee of **2a**).

3. Conclusions

In conclusion, we found that C–N bond axially chiral aminophosphine (*S*)-**1c** was an effective ligand for the kinetic resolution in the palladium-catalyzed asymmetric allylic alkylation. Chiral allylic esters, such as (*R*)-1,3-diphenyl-2-propenyl acetate (*R*)-**2a**, were obtained by kinetic resolution with good enantioselectivities.

4. Experimental

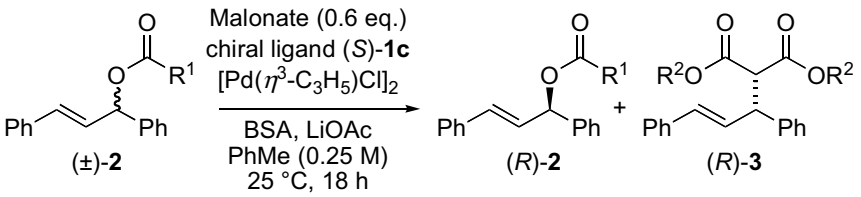
4.1. General procedure for the kinetic resolution in palladium-catalyzed allylic alkylation: optimization of reaction conditions (Table 1, entry 14)

To a mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.01 mmol, 3.9 mg), chiral aminophosphine ligand (*S*)-**1c** (0.02 mmol, 9.0 mg), and LiOAc (0.004 mmol, 0.3 mg) in PhMe (0.7 mL) was added racemic allylic ester **2a** (0.2 mmol, 50.5 mg) at room temperature under an Ar atmosphere. After 30 min, BSA (0.6 mmol, 0.15 mL) and dimethyl malonate (0.12 mmol) in PhMe (1.2 M, 0.1 mL) was added at 25 °C. After 18 h, the reaction mixture was diluted with diethyl ether and water. The organic layer was washed with brine and dried over $MgSO_4$. The filtrate was concentrated with a rotary evaporator and the residue was passed through a pipette plug of silica gel (diethyl ether) to give a mixture of **2a** and **3a**. The reaction conversion was determined by ^1H NMR. The ee of **2a** and **3a** was determined by HPLC analysis using a chiral column (Daicel CHIRALCEL® OD-H, flow rate = 0.2 mL/min, hexane/^{i}PrOH = 99:1, detection at 254 nm: t_R 32.3 min ((*S*)-**2a**), t_R 36.6 min ((*R*)-**2a**), t_R 41.4 min [(*R*)-**3a**], t_R 44.5 min [(*S*)-**3a**)].

4.2. General procedure for kinetic resolution in palladium-catalyzed allylic alkylation in PhMe (Table 1, entry 19)

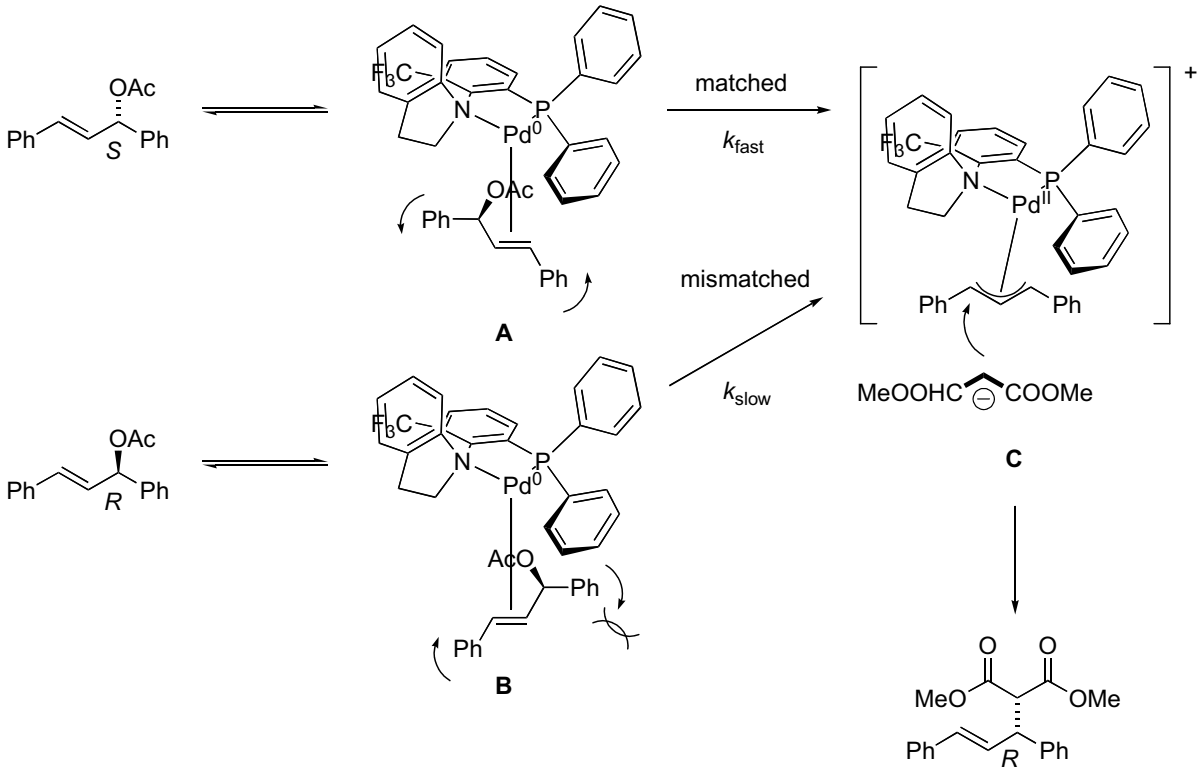
To a mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.01 mmol, 3.9 mg), chiral aminophosphine ligand (*S*)-**1c** (0.02 mmol, 9.0 mg), and LiOAc

Table 3
Kinetic resolution in palladium-catalyzed asymmetric allylic alkylation of various allylic esters using (*S*)-**1c**[a]



Entry	R^1	R^2	Conv.[b] (%)	ee of recovered allylic ester[c] (%)	ee of product[c] (%)	S[d]
1	Me	Me	54	92 (*R*)-**2a**	95 (*R*)-**3a**	23.9
2	*t*-Bu	Me	44	55[e](49)[f] (*R*)-**2b**	94(43)[f] (*R*)-**3a**	9.7
3	Ph	Me	56	59(42)[f] (*R*)-**2c**	94(55)[f] (*R*)-**3a**	5.0
4	Me	Et	53	78(43)[f] (*R*)-**2a**	94 [g](49)[f] (*R*)-**3b**	13.8

[a] The reactions were carried with malonate (0.6 equiv) and BSA (3.0 equiv), in the presence of LiOAc (2 mol %) and ligand (*S*)-**1c** (10 mol %) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (5 mol %) in PhMe (0.25 M) at 25 °C for 18 h.
[b] Determined by ^{1}H NMR.
[c] Determined by HPLC analysis using a chiral column (Daicel CHIRALCEL® OD-H).
[d] $S = \ln[(1 - C/100)(1 - ee/100)]/\ln[(1 - C/100)(1 + ee/100)]$ (C = conversion; ee = ee of **2**).
[e] Determined by HPLC analysis using a chiral column (Daicel CHIRALPAK® AS-H).
[f] Values in parentheses are isolated yields.
[g] Determined by HPLC analysis using a chiral column (Daicel CHIRALCEL® OJ).



Scheme 1. Plausible asymmetric induction process during kinetic resolution in palladium-catalyzed asymmetric allylic alkylation using chiral ligands (*S*)-**1c**.

(0.004 mmol, 0.3 mg) in PhMe (0.7 mL) was added racemic allylic ester **2a** (0.2 mmol, 50.5 mg) at room temperature under an Ar atmosphere. After 30 min, BSA (0.6 mmol, 0.15 mL) and dimethyl malonate (0.13 mmol) in PhMe (1.3 M, 0.1 mL) were added at 25 °C. After 40 h, the reaction mixture was diluted with diethyl ether and water. The organic layer was washed with brine and dried over $MgSO_4$. The filtrate was concentrated with a rotary evaporator and the reaction conversion was determined by ^{1}H NMR. The residue was purified by column chromatography (hexane/ethyl acetate/triethylamine = 34:1:6) to give (*R*)-**2a** (19 mg, 0.07 mmol) and (*R*)-**3a** (38 mg, 0.12 mmol).

4.2.1. Compound (*R*)-2a[10e]

37% yield; 95% ee; $[\alpha]_D^{20} = -4.9$ (*c* 0.30, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.14 (s, 3H), 6.35 (dd, *J*= 6.9 and 15.7 Hz, 1H), 6.44 (d, *J*= 6.9 Hz, 1H), 6.64 (d, *J*= 15.7 Hz, 1H), 7.21-7.43 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 76.1, 126.7, 127.0, 127.5, 128.0, 128.1, 128.6, 128.6, 132.6, 136.2, 139.2, 170.0; EI-MS *m/z* (rel intensity) 252 (M^+, 9).

4.2.2. Compound (*R*)-3a[9a]

59% yield; 95% ee; $[\alpha]_D^{20} = +11.8$ (*c* 0.20, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.51 (s, 3H), 3.70 (s, 3H), 3.95 (d, *J* = 10.9 Hz,

1H), 4.27 (dd, J = 8.5 and 10.9 Hz, 1H), 6.33 (dd, J = 8.5 and 15.8 Hz, 1H), 6.48 (d, J = 15.8 Hz, 1H), 7.17–7.34 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.2, 52.4, 52.6, 57.6, 126.4, 127.1, 127.5, 127.8, 128.5, 128.7, 129.1, 131.8, 136.8, 140.1, 167.8, 168.2; EI-MS m/z (rel intensity) 324 (M^+, 13).

4.3. General procedure for the kinetic resolution of various allylic esters 2 in palladium-catalyzed allylic alkylation (Table 3)

To a mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.01 mmol, 3.9 mg), chiral aminophosphine ligand (*S*)-**1c** (0.02 mmol, 9.0 mg), and LiOAc (0.004 mmol, 0.3 mg) in PhMe (0.7 mL) was added racemic allylic ester **2** (0.2 mmol) at room temperature under an Ar atmosphere. After 30 min, BSA (0.6 mmol, 0.15 mL) and malonate (0.12 mmol) in PhMe (1.2 M, 0.1 mL) were added at 25 °C. After 18 h, the reaction mixture was diluted with diethyl ether and water. The organic layer was washed with brine and dried over $MgSO_4$. The filtrate was concentrated with a rotary evaporator and the reaction conversion was determined by ^{1}H NMR. The residue was purified by column chromatography (hexane/ethyl acetate/triethylamine = 34:1:6) to give (*R*)-**2** and (*R*)-**3**.

4.3.1. Compound (*R*)-2b[11]

(Table 3, entry 2) 29 mg, 0.10 mmol, 49% yield; 55% ee (Daicel CHIRALPAK® AS-H, flow rate = 0.25 mL/min, hexane/^{i}PrOH = 99:1, detection at 254 nm: t_R 17.0 min ((*R*)-**2b**), t_R 18.8 min ((*S*)-**2b**)); $[\alpha]_D^{20} = +3.4$ (c 0.35, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 9H), 6.32 (dd, J = 6.8 and 15.6 Hz, 1H), 6.41 (d, J = 6.9 Hz, 1H), 6.63 (d, J = 15.6 Hz, 1H), 7.23–7.41 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.1, 38.9, 75.7, 126.67, 126.72, 127.8, 127.9, 128.0, 128.5, 128.5, 132.2, 136.3, 139.6, 177.3; EI-MS m/z (rel intensity) 294 (M^+, 4).

4.3.2. Compound (*R*)-3a

(Table 3, entry 2) 28 mg, 0.09 mmol, 43% yield; 94% ee.

4.3.3. Compound (*R*)-2c[10a,12]

(Table 3, entry 3) 26 mg, 0.08 mmol, 42% yield; 59% ee (Daicel CHIRALCEL® OD-H + OD-H, flow rate = 0.30 mL/min, hexane/^{i}PrOH = 99:1, detection at 254 nm: t_R 49.1 min (CD: λ_{ext} ($\Delta\varepsilon$) 254 (−)) ((*S*)-**2c**), t_R 55.0 min (CD: λ_{ext} ($\Delta\varepsilon$) 254 (+)) ((*R*)-**2c**)); $[\alpha]_D^{20} = +8.0$ (c 0.30, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.47 (dd, J = 6.8 and 15.9 Hz, 1H), 6.69–6.76 (m, 2H), 7.21–7.59 (m, 13H), 8.13 (d, J = 8.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 76.6, 126.7, 127.0, 127.5, 128.0, 128.2, 128.4, 128.6, 128.6, 129.7, 130.3, 132.8, 133.1, 136.1, 139.3, 165.6; EI-MS m/z (rel intensity) 314 (M^+, 3).

4.3.4. Compound (*R*)-3a

(Table 3, entry 3) 35 mg, 0.11 mmol, 55% yield; 94% ee.

4.3.5. Compound (*R*)-2a

(Table 3, entry 4) 22 mg, 0.09 mmol, 43% yield; 78% ee.

4.3.6. Compound (*R*)-3b[8c]

(Table 3, entry 4) 35 mg, 0.10 mmol, 49% yield; 94% ee (Daicel CHIRALCEL® OJ, flow rate = 0.7 mL/min, hexane/^{i}PrOH = 95:5, detection at 254 nm: t_R 13.6 min ((*R*)-**3b**), t_R 16.0 min ((*S*)-**3b**)); $[\alpha]_D^{20} = +16.8$ (c 0.31, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H), 3.90–4.00 (m, 3H), 4.17 (q, J = 7.1 Hz, 2H), 4.26 (dd, J = 8.4 and 10.9 Hz, 1H), 6.33 (dd, J = 8.4 and 15.7 Hz, 1H), 6.48 (d, J = 15.8 Hz, 1H), 7.16–7.33 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 14.1, 49.2, 57.7, 61.3, 61.5, 126.3, 127.1, 127.5, 128.0, 128.4, 128.6, 129.3, 131.6, 136.8, 152.2, 167.4, 167.8; EI-MS m/z (rel intensity) 352 (M^+, 15).

4.4. Determination of absolute configuration of 2b

4.4.1. Resolution of 1,3-diphenyl-2-propene-1-ol

The resolution was carried out by the use of a chiral stationary phase column [Chiralcel OD-H (1.0 ϕ × 25 cm), flow rate = 0.5 mL/min, hexane/^{i}PrOH = 95:5] to give both enantiomers. A 0.25 mL of solution was injected for each batch using 110 mg of (±)-1,3-diphenyl-2-propene-1-ol in EtOH (4.25 mL). Enantiomers were eluted at 38 min for (*S*)-isomer and 48 min for (*R*)-isomer.[14]

4.4.2. (*S*)-1,3-Diphenyl-2-propene-1-ol

38 mg, 68%; >99% ee; $[\alpha]_D^{20} = -31.9$ (c 0.29, $CHCl_3$); HPLC (Daicel CHIRALCEL® OD-H, 0.46 ϕ × 25 cm, flow rate = 0.5 mL/min, hexane/^{i}PrOH = 90:10, detection at 254 nm) t_R = 33.1 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03 (s, br, 1H), 5.40 (d, J = 4.6 Hz, 1H), 6.39 (dd, J = 6.5 and 15.8 Hz, 1H), 6.70 (d, J = 15.8 Hz, 1H), 7.21–7.46 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.1, 126.3, 126.6, 127.8, 127.8, 128.6, 128.6, 130.6, 131.5, 136.5, 142.7; EI-MS m/z (rel intensity) 210 (M^+, 34).

4.4.3. (*R*)-1,3-Diphenyl-2-propene-1-ol

38 mg, 68%; >99% ee; $[\alpha]_D^{20} = +34.8$ (c 0.30, $CHCl_3$); HPLC (Daicel CHIRALCEL® OD-H, 0.46 ϕ × 25 cm, flow rate = 0.5 mL/min, hexane/^{i}PrOH = 90:10, detection at 254 nm) t_R = 43.0 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03 (s, br, 1H), 5.40 (d, J = 4.6 Hz, 1H), 6.39 (dd, J = 6.5 and 15.8 Hz, 1H), 6.70 (d, J = 15.8 Hz, 1H), 7.24–7.46 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.1, 126.3, 126.6, 127.8, 127.8, 128.6, 128.6, 130.6, 131.5, 136.5, 142.7; EI-MS m/z (rel intensity) 210 (M^+, 30).

4.4.4. Preparation of (*R*)-2b

To a mixture of (*R*)-1,3-diphenyl-2-propene-1-ol (0.179 mmol, 38 mg), triethylamine (0.9 mL), and DMAP (0.04 mmol, 4 mg) was added pivaloyl chloride (0.179 mmol, 23 μL) at room temperature. After 21 h, the reaction mixture was diluted with 2 M HCl aq and diethyl ether. The organic layer was washed with water, brine, and dried over $MgSO_4$. The filtrate was concentrated with a rotary evaporator and the residue was purified by column chromatography (hexane/ethyl acetate = 100:1) to give (*R*)-**2b** (16 mg, 0.054 mmol).

4.4.5. Compound (*R*)-2b

30% yield; 97% ee (Daicel CHIRALPAK® AS-H, flow rate = 0.25 mL/min, hexane/^{i}PrOH = 99:1, detection at 254 nm): t_R 20.2 min (major, (*R*)-**2b**), t_R 23.0 min (minor, (*S*)-**2b**)); $[\alpha]_D^{20} = +4.1$ (c 0.30, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 9H), 6.32 (dd, J = 6.7 and 15.6 Hz, 1H), 6.41 (d, J = 7.0 Hz, 1H), 6.63 (d, J = 15.5 Hz, 1H), 7.24–7.41 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.1, 38.9, 75.7, 126.67, 126.72, 127.8, 127.9, 128.0, 128.5, 128.5, 132.2, 136.3, 139.6, 177.3; EI-MS m/z (rel intensity) 294 (M^+, 4).

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