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Highly Diastereoselective Palladium-Catalyzed Cyclizations of 3,4-Allenylic Hydrazines and Organic Halides—Highly Stereoselective Synthesis of Optically Active Pyrazolidine Derivatives and the Prediction of the Stereoselectivity

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Abstract: Pyrazolidines containing two chiral centers, an interesting class of heterocyclic compounds possessing a range of biological activities, have been prepared highly diastereoselectively (up to 95:5) through asymmetric Pd-$(OAc)_2$-catalyzed cyclizations between the easy available optically active allenylic hydrazines and organic halides in THF in the presence of (*R*,*R*)-Bn-Box (**L2**) as the ligand. It was observed 1) that in most cases (3*R*,5*S*)-pyrazolidines were obtained in good yields with very high enantiopurities (>99%) and high diastereoselectivities (up to 95:5) in the presence of (*R*,*R*)-Bn-Box (**L2**), 2) that aryl halides containing electron-donating or -withdrawing groups, heteroaryl, and 1-alkenyl iodides are all suitable substrates for this diastereoselective cyclization, 3) that the absolute configurations of the newly formed chiral centers in the pyrazolidines depend on the structure of substrate **1**, and 4) that the enantio- and diastereopurities of the *trans*-pyrazolidines are co-controlled by the chiralities of the chiral catalysts and the substrates. A model for prediction of the enantiopurities of the products and the diastereoselectivities of the reactions based on an HPLC study of the starting hydrazines and the products was established.

Keywords: allenes · asymmetric catalysis · heterocycles · hydrazines · palladium

Introduction

Pyrazolidines are an interesting class of heterocyclic compounds with biological activities that have stimulated scientists to design novel therapeutic agents with mimetic scaffolds.[1] One of the major challenges in these objectives is the development of efficient methods for the stereoselective synthesis of optically active pyrazolidines.[2] Although transition-metal-catalyzed reactions for the synthesis of heterocyclic compounds have been demonstrated as one of the most powerful protocols in modern synthetic organic chemistry,[3] transition-metal-catalyzed asymmetric reactions for optically active pyrazolidines have not been well developed.[4]

Recently, we and others have developed transition-metal-catalyzed coupling cyclization reactions between functionalized allenes and organic halides.[5] However, there are only a few reports on catalytic diastereo- or enantioselective coupling cyclization reaction between these building blocks to afford optically active heterocyclic compounds. Larock et al. reported asymmetric palladium-catalyzed hetero- and carboannulation of allenes using functionalized aryl and vinylic halides with *ee*s of up to 86%,[6] while in 2004 we reported a method for the synthesis of pyrazolidine derivatives through Cu- and Pd-catalyzed one-pot tandem reactions of functionalized 2-(2′,3′-allenyl)-β-keto esters, dibenzyl azodicarboxylate, and organic halides with poor diastereoselectivity (*cis*/*trans* 33:77–45:55).[7b] In this paper we report a double asymmetric induction method[8] for highly diastereoselective syntheses of pyrazolidine derivatives with high enantiopurities through asymmetric cyclizations between optically active 3,4-allenylic hydrazines and organic halides.

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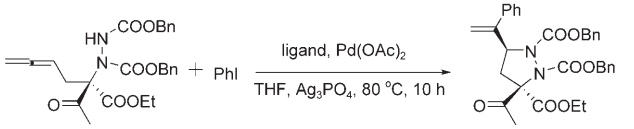
Results and Discussion

Our initial efforts started with the cyclization of optically active allenylhydrazine **1a**[7b] (Table 1) with organic halides.

Table 1. Ligand and solvent effects on Pd-catalyzed asymmetric coupling—cyclization of **1a** with PhI.[a]

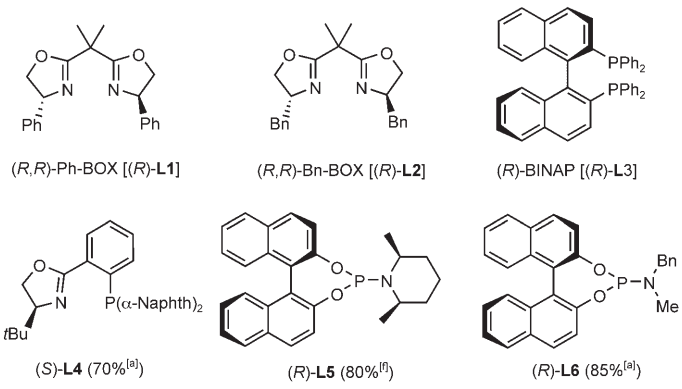


(*R*)-**1a** 98% *ee* — **2a** — *trans*-(3*R*,5*S*)-**3aa**

Entry	Ligand	Yield of **3aa** [%][b]	*ee* [%] (3*R*,5*S*)[c]	*ee* [%] (3*R*,5*R*)[c]	dr[d]
1	**L1**	69	99	88	87:13
2	**L2**	81	98	85	95:5
3	**L3**	83	98	99	57:43
4[e]	**L2**	83	97	90	86:14
5[f]	**L2**	76	99	76	93:7

[a] Reactions were typically conducted with 0.2 mmol of **1a**, 0.4 mmol of **2a**, 0.08 mmol Ag_3PO_4, 5 mol% $Pd(OAc)_2$, and 10 mol% ligand in 2 mL THF in a tube with a screw cap at 80°C. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] dr = *trans*/*cis*. [e] DMF was used as solvent. [f] 1,4-Dioxane was used as solvent.

Accordingly, we screened several optically active palladium catalysts prepared in situ from easily available chiral ligands and $Pd(OAc)_2$ (Table 1). In view of the fact that significantly enhanced levels of enantioselectivity could be achieved in the presence of silver salts,[6,9] we tried the use of Ag_3PO_4 as the base. As shown in Table 1, the reaction in THF at 80°C in the presence of 0.4 equiv of Ag_3PO_4 as the base afforded the desired products with interesting diastereoselectivities when bisoxazoline (*R*,*R*)-**L1** and $Pd(OAc)_2$ were used as the catalyst (entry 1, Table 1). To our surprise, when bisoxazoline (*R*,*R*)-**L2** was then used as the ligand, the desired pyrazolidine **3aa** was produced with very high enantiopurity (98%) and in good yield (81%) and diastereoselectivity (95:5) (entry 2, Table 1). The use of BINAP ((*R*)-**L3**), however, provided the desired heterocycle **3aa** with a poor diastereoselectivity (entry 3, Table 1). Notably, the bulky ligand (*S*)-**L4** and the P-N ligands (*R*)-**L5** and (*R*)-**L6** were ineffective for the cyclization reaction. It was found that the reaction carried out in DMF and catalyzed by (*R*,*R*)-**L2**/$Pd(OAc)_2$ gave the product with a lower diastereoselectivity (entry 4, Table 1). When 1,4-dioxane was used as the solvent, the result was similar to that seen in the reaction carried in THF (entry 5, Table 1). On the basis of these results, 1.0 equiv of **1**, 1.2 equiv of **2**, 0.4 equiv of Ag_3PO_4, 5 mol% of $Pd(OAc)_2$, and 10 mol% of (*R*,*R*)-Bn-Box **L2** in THF were defined as the standard conditions.



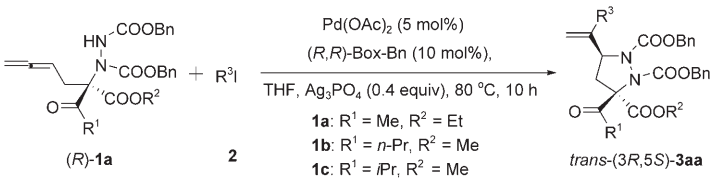
(*R*,*R*)-Ph-BOX [(*R*)-**L1**] (*R*,*R*)-Bn-BOX [(*R*)-**L2**] (*R*)-BINAP [(*R*)-**L3**]

(*S*)-**L4** (70%[a]) (*R*)-**L5** (80%[f]) (*R*)-**L6** (85%[a])

[a] Yield of **1a** recovered.

Next, the scope of the highly diastereoselective catalytic cyclization reactions between optically active allenylhydrazines and organic halides was studied under the standard conditions (Table 2). It can be concluded: 1) that in most cases (3*R*,5*S*)-pyrazolidines were obtained in good yields and with very high enantiopurities (>99%) and high diastereoselectivities (up to 95:5), 2) that aryl halides containing electron-donating or -withdrawing groups can be used (entries 2–5, Table 2), 3) that heteroaryl or 1-alkenyl iodides are also suitable substrates for this diastereoselective cyclization process (entries 6 and 7, Table 2), the configuration of the C=C bond in the 1-alkenyl iodide remained unchanged during the reaction (entry 6, Table 2), 4) that R^1 and R^2 can be different alkyl groups (entries 9 and 10, Table 2), and 5) that the reaction favors the formation of

Table 2. $Pd(OAc)_2$/(*R*,*R*)-Bn-Box-catalyzed asymmetric coupling-cyclization reactions of **1** with different organic halides.[a]



(*R*)-**1a** — **2** — *trans*-(3*R*,5*S*)-**3aa**

Entry	(*R*)-**1** (% *ee*)	R^3I (**2**)	Yield **3** [%][b]	*ee* [%][c] (3*R*,5*S*)	dr[d]
1	**1a** (98)	C_6H_5I	81 (**3aa**)	99	94:6
2	**1a** (98)	4-MeC_6H_4I	81 (**3ab**)	99	92:8
3[e]	**1a** (98)	4-MeC_6H_4I	80 (**3ab**)	99	93:7
4	**1a** (98)	4-$MeOC_6H_4I$	85 (**3ac**)	99	94:6
5	**1a** (98)	4-$MeO_2CC_6H_4I$	83 (**3ad**)	97	95:5
6	**1a** (98)	(*E*)-*n*-$C_4H_9C_2H_2I$	82 (**3ae**)	99	93:7
7	**1a** (98)	2-iodothiophene	67 (**3af**)	99	95:5
8	**1a** (98)	4-BrC_6H_4I	86 (**3ag**)	>95	93:7
9[f]	**1b** (98)	C_6H_5I	81 (**3ba**)	99	91:9
10[f]	**1c** (98)	C_6H_5I	78 (**3ca**)	99	92:8

[a] Reactions were typically conducted under standard conditions. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] dr = *trans*/*cis*. [e] 1,4-Dioxane was used as solvent. [f] Reaction temperature: 70°C.

trans-pyrazolidines in the presence of (*R*,*R*)-**L2**/$Pd(OAc)_2$ as the catalyst.

In order to determine the origin of the asymmetric induction more precisely, a series of control experiments were conducted. As discussed above, the reaction between (*R*)-**1a** and PhI in the presence of $Pd(OAc)_2$/(*R*,*R*)-**L2** as the catalyst is diastereoselective (*cis*/*trans* 6:94), affording the *trans*-pyrazolidine (3*R*,5*S*)-**3aa** with high enantiopurity (99% *ee*) (Table 3, Entry 1). In contrast, when (*S*,*S*)-**L2** was used, (3*R*,5*R*)-**3aa** was obtained as the major product with high enantiopurity but moderate diastereoselectivity, which may be attributed to the mismatch situation between the substrate and the ligand. On the other hand, when (*S*)-**1** was used as the substrate in the presence of $Pd(OAc)_2$/(*R*,*R*)-**L2**, products (3*S*,5*S*)-**3aa** and (3*S*,5*R*)-**3aa** with inverted configurations were formed in 99% *ee* and 92% *ee*, respectively, though the diastereoselectivity was poor. When the chiral ligand was changed to (*S*,*S*)-**L2**, the corresponding *trans*-(3*S*,5*R*)-**3aa** was obtained from (*S*)-**1** with excellent enantiopurity and highly diastereoselectively. From these results, it can be concluded: 1) that the absolute configurations of the newly formed chiral centers in the pyrazolidines depend on the structure of substrate **1**, and 2) that the enantio- and diastereopurities for the pyrazolidines are co-controlled by the chirality of the chiral catalysts and substrates.

Furthermore, after monitoring of the reaction between (*R*)-**1a** and PhI shown in entry 1 of Table 1, it was found that no racemization was observable for the starting material (*R*)-**1a**, the major product (3*R*,5*S*)-**3aa**, or the minor product (3*R*,5*R*)-**3aa**.

However, it should be noted that the enantiopurity of the minor product [(3*R*,5*R*)-**3aa** vs (3*S*,5*S*)-**3aa**] is lower than that of the starting (*R*)-**1a** (entry 1, Table 1), which may be easily explained by careful analysis of the HPLC results relating to the preparation of **3aa** from (*R*)-**1** with 98.0% *ee* and from (*S*)-**1** with 97.6% *ee*: 98.87% of starting material **1**—that is, pure (*R*)-**1**—was converted into 5.16% of (3*R*,5*R*)-**3aa** and 93.71% of (3*R*,5*S*)-**3aa**, while 1.13% of starting material **1**—that is, pure (S)-**1**—was converted into 0.80% of (3*S*,5*S*)-**3aa** and 0.33% of (3*S*,5*R*)-**3aa** (entry 1, Table 4), due to the mismatched situation of (*S*)-**1** with (*R*,*R*)-Box-Bn **L2** (entry 2, Table 4). With this analysis, it is reasonable to predict that the racemic **1** should also yield the major isomer (3*R*,5*S*)-**3aa** with 42% *ee* and the minor isomer (3*S*,5*S*)-**3aa** with 84% *ee* (entry 3, Table 4). Actually, the corresponding treatment of *rac*-**1** by the standard procedure in Table 2 did yield the major isomer (3*R*,5*S*)-**3aa** with 43% *ee* and the minor isomer (3*S*,5*S*)-**3aa** with 86% *ee* [Eq. (1) in Table 4].

Furthermore, the reaction between (*R*)-**1a** with 84% *ee* and PhI under the standard conditions afforded *trans*-(3*R*,5*S*)-**3aa** with 95% *ee* as expected (Scheme 1).

Table 4. Chiral HPLC analysis of different **3aa** samples.[a]

Entry	Sample source of **3aa** (% *ee*)	Integration of HPLC peaks for each stereoisomer of **3a**					
		Isomers **3aa** from (*R*)-**1a** [%]			Isomers **3aa** from (*S*)-**1a** [%]		
		Total	(3*R*,5*R*)	(3*R*,5*S*)	Total	(3*S*,5*S*)	(3*S*,5*R*)
1	(*R*)-**1a** (98)	*98.87*	5.16	93.71	*1.13*	0.80	0.33
2	(*S*)-**1a** (97.6)	***1.46***	**0.36**	**1.10**	***98.54***	60.56	37.98
3[b]	*rac*-**1a** (0)	*50.00*	2.61	47.39	*50.00*	30.73	19.27
4	*rac*-**1a** (0)	*49.00*	2.38	46.62	*51.00*	32.42	18.58
5[b]	(*R*)-**1a** (84)	*92.00*	4.80	87.20	*8.00*	4.92	3.08
6	(*R*)-**1a** (84)	*93.13*	4.82	88.31	*6.68*	4.56	2.31

[a] See footnote a of Table 2. [b] Predicted by the results in entries 1 and 2 of Table 4 as follows:

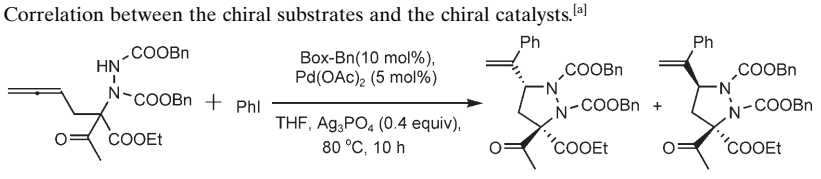
$$\%\ \text{of } (3R,5R)\text{-}\mathbf{3aa} = \frac{5.16}{5.16 + 93.71} \times \%\ \text{of } (R)\text{-}\mathbf{1a} \text{ in the starting } \mathbf{1a}$$

$$\%\ \text{of } (3R,5S)\text{-}\mathbf{3aa} = \frac{93.71}{5.16 + 93.71} \times \%\ \text{of } (R)\text{-}\mathbf{1a} \text{ in the starting } \mathbf{1a}$$

$$\%\ \text{of } (3S,5S)\text{-}\mathbf{3aa} = \frac{60.56}{60.56 + 37.98} \times \%\ \text{of } (S)\text{-}\mathbf{1a} \text{ in the starting } \mathbf{1a}$$

$$\%\ \text{of } (3S,5R)\text{-}\mathbf{3aa} = \frac{37.98}{56.56 + 37.98} \times \%\ \text{of } (S)\text{-}\mathbf{1a} \text{ in the starting } \mathbf{1a}$$

Table 3. Correlation between the chiral substrates and the chiral catalysts.[a]



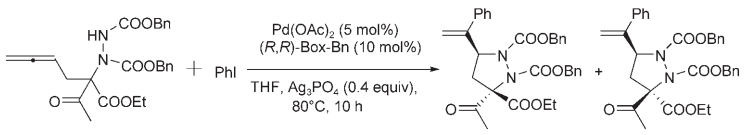
1 **2a** *cis*-(3*R*,5*R*)-**3aa** *trans*-(3*R*,5*S*)-**3aa**

Entry	**1a** (98% *ee*)	Ligand	Yield [%][b]	*ee* (*cis*) [%][c]	*ee* (*trans*) [%] [c]	dr[d]
1	(*R*)-**1a**	(*R*,*R*)-**L2**	81	73 (3*R*,5*R*)	99 (3*R*,5*S*)	6:94
2	(*R*)-**1a**	(*S*,*S*)-**L2**	81	97 (3*R*,5*R*)	90 (3*R*,5*S*)	65:35
3	(*S*)-**1a**	(*R*,*R*)-**L2**	80	99 (3*S*,5*S*)	94 (3*S*,5*R*)	61:39
4	(*S*)-**1a**	(*S*,*S*)-**L2**	85	85 (3*S*,5*S*)	99 (3*S*,5*R*)	6:94

[a] See footnote [a] of Table 2. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] dr = *cis*/*trans*.

Conclusions

In conclusion, asymmetric palladium-catalyzed cyclizations between the easily available 3,4-allenylic hydrazines and organic halides have been developed for the highly diastereoselective synthesis of highly optically active pyrazolidines. We have also established a model with which the enantiopurities of the products and the diastereoselectivities of the



	Yield of **3aa**	dr (*cis* / *trans*)	*ee* of *cis*-(3*S*,5*S*)-**3aa**	*ee* of *trans*-(3*R*,5*S*)-**3aa**
rac-**1a** (0% *ee*)	79%	35:65 (33.3:66.7)[a]	86% (84%)[a]	43% (42%)[a]
(*R*)-**1a** (84% *ee*)	85%	9:91 (10.7:90.3)[a]	-3% (1%)[a]	95% (93%)[a]

Scheme 1. [a] The numbers in parentheses are the predicted ones based on the data presented in entries 3 and 5 in Table 4.

reactions may be easily predicted. This reaction has paved the way for asymmetric cyclizations of functionalized allenes for asymmetric synthesis of enantiomerically enriched cyclic compounds. Further study in this area is now in progress in our laboratory.

Experimental Section

Typical procedure for the synthesis of optically active 3,4-allenylic hydrazines with 2-(*N*,*N*-Bis(benzyloxycarbonyl)hydrazino)-2-(buta-2,3-dienyl)-3-oxobutyric acid ethyl ester [(*R*)-1a] as an example:[7b] Ethyl 2-(buta-2,3-dienyl)-3-oxobutanoate (1.328 g, 7.2 mmol) and dibenzyl azodicarboxylate (DBAD, 2.999 g, 9.1 mmol) were added at 0 °C to a solution of $Cu(OTf)_2$ (270 mg, 0.75 mmol) and (*S*,*S*)-(−)-2,2′-isopropylidenebis(4-phenyl-2-oxazoline) (255 mg, 0.78 mmol) in dry CH_2Cl_2 (60 mL), previously stirred at room temperature for 1 h. The mixture was then stirred at this temperature for a further 4 h with monitoring by TLC. After evaporation, the residue was purified by flash chromatography on silica gel (petroleum ether/ether 2:1) to afford (*R*)-**1a** (3.373 g, 97%) in 98% *ee* as determined by HPLC analysis (Chiralcel AD, 25% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 39.3 (major), 50.1 min (minor); viscous liquid; $[\alpha]_{20}^{D}$ = +4.0 (*c* = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.38–7.22 (m, 10H), 6.70–6.30 (m, 1H), 5.30–5.02 (m, 5H), 4.70–4.50 (m, 2H), 4.30–3.98 (m, 2H), 2.92–2.60 (m, 2H), 2.50–2.00 (m, 3H), 1.28–1.02 ppm (m, 3H); IR (neat): $\tilde{\nu}$ = 3309, 2982, 1956, 1731, 1221 cm^{-1}; MS (MALDI): *m*/*z*: found: 503.2 [*M*+Na]$^+$; HRMS (MALDI): *m*/*z*: calcd for $C_{26}H_{28}N_2O_7Na^+$: 503.1789; found: 503.1794 [*M*+Na]$^+$.

2-(*N*,*N*-Bis(benzyloxycarbonyl)hydrazino)-2-(buta-2,3-dienyl)-3-oxobutyric acid ethyl ester [(*S*)-1a]: The reaction of ethyl 2-(buta-2,3-dienyl)-3-oxobutanoate (258 mg, 1.42 mmol), dibenzyl azodicarboxylate (DBAD, 663 mg, 2.0 mmol), $Cu(OTf)_2$ (53 mg, 10 mol%), and (*R*,*R*)-(+)-2,2′-isopropylidenebis-(4-phenyl-2-oxazoline) (54 mg, 10.4 mol%) in dry CH_2Cl_2 (12 mL) afforded (S)-**1a** (627 mg, 92%) of 97.6% *ee* as determined by HPLC analysis (Chiralcel AD, 25% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 37.3 (minor), 45.7 min (major); viscous liquid; $[\alpha]_{20}^{D}$ = −3.0 (*c* = 0.92, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.38–7.22 (m, 10H), 6.88–6.60 (m, 1H), 5.30–5.01 (m, 5H), 4.68–4.50 (m, 2H), 4.26–3.98 (m, 2H), 2.92–2.60 (m, 2H), 2.50–1.90 (m, 3H), 1.29–0.98 ppm (m, 3H).

2-(*N*,*N*-Bis(benzyloxycarbonyl)hydrazino)-2-(buta-2,3-dienyl)-3-oxo-hexanoic acid methyl ester [(*R*)-1b]: The reaction of methyl 2-(buta-2,3-dienyl)-3-oxohexanoate (409 mg, 2.09 mmol), dibenzyl azodicarboxylate (DBAD, 884 mg, 2.67 mmol), $Cu(OTf)_2$ (76 mg, 10 mol%), and (*S*,*S*)-(+)-2,2′-isopropylidenebis(4-phenyl-2-oxazoline) (73 mg, 10.4 mol%) in dry CH_2Cl_2 (20 mL) afforded (*R*)-**1b** (808 mg, 78%) of 98% *ee* as determined by HPLC analysis (Chiralcel AD, 25% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 47.9 (major), 55.0 min (minor); viscous liquid; $[\alpha]_{20}^{D}$ = +2.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.40–7.22 (m, 10H), 6.85–6.60 (m, 1H), 5.30–5.05 (m, 5H), 4.63 (br, 2H), 3.80–3.50 (m, 3H), 2.90–2.50 (m, 4H), 1.80–1.40 (m, 2H), 0.88 ppm (br, 3H); IR (neat): $\tilde{\nu}$ = 3311, 2960, 1956, 1743, 1218, 1028 cm^{-1}; MS (MALDI): *m*/*z*: found: 517 [*M*+Na]$^+$; HRMS (MALDI): *m*/*z*: calcd for $C_{27}H_{30}N_2O_7Na^+$: 517.1945; found: 517.1958 [*M*+Na]$^+$.

2-(*N*,*N*-Bis(benzyloxycarbonyl)hydrazino)-2-(buta-2,3-dienyl)-4-methyl-3-oxopentanoic acid methyl ester [(*R*)-1c]: The reaction of methyl 2-(buta-2,3-dienyl)-4-methyl-3-oxopentanoate (490 mg, 2.50 mmol), dibenzyl azodicarboxylate (DBAD, 994 mg, 3.00 mmol), $Cu(OTf)_2$ (90 mg, 10 mol%), and (*S*,*S*)-(+)-2,2′-isopropylidenebis(4-phenyl-2-oxazoline) (88 mg, 10.6 mol%) in dry CH_2Cl_2 (20 mL) afforded (*R*)-**1c** (1.107 g, 90%) in 98% *ee* as determined by HPLC analysis (Chiralcel OD, 15% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 12.2 (minor), 13.5 min (major); viscous liquid; $[\alpha]_{20}^{D}$ = −3.0 (*c* = 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.40–7.20 (m, 10H), 7.70–6.38 (m, 1H), 5.28–5.01 (m, 5H), 4.62 (br, 2H), 3,82–3.30 (m, 4H), 2.90–2.62 (m, 2H), 1.15–0.80 (m, 6H); IR (neat): $\tilde{\nu}$ = 3304, 2953, 1952, 1732, 1456, 1219 cm^{-1}; MS (MALDI): *m*/*z*: found: 517 [*M*+Na]$^+$; HRMS (MALDI): *m*/*z*: calcd for $C_{27}H_{30}N_2O_7Na^+$: 517.1945; found: 517.1959 [*M*+Na]$^+$.

All the spectral data for the known products have been published in the Supporting Information of ref. [7b]. The diastereoisomers can be easily separated by chromatography on silica gel.

General procedure for the in situ synthesis of optically active palladium catalysts from chiral ligands and $Pd(OAc)_2$: A solution of $Pd(OAc)_2$ (22.4 mg, 0.1 mmol) and chiral ligand (**L1**–**L6**, 0.2 mmol) in dry THF (10 mL) was stirred at room temperature for 1 h as the catalyst for the following reactions.

General procedure for synthesis of optically active pyrazolidine derivatives: The solution of catalyst in THF (1 mL), prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%), was added to a solution of (*R*)-**1** (0.21 mmol), PhI (50 mg, 0.24 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL), and the reaction was allowed to proceed at 80 °C in a tube with a screw cap. After the reaction was complete as monitored by TLC (petroleum ether/ethyl acetate 3:1), rotary evaporation and flash chromatography on silica gel (petroleum ether/ethyl acetate 5:1) afforded **3** ((3*R*,5*R*)-**3** and (3*R*,5*S*)-**3**). All the known products were identified by comparison with authentic samples prepared in this group.[7b]

3-Acetyl-1,2-dibenzyloxycarbonyl-3-ethoxycarbonyl-5-(1′-phenylethenyl)-pyrazolidine (3aa) ((3*R*,5*R*)-3aa and (3*R*,5*S*)-3aa; entry 1, Table 2): The solution of catalyst in THF (1 mL) prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) was added to a solution of (*R*)-**1a** (102 mg, 0.21 mmol), PhI (50 mg, 0.24 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3aa**[7] (96 mg, 81%) ((3*R*,5*R*)-**3aa**/3*R*,5*S*)-**3aa** 6:94 as determined by HPLC analysis).

*Isomer (3*R,5R*)-3aa*: 73% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 13.4 (minor), 17.6 min (major).

*Isomer (3*R,5S*)-3aa*: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 22.2 (major), 30.5 min (minor).

3-Acetyl-1,2-dibenzyloxycarbonyl-3-ethoxycarbonyl-5-(1′-(4″-methylphenyl)ethenyl)pyrazolidine (3ab) ((3*R*,5*R*)-3ab and (3*R*,5*S*)-3ab) (entries 2 and 3, Table 2): The solution of catalyst in THF (1 mL) prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis-(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol) was added to a solution of (*R*)-**1a** (91 mg, 0.19 mmol), 4-iodotoluene (55 mg, 0.25 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3ab**[7] (87 mg, 81%) ((3*R*,5*R*)-**3ab**/(3*R*,5*S*)-**3ab** 8:92 as determined by HPLC analysis).

*Isomer (3*R,5R*)-3ab*: 85% *ee* as determined by HPLC analysis (Chiralcel AD, 10% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 25.9 (minor), 28.6 min (major).

*Isomer (3*R,5S*)-**3ab***: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 10% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 41.0 (minor), 43.8 min (major).

The solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in 1,4-dioxane (1 mL) was added to a solution of (*R*)-**1a** (96 mg, 0.20 mmol), 4-iodotoluene (54 mg, 0.25 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in 1,4-dioxane (1 mL). The reaction afforded **3ab** (91 mg, 80%) ((3*R*,5*R*)-**3ab**/(3*R*,5)-**3ab** 7:93 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3ab***: 80% *ee* as determined by HPLC analysis (Chiralcel AD, 10% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 26.4 (minor), 29.1 min (major).

*Isomer (3*R,5S*)-**3ab***: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 10% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 41.3 (major), 43.9 min (minor).

3-Acetyl-1,2-dibenzyloxycarbonyl-3-ethoxycarbonyl-5-(1′-(4″-methoxyphenyl)ethenyl)pyrazolidine (3ac) ((3*R*,5*R*)-3ac and (3*R*,5*S*)-3ac; Entry 4, Table 2): The solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidene-bis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1a** (94 mg, 0.20 mmol), 4-iodoanisole (58 mg, 0.25 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3ac**[7] (97 mg, 85%) ((3*R*,5*R*)-**1ac**/(3*R*,5*S*)-**3ac** 6:94 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3ac***: 85% *ee* as determined by HPLC analysis (Chiralcel AD, 15% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 28.1 (minor), 32.1 min (major).

Isomer (3*R*,5*S*)-**3ac**: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 15% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 40.7 (major), 48.5 min (minor).

3-Acetyl-1,2-dibenzyloxycarbonyl-3-ethoxycarbonyl-5-(1′-(4″-methoxycarbonylphenyl)ethenyl)pyrazolidine (3ad) ((3*R*,5*R*)-3ad and (3*R*,5*S*)-3ad) (entry 5, Table 2): The solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1a** (98 mg, 0.20 mmol), 4-iodobenzoic acid methyl ester (64 mg, 0.24 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3ad**[7] (101 mg, (81%) ((3*R*,5*R*)-**3ad**/(3*R*,5*S*)-**3ad** 5:95 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3ad***: 81% *ee* as determined by HPLC analysis (Chiralcel AD, 15% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 28.3 (minor), 34.1 min (major).

*Isomer (3*R,5S*)-**3ad***: 97% *ee* as determined by HPLC analysis (Chiralcel AD, 15% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 38.9 (major), 55.9 min (minor).

3-Acetyl-1,2-dibenzyloxycarbonyl-3-ethoxycarbonyl-5-((*E*)-1′-methylene-hept-2′enyl)pyrazolidine (3ae) ((3*R*,5*R*)-3ae and (3*R*,5*S*)-3ae) (entry 6, Table 2): The solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1a** (94 mg, 0.20 mmol), (*E*)-1-iodohex-1-ene (56 mg, 0.26 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3ae**[7] (90 mg, 82%) ((3*R*,5*R*)-**3ae**/(3*R*,5*S*)-**3ae** 7:93 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3ae***: 83% *ee* as determined by HPLC analysis (Chiralcel AD, 5% *i*PrOH in hexane, 0.8 mL min^{-1}, 230 nm), t_R = 20.3 (minor), 21.5 min (major).

*Isomer (3*R,5S*)-**3ae***: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 5% *i*PrOH in hexane, 0.8 mL min^{-1}, 230 nm), t_R = 29.2 (major), 35.0 min (minor).

3-Acetyl-1,2-dibenzyloxycarbonyl-3-ethoxycarbonyl-5-(1′-(2″-thienyl)-ethenyl)pyrazolidine (3af) ((3*R*,5*R*)-3af and (3*R*,5*S*)-3af) (entry 7, Table 2): The solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis-(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1a** (101 mg, 0.21 mmol), 2-iodothiophene (53 mg, 0.25 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3af**[7] (78 mg, 66%) ((3*R*,5*R*)-**3af**/(3*R*,5*S*)-**3af** 5:95 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3af***: 79% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 17.1 (minor), 20.3 min (major).

*Isomer (3*R,5S*)-**3af***: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 33.9 (minor), 44.8 min (major).

3-Acetyl-1,2-dibenzyloxycarbonyl-3-ethoxycarbonyl-5-(1′-(4″-bromo-phenyl)ethenyl)pyrazolidine (3ah) ((3*R*,5*R*)-3ah and (3*R*,5*S*)-3ah) (entry 8, Table 2): The solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,R)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1a** (99 mg, 0.21 mmol), 1-bromo-4-iodobenzene (70 mg, 0.25 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3af**[7] (112 mg, 86%) ((3*R*,5*R*)-**3af**/(3*R*,5*S*)-**3ah** 7:93 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3ah***: 85% *ee* as determined by HPLC analysis (Chiralcel AD, 15% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 37.4 (major), 41.2 min (minor).

*Isomer (3*R,5S*)-**3ah***: >95% *ee* as determined by HPLC analysis (Chiralcel OD, 15% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 15.1 (minor), 17.1 min (major).

1,2-Dibenzyloxycarbonyl-3-butyryl-3-methoxycarbonyl-5-(1′-phenyl-ethenyl)pyrazolidine (3ba) ((3*R*,5*R*)-3ba and (3*R*,5*S*)-3ba) (entry 9, Table 2): The solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1b** (99 mg, 0.20 mmol), PhI (55 mg, 0.26 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3ba** (96 mg, 81%) ((3*R*,5*R*)-**3ba**/(3*R*,5*S*)-**3ba** 9:91 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3ba***: 83% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 28.1 (minor), 33.6 (major); viscous liquid; $[\alpha]_{20}^{D}$ = +22.0 (c = 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.39–7.22 (m, 15H), 5.62 (s, 1H), 5.42 (d, J = 8.10 Hz, 1H), 5.33–5.05 (m, 5H), 3.56 (s, 3H), 3.20 (dd, J = 13.50, 9.30 Hz, 1H), 2.90–2.60 (m, 2H), 2.29 (dd, J = 13.50, 3.30 Hz, 1H), 1.60–1.35 (m, 2H), 0.76 ppm (t, J = 7.35 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 204.3, 167.5, 156.6, 153.9, 144.7, 138.8, 135.3, 135.1, 128.6, 128.50, 128.47, 128.45, 128.39, 128. 2, 128.0, 127.9, 126.7, 113.2, 75.6, 68.8, 68.6, 62.0, 52.8, 40.2, 39.1, 16.8, 13.3 ppm; IR (neat): $\tilde{\nu}$ = 3033, 2961, 1725, 1497, 1412, 1152 cm^{-1}; MS (MALDI): m/z: found: 593.4 $[M+Na]^+$; HRMS (MALDI): m/z: calcd for $C_{33}H_{34}N_2O_7Na$: 593.2258; found: 593.2280 $[M+Na]^+$.

*Isomer (3*R,5S*)-**3ba***: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 37.2 (major), 42.5 min (minor); viscous liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.39–7.22 (m, 15H), 5.63 (s, 1H), 5.46 (d, J = 6.90 Hz, 1H), 5.34–5.06 (m, 5H), 3.58 (s, 3H), 3.11 (dd, J = 13.80, 9.60 Hz, 1H), 2.46–2.14 (m, 3H), 1.60–1.41 (m, 2H), 0.78 ppm (t, J = 7.35 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 199.2, 169.7, 157.0, 153.4, 144.6, 138.3, 135.42, 135.37, 128.6, 128.5, 128.4, 128.3, 128.24, 128.21, 128.1, 127.8, 126.6, 113.4, 76.9, 68.6, 68.4, 61.4, 53.1, 39.97, 39.94, 17.3, 13.5 ; IR (neat): $\tilde{\nu}$ = 3033, 2962, 1725, 1498, 1412, 1151 cm^{-1}; MS (MALDI): m/z: found: 593.4 $[M+Na]^+$; HRMS (MALDI): m/z: calcd for $C_{33}H_{34}N_2O_7Na^+$: 593.2258; found: 593.2280 $[M+Na]^+$.

1,2-Dibenzyloxycarbonyl-3-isobutyryl-3-methoxycarbonyl-5-(1′-phenyl-ethenyl)pyrazolidine (3ca) ((3*R*,5*R*)-3ca and (3*R*,5*S*)-3ca) (entry 10, Table 2): The solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1c** (98 mg, 0.20 mmol), PhI (55 mg, 0.26 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3ca** (90 mg, 78%) ((3*R*,5*R*)-**3ca**/(3*R*,5*S*)-**3ca** 8:92 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3ca***: 81% *ee* as determined by HPLC analysis (Chiralcel OD, 3% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 16.4 (major), 18.0 min (minor); viscous liquid; $[\alpha]_{20}^{D}$ = +55.0 (c = 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.35–7.18 (m, 15H), 5.57 (d, J = 1.20 Hz, 1H), 5.41 (dd, J = 8.55, 1.35 Hz, 1H), 5.25–5.01 (m, 5H), 3.49 (s, 3H), 3.27–3.17 (m, 1H), 3.08 (dd, J = 13.50, 9.00 Hz, 1H), 2.24 (dd, J = 13.50,

2.40 Hz, 1H), 0.98 (d, $J=6.60$ Hz, 3H), 0.87 ppm (d, $J=6.60$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): $\delta=208.2$, 167.8, 156.2, 154.4, 144.2, 138.7, 135.25, 135.22, 128.50, 128.47, 128.43, 128.35, 128.33, 128.30, 128.0, 127.9, 126.6, 113.6, 76.0, 68.68, 68.64, 61.5, 52.6, 38.9, 36.3, 20.6, 20.3 ppm; IR (neat): $\tilde{\nu}=3032$, 2954, 1741, 1716, 1497, 1456, 1002, 698 cm^{-1}; MS (MALDI): m/z: found: 571.2 $[M+H]^+$; HRMS (MALDI): m/z: calcd for $C_{33}H_{34}N_2O_7Na^+$: 593.2258; found: 593.2272 $[M+Na]^+$.

*Isomer (3*R,5S*)-**3ca***: 99% *ee* as determined by HPLC analysis (Chiralcel OD, 3% *i*PrOH in hexane, 0.7 mL min^{-1}, 230 nm), t_R = 21.2 (minor), 32.2 min (major); viscous liquid; $[\alpha]_{20}^{D}=+19.9$ ($c=3.5$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=7.40$–7.25 (m, 15H), 5.64 (s, 1H), 5.45 (d, $J=$ 7.20 Hz, 1H), 5.35–5.02 (m, 5H), 3.56 (s, 3H), 3.09 (dd, $J=13.50$, 9.00 Hz, 1H), 2.84–2.74 (m, 1H), 2.36 (d, $J=13.50$, 1H), 0.99 (d, $J=$ 6.60 Hz, 3H), 0.90 ppm (d, $J=6.60$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): $\delta=203.8$, 169.9, 157.0, 153.6, 144.1, 138.4, 135.5, 135.4, 128.5, 128.3, 128.16, 128.13, 128.09, 127.9, 127.7, 126.7, 113.5, 76.7, 68.5, 68.2, 61.2, 53.0, 40.2, 37.5, 20.3, 20.0 ppm; IR (neat): $\tilde{\nu}=3033$, 2952, 1716, 1498, 1455, 1395, 1338, 1154, 698 cm^{-1}; MS (MALDI): m/z: found: 571.2 $[M+H]^+$; HRMS (MALDI): m/z: calcd for $C_{33}H_{34}N_2O_7Na^+$: 593.2258; found: 593.2271 $[M+Na]^+$.

Correlation between the chiral substrates and the chiral catalysts

Entry 2, Table 3: A solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*S*,*S*)-(+)-2,2′-isopropylidenebis-(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1a** (96 mg, 0.20 mmol), PhI (50 mg, 0.24 mmol), and Ag_3PO_4 (33 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3aa** (90 mg, 81%) ((3*R*,5*R*)-**3aa**/(3*R*,5*S*)-**3aa** 65:35 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3aa***: 97% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 12.1 (minor), 16.1 min (major).

*Isomer (3*R,5S*)-**3aa***: 90% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 20.0 (major), 27.5 min (minor).

Entry 3, Table 3: A solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-L1, 10 mol%) in THF (1 mL) was added to a solution of (*S*)-**1a** (98 mg, 0.20 mmol), PhI (50 mg, 0.24 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3aa** (91 mg, 80%) ((3*S*,5*S*)-**3aa**/(3*S*,5*R*)-**3aa** 61:39 as determined by HPLC analysis).

*Isomer (3*S,5S*)-**3aa***: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 12.1 (major), 16.2 min (minor).

*Isomer (3*S,5R*)-**3aa***: 94% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 19.9 (minor), 27.3 min (major).

Entry 4, Table 3: A solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*S*,*S*)-(+)-2,2′-isopropylidenebis(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*S*)-**1a** (96 mg, 0.20 mmol), PhI (50 mg, 0.24 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3aa** (95 mg, 85%) ((3*S*,5*S*)-**3aa**/(3*S*,5*R*)-**3aa** 6:94 as determined by HPLC analysis).

*Isomer (3*S,5S*)-**3aa***: 85% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 12.1 (major), 16.1 min (minor).

*Isomer (3*S,5R*)-**3aa***: 99% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 19.9 (minor), 27.1 min (major).

Entry 4, Table 4: A solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis-(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of *rac*-**1a** (96 mg, 0.20 mmol), PhI (82 mg, 0.4 mmol), and Ag_3PO_4 (34 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3aa** (88 mg, 79%) ((3*S*,5*S*)-**3aa**/(3*R*,5*S*)-**3aa** 35:65 as determined by HPLC analysis).

*Isomer (3*S,5S*)-**3aa***: 43% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 12.5 (major), 16.7 min (minor).

*Isomer (3*S,5R*)-**3aa***: 86% *ee* as determined by HPLC analysis (Chiralcel AD, 7% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 20.9 (major), 28.5 min (minor).

Entry 6, Table 4: A solution of catalyst prepared from $Pd(OAc)_2$ (5 mol%) and (*R*,*R*)-(+)-2,2′-isopropylidenebis-(4-benzyl-2-oxazoline) ((*R*,*R*)-**L1**, 10 mol%) in THF (1 mL) was added to a solution of (*R*)-**1a** (84% *ee*) (95 mg, 0.20 mmol), PhI (84 mg, 0.4 mmol), and Ag_3PO_4 (33 mg, 0.08 mmol) in THF (1 mL). The reaction afforded **3aa** (93 mg, 85%) ((3*R*,5*R*)-**3aa**/(3*R*,5*S*)-**3aa** 9:91 as determined by HPLC analysis).

*Isomer (3*R,5R*)-**3aa***: 2.7% *ee* as determined by HPLC analysis (Chiralcel AD, 5% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 19.2 (minor), 25.7 min (major).

*Isomer (3*R,5S*)-**3aa***: 95% *ee* as determined by HPLC analysis (Chiralcel AD, 5% *i*PrOH in hexane, 1 mL min^{-1}, 230 nm), t_R = 34.3 (major), 46.5 min (minor).

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