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Palladium-Catalyzed Asymmetric Construction of Vicinal All-Carbon Quaternary Stereocenters and its Application to the Synthesis of Cyclotryptamine Alkaloids

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Abstract

We report the use of a two-fold Pd-catalyzed decarboxylative allylic alkylation (Pd-DAAA) to construct two vicinal all carbon quaternary stereocenters in a diastereo- and enantioselective fashion. To demonstrate the synthetic utility of this process, the products of the Pd-DAAA were elaborated to complete the formal syntheses of the cyclotryptamine alkaloids. Mechanistic investigations have revealed that the two-fold Pd-catalyzed transformation proceeds through an initial matched first allylation followed by a second mismatched allylation to deliver the desired product.

Keywords

asymmetric catalysis; palladium; allylic alkylation; quaternary stereocenters; alkaloids

The cyclotryptamine alkaloids are a diverse group of natural products with a wide array of biological activities (Figure 1).¹ This family of alkaloids consists of hexahydropyrroloindole units linked to form oligomers of varying sizes (Figure 1). Cyclotryptamine alkaloids are found in a number of different types of plants and animals.

From a structural perspective, cyclotryptamines are found in both *meso*- and optically active form. Due to their diverse biological profiles and unique structural features, the cyclotryptamine alkaloids have gained extensive attention from the synthetic community. Many elegant strategies have been devised to assemble these targets in enantiopure form.²

A pronounced feature found in these natural products is the presence of two vicinal quaternary stereocenters. Quaternary all carbon stereocenters are present in a variety of natural products and biologically active compounds. The presence of this structural element greatly complicates the asymmetric assembly of such molecular architectures due to the steric congestion present when bringing four carbon substituents together. Over the last

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several decades, extensive research has been devoted to develop methods that can assemble quaternary all carbon stereocenters in an asymmetric fashion, including cycloadditions, pericyclic reactions, and metal-catalyzed alkylation strategies.³ When a second vicinal quaternary center is present in a synthetic target, the asymmetric assembly is complicated further. In fact, the construction of adjacent quaternary stereocenters has been referred to as “a daunting challenge in natural product synthesis.”⁴ Currently, few methods exist for the construction of vicinal quaternary carbon centers in a single synthetic operation; hence each stereocenter is typically assembled sequentially. Furthermore, relatively few examples have been reported for the assembly of this structural motif in a catalytic asymmetric manner.⁵

The Pd decarboxylative asymmetric allylic alkylation (Pd-DAAA) has proven to be a mild, robust and functional group-tolerant method for the construction of stereocenters with high levels of diastereo- and enantioselectivity.⁶ This transformation has been performed with a variety of nucleophiles, including ketones, α -ketoesters, acyl imidazoles, *N*-acyl oxazolidinones, and 2-oxindoles.⁷ Recently, the Pd-DAAA was used to construct two quaternary carbon stereocenters bearing a 1,4-relationship.⁸ We sought to test the limits of the Pd-DAAA by constructing two *vicinal* quaternary carbon stereocenters in a single operation. Unlike two stereocenters bearing a distal 1,4-relationship, construction of two vicinal quaternary carbon stereocenters leads to sterically congested intermediates and products. Furthermore, the stereochemistry of the second stereocenter would likely be affected by the result of the first allylation event; that is, substrate control will compete with chiral catalyst control.

Our retrosynthetic strategy to access the cyclotryptamine core is outlined in Scheme 1. We envisioned that cyclotryptamines (–)-chimonanthine (**1**), (–)-folicanthine, (**2**) (+)-calycanthine (**3**), (–)-WIN 64821 (**4**), and (–)-ditryptophenaline (**5**) could be accessed by manipulation of common intermediate **6**. Intermediate **6**, which contains both vicinal quaternary stereocenters, would arise from a Pd-DAAA of dienol dicarbonate **7**. Dienol dicarbonate **7** would be formed by treatment of bisoxindole **8** with allyl chloroformate under basic conditions.

To determine whether the Pd-DAAA could be used to access the cyclotryptamine core in an enantio- and diastereoselective fashion, dienol dicarbonate **7** was prepared as outlined in Scheme 2. Condensation of oxindole (**9**) and isatin (**10**) afforded isoindigo in 82% yield.⁹ Isoindigo was treated with di-*tert*-butyl dicarbonate in THF followed by hydrogenation with Pearlman's catalyst to provide bisoxindole **8**. The reaction of bisoxindole **8** with allyl chloroformate and triethylamine facilitated smooth formation of dienol dicarbonate **7** in 90% yield.¹⁰ Surprisingly, dienol dicarbonate **7** proved to be a bench-stable intermediate that could be accessed on >16 g scale using the sequence shown in an overall 63% yield from inexpensive commercially available starting materials **9** and **10**.

With key dienol dicarbonate **7** in hand, the Pd-DAAA was explored. Initial studies were performed using achiral ligands to determine the influence of ligand structure on the diastereoselectivity of the reaction. Ideally, ligand control would override substrate control and could be used to favor either the d/l (**6**) or *meso* (**11**) products. This would provide access to both chiral and *meso* cyclotryptamine natural products. Treatment of the dienol dicarbonate **7** with Pd₂(dba)₃•CHCl₃ and PPh₃ facilitated the desired allylation with >95% conversion but in a mere 2:1 d.r. favoring the chiral product **6** (Table 1, entry 1). Switching to the electron-deficient ligand tri-2-furylphosphine led to an improvement in the diastereoselectivity of the transformation and delivered the products in a 5.4:1 d.r. still favoring the C₂ symmetric product **6** (entry 2). Employing the bulky ^tBu-XPhos ligand resulted in further enhancement of the diastereoselectivity to 5.8:1, but continued to favor the C₂ symmetric product **6** (entry 3). Bidentate ligands were studied next in the

transformation; utilizing dppe, improved the d.r. to 6:1, still favoring the chiral product **6** (entry 4). Xantphos led to a reduced 1.7:1 d.r. in favor of the chiral product **6** (entry 5).

Based on the results obtained employing achiral ligands (entries 1–5), it appeared that substrate control was favoring the C₂ symmetric product **6** over the *meso* product **11** but ligand structure still influenced this selectivity as seen through the varying diastereomeric ratios. With this bias, we were interested in determining if chiral ligands could provide the C₂ symmetric product **6** with high levels of enantioselectivity. Employing ^tPr-PHOX¹¹ in the transformation provided the products **6** and **11** with an excellent 7:1 d.r. but in only 24% ee (entry 6). Screening our modular ligands **L1**–**L4** (entries 7–10) revealed that (*S,S*)-**L3**, which contains a stilbene backbone, performed best both in terms of diastereo- and enantioselectivity, facilitating the allylation in a 3.3:1 d.r. and with 87% ee (entry 9). Continuing with (*S,S*)-**L3** as the ligand, a solvent screen revealed that the Pd-DAAA was best performed in THF (entries 9, 11, 12). Temperature and additives were examined for their ability to impart an effect on the diastereoselectivity and enantioselectivity of the transformation. Performing the reaction at reduced temperature led to a slightly diminished d.r., but a slight increase in enantioselectivity (entry 13). Adding 10 mol% of (*n*-hex)₄NBr to the reaction led to an increase in both diastereoselectivity and enantioselectivity (entry 14). It has been demonstrated that addition of (*n*-hex)₄NBr to the Pd-catalyzed allylic alkylations can have a beneficial effect on enantioselectivity by decreasing the rate of nucleophilic attack.¹² In hopes of seeing a synergistic effect on selectivity, the Pd-DAAA was conducted at 0 °C in the presence of 10 mol% (*n*-hex)₄NBr. To our delight, running the reaction under these conditions resulted in >95% conversion in a 3.2:1 d.r. and 92% ee (entry 15).

With optimized conditions in hand, the scalability of the Pd-DAAA was explored. The transformation proved quite amenable to scale-up, and was easily conducted on > 9 g scale (eq 1). When conducted on this scale, the Pd and ligand loading could be reduced five-fold, and only 0.5 mol% Pd₂(dba)₃•CHCl₃ and 1.5 mol% (*S,S*)-**L3** were needed to drive the transformation to completion. Under these reaction conditions, the products could be obtained in a 96% isolated yield, in a 3.3:1 d.r. and 91% ee.

(eq. 1)

With gram quantities in hand, chiral bisallyl oxindole **6** was elaborated into diol **14** (Scheme 3). Treatment of bisallyl oxindole **6** with TFA in CH₂Cl₂ followed by benzylation with BnBr provided alkylated oxindole **12** in near quantitative yield. Oxidative cleavage of the alkylated oxindole **12** under modified Johnson-Lemieux conditions afforded unstable bisaldehyde **13**. Reduction of bisaldehyde **13** with NaBH₄ provided diol **14**. At this stage, optical rotation was used to determine the absolute configuration of diol **14**. Previously, Overman and coworkers have used the (+) enantiomer of diol **14** to complete the syntheses of (+)-chimonanthine^{2a, 2b}, (+)-folicanthine,^{2c} (–)-calycanthine^{2a, 2b}. Our synthetic sample of **14** had a rotation of –192 (c = 1.2 in CHCl₃), indicating the enantiomer shown, which corresponds to the formal syntheses of (–)-chimonanthine (**1**), (–)-folicanthine (**2**), and (+)-calycanthine (**3**).^{2a} Likewise, bisaldehyde **13** has been used by Overman and coworkers to

complete the total synthesis of (–)-WIN 64821 (**4**) and (–)-ditryptophenaline (**5**)¹³ and constitutes a formal synthesis of these targets with the same absolute configuration.

The Pd-DAAA described is intriguing from a mechanistic perspective since the process proceeds through two independent allylation steps (Scheme 4). The first allylation (**A**) is enantiodetermining in the transformation, and gives rise to two intermediates, **15**, and *ent*-**15**, which are not observed. Instead, the enantiomeric mixture of **15** and *ent*-**15** undergoes a second, diastereoselective allylation step (**B**), which affords the observed products **6** and **11** in 95% yield, in a 3.3:1 d.r. and 91% ee (eq 1).

Several outcomes for allylations **A** and **B** are possible that can provide the enantio- and diastereoselectivity observed in the double allylation process. For instance, the first allylation **A** can proceed with lower levels of enantioselectivity than what is observed at the end of the transformation (91% ee), while the second allylation **B** can enhance the ee to 91% by transforming the minor intermediate enantiomer *ent*-**15** to the *meso* product **11**. Conversely, the first allylation **A** can proceed with higher levels of enantioselectivity than what is observed at the end of the transformation (91%), and the second allylation **B** could be eroding the %ee observed by transforming the major intermediate enantiomer **15** to the *meso* product. Additionally, the second allylation step **B** can occur in a matched sense, where the stereocenter constructed in allylation step **A** reinforces the formation of the second stereocenter in step **B** to favor the C₂ symmetric product **6**. Conversely, the second allylation **B** can occur in a mismatched fashion, such that the first stereocenter leads to unfavorable interactions in the transition state in step **B**, which would disfavor formation of the C₂ symmetric product **6**.

To probe the effect that allylation step **B** has on the ee and d.r. of the transformation, monoallylated enol carbonates **15** and *rac*-**15** were studied in the Pd-DAAA. Monoallylated enol carbonate **15** is the intermediate obtained in the double allylation process after the enantiodetermining allylation step **A**. Subjecting this intermediate (**15**) with known enantiopurity to the reaction conditions of the Pd-DAAA would reveal what effect the second allylation step **B** has on the enantioselectivity and diastereoselectivity of the overall reaction.

Enantioenriched (62% ee) monoallylated enol carbonate **15** was prepared by treatment of oxindole dimer **8** with a single equivalent of allyl acetate and (*S,S*)-**L1**¹⁴, under Pd catalysis followed by enol carbonate formation with allyl chloroformate (Scheme 5). Racemic monoallylated enol carbonate *rac*-**15** was prepared in an analogous fashion.

Both enol carbonates **15** and *rac*-**15** were subjected to the Pd-DAAA reaction conditions using different enantiomers of **L3** (Table 2). The reaction of enantioenriched monoallyl enol carbonate **15** under optimized conditions employing (*S,S*)-**L3**, the enantiomer of ligand which is present in the double allylation, resulted in formation of the desired product **6** with >95% conversion, 3.6:1 d.r., and a 57% ee (entry 1). The d.r. obtained in this reaction was comparable to the d.r. obtained in the double Pd-DAAA (compare to eq 1), and a 5 point drop in ee was observed from the starting material. The result in entry 1 suggests that the first allylation step **A** proceeds with higher enantioselectivity (>91%) than what is observed at the end of the double allylation process (91%) since a 5% enantioerosion is observed going from **15** to **6**. Enantioenriched monoallyl enol carbonate **15** was next treated under the optimized reaction conditions with (*R,R*)-**L3**, the antipode of the ligand present in the Pd-DAAA. This reaction resulted in formation of the desired product **6** with >95% conversion, 6.5:1 d.r., and a 69% ee (entry 2). The d.r. obtained from this reaction was significantly higher than the d.r. obtained in the Pd-DAAA (compare table 2 entry 2 to eq 1), and a 7 point increase in ee was observed. The increased enantiopurity of the product observed in

entry 2 supports the notion that the first allylation step **A**, proceeds with >91% ee. Additionally, entry 2 suggests that the second allylation step **B**, is mismatched with (*S,S*)-**L3**, the enantiomer of ligand that is present in the double Pd-DAAA, since the d.r. is improved when (*R,R*)-**L3**, is used. Reaction of enantioenriched monoallyl enol carbonate **15** employing (*rac*)-**L3** resulted in formation of the desired product with >95% conversion, 5.4:1 d.r., and a 62% ee (entry 3). In this reaction, the d.r. was slightly higher than the d.r. obtained in the double Pd-DAAA (compare entry 3 to eq 1), and no change in % ee was observed. Finally, treatment of *racemic* monoallyl enol carbonate *rac*-**15** under optimized conditions employing (*S,S*)-**L3**, resulted in formation of the desired product **6** with >95% conversion, 4:1 d.r., and a –8% ee favoring the *opposite* enantiomer than what is observed in the double allylation process with (*S,S*)-**L3** (entry 4). This result supports the notion that the second allylation event **B** is mismatched, since the *minor* enantiomer of product is favored from what is expected when using (*S,S*)-**L3** for the double Pd-DAAA.

To gain further insight into the first allylation **A** of the double Pd-DAAA process, we were interested in isolating and assaying the intermediate monoallyl enol carbonate **15** by stopping the double Pd-DAAA reaction at partial conversion. Monoallyl enol carbonate **15** could be observed on TLC after running the double Pd-DAAA reaction for 10 min. However, attempts to stop the reaction at partial conversion after 5, 10, 15, 30, and 60 min by dilution of reaction aliquots with oxygenated diethyl ether led only to observation of double allylation products **6** and **11** by ¹H NMR. This unexpected result indicated that the double Pd-DAAA was occurring more quickly than the catalyst oxidation with oxygen. To overcome this limitation, aliquots of the reaction mixture were loaded directly onto preparatory TLC plates at 0, 5, 10, and 15 min reaction times (Table 3), and the monoallyl enol carbonate **15** and the double allylation products **6** and **11** were separated from the active catalyst species. The enantiopurities of **15** and **6** were assayed by chiral HPLC to determine if the conclusions drawn from table 2 were valid. At t = 0 min, only trace quantities of **15** and **6** were observed. At t = 5, t = 10, and t = 15 min on the other hand, **15** and **6** could be isolated and assayed by chiral HPLC. At these time intervals, both the intermediate monoallyl enol carbonate **15** and the double allylation products **6** and **11** were detected, indicating that the second, mismatched allylation step (**B**), had a rate comparable to the first, enantiodetermining step **A**. Monoallyl enol carbonate **15** was observed in 93% ee at t = 5, t = 10, and t = 15 min, while the double allylation product **6** was isolated with 91% ee at t = 5, t = 10, and t = 15 min. As suggested by table 2, the enantiopurity of monoallyl enol carbonate **15** is higher than the ee of the double allylation product **6**.

Based on the results obtained from Table 2 and Table 3, several conclusions can be drawn about enantioselectivity of the double allylation process (Scheme 4). The first, enantiodetermining allylation **A**, provides intermediates **15** and *ent*-**15**, with greater enantiopurity (~93% ee) than what is observed at the end of the transformation (91% ee). The second allylation **B** is more substrate controlled than ligand controlled and occurs in a mismatched fashion. This event reduces the enantiopurity of intermediate **15** to the product **6** from 93% to 91% ee. This occurs because the second mismatched allylation step **B** proceeds at different rates for **15** and *ent*-**15** to yield the *meso* and chiral products. Both **15** and *ent*-**15** react in the second allylation to form the chiral products **6** and *ent*-**6** with a greater rate than forming the *meso* product.

However, the relative rate of formation for *ent*-**6**:**11** is greater than the rate of formation for **6**:**11**, which leads to a greater portion of *meso* product to come from **15**, and leads to the observed reduction in enantiopurity in the product from monoallyl enol carbonate intermediate **15**. These conclusions are supported by the result obtained in Table 2 entry 1, where the starting material **15**, with 62% ee was treated under the reaction conditions with

(*S,S*)-**L3**, the same enantiomer of ligand that is present under the optimized reaction conditions in eq 1 and produced the product with a reduced 57% ee. Likewise, Table 2 entry 2 supports the same conclusion since treatment of the monoallyl enol carbonate **15** with (*R,R*)-**L3**, the opposite enantiomer of ligand from what is present in the reaction mixture, resulted in an improvement in enantiopurity from 62% to 69% ee. Table 2 entry 4 also supports these conclusions since treatment of racemic monoallyl enol carbonate *rac*-**15** with (*S,S*)-**L3** produced a product with –8% ee favoring the *opposite* enantiomer from what is observed under the optimized reaction conditions also employing (*S,S*)-**L3** as the ligand (eq 1). Finally, direct isolation of the monoallyl enol carbonate **15** from the double Pd-DAAA also supports this conclusion, since this intermediate was observed in 93% ee, which is higher than the 91% ee obtained in the final product.

Based on the mechanistic experiments in Table 2 and Table 3, several conclusions can be drawn about the diastereoselectivity of the Pd-DAAA. Under the optimized reaction conditions, monoallyl enol carbonate **15**, reacts with the catalyst in a mismatched fashion and produces a greater quantity of *meso* product **11** than the reaction of catalyst with *ent*-**15**. This occurs because the monoallyl enol carbonate intermediate **15** is present in much greater quantity than *ent*-**15**. (at 62% ee, the ratio of **15** to *ent*-**15** is 81:19) This conclusion is supported by Table 2 entry 2, where the monoallyl enol carbonate was treated with (*R,R*)-**L3** to produce the chiral product **6** in a 6.5:1 d.r., which is higher than the 3.3:1 d.r. observed under the optimized reaction conditions (eq 1). Under the conditions in Table 2 entry 2, the allylation is conducted with the opposite enantiomer of ligand from that what is present under the optimized reaction conditions, and is therefore *matched* for monoallyl enol carbonate **15** and is *mismatched* for the enantiomer *ent*-**15**. Since the matched monoallyl enol carbonate **15** is now present in much greater quantity than the mismatched monoallyl enol carbonate *ent*-**15**, the diastereoselectivity of the reaction increases from what is observed under the optimized reaction conditions (eq 1).

The observed stereochemical outcome for the double Pd-DAAA can be rationalized using a “wall and flap” mnemonic which represents the chiral π -allyl palladium species (Figure 3).¹⁵ Approach of the oxindole enolate under the “flap” of the chiral ligand environment in trajectory **I** is favored, and minimizes steric clash with the “walls”. On the other hand, approach of the oxindole enolate from the opposite face as depicted in trajectory **II** leads to several unfavorable steric interactions. Trajectory **I** leads to formation of monoallyl enol carbonate **15**, the enantiomer observed in the double Pd-DAAA.

In conclusion we have successfully developed a scalable twofold Pd-DAAA of oxindole dienol dicarbonate **7** to construct two vicinal carbon quaternary stereocenters in near quantitative yield and high levels of diastereo- and enantioselectivity. The bisoxindole product (**6**) of this challenging transformation was elaborated onto the formal synthesis of the cyclotryptamine alkaloids (–)-chimonanthine (**1**), (–)-folicanthine, (**2**) (+)-calycanthine (**3**), and (–)-WIN 64821 (**4**), (–)-ditryptophenaline (**5**). Detailed mechanistic studies on the two-fold allylation process have revealed that the reaction proceeds through an enantiodetermining allylation step **A** in 93% ee followed by a mismatched second allylation step **B** to arrive at the chiral product in 3.3:1 d.r. and 91% ee.

Supplementary Material

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14. (*S,S*)-**L1**, and (*S,S*)-**L3**, provide the same enantiomer of product **11** when employed in the double allylation process.
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Figure 1.
Representative cyclotryptamine alkaloids

Figure 2.
Ligands employed in optimization studies

Figure 3.
Rationale for observed absolute configuration

Scheme 1. Retrosynthesis. Boc = *tert*-butoxycarbonyl

Scheme 2.

Synthesis of dienol carbonate **7**. Reagents and conditions: a) HCl, HOAc, reflux, 82%; b) Boc_2O , DMAP, NEt_3 , THF, 0 °C to rt, 89%; c) 10 wt% $\text{Pd}(\text{OH})_2/\text{C}$, EtOH, RT, 96%. d) allyl chloroformate, NEt_3 , THF, 0 °C to RT, 90%. DMAP = 4-dimethylaminopyridine.

Scheme 3.

Completion of the formal syntheses. Reagents and conditions: a) TFA, CH_2Cl_2 , RT; (b) NaH, DMF, 0 °C, then BnBr to RT, 95% over two steps; c) OsO_4 , NaIO₄, 2,6-lutidine, dioxane/ H_2O , RT; d) NaBH_4 , MeOH, 0 °C, 52% over two steps. DMF = *N,N*-dimethylformamide, TFA = trifluoroacetic acid.

Scheme 4.
Mechanistic rationale for double Pd-DAAA

Scheme 5.

Preparation of monoallyl enol carbonates **15** and *rac*-**15**. ^aReagents and conditions: (a) 2.5 mol% Pd₂(dba)₃•CHCl₃, 7.5 mol% (rac)-**L1**, allyl acetate, Cs₂CO₃, THF, RT; (b) allyl chloroformate, NEt₃, THF, 0 °C, 95% over two steps; (c) 2.5 mol% Pd₂(dba)₃•CHCl₃, 7.5 mol% (*S,S*)-**L1**, allyl acetate, Cs₂CO₃, THF, RT; (d) allyl chloroformate, NEt₃, THF, 0 °C, 95% over two steps.

Table 1

Selected optimization studies

entry	ligand	solvent	additive	d.r. ^b	%ee ^c
1 ^d	PPh ₃	THF	-	2.0:1	-
2 ^d	(2-furyl) ₃ P	THF	-	5.4:1	-
3	^t Bu-XPhos	THF	-	5.8:1	-
4	dppf	THF	-	6.0:1	-
5	Xantphos	THF	-	1.7:1	-
6	Pt-PHOX	THF	-	7.0:1	24
7	(<i>S,S</i>)-L1	THF	-	1.6:1	89
8	(<i>S,S</i>)-L2	THF	-	1.6:1	26
9	(<i>S,S</i>)-L3	THF	-	3.3:1	87
10	(<i>S,S</i>)-L4	THF	-	3.0:1	47
11	(<i>S,S</i>)-L3	dioxane	-	2.7:1	58
12	(<i>S,S</i>)-L3	DME	-	3.0:1	83
13 ^e	(<i>S,S</i>)-L3	THF	-	2.8:1	86
14	(<i>S,S</i>)-L3	THF	10 mol% (<i>n</i> -hex) ₄ NBr	3.5:1	88
15 ^e	(<i>S,S</i>)-L3	THF	10 mol% (<i>n</i> -hex) ₄ NBr	3.2:1	92

^a All reactions were performed with 2.5 mol% Pd₂(dba)₃•CHCl₃, 7.5 mol% of ligand, 0.02 mmol of dienol dicarbonate **7** in the indicated solvent. All reactions proceeded with >95% conversion as determined by ¹H NMR of the crude reaction mixture.

^b d.r. determined by ¹H NMR of the crude reaction mixture.

^c %ee determined by chiral HPLC

^d 22.5 mol% of ligand was used.

^e reaction was conducted at 0 °C. dba = dibenzylideneacetone, DME = 1,2-dimethoxyethane, dppe = 1,1'-Bis(diphenylphosphino)ferrocene.

Table 2

Pd-DAAA of monoallyl enol carbonate **15**^a

entry	%ee of 15	ligand	d.r. ^b	%ee ^c
1	62	(<i>S,S</i>)- L3	3.6:1	57
2	62	(<i>R,R</i>)- L3	6.5:1	69
3	62	(<i>racemic</i>)- L3	5.4:1	62
4	0	(<i>S,S</i>)- L3	4.0:1	-8

^a All reactions were performed with 2.5 mol% Pd₂(dba)₃•CHCl₃, 7.5 mol% of ligand, 10 mol% of (*n*-hex)₄NBr, 0.02 mmol of dienol dicarbonate **7** in THF (0.1M) at 0 °C. All reactions proceeded with >95% conversion as determined by ¹H NMR of the crude reaction mixture.

^b d.r. determined by ¹H NMR of the crude reaction mixture.

^c %ee determined by chiral HPLC.

Table 3

Isolation of monoallyl enol carbonate **15**

entry	t (min)	%ee ^b	%ee ^b
1	0 ^c	-	-
2	5	93	91
3	10	93	91
4	15	93	91

^a All reactions were performed with 2.5 mol% Pd₂(dba)₃•CHCl₃, 7.5 mol% of ligand, 10 mol% of (*n*-hex)₄NBr, 0.02 mmol of dienol dicarbonate **7** in THF (0.1M) at 0 °C.

^b %ee determined by chiral HPLC.

^c Only traces **15** and **6** were observed.