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Multiple Absolute Stereocontrol in Pd-Catalyzed [3+2] Cycloaddition of Oxazolidinones and Trisubstituted Alkenes Using Chiral Ammonium–Phosphine Hybrid Ligands

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Abstract

The development of a Pd-catalyzed highly enantio- and diastereoselective [3+2] cycloaddition of 5-vinyloxazolidinones and activated trisubstituted alkenes is described in detail. This protocol for the single-step construction of densely functionalized pyrrolidines with three contiguous stereocenters including vicinal quaternary stereocenters depends on the remarkable ability of phosphine ligands possessing a chiral ammonium ion to promote intermolecular cycloaddition reactions with a precise control of absolute stereochemistry. A series of control experiments show that a chiral ammonium–phosphine hybrid ligand enabled the individual, yet simultaneous stereocontrol of each chiral center in the annulation reaction. The reaction mechanism is also discussed with particular focus on the stereodetermining processes.

Introduction

Efficient access to complex chiral molecules from simple materials represents one of the most important objectives in organic synthesis; numerous efforts have been devoted to the development of reliable and general methods instrumental in addressing this issue.[1–6] Among the approaches based on transition-metal catalysis, Pd-catalyzed asymmetric cycloaddition mediated by a zwitterionic π-allylpalladium intermediate offers a powerful tool for the stereoselective synthesis of highly substituted carbocycles and heterocycles.[7] The prominent feature of this methodology is that it allows the facile construction of multiple stereocenters in a single synthetic operation. An increase in the number of target stereogenic centers and the complexity of molecular scaffolds make this type of transformation more valuable, yet more difficult with respect to absolute stereocontrol. In fact, while the development of catalytic stereoselective cycloaddition reactions that enable the installation of three or more contiguous stereocenters is in demand, viable strategies to address this challenge have been limited.[8–15]

The Pd-catalyzed [3+2] cycloaddition of 5-vinyloxazolidinones and activated trisubstituted alkenes[16] provides a straightforward method to construct highly functionalized pyrrolidines, a ubiquitous core structure of natural products and pharmaceuticals.[17–19] When readily accessible, differently trisubstituted alkenes are used as the coupling partner for the cycloaddition, the initial intermolecular addition of allylpalladium species to the alkene generates a zwitterionic intermediate possessing a trisubstituted prochiral carbanion site (Figure 1). At the same time, this intermediate is endowed with a 1,1-disubstituted allylpalladium moiety by using vinyloxazolidinones with a tetrasubstituted chiral carbon. The subsequent

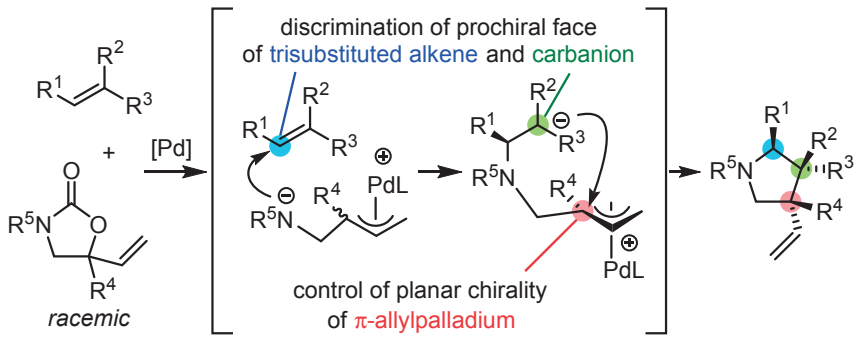


Figure 1. Multiple stereocontrol in Pd-catalyzed [3+2] cycloaddition of 5-vinyloxazolidinones and trisubstituted alkenes.

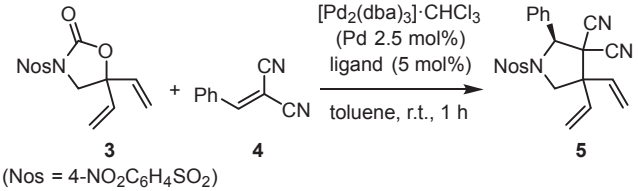
ring-closing bond formation between these two reactive sites gives rise to a cyclic product with three contiguous chiral carbons including two quaternary carbons. A main obstacle to achieve this type of annulation reaction in an asymmetric manner is the need of three simultaneous stereocontrols: (i) enantiofacial discrimination of the trisubstituted alkene, (ii) recognition of the prochiral face of the trisubstituted carbanion site of the zwitterionic intermediate, and (iii) control of the chirality of its π-allylpalladium moiety.[20,21] To establish a cycloaddition protocol involving such a multiple stereocontrol, a new type of phosphine ligand bearing a chiral ammonium ion component was designed; upon coordination to the Pd center, this was expected to precisely recognize the remote anionic site of the zwitterionic intermediate through ion pairing. In this article, we describe a detailed study on the development of a Pd-catalyzed highly enantio- and diastereoselective [3+2] cycloaddition of 5-vinyloxazolidinones and activated trisubstituted alkenes based on the judicious utilization of the unique properties of chiral ammonium–phosphine hybrid ligands.[22,23]

Results and Discussion

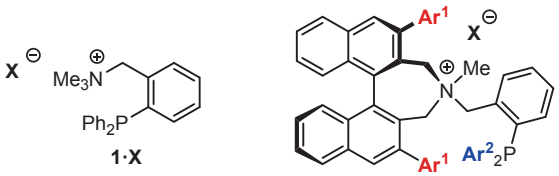
Our initial study was focused on the identification of an effective ligand for promoting the Pd-catalyzed asymmetric [3+2] cycloaddition. To this end, we selected *N*-(4-nitrobenzenesulfonyl)-5,5-divinyloxazolidin-2-one (**3**) and 2-benzylidenemalononitrile (**4**) as the model substrates. The reaction between these substrates would provide a suitable platform to verify our hypothesis that chiral ammonium phosphines act as a ligand that could control the absolute stereochemistry in the addition of the anionic site of the allylpalladium intermediate generated from **3** to prochiral **4**.

First, we investigated the reaction of **3** with **4** under the influence of the catalyst prepared in situ from tris(dibenzylideneacetone)dipalladium–chloroform complex ($[Pd_2(dba)_3]\cdot CHCl_3$) and triphenylphosphine (PPh_3) in toluene at room temperature. After 1 h of stirring, the desired pyrrolidine **5** was obtained in moderate yield (Table 1, Entry 1). The insufficient reactivity can be attributed to the reluctant addition of the sulfonamide ion moiety of the zwitterionic allylpalladium to **4**, probably because of the internal association of this weak nitrogen nucleophile with the cationic Pd center (Figure 2). This unproductive interaction could be suppressed by the addition of an external anion that has a strong coordinating ability to Pd such as a halide ion,[24] as previously observed by Knight and Aggarwal in related reaction systems.[16,25] Indeed, in the presence of a catalytic amount of tetrabutylammonium bromide (TBAB), the cycloaddition proceeded much faster under otherwise identical conditions, affording **5** in 79% yield (Entry 2). This observation led us to envision further reactivity enhancement by the use of a phosphine ligand incorporating a quaternary ammonium halide component in view of not only assisting the preferable halide–Pd contact, but also recognizing

Table 1. Optimization of catalytic system for cycloaddition of 5-vinyloxazolidinone **3** and benzylidenemalononitrile **4**[a)]



3 (Nos = 4-$NO_2C_6H_4SO_2$) **4** **5**



1·X

2a·X (Ar[1] = Ar[2] = Ph)
2b·X (Ar[1] = β-Naph, Ar[2] = Ph)
2c·X (Ar[1] = Ph, Ar[2] = 4-$CF_3C_6H_4$)
2d·X (Ar[1] = β-Naph, Ar[2] = 4-$CF_3C_6H_4$)

Entry	Ligand	Yield/%[b)]	ee/%[c)]
1	PPh_3	43	—
2[d)]	PPh_3	79	—
3	**1·Br**	99	—
4	**1·OAc**	49	—
5	**2a·Br**	94	63
6	**2b·Br**	99	63
7	**2c·Br**	99	57
8	**2d·Br**	99	75
9	**2d·Cl**	99	72
10	**2d·I**	99	90
11[e)]	**2d·I**	99	92

a) Unless otherwise noted, reactions were carried out with 0.10 mmol of **3** and 0.12 mmol of **4** in the presence of $[Pd_2(dba)_3]\cdot CHCl_3$ (Pd, 2.5 mol %) and ligand (5 mol %) in 1.0 mL of toluene at room temperature for 1 h. b) Isolated yield. c) Determined by HPLC analysis. d) Performed with 5 mol % of TBAB. e) Carried out at 0 °C for 3 h.

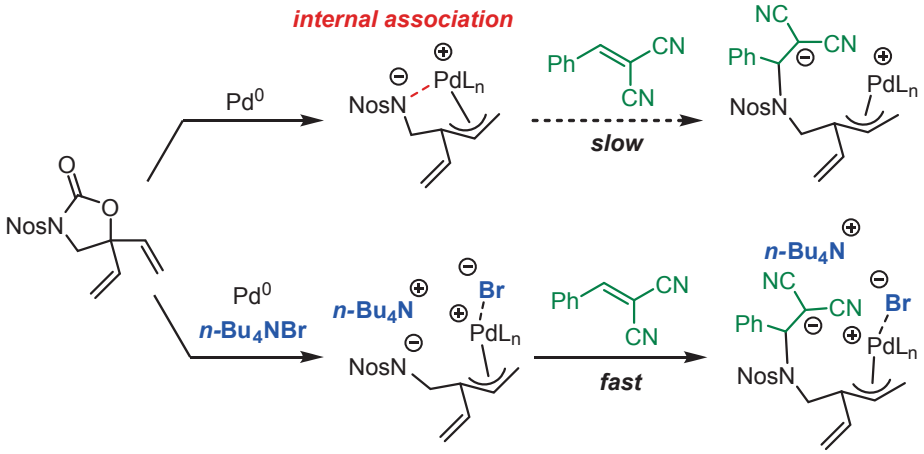
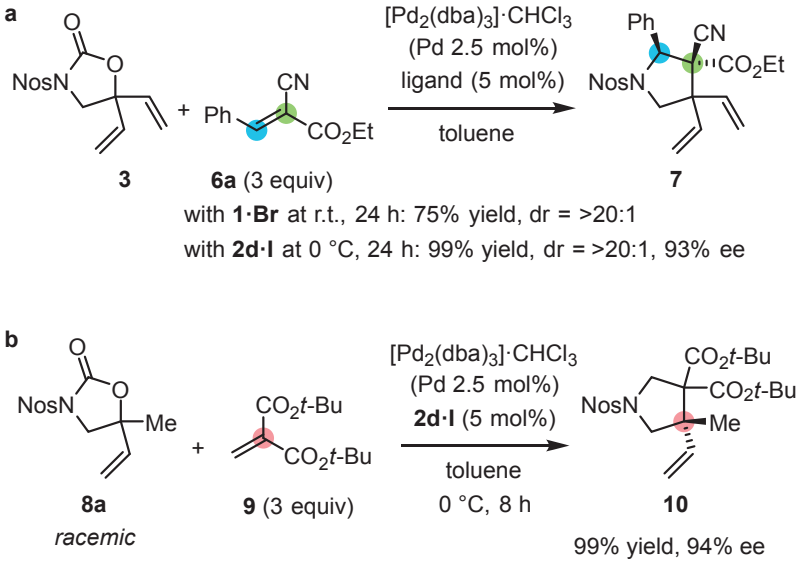


Figure 2. Effect of halide ion.

the anionic site via facile pairing with the ammonium ion. Therefore, the performance of *o*-diphenylphosphinobenzylammonium bromide **1·Br** was evaluated as a ligand.[26–29] As expected, the bond formation was completed within 1 h, affording **5** quantitatively (Entry 3). Notably, switching the bromide ion of the ligand to acetate ion caused a substantial decrease in the reactivity, reinforcing the assumption that the coordinating ability of the anion is crucial for the catalytic efficiency (Entry 4). These findings showed that *o*-diarylphosphinobenzylammonium halide is a core structure requisite for effective ligands for promoting the zwitterionic allylpalladium-mediated cycloaddition. With this information, we sought to develop chiral ammonium phosphines capable of rigorously discriminating the prochiral faces of **4** in the conjugate addition stage of annulation. For this purpose, we chose to introduce a chiral 1,1′-binaphthyl-derived azepinium skeleton[30] into the ammonium ion component and fortunately found that **2a·Br** with simple phenyl appendages at both the 3,3′-positions of the binaphthyl unit (Ar^1) and phosphorus center (Ar^2) induced an appreciable level of enantiocontrol on **5** without detrimental effect on the reactivity profile (Entry 5). Subsequent structural modifications of the aromatic substituents showed that chiral ammonium phosphine **2d·Br** is a promising candidate for further optimization (Entries 5–8). Then, we examined the effect of the identity of halide ion on the competence of the ligand for stereocontrol. Interestingly, while the use of chloride variant **2d·Cl** subtly affected the selectivity (Entry 9), a dramatic improvement in enantioselectivity was attained when the counter ion was exchanged to iodide **2d·I** (Entry 10). This indicates the intimate contact of the halide ion with the positively charged Pd center in the transition state and also highlights a distinct feature of the chiral ammonium phosphine ligands. Finally, lowering the reaction temperature to 0 °C increased the enantioselectivity to 92% ee (Entry 11).

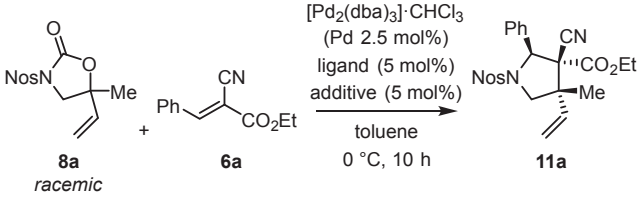
With the optimal ligand **2d·I** and reaction conditions, we turned our attention to the stereoselective construction of consecutive tertiary and all-carbon quaternary stereocenters with a trisubstituted alkene bearing different geminal substituents as the substrate. We initially attempted the reaction of oxazolidinone **3** with (*E*)-ethyl 2-cyano-3-phenylacrylate (**6a**) under the catalysis of the Pd complex bearing an achiral ligand **1·Br** at room temperature, which afforded diastereomerically pure pyrrolidine **7** in good yield (Scheme 1a). This result suggested that the relative stereochemistry of C(2) and C(3) stereocenters in **7** originated from the geometry of the starting alkene **6a**. Thus, considering the capability of **2d·I** to precisely discriminate prochiral **6a**, we assumed that the use of this chiral ligand would lead to the formation of stereochemically homogeneous **7**. In fact, the reaction of **3** with **6a** under the optimized conditions with **2d·I** as the ligand resulted in the quantitative production of diastereomerically pure **7** with high enantioselectivity. Meanwhile, we interrogated the potential ability of **2d·I** to control the planar chirality of the π-allylpalladium by subjecting a combination of racemic 5-methyl-5-vinyloxazolidinone **8a** and 2-methylidenemalonate **9** to similar annulation. This trial stereoconvergently produced pyrrolidine **10** with high efficiency and enantioselectivity (Scheme 1b). These data manifested the possibility that chiral ammonium phosphine **2d·I** would pave the way to individual, yet simultaneous absolute stereocontrol in multiple bond-forming events in asymmetric cycloaddition reactions.

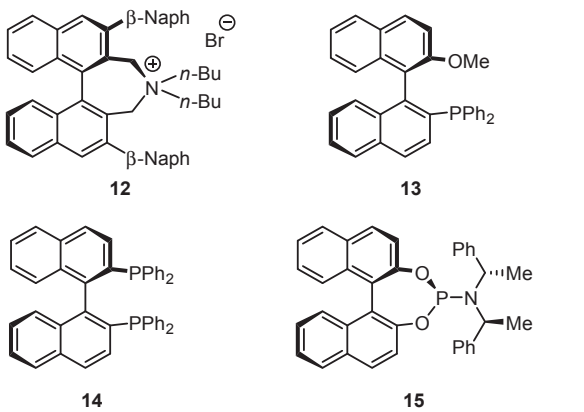
From this standpoint, we assessed the viability of the asymmetric construction of three contiguous stereocenters including vicinal all-carbon quaternary stereocenters[8,12,31–35] through the [3+2] annulation of racemic 5-vinyloxazolidinone **8a** and 2-cyano-3-phenylacrylate **6a** (Table 2). Thus, the reaction of **8a** with **6a** catalyzed by $[Pd_2(dba)_3]\cdot CHCl_3$ and **2d·I** in toluene at 0 °C furnished the desired densely substituted pyrrolidine **11a** in an almost stereochemically pure form (Entry 1).[36] Then, several control experiments were carried out to figure out the crucial elements for the catalytic system to facilitate this cycloaddition with satisfactory levels of efficiency and multiple stereocontrol. As shown in Table 2, the reaction of **8a** with **6a** using tris(4-trifluoromethyl)phenylphosphine as the ligand in the presence of chiral ammonium bromide **12**[37] proceeded at room temperature to afford **11a** quantitatively, but as a 1:1 mixture of diastereomers of low enantiopurity (Entry 2). Important comparison was that the annulation with the same phosphine ligand in the absence of **12** showed no indication of the product formation (Entry 3). While the combined use of common chiral phosphine ligands, such as MOP[38] (**13**) or BINAP[39] (**14**) with TBAB was ineffective in promoting the cycloaddition (Entry 4) or inducing stereoselectivity (Entry 5), BINOL-derived phosphoramidite[40,41] **15** could impart sufficient cata-



Scheme 1. Examinations of individual absolute stereocontrol.

Table 2. Attempt at asymmetric construction of contiguous all-carbon quaternary stereocenters[a)]





Entry	Ligand	Additive	Yield/%[b)]	dr[c)]	ee/%[d)]
1	**2d·I**	—	98	>20:1	98/nd
2[e)]	P(4-$CF_3C_6H_4$)$_3$	**12**	99	1:1	14/−33
3[e)]	P(4-$CF_3C_6H_4$)$_3$	—	0	—	—
4[e)]	**13**	TBAB	trace	—	—
5[e),f)]	**14**	TBAB	13	1:1.9	<1/<1
6[e)]	**15**	TBAB	95	1:1.2	−15/−23

a) Unless otherwise noted, reactions were carried out with 0.10 mmol of **8a** and 0.30 mmol of **6a** in the presence of [$Pd_2(dba)_3$·$CHCl_3$] (Pd, 2.5 mol %), ligand (5 mol %), and additive (5 mol %) in 1.0 mL of toluene at 0 °C for 10 h. b) Isolated yield. c) Determined based on ^{1}H NMR analysis of crude reaction mixture. d) Determined by HPLC analysis. nd: not detected. e) Carried out at r.t. for 24 h. f) With 2.5 mol % of **14**.

lytic activity to the corresponding Pd complex (Entry 6).[12] However, the observed poor stereoselectivity could not be improved by a further screening of structurally different chiral phosphoramidites. These results emphasize the critical importance of the molecular architecture of **2·X** that features the triarylphosphine incorporating chiral ammonium ion component paired with an appropriate halide ion for achieving an otherwise difficult multiple stereocontrol in the Pd-catalyzed [3+2] cycloaddition.

Next, the substrate scope of this asymmetric [3+2] cycloaddition of racemic 5-vinyloxazolidinones **8** and geometrically pure trisubstituted alkenes **6** was explored, and the representative results are listed in Figure 3. In the reactions of **8a** with 2-cyanoacrylates **6** possessing aromatic or heteroaromatic substituents at the 3-positions, excellent chemical yield and almost complete enantio- and diastereoselectivity were uniformly observed (**11b**–**11e**). A significant variation in the structure of the 5-alkyl substituent of **8** was feasible, and the corresponding cycloadducts were obtained in a virtually stereochemically pure form **11f**–**11i**. The reaction also tolerated the 5-aromatic groups on **8**, producing *N*-protected pyrrolidines **11j**–**11l** quantitatively with high levels of relative and absolute stereocontrol.[36]

To further expand the potential of our strategy for multiple absolute stereocontrol, the annulation reactions of oxazolidinones with a geometrical mixture of trisubstituted alkenes were investigated in detail. We reasoned that, if the absolute stereochemistry in the construction of C(3) chiral carbon of annulation product can be established individually by the virtue of chiral ammonium–phosphine ligand **2d·I** (Figure 4), this ligand-controlled catalysis would override the geometrical nature of trisubstituted alkenes. For obtaining a vital clue to validate this possibility, the cycloaddition of oxazolidinone **3** and ethyl 2-cyanoacrylate (**16**) was performed. Although a complex mixture was obtained due to the strong tendency of **16** towards polymerization, the desired pyrrolidine **17** was isolated in 25% yield with moderate enantioselectivity (Scheme 2). The observed asymmetric induction could be accounted for by assuming the doubly ion-pairing intermediate, where the

conformation of the C(3) carbanion is controlled by the ligand, particularly the chiral ammonium ion component.

Based on this prospect, this catalytic system was applied to the reactions of racemic 5-vinyloxazolidinones **8** with 2-nitro-3-arylacrylates **18** that are difficult to prepare in a geometrically pure form because of their facile E/Z isomerization (Table 3). Initially, the cycloaddition of **8a** and ethyl 2-nitro-3-phenylacrylate (**18a**; $E/Z = 1{:}2$) was attempted using achiral ammonium phosphine **1·Br**. The reaction turned out to be sluggish even at room temperature, furnishing cycloadduct **19a** in low yield and as a 5:8:3:1 mixture of four diastereomers (Entry 1). This indicates the difficulty of controlling the stereochemical outcome of this cycloaddition. In contrast, however, the use of **2d·I** as the ligand led to the quantitative formation of **19a** with high diastereo- (11:1.4:1:<1) and excellent enantioselectivity (95% ee) (Entry 2). It should be noted that the E/Z ratio of the remaining **18a** was confirmed to be almost unchanged. These observations demonstrate the inherent power of chiral ammonium phosphine **2d·I** for enabling efficient individual absolute stereocontrol over the array of three contiguous stereocenters in the single annulation. Further experiments were carried out to probe the scope of this protocol. With respect to 2-nitroacrylates **18**, the incorporation of diverse 3-aryl substituents including fused and heteroaromatic substituents was tolerated, and the corresponding pyrrolidines were obtained almost quantitatively with high diastereo- and enantioselectivity (Entries 3–6). The reaction accommodated oxazolidinones with various 5-alkyl substituents without a considerable loss of chemical yield and stereoselectivity (Entries 7–11). Moreover, 5-aryloxazolidinones were also employable with a similar degree of efficiency and diastereoselectivity, albeit a certain decrease in enantioselectivity was detected (Entries 12–14).

As clearly shown by this study, chiral ammonium–phosphine hybrid ligand **2d·I** played a pivotal role in achieving rigorous multiple absolute stereocontrol over the [3+2] annulation reaction. Among the critical stereodetermining events involved in the asymmetric five-membered ring construction, the C(2) and C(3) stereocenters of the resulting pyrrolidine framework would be determined through the enantiofacial discrimination of the starting trisubstituted alkene in the aza-Michael addition and of the subsequently generated carbanion in the ring-closing step, respectively (Figure 1). With regard to the C(4) stereocenter derived from the C(5) chiral carbon of racemic oxazolidinone, however, two possible scenarios existed for the stereoconvergent establishment of this stereocenter (Figure 5): (i) It was installed through the isomerization of planar chiral π-allylpalladium via π–σ–π interconversion; (ii) racemic oxazolidinone was directly transformed into a single stereoisomer of π-allylpalladium intermediate through direct enantioconvergent mechanism, where one enantiomer of oxazolidinone undergoes an *anti*-S_N2'-type addition pathway, and the other reacts via a *syn*-S_N2' pathway.[42]

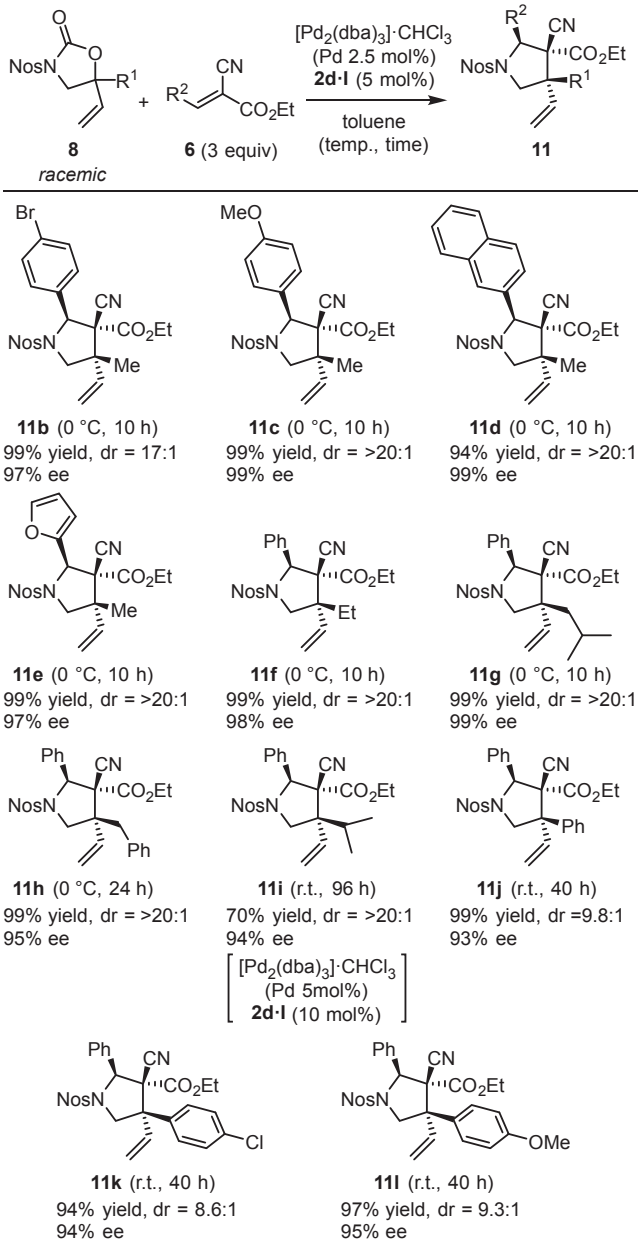


Figure 3. Substrate scope of catalytic asymmetric [3+2] cycloaddition of oxazolidinones **8** and 2-cyanoacrylates **6**.

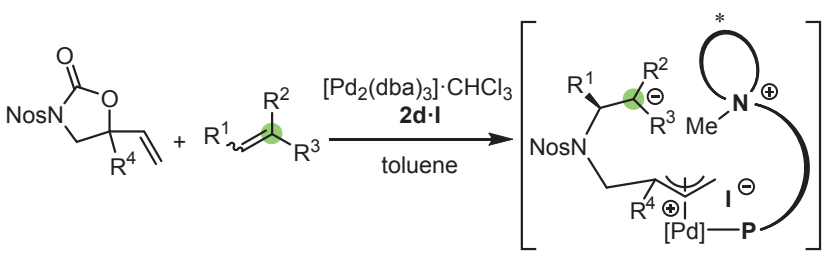
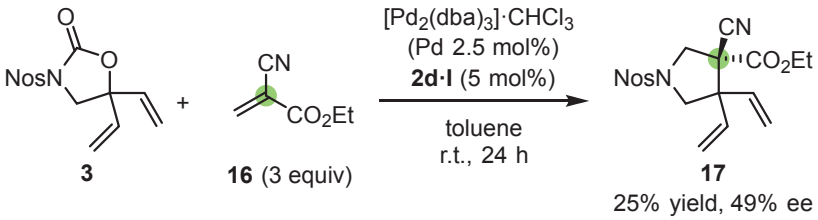
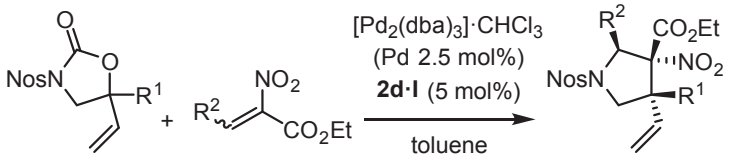


Figure 4. Individual stereocontrol in the construction of C(3) chiral carbon.



Scheme 2. Examination of the construction of C(3) chiral carbon.

Table 3. Asymmetric [3+2] cycloaddition of oxazolidinones **8** and 2-nitro-3-arylacrylates **18**[a)]



Entry	R^1	**8**	R^2	**18**	Conditions	**19**	Yield /%[b)]	dr[c)]	ee /%[d)]
1[e)]	Me	**8a**	Ph	**18a**	r.t., 24 h	**19a**	27	5:8:3:1	—
2	Me	**8a**	Ph	**18a**	0 °C, 8 h	**19a**	99	11:1.4:1:<1	95
3	Me	**8a**	4-Me-C_6H_4	**18b**	0 °C, 10 h	**19b**	99	12:1.1:1:<1	92
4	Me	**8a**	4-CF_3-C_6H_4	**18c**	0 °C, 10 h	**19c**	99	5.9:1.1:1:<1	89
5	Me	**8a**	2-naphthyl	**18d**	0 °C, 10 h	**19d**	99	11:1.2:1:<1	96
6	Me	**8a**	2-furyl	**18e**	r.t., 24 h	**19e**	97	11:1.1:1:<1	94
7	Et	**8b**	Ph	**18a**	0 °C, 24 h	**19f**	99	15:2.8:1:<1	96
8	*n*-Bu	**8c**	Ph	**18a**	0 °C, 24 h	**19g**	80	17:3.8:1:<1	92
9	*i*-Bu	**8d**	Ph	**18a**	r.t., 24 h	**19h**	83	11:1:<1:<1	97
10	$PhCH_2CH_2$	**8e**	Ph	**18a**	r.t., 36 h	**19i**	99	14:1.3:1:<1	95
11	*i*-Pr	**8f**	Ph	**18a**	r.t., 48 h	**19j**	78	>20:2.6:1:<1	96
12	Ph	**8g**	Ph	**18a**	r.t., 48 h	**19k**	92	16:1:<1:<1	71
13	4-Cl-C_6H_4	**8h**	Ph	**18a**	r.t., 36 h	**19l**	81	19:1:<1:<1	83
14	4-MeO-C_6H_4	**8i**	Ph	**18a**	r.t., 36 h	**19m**	79	17:1:<1:<1	77

a) Unless otherwise noted, reactions were carried out with 0.10 mmol of **8** and 0.3 mmol of **18** in the presence of $[Pd_2(dba)_3 \cdot CHCl_3]$ (Pd, 2.5 mol %) and **2d·I** (5 mol %) in 1.0 mL of toluene. b) Isolated yield. c) Determined based on ^{1}H NMR analysis of crude reaction mixture. d) Enantiomeric excesses of the major diastereomer were indicated, which were analyzed by chiral stationary phase HPLC. The absolute configurations of **19a** was confirmed by X-ray diffraction analysis, and the stereochemistries of other examples were assumed by analogy. e) The reaction was performed with **1·Br** (5 mol %) instead of **2d·I**.

To gain insight into the course of the determination of C(4) stereochemistry, the asymmetric cycloaddition with racemic oxazolidinone **20** bearing a geometrically pure, deuterated vinyl substituent was investigated. Thus, **20** was treated with 2-cyano-3-phenylacrylate **6a** under the influence of the Pd/**2d·I** complex, which afforded a 1:1 ratio of the geometrical isomers of pyrrolidine **21** (Scheme 3), indicating that the absolute stereochemistry of the C(4) carbon was established through the isomerization of planar chiral π-allylpalladium.

Conclusion

A highly enantio- and diastereoselective [3+2] annulation reaction of 5-vinyloxazolidinones with trisubstituted alkenes was successfully developed based on the utilization of a Pd complex bearing a chiral ammonium–phosphine hybrid ligand. This asymmetric cycloaddition system, characterized by ligand-enabled multiple absolute stereocontrol over the single-step construction of three contiguous stereocenters in a five-membered heterocycle, allows the straightforward access to diverse densely functionalized pyrrolidines of high stereochemical purity. This study not only provides an efficient synthetic protocol, but also offers unprecedented, yet fruitful opportunities for the molecular design of chiral phosphine ligands and their applications to the development of previously elusive, catalytic stereoselective transformations.

Experimental

General. All air- and moisture-sensitive reactions were performed under an atmosphere of argon (Ar) in dried glassware. The manipulations for Pd-catalyzed reactions were carried out with standard Schlenk techniques under Ar. Toluene was supplied from Kanto Chemical Co., Inc. as "Dehydrated" and further purified by both A2 alumina and Q5 reactant using a GlassContour solvent dispensing system. $[Pd_2(dba)_3] \cdot CHCl_3$ was purchased from Sigma-Aldrich Co. and purified by following a literature procedure.[43] Ammonium phosphines **2·X**,[22]

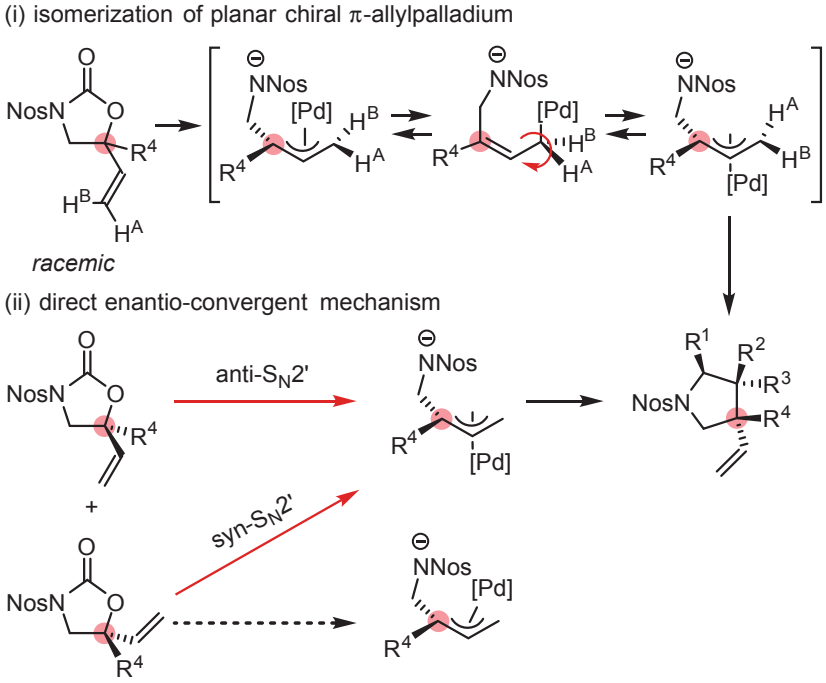
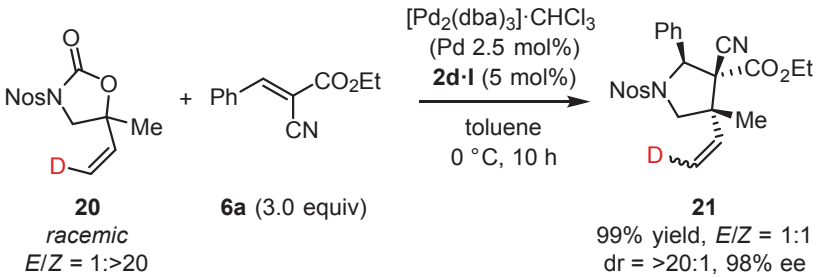


Figure 5. Two possible scenarios for the determination of C(4) stereocenter.



Scheme 3. Asymmetric cycloaddition of deuterated oxazolidinone **20**.

oxazolidinones,[22] and alkenes[44,45] were synthesized by following procedures described in the literature. Deuterated oxazolidinone **20** was synthesized as described in Supporting Information. Other simple chemicals were purchased and used as such.

Representative Procedure for Pd-Catalyzed Asymmetric Cycloaddition of 5-Vinyloxazolidinones with Trisubstituted Alkenes. To a Schlenk flask was added $[Pd_2(dba)_3]\cdot CHCl_3$ (1.29 mg, 1.25 µmol), **2d·I** (5.50 mg, 5 µmol), and ethyl 2-cyano-3-phenylacrylate (**6a**) (60.4 mg, 0.3 mmol) and the flask was evacuated and refilled with Ar three times. Then, toluene (1 mL) was introduced, and the resulting catalyst mixture was degassed by alternating vacuum evacuation/Ar backfill. The mixture was cooled to 0 °C and 5-vinyloxazolidinone **8a** (31.2 mg, 0.1 mmol) was successively added into the reaction flask. After stirring for 10 h, the reaction mixture was filtered through a pad of short silica gel and washed with acetone. The resulting filtrates were concentrated and purified by column chromatography on silica gel (Hex/Et_2O = 9:1 to 3:1 as eluent) to afford **11a** (46.1 mg, 0.098 mmol, 98% yield) as a white solid. **11a**: ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (2H, d, J = 8.9 Hz), 7.59 (2H, d, J = 8.9 Hz), 7.26–7.22 (1H, m), 7.19–7.11 (4H, m), 5.86 (1H, dd, J = 17.4, 11.0 Hz), 5.68 (1H, s), 5.45 (1H, d, J = 17.4 Hz), 5.37 (1H, d, J = 11.0 Hz), 4.33 (1H, d, J = 11.5 Hz), 4.28 (1H, dq, J = 11.0, 7.3 Hz), 4.15 (1H, dq, J = 11.0, 7.3 Hz), 3.76 (1H, d, J = 11.5 Hz), 1.57 (3H, s), 1.28 (3H, t, J = 7.3 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.4, 149.9, 145.4, 135.2, 134.1, 129.3, 128.8, 128.5, 128.2, 123.9, 118.4, 115.1, 66.9, 65.0, 63.8, 58.3, 50.6, 19.4, 14.2; IR (film): 3105, 3069, 3036, 2984, 2936, 1744, 1531, 1350, 1240, 1165, 1090, 1042, 741, 698, 563 cm^{-1}; HRMS (ESI): Calcd for $C_{23}H_{23}N_3O_6SNa^+$ ($[M + Na]^+$) 492.1200, Found 492.1200; HPLC OZ3, Hex/IPA = 80:20, flow rate: 1.0 mL min^{-1}, λ = 254 nm, retention time: 29.3 min (major), 38.9 min (minor).

Representative Procedure for Pd-Catalyzed Asymmetric Cycloaddition of 5-Vinyloxazolidinones with 2-Nitro-3-arylacrylates. To a Schlenk flask was added $[Pd_2(dba)_3]\cdot CHCl_3$ (1.29 mg, 1.25 µmol) and **2d·I** (5.50 mg, 5 µmol) and the flask was evacuated and refilled with Ar three times. Then, toluene (1 mL) was introduced, and the resulting catalyst mixture was degassed by alternating vacuum evacuation/Ar backfill. The mixture was cooled to 0 °C and 2-nitro-3-phenylacrylate **18a** (66.4 mg, 0.3 mmol) and 5-vinyloxazolidinone **8a** (31.2 mg, 0.1 mmol) were successively added into the reaction flask. After stirring for 8 h, the reaction mixture was filtered through a pad of short silica gel and rinsed with acetone and

the filtrates were concentrated. Purification of the residue by column chromatography on silica gel ($H/Et_2O = 11:1$ to 3:1 as eluent) gave **19a** (48.4 mg, 0.0989 mmol, 99% yield) as a white solid. **19a**: ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (2H, d, $J =$ 8.7 Hz), 7.59 (2H, d, $J = 8.7$ Hz), 7.22–7.17 (1H, m), 7.07–7.05 (4H, m), 6.08 (1H, s), 5.91 (1H, dd, $J = 17.2$, 11.0 Hz), 5.50 (1H, d, $J = 17.2$ Hz), 5.38 (1H, d, $J = 11.0$ Hz), 4.30 (1H, d, $J = 10.5$ Hz), 4.21 (1H, d, $J = 10.5$ Hz), 3.76 (1H, dq, $J = 10.5$, 7.3 Hz), 3.45 (1H, dq, $J = 10.5$, 7.3 Hz), 1.56 (3H, s), 0.68 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.3, 149.9, 145.7, 136.0, 133.7, 129.1, 128.8, 128.4, 128.0, 123.9, 119.2, 105.0, 66.4, 63.1, 58.2, 50.9, 16.5, 13.2; IR (film): 3105, 3069, 3038, 2984, 2922, 1744, 1557, 1530, 1348, 1236, 1161, 1042, 853, 735, 702, 617, 565 cm^{-1}; HRMS (ESI): Calcd for $C_{22}H_{23}N_3O_8SNa^+$ ($[M + Na]^+$) 512.1098, Found 512.1101; HPLC IA, H/EtOH = 83.3:16.7, flow rate: 0.5 mL min^{-1}, $\lambda =$ 254 nm, retention time: 15.8 min (minor), 20.1 min (major).

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Supporting Information

Analytical data for cyclization products, procedure for the synthesis of deuterated oxazolidinone **20**, NMR spectra of new compounds, and HPLC charts. This material is available on http://dx.doi.org/10.1246/bcsj.20160053.

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