Highly Enantioselective Synthesis of 1,3-Oxazolidin-2-imine Derivatives by Asymmetric Cycloaddition Reactions of Vinyloxiranes with Unsymmetrical Carbodiimides Catalyzed by Palladium(0) Complexes

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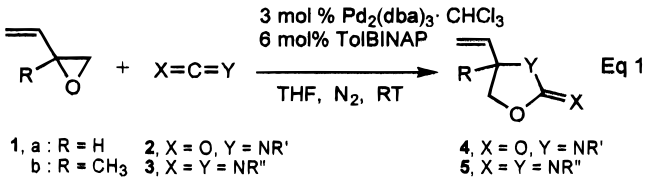
4-Vinyl-1,3-oxazoilidin-2-imine derivatives have been synthesized by cycloaddition reactions of 2-vinyloxiranes with unsymmetrical carbodiimides catalyzed by palladium(0) complexes in excellent total isolated yields. After reaction two compounds were always formed, one of which was isolated as the major product. A bulky alkyl group on one of the nitrogen atoms of the carbodiimide enhanced the product ratio in favor of the *N*-aryl-3-alkyl-1,3-oxazolidin-2-imine. Highly enantioselective cycloadducts (up to >99% ee) were formed by using TolBINAP as the chiral phosphine ligand, in THF at ambient temperatures. The enantiodetermination is believed to be dependent on nucleophilic attack of the anionic nitrogen of the carbodiimide due to the steric interaction of the carbodiimide substituents with the chiral phosphine ligand.

Introduction

Asymmetric synthesis is an important strategy for the preparation of enantiomerically pure or enriched compounds.[1] The cycloaddition and ring expansion reactions of three-membered-ring heterocycles such as aziridines[2] and oxiranes[3] with heterocumulenes to form five-membered ring products have been widely studied in the past several years. For example, some 2-oxazolidine derivatives have been prepared which may have interesting biological activities.[4] Palladium is a useful catalyst for the cycloaddition reactions.[5] π-Allylpalladium intermediates are likely key intermediates for the regio- and stereoselective synthesis of 1,3-oxazolidines. For instance, the asymmetric cyclization of 2-butenylenedicarbamate catalyzed by chiral ferrocenylphosphine−palladium(0) complexes afforded 4-vinyl-1,3-oxazolidin-2-ones in up to 77%ee.[6] A series of 2-(diphenylphosphino)-benzoic acid and 2-(diphenylphosphino)aniline based ligands have been utilized along with a catalytic amount of $Pd_2(dba)_3{\cdot}CHCl_3$ for the stereoselective formation of 1,3-oxazolidine-2-ones from urethanes.[7] In addition, use of Pd(0)−triisopropyl phosphite as the catalyst for the diastereoselective conversion of vinyloxirane gives *cis*-oxazolidin-1-ones.[8]

In a previous publication,[9] we described the stereoselective synthesis of 4-vinyl-1,3-oxazolidone and 4-vinyl-1,3-oxazolidin-2-imine derivatives by using palladium complexes and chiral phosphine ligands as the catalyst system for the cycloaddition reaction of 2-vinyloxiranes and heterocumulenes (eq 1). By introducing chiral phos-



phine ligands, such as (*S*)- or (*R*)-TolBINAP, 4-vinyl-1,3-oxazolidin-2-imines derivatives were obtained in high yields and in up to 95% ee. The question arises as to the degree of regioselectivity of the cycloaddition reaction of *unsymmetrical* carbodiimides with vinyloxiranes, i.e.,

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(3) (a) Speranza, G. P.; Pepel, W. J. *J. Org. Chem.* **1958**, *23*, 1922. (b) Herweh, J. E.; Foglia, T. A.; Swern, D. *J. Org. Chem.* **1968**, *33*, 4029. (c) Herweh, J. E.; Kauffman, W. J. *Tetrahedron Lett.* **1971**, *12*, 809. (d) Baba, A.; Fujiwara, M.; Matsuda, H. *Tetrahedron Lett.* **1986**, *27*, 77. (e) Fujiwara, M.; Baba, A.; Matsuda, H. *J. Heterocycl. Chem.* **1988**, *25*, 1351. (f) Shibata, I.; Seki, K.; Matsuda, H. *J. Org. Chem.* **1986**, *51*, 7. (g) Baba, A.; Seki, K.; Matsuda, H. *J. Heterocycl. Chem.* **1990**, *27*, 1925. (h) Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792. (i) Qian, C.; Zhu, D. *Syn Lett.* **1994**, 129. (j) Brunner, M.; Mussmann, D. V. *Syn Lett.* **1994**, 69.

(4) (a) Boyd, G. V. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Gilchrist, T. L., Eds.; Elsevier Science Ltd.: U.K., 1997; Vol. 9, pp 217−218. (b) Boyd, G. V. In *Progress in Heterocyclic Chemistry*; Suschitzky, H., Gribble, G. W., Eds.; Elsevier Science Ltd.; U.K., 1996; Vol. 8, pp 187−191. (c) Boyd, G V. In *Progress in Heterocyclic Chemistry*; Suschitzky, H., Scriven, E. F. V., Eds.; Elsevier Science Ltd.: U.K., 1995; Vol. 7, pp 198−201 (d) Katritzky, A. R.; Rees, C. W. *Comprehensive Heterocyclic Chemistry,* Vol. 1, Part 1; Pergamon Press: U.K., 1984. (e) Shibata, I.; Toyota, M.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1990**, *55*, 2487. (f) Dyen, M. E.; Swern, D. *Chem. Rev.* **1967**, *67*, 197. (g) Murthy, K. S. K.; Dhar, D. N. *J. Heterocycl. Chem.* **1984**, *21*, 1721. (h) Karikomi, M.; Yamazaki, T.; Toda, T. *Chem. Lett.* **1993**, 1965. (i) Paleo, M. R.; Calaza, M.I. Sardina, F. J. *J. Org. Chem.* **1997**, *62*, 6862.

(5) Tsuji, J. *Palladium Reagents and Catalysts. Innovations in Organic Synthesis*; John Wiley & Sons: U.K., 1995.

(6) Hayashi, T.; Yamamoto, A.; Ito, Y. *Tetrahedron Lett.* **1988**, *29*, 99.

(7) Trost, B. M.; Van Venkren, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 444.

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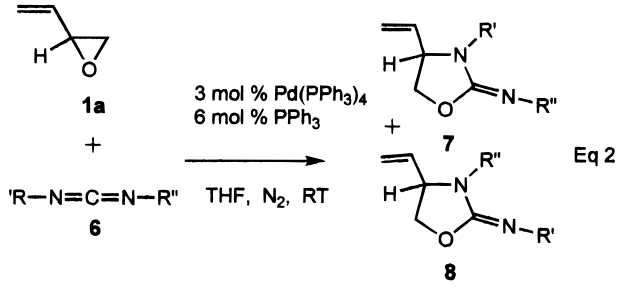
is there any preference for one of the two possible 4-vinyl-1,3-oxazolidin-2-imines? Also can one attain significant chiral discrimination using TolBINAP as an added ligand? We now wish to report that regioselectivities of 2−4:1 (9:1 in one case) were obtained in the reactions with impressive enantiomeric excesses realized by using TolBINAP as the chiral ligand.

Results and Discussion

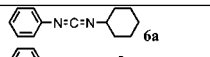
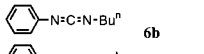
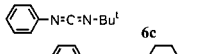
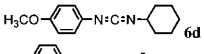
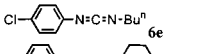
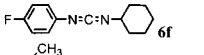
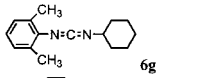
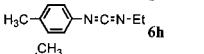
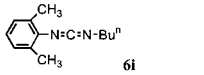
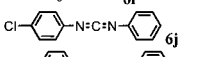
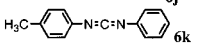
Cycloaddition Reactions of Vinyloxirane with Unsymmetrical Carbodiimides. As previously reported,[9] 3 mol % of $Pd(PPh_3)_4$ and 6 mol % of PPh_3 were required in order to obtain products from the cycloaddition reactions of 2-vinyloxiranes with heterocumulenes. Cycloaddition reactions of 2-vinyloxirane with unsymmetrical carbodiimides were carried out in the same manner providing good to excellent isolated yields of products. The reactions were performed by treatment of 2-vinyloxirane **1a** with unsymmetrical carbodiimides **6** in the presence of $Pd(PPh_3)_4$ and 2 equiv of triphenylphosphine relative to palladium, in dried THF at room temperature, until there was full conversion of carbodiimide (monitored by IR) (eq 2).



Two products (4-vinyl-1,3-oxazolidin-2-imines), **7** and **8**, were formed using carbodiimides containing alkyl and aryl substituents. The products were isolated in pure form (preparative TLC) in a total yield of 79−96% (Table 1).[10] It is noteworthy that one of the two five-membered-ring heterocycles was always obtained as the major product (**7**) and it is less polar than isomeric (**8**). The ratios of **7** to **8** were usually determined by gas chromatography of the reaction mixture after complete conversion of the carbodiimide. Nuclear magnetic resonance (^1H, ^{13}C) spectra indicated that two products were formed from unsymmetrical diaryl carbodiimides (entries 10 and 11) but the ratio could not be determined, and the products were inseparable by GC and TLC.

The cycloaddition reaction may proceed via zwitterionic (π-allyl)palladium intermediates formed by oxidative addition of **1** to a palladium(0) species[11] followed by reaction with the unsymmetrical carbodiimide. Rotation about the C-6 carbon of **9** and **10** (Scheme 1) enables two types of intramolecular ring closure to occur, by either of the nitrogen nucleophiles at the C-3 carbon to give the five-membered-ring, 4-vinyl-1,3-oxazolidine-2-imines derivatives, **7** and **8**.

Table 1. Cycloaddition Reactions of 2-Vinyloxirane 1a with Unsymmetrical Carbodiimides 6 in the Presence of $Pd(PPh_3)_4$ and PPh_3[a]

entry	Carbodiimides	Reaction Time (hr)	Ratio[b] of **7** : **8**	Isolated yield[c] **7** + **8**
1	 **6a**	12	2.4 : 1	84 %
2	 **6b**	12	2 :1	82 %
3	 **6c**	24	1.4 : 1	84 %
4	 **6d**	12	2 : 1	81 %
5	 **6e**	12	2 : 1	84 %
6	 **6f**	12	2 :1	90 %
7	 **6g**	15	4 : 1	96 %
8	 **6h**	12	2 :1	82 %
9	 **6i**	15	4.5 : 1	79 %
10	 **6j**	15	*d*	81 %
11	 **6k**	15	*d*	94 %

[a] Reaction conditions: 2-vinyloxirane, **1a** (1.5 mmol), carbodiimide **6** (1.0 mmol), $Pd(PPh_3)_4$ (0.03 mmol), PPh_3 (0.06 mmol), THF (5 mL), room temperature, N_2 atmosphere. [b] Determined by GC. [c] Purified by preparative TLC. [d] The two isomers could not be separated by GC or TLC.

Since there are two possible structures for the major products from alkylarylcarbodiimides, one with the aryl group attached to the nitrogen of the oxazolidine ring and the other with the alkyl group attached to the heterocyclic nitrogen, the structure of the major products need to be determined. Attempts to hydrolyze 4-vinyl-1,3-oxazolidin-2-imines to 4-vinyl-1,3-oxazolidin-2-ones led to only partial conversion. Therefore, a single-crystal X-ray determination was made to establish the structure of the major product of entry 7 (Table 1). The result shows that the structure of the major product (**7g**) of this cycloaddition reaction is the 4-vinyl-1, 3-oxazolidin-2-imine, which contains a cyclohexyl group attached to the heterocyclic ring nitrogen (Figure 1). Comparison[12] of the spectral data of the major and minor products from each reaction to those obtained from entry 7 reveals that the major product formed (**7**) is the isomer with the alkyl group attached to the nitrogen of the ring. This may be due to the fact that the nucleophilicities of anionic nitrogen containing alkyl substituents is higher than that in which an aryl group is the substituent.

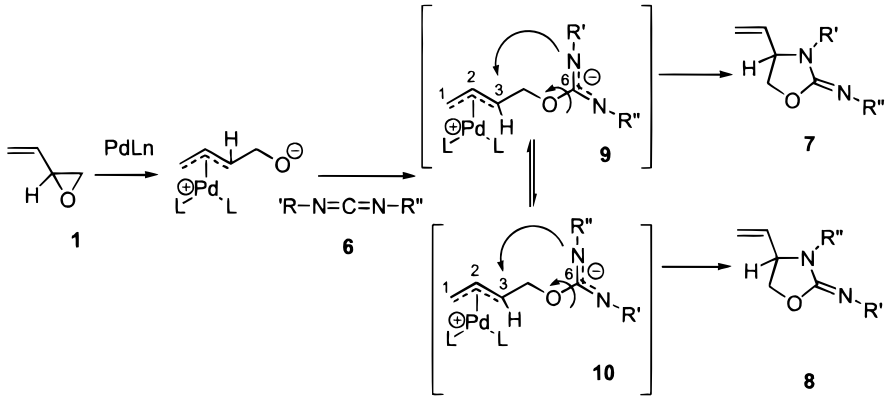
Attempts to improve the regioselectivity of this reaction by introducing a more bulky alkyl group (R′), such as *tert*-butyl or cyclohexyl, on one nitrogen atom of the carbodiimide proved to be ineffective (entries 1−3). Phenyl rings (R″) which contain a substituent at the *para* position also did not enhance the regioselectivity of the reactions (entries 4−6). Furthermore, the reaction temperature does not affect the regioselectivity of the reaction. Similar results were obtained when performing the reaction (entry 1) either at higher (80 °C, 2 h) or lower (5 °C, 24 h) reaction temperatures. Using other phosphine ligands in the cycloaddition reaction such as

(10) After complete conversion of carbodiimide, the reaction mixture was concentrated and the residue was separated by preparative silica gel TLC using pentane/ether as the developer.

(11) (a) Hayashi, T.; Yamamoto, A.; Hagihara, T.; Ito, Y. *Tetrahedron Lett.* **1986**, *27*, 191. (b) Hayashi, T.; Yamamoto, A.; Ito, Y. *Chem. Lett.* **1987**, 177. (c) Hayashi, T.; Konishi, M.; Kumada, M. *Chem. Soc., Chem. Commun.* **1984**, 107. (d) Fiaud, J.-C.; Legros, J.-Y. *J. Org. Chem.* **1990**, *55*, 4840. (e) Tsuji, J. *Pure Appl. Chem.* **1982**, *54*, 197.

(12) Spectral data were compared by means of ^1H NMR spectra (pattern of the coupling constants) and the C=N absorption band in the IR spectrum (~1970 cm^{-1} for the major products and ~1990 cm^{-1} for the minor products).

Scheme 1



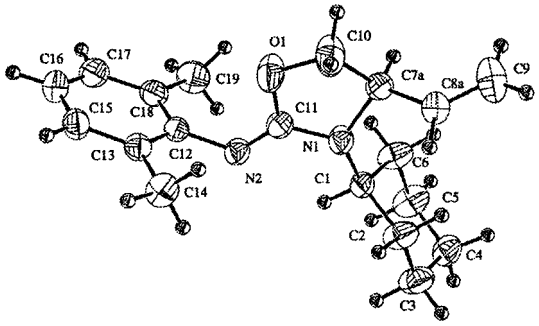
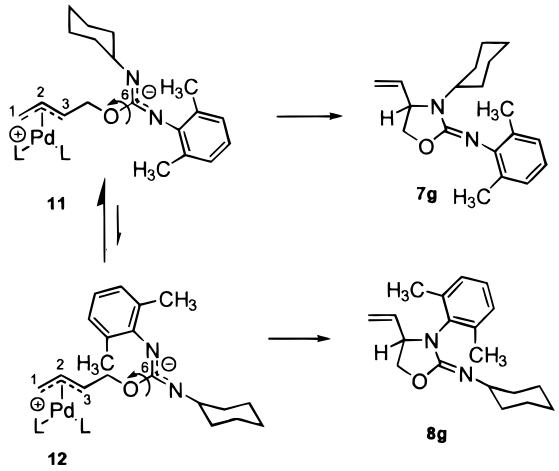


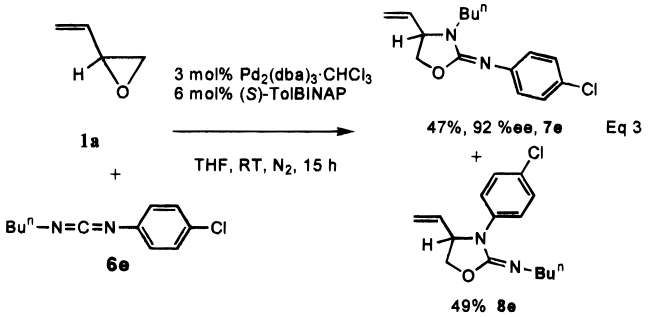
Figure 1. X-ray structure of the major product (**7g**) obtained from entry 7, Table 1.

Scheme 2



tricyclohexylphosphine, dppp or dppb had no effect on the selectivity.[13] However, greater selectivity resulted using carbodiimides containing a phenyl ring with *ortho* substituents (entries 7 and 9), possibly because of steric hindrance of the *ortho* substituents on the phenyl ring during rotation about C-6 of the intermediates. Therefore, it can be reasoned that intermediate **11** is preferred to **12** prior to intramolecular nucleophilic attack at C-3 (Scheme 2) and thus isomer **7g** is generated as the major product. The noted anion nucleophilicity effect could be responsible for a greater rate of cyclization of **11** than **12**, thus leading to **7g** as the primary product.[14]

Asymmetric Palladium-Catalyzed Cycloaddition Reactions of Vinyloxiranes with Unsymmetrical Carbodiimides. As previously reported on the cycloaddition reactions of 2-vinyloxiranes with symmetrical carbodiimides, the highest enantioselectivities were attained when TolBINAP was used as the chiral ligand.[9,15] Impressive results were also realized in the asymmetric cycloaddition reaction of 2-vinyloxirane with unsymmetrical carbodiimides. We initially performed this reaction by using 1.5 mmol of **1a** and 1 mmol of **6e** (R′ = *n*-butyl, R″ = *p*-ClC_6H_4) in the presence of $Pd_2(dba)_3$·$CHCl_3$ (0.03 mmol) and (*S*)-TolBINAP (0.06 mmol) for 15 h in THF at room temperature under a nitrogen atmosphere. After reaction, *N*-(*p*-chlorophenyl)-3-*n*-butyl-4-vinyl-1,3-oxazolidin-2-imine **7e** and *N*-(*n*-butyl)-3-*p*-chlorophenyl-4-vinyl-1,3-oxazolidin-2-imine **8e** were obtained in 96% isolated yield (**7e** + **8e**), with **7e** in 92% ee (eq 3). The % ee of **7e** was determined by chiral HPLC using a Chiracel OD column and 15% *i*-PrOH in hexane as the eluant. The enantiomers of **8e** could not be resolved by the same column.



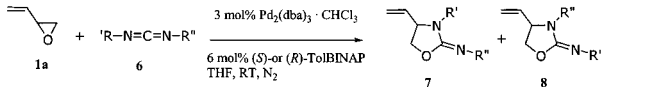
Some results for the asymmetric cycloaddition of unsymmetrical carbodiimides (**6**) with 2-vinyloxirane using the Pd(0)−TolBINAP catalyst system are presented in Table 2. The catalyst was generated in situ by reaction of 3 mol % of $Pd_2(dba)_3$·$CHCl_3$ with 2 equiv of (*S*)- or (*R*)-TolBINAP relative to palladium. The reaction mixtures were stirred under an inert atmosphere at room temperature until the conversion of the carbodiimides was complete (monitored by IR). Remarkable results for asymmetric induction were observed by employing carbodiimides **6** containing quite bulky alkyl substituents such as cyclohexyl (entries 1 (>99%ee of **7a**) and 4 (>99%

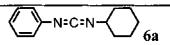
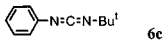
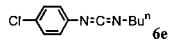
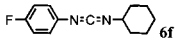
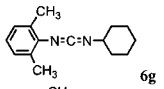
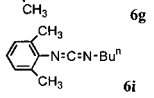
(13) The product ratios of the **7** to **8** of the reaction (entry 5), by using tricyclohexylphosphine, dppp, and dppb were 1.6:1,1:1 and 0.8:1, respectively.

(14) We thank one of the referees for this suggestion.

(15) TolBINAP = 2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl. See: Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem*, **1986**, *51*, 629.

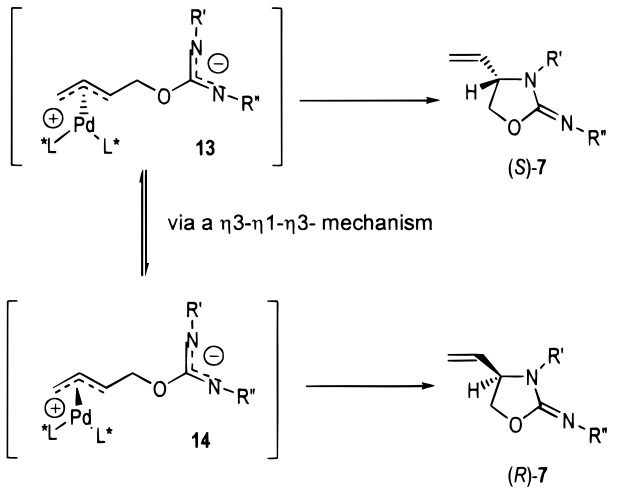
Table 2. Asymmetric Cycloadditions of 2-Vinyloxirane 1a with Unsymmetrical Carbodiimides 6 in the Presence of $Pd_2(dba)_3 \cdot CHCl_3$−(*S*)− or (*R*)-TolBINAP[a]



entry	Carbodiimides, 6	Reaction time	Ratio[b] of 7 : 8	Isolated yield[c] 7+8	% ee[d] of 7	$[\alpha]^{22}_D$ of 7 in $CHCl_3$
1	 6a	15 h	4 :1	94 %	>99	+18.9 (*c*, 2.74)[e]
2	 6c	4 days	9:1	58 %	>99	+ 45.1 (*c*, 5.30)[e]
3	 6e	15 h	1:1	96 %	93	-75.8 (*c*, 5.15)[f]
4	 6f	15 h	2:1	87 %	>99 97	-22.9 (*c* ,3.80)[f] +21.9 (*c*, 2.74)[e]
5	 6g	36 h	3.5:1	55 %	88 %	+70.5 (*c*, 2.06)[e]
6	 6i	36 h	4:1	69 %	94%	+27.9 (*c*, 1.80)[e]

[a] Reaction conditions: refer to the Experimental Section for the general procedure for the asymmetric cycloaddition. [b] Determined by GC. [c] Isolated by preparative TLC. [d] Enantiomeric excess determined by HPLC using a Chiracel OD column. [e] Using (*S*)-TolBINAP. [f] Using (*R*)-TolBINAP.

Scheme 3



ee of **7f**)) and *tert*-butyl (entry 2 (>99% ee of **7c**)). The enantiomers of each regioisomer of **7** were resolved by using HPLC with a chiral column (Chiracel OD), and a single signal was observed (using the same column and conditions) in the determination of the % ee of products from entries 1, 2, and 4.[16] In addition, moderate to good enantiomeric selectivities were obtained from entries 3 (92−93%ee of **7e**), 5 (88%ee of **7i**), and 6 (94%ee of **7g**). When both substituents on the carbodiimides are of considerable effective steric bulk, the yields of the products are appreciably lower (entries 2, 5, and 6).

The high degree of asymmetric induction observed in the cycloaddition reactions can be explained by the pathway shown in Scheme 3. The stereodetermination step in the reaction depends on the intramolecular attack of nitrogen nucleophiles on C-3 of the (π-allyl)palladium intermediates. It has been suggested that[7,9] the rate of interconversion between intermediates **13** and **14** (via a $\eta^3-\eta^1-\eta^3$ mechanism)[17] is much faster than nucleophilic attack of the nitrogen nucleophile. In this case, bulky alkyl substituents (cyclohexyl and *tert*-butyl) of unsymmetrical carbodiimides may influence the steric interaction during the enantiodetermination step, resulting in one of the intermediates reacting significantly faster than the others and thus accounting for the high enantiomeric excess. In the experiment using (*S*)-TolBINAP as an added chiral phosphine ligand, intermediate **14** reacts at a greater rate and affords solely the (*R*)-enantiomer.

The assignment of absolute stereochemistry was based on comparison of the sign of $[\alpha]^{22}_D$ with 4-vinyl-1,3-oxazolidin-2-imine products obtained previously,[9] and where absolute configuration was based on crystallographic data. All (*R*)-enantiomers were eluted first from the chiral column.

Conclusion

We have successfully extended the scope of the ring expansion reaction catalyzed by palladium complexes for the synthesis of 4-vinyl-1,3-oxazolidin-2-imine derivatives (**7** and **8**). Vinyloxazolidine derivatives were produced in high enantiomeric excess from the cycloaddition reaction of 2-vinyloxiranes with *unsymmetrical* carbodiimides in the presence of catalytic quantities of $Pd_2(dba)_3 \cdot CHCl_3$ and TolBINAP. When the reaction was performed in THF at room temperature, compounds **7a**, **7c**, and **7f** were obtained in good yield and in >99% optical purity.

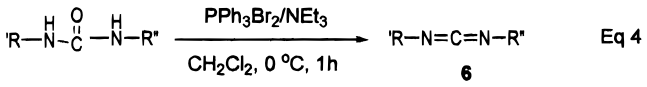
Experimental Section

General Methods. All NMR spectra were recorded in 200 and 300 MHz instruments. Infrared spectra were recorded on a Fourier transform spectrometer and are reported in wavenumbers (cm^{-1}). Optical rotations were measured using a polarimeter in a 10-cm cell at 22 °C. Melting points are uncorrected.

Assessment of % ee was achieved using an analytical HPLC instrument equipped with an automatic injector, diode array detector monitoring at 220 nm, and a Chiracel OD column. A 85:15, *n*-hexane:2-propanol mixture was used as the mobile phase at a flow rate of 1 mL/min.

Vinyloxiranes and $Pd(PPh_3)_4$ were purchased from Aldrich and were used as received. Palladium catalysts were prepared according to literature procedures.[18] The organic solvents were dried and distilled prior to use.

Synthesis of Unsymmetrical Carbodiimides 6a−k. Carbodiimides were prepared according to literature procedures[19] by dehydration of the appropriate urea (eq 4). The



substituted urea (8 mmol) was added portionwise during 60 min to a stirred suspension of bromotriphenylphosphonium

(16) Enantiomers of regioisomers **8** could not be separated up to acceptable standard by using Chiracel OD column.

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(18) Ukai, T.; Kawazura, H.; Ishii, Y. *J. Organomet. Chem.* **1974**, *65*, 253.

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bromide (10 mmol) and triethylamine (20 mmol) in dichloromethane (15 mL) at 0 °C. The resulting mixture was then washed with water and dried with anhydrous sodium sulfate. Evaporation of the solvent gave crude carbodiimide (**6**) which was distilled at reduced pressure to yield the desired unsymmetrical carbodiimide **6**. IR, NMR, MS, and analytical data of an example unsymmetrical carbodiimide **6a** are shown below (see Supporting Information for all **6**).

***N*-Cyclohexyl-*N*′-phenylcarbodiimide (6a) (R′ = C_6H_{11}, R″ = C_6H_5):** oily liquid; IR (C═N) 2116 cm^{-1}; ^1H NMR($CDCl_3$) δ 1.20−2.20 (m, 10 H), 3.48 (m, 1H), 7.05−7.39 (m, 5H) ^{13}C NMR ($CDCl_3$) 24.34, 25.30, 34.91, 56.61, 123.31, 124.47, 129.30, 140.88 ppm; MS (*m*/*e*) 200 $[M]^+$, HRMS calcd for $C_{13}H_{16}N_2$ 200.1313, found 200.1291.

General Procedure for the Palladium-Catalyzed Cycloaddition Reaction of Vinyloxiranes and Heterocumulenes. A mixture of $Pd(PPh_3)_4$ (0.03 mmol), PPh_3 (0.06 mmol), and THF (3 mL) was stirred under nitrogen at room temperature for 30 min. Vinyloxirane **1** (1.5 mmol) and unsymmetrical carbodiimide **6** (1 mmol) were added to the solution. The mixture was then stirred under nitrogen at room temperature until the conversion of the carbodiimide was complete (monitored by the shift of the IR absorption of the C═N band in the free carbodiimide (∼2100 cm^{-1}) to that of the oxazolidine (1670−1690 cm^{-1})). The light yellow homogeneous solution was then concentrated by rotary evaporation, and the residue was purified by silica gel TLC using pentane/ether mixture as the developer. Melting points, IR, NMR, MS and analytical data for selected representatives **7** and **8** are as follows (see Supporting Information for all cases).

***N*-Phenyl-3-cyclohexyl-4-vinyl-1,3-oxazolidin-2-imine (7a) (R = H, R′ = C_6H_{11}, R″ = C_6H_5):** oily liquid; IR (C═N) 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95−2.05 (m, 10H), 3.88 (m, 2H), 4.28 (m, 2H), 5.18−5.34 (m, 2H), 5.75−5.93 (m, 1H), 6.90−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.61, 25.82, 25.94, 29.55, 31.69, 54.30, 58.38, 69.54, 118.15, 121.74, 123.37, 128.35, 138.16, 148.13,152.38 ppm; MS (*m*/*e*) 270 $[M]^+$. Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20; N, 10.36 Found: C, 75.53; H, 8.37; N, 10.38.

***N*-Cyclohexyl-3-phenyl-4-vinyl-1,3-oxazolidin-2-imine (8a) (R = H, R′ = C_6H_5, R″ = C_6H_{11}):** oily liquid; IR (C═N) 1673 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10−2.00 (m, 10H), 3.50 (m, 2H), 4.03 (dd, 1H, *J* = 8.1 and 4.7 Hz), 4.42 (dd, 1H, *J* = 8.1 and 8.1 Hz), 4.65 (m, 1H), 5.32 (m, 2H), 5.85 (m, 1H), 6.95−7.70 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.56, 25.76, 25.89, 29.45, 31.66, 54.18, 58.27, 69.42, 118.01, 113.64, 123.96, 141.25, 138.17, 152.29, 154.53 ppm; MS (*m*/*e*) 270 $[M]^+$; HRMS calcd for $C_{17}H_{22}N_2O$ 270.1732. found 270.1725.

***N*-*n*-Butyl-3-phenyl-4-vinyl-1,3-oxazolidin-2-imine (7b) (R = H, R′ = C_4H_9, R″ = C_6H_5):** oily liquid; IR (C═N) 1677 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3H), 1.28−1.65 (m, 4H), 3.17 (m, 1H), 3.99 (dd, 1H, *J* = 8.12 and 7.19 Hz), 4.23 (dd, 1H, *J* = 15.57 and 7.69 Hz), 4.45 (dd, 1H, *J* = 7.95 and 7.95 Hz), 5.47 (m, 2H), 5.80 (m, 1H), 6.90−7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.89, 20.06, 28.91, 42.52, 60.25, 69.27, 120.57, 121.89, 123.40, 128.43, 135.23, 147.94, 152.64 ppm; MS (*m*/*e*) 244 $[M]^+$; HRMS calcd for $C_{15}H_{20}N_2O$ 244.1576, found 244.1567.

***N*-Phenyl-3-*n*-butyl-4-vinyl-1,3-oxazolidin-2-imine (8b) (R = H, R′ = C_6H_5, R″ = C_4H_9):** oily liquid; IR (C═N) 1697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (t, 3H), 1.26−1.63 (m, 4H), 3.29 (m, 1H), 4.02 (dd, 1H, *J* = 8.1 and 5.4 Hz), 4.45 (m, 1H), 4.66 (m, 1H), 5.29 (m, 2H), 5.81 (m, 1H), 6.97−7.59 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.04, 20.66, 33.84, 46.47, 60.31, 68.62, 119.07, 120.74, 122.74, 128.48, 135.53, 139.48, 150.01 ppm; MS (*m*/*e*) 244 $[M]^+$; HRMS calcd for $C_{15}H_{20}N_2O$ 244.1576, found 244.1587.

General Procedure for the Asymmetric Palladium-Catalyzed Cycloaddition Reaction of Vinyloxirane with Unsymmetrical Carbodiimides. A mixture of $Pd_2(dba)_3 \cdot CHCl_3$ (0.03 mmol), TolBINAP (0.06 mmol), and THF (5 mL) was stirred at room temperature for 30 min. Vinyloxirane **1a** (1.5 mmol) and unsymmetrical carbodiimide **6** (1.0 mmol) were added, and the mixture was then stirred under nitrogen at room temperature until the conversion of the carbodiimide was complete. The orange brown solution was subjected to rotary evaporation, and the residue was purified by preparative silica gel TLC using pentane/ether mixture as the developer. The purified product was rechromatographed on preparative HPLC in order to eliminate any residual chiral phosphine ligand. The enantiomeric excess was calculated by determining peak area (using a programming analytical HPLC integrator).

Single-Crystal X-ray Diffraction Study of 7g. Crystals of **7g** were obtained by purification using preparative TLC, preparative HPLC, and recrystallization from an ether−hexane solution. One of the crystals having a proximate dimension of 0.2 × 0.2 × 0.2 mm was mounted on a glass capillary. All measurements were made on a Siemens SMART diffractometer using the ω scan mode. Cell dimensions and an orientation matrix for data collection were obtained from least-squares refinement using the setting angles of 8192 reflections in the range $3° < 2\theta < 57°$ and corresponded to a monoclinic cell with dimensions $a = 13.0399(2)$ Å, $b = 16.4639(2)$ Å, $c = 17.2130(2)$ Å, $\beta = 109.273(1)$. For $Z = 4$ and FW = 596.85, the calculated density is 1.136 g/cm^3. On the basis of the systematic absences, the space group was determined to be *P*21. The data were collected at −100 °C using the $\omega-2\theta$ scan technique to a maximum 2θ value of 57°.

A total of 23988 reflections were collected. The unique set contained only 8855 reflections. The final cycle of full matrix least-squares refinement was based on 5999 observed reflections ($I > 2.5\sigma(I)$) and 398 variable parameters. Weights based on counting statistics were used. The maximum and minimum peaks on the final differences Fourier map corresponded to 0.300 and −0.400 e/a^3, respectively.

All the calculations were performed using the NRCVAX crystallographic software package.[20]

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Supporting Information Available: ^1H and ^{13}C NMR spectra of compounds **6a**−**k**, **7b**−**f**, **7h**, and **8a**−**i**. Spectral data of compounds **6a**−**k**, **7a**−**i**, and **8a**−**i**. Text giving full details of the X-ray structure determination of **7g** including the experimental procedure and tables of bond distances and angles and torsion angles (75 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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