Palladium(0)-Catalyzed Asymmetric Cycloaddition of Vinyloxiranes with Heterocumulenes Using Chiral Phosphine Ligands: An Effective Route to Highly Enantioselective Vinyloxazolidine Derivatives

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Abstract: Cycloaddition reaction of 2-vinyloxiranes with carbodiimides using $Pd_2(dba)_3$·$CHCl_3$, and TolBINAP as the chiral ligand, in THF at ambient temperature, afforded 4-vinyl-1,3-oxazolidin-2-imines in 70−99% yield and in up to 95% ee. The stereoselectivity is strongly influenced by the structure of the chiral phosphine ligands and substrates, as well as by the reaction conditions. The enantiodetermination step is assumed to be nucleophilic attack of a nitrogen nucleophile on a π-allyl palladium intermediate. Reaction of 2-vinyloxiranes with isocyanates using the same catalyst system afforded 4-vinyl-1,3-oxazolidin-2-ones in high yield but in no greater than 50% ee.

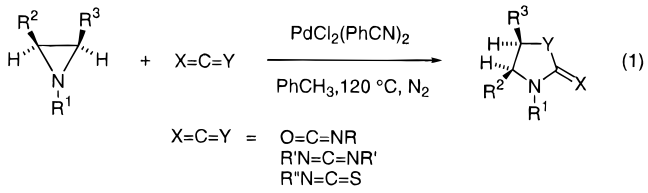
Introduction

The cycloaddition reaction of oxiranes with heterocumulenes is an efficient method to prepare five-membered ring heterocycles.[1] For instance, 1,3-cycloaddition reactions of isocyanates with oxiranes have been extensively studied due to the potential biological activities of 2-oxazolidine derivatives.[2−3]

Stoichiometric cycloaddition reaction of unsymmetrical epoxides with heterocumulenes usually occurs under relatively vigorous reaction conditions (reaction temperature of ca. 150 °C or higher) and with low regioselectivity. Better yields and regioselectivity can be achieved by introducing catalysts such as quaternary ammonium salts,[4a] a lithium halide,[4b,c] organostibonium,[4d,e] or organotin compounds,[4f,g] and transition metal complexes such as Pd(0) complexes have been shown to be very effective catalysts.[4h]

It is well-known that only one of a pair of enantiomers is usually pharmacologically active while the other could either be innocuous or damaging to human health. Therefore, the development of enantioselective approaches to chiral molecules of biological interest is currently receiving significant attention.[5]

One of us reported that the $PdCl_2(PhCN)_2$-catalyzed reaction of the 1,2- or 1,2,3-trisubstituted aziridines with heterocumulenes proceeds regio- and stereospecifically to give five-membered heterocycles in high yield[6] (eq 1). As a part of our study on



(1)

the ring expansion reaction of three-membered-ring heterocycles catalyzed by transition metal complexes, we have undertaken an investigation of the possibility of stereoselective cycloaddition of vinyloxiranes with heterocumulenes catalyzed by palladium(0) complexes modified with chiral ligands.

Methods for the stereoselective or chiral synthesis of 4-vinyl-1,3-oxazolidin-2-ones have previously been reported. Hayashi and co-workers[7] described the asymmetric cyclization of 2-butenylenedicarbamate catalyzed by chiral ferrocenylphosphine−palladium(0) complexes providing 4-vinyl-1,3-oxazolidin-2-ones in up to 77% ee and in high yield (eq 2). Trost and Sudhakar[8] reported the effective stereoselective conversion of vinyloxiranes to *cis*-oxazolidin-2-ones catalyzed by $Pd_2(dba)_3$·$CHCl_3$ and trialkyl phosphite (eq 3), and the stereochemical features were rationalized on the basis of steric interactions between the R group on the vinyloxirane and triisopropyl phosphite ligands. In recent work, Trost and co-workers[9] have investigated a series of 2-(diphenylphosphino)benzoic acid and 2-(diphenylphosphino)aniline based ligands and used them in reactions of urethanes leading to the formation of oxazolidinones in good to high enantiomeric excess (eq 4). To our knowledge, there are no examples of the synthesis of 1,3-oxazolidin-2-imines in high enantiomeric excess by the cycloaddition of oxiranes to carbodiimides.

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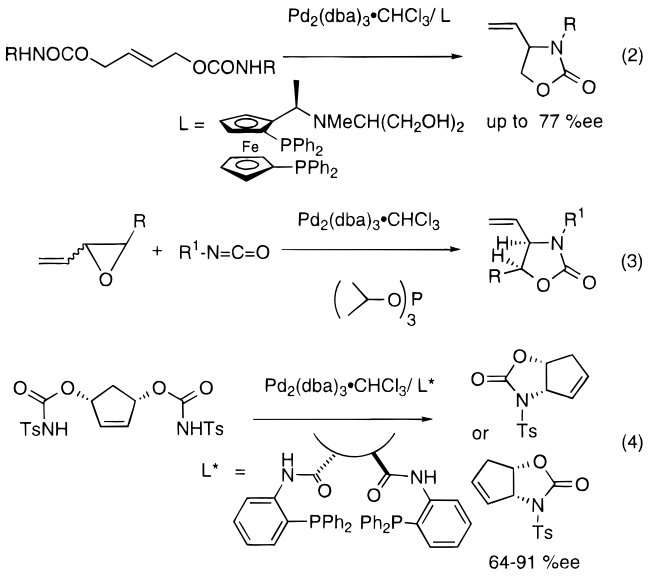
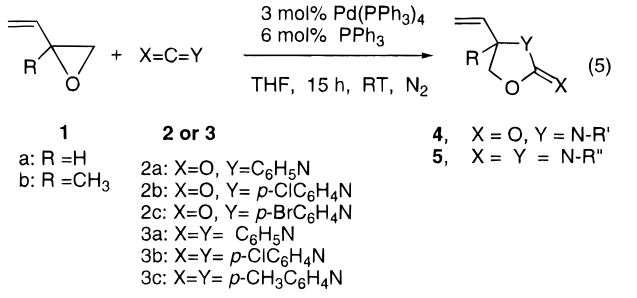


We now wish to report a highly enantioselective method for the synthesis of oxazolidine derivatives in good to excellent yield, by palladium(0)/2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl (TolBINAP)-catalyzed cycloaddition of heterocumulenes with vinyloxiranes.

Results and Discussion

Cycloaddition Reaction of Vinyloxirane with Heterocumulenes. To examine the feasibility of the cycloaddition pathway for obtaining optically active oxazolidine derivatives from the reaction of 2-vinyloxiranes with heterocumulenes, we initially performed this reaction using an achiral-Pd(0) catalyst such as $Pd(PPh_3)_4$. This reaction was successfully carried out by treatment of the 2-vinyloxirane **1** (R = H or CH_3) with heterocumulenes **2** or **3** in the presence of $Pd(PPh_3)_4$ and triphenylphosphine in anhydrous THF at room temperature for 15 h. In this manner, the 4-vinyl-1,3-oxazolidin-2-one (**4**) (X = O, Y = NR′) or 4-vinyl-1,3-oxazolidin-2-imine (**5**) (X = Y = NR″) was formed regioselectively and in 90−98% yield (eq 5 and Table 1). This reaction required 3 mol % of $Pd(PPh_3)_4$



and 2 equiv of added triphenylphosphine ligand relative to Pd. Reduced amounts of $Pd(PPh_3)_4$ or no additional PPh_3, resulted in lower product yields.[10] *p*-Nitrophenyl isocyanate and bis(*p*-nitrophenyl)carbodiimide failed to give the desired products presumably because of their poor electrophilicity.

The cycloaddition reaction may proceed via zwitterionic (π-allyl) palladium intermediates generated by oxidative addition of vinyloxirane **1** to a palladium(0) species[11] followed by reaction with the heterocumulene. Intramolecular attack of the nitrogen nucleophile at the C-3 carbon of **6** would generate the five-membered heterocyclic product (Scheme 1).

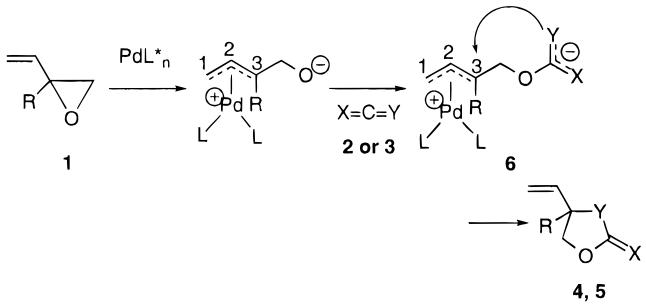
(10) Reaction with 1 or 2 mol % $Pd(PPh_3)_4$ provided no cycloaddition reaction and 25% isolated products, respectively. The reaction performed using 3 mol % $Pd(PPh_3)_4$ but without addition of PPh_3 afforded **3b** in 90% yield.

Table 1. Cycloadducts Obtained from the Reaction of 2-Vinyloxiranes (**1**) and Heterocumulenes **2** or **3** in the Presence of $Pd(PPh_3)_4$ and PPh_3[a]

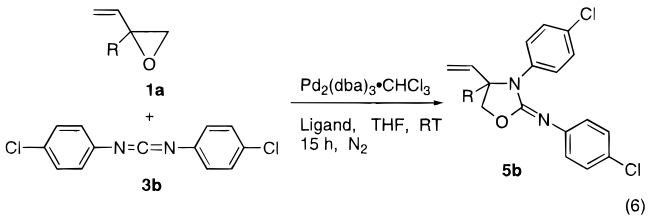
compds	R	X	Y	isolated yield (%)[b]
4a	H	O	C_6H_5N	90
4b	H	O	*p*-ClC_6H_4N	98
4c	H	O	*p*-BrC_6H_4N	95
4d	CH_3	O	*p*-ClC_6H_4N	94
5a	H	C_6H_5N	C_6H_5N	98
5b	H	*p*-ClC_6H_4N	*p*-ClC_6H_4N	96
5j	CH_3	*p*-$CH_3C_6H_4N$	*p*-$CH_3C_6H_4N$	90

[a] Reaction conditions: 2-vinyloxirane (1.0 mmol), heterocumulene (1.0 mmol), $Pd(PPh_3)_4$ (0.03 mmol), PPh_3 (0.06 mmol), 3 mL of THF, room temperature, 15 h, N_2 atmosphere. [b] Purified by preparative TLC.

Scheme 1



A high degree of asymmetric induction could be achieved in the cycloaddition of vinyloxiranes and heterocumulenes, especially carbodiimides. Success depends on the choice of the appropriate combination of metal and chiral ligands as well as the reaction conditions.[5,12] When the cycloaddition of 1 mmol each of **1a** (R = H) and **3b** (X = Y = *p*-ClC_6H_4N) was performed in THF at room temperature in the presence of $Pd_2(dba)_3$·$CHCl_3$ (0.03 mmol) and (*S*)-TolBINAP[13] (0.06 mmol) for 15 h under an inert atmosphere, *N*-(*p*-chlorophenyl)-3-(*p*-chlorophenyl)-4-vinyl-1,3-oxazolidin-2-imine (**5b**) was isolated in 95% yield and in 94 %ee as determined by chiral HPLC (Chiracel OD) (eq 6). Other commercially available chiral



ligands such as (−)DIOP[14] (94% yield, 20% ee), (−)-MeDUPHOS[15] (87% yield, 45% ee), (*R*,*R*)-NORPHOS,[16] (95% yield, 6% ee), and (*R*)-PROPHOS[17] (96% yield, 3% ee) were less effective in terms of asymmetric induction, whereas (*R*)-

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(13) (*S*)-TolBINAP = (*S*)-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. Pd-Catalyzed Asymmetric Cycloaddition of 2-Vinyloxirane (**1a**) and Bis(*p*-chlorophenyl)carbodiimide (**3b**) Using Various Chiral Phosphine Ligands

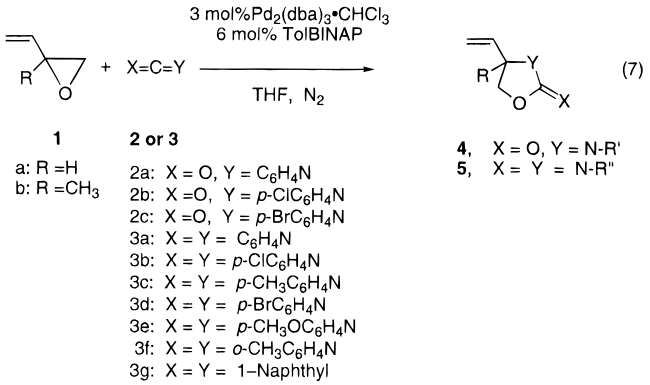
ligand	% isolated yield of **5b**[a]	% ee[b]	$[\alpha]^{22}_D$ in $CHCl_3$
(*S*)-TolBINAP	95	94	+38.7 (*c* 5.04)
(−)DIOP	94	20	−7.1 (*c* 5.14)
(−)Me-DUPHOS	87	45	−18.2 (*c* 5.03)
(*R*,*R*)-NORPHOS	95	6	−2.0 (*c* 5.04)
(*R*)-PROPHOS	96	3	−0.5 (*c* 5.04)
(*R*)-BINAP	93	94	−38.7 (*c* 5.07)

[a] Purified by preparative TLC. [b] Determined by HPLC (Chiracel OD, 15% *i*-PrOH in hexane).

BINAP[18] (93% yield, 94% ee) gave essentially the same yield and % ee as that obtained by using (*S*)-TolBINAP but, as anticipated, for the other enantiomer (Table 2).

The chromatographic separation of racemic **5b,** on a chiral stationary phase using 15% 2-propanol in *n*-hexane as the mobile phase produced a chromatogram with two peaks for the two enantiomers in a 1:1 ratio (Figure 1a). The chromatogram of **5b,** obtained by cyclization utilizing Pd/(*S*)-TolBINAP, showed a signal due to the predominant enantiomer with retention time corresponding to that of the first eluted enantiomer (Figure 1b). *N*-(*p*-Chlorophenyl)-3-(*p*-chlorophenyl)-4-vinyl-1,3-oxazolidin-2-imine (**5b**) can be readily obtained in purified form, as crystalline white needles, by preparative silica gel TLC followed by preparative HPLC. A single-crystal X-ray diffraction analysis of **5b** revealed it to possess the (*R*)-configuration (see Figure 2 for the ORTEP diagram).

A series of other 4-vinyl-1,3-oxazolidines (eq 7) were similarly synthesized, usually in high optical purity, using the



Pd(0)−TolBINAP catalyst system which was generated *in situ* by reaction of 3 mol % of $Pd_2(dba)_3$•$CHCl_3$ with 2 equiv of bidentate ligand relative to palladium. The reaction mixtures were stirred under nitrogen at room temperature until the conversion of the heterocumulenes was complete (monitored by IR). The results are shown in Table 3.

Attempts to improve the enantioselectivity of this reaction by introducing an *ortho* substituent such as a methyl group (Table 3, entries 6 and 7) on the phenyl ring of carbodiimides proved to be ineffective. The increased steric hindrance resulted in lower enantioselectivity. A naphthyl substituent on the nitrogen nucleophile also failed to improve the optical yield of the product (entry 8). Nevertheless, it must be noted that the % ee is still high (84−89%). 2-Methyl-2-vinyloxirane (**1**, R = CH_3) (entries 9−12) reacted at a lower rate and provided products in somewhat lower % ee (69−91%) compared to that obtained from 2-vinyloxirane (**1**, R = H).

The generally high degree of asymmetric induction found in the cycloaddition reaction can be explained by the pathway outlined in Scheme 2. Oxidative addition of a chiral phosphine−palladium complex to racemic vinyl oxirane **1** followed by heterocumulene interception affords the diastereomeric π-allyl palladium complexes **7** and **8**. Intramolecular attack of the nitrogen nucleophile (X = Y = NAr) at the C-3 carbon of **7** and **8** can give the corresponding (*S*)- and (*R*)-oxazolidine derivatives, respectively. The enantiodetermination step in this asymmetric cycloaddition may involve nucleophilic addition. The asymmetric cyclization reactions of 2-butenylenedicarbamate in the presence of Pd(0) and chiral phosphine ligands[7] are believed to proceed via similar intermediates, indicating that the interconversion between π-allyl palladium complexes **7** and **8** occurs via a $\eta^3-\eta^1-\eta^3$ mechanism[19] and is much faster than attack of the nitrogen nucleophile. Thus, one of the two intermediate complexes (**7** and **8**) reacts faster than the other and consequently gives the major enantiomer. In the case of using (*S*)-TolBINAP as the chiral ligand, the intermediate **8** reacts at a greater rate affording the (*R*)-enantiomer as the major stereoisomer.

4-Vinyl-1,3-oxazolidin-2-ones **4b**,**c** (Table 3, entries 13 and 14) were obtained from reaction of **1** with isocyanates by employing a procedure identical to that used for carbodiimides. The % ee of these products is appreciately lower than those derived from carbodiimides, suggesting that TolBINAP has less influence in the steric interaction in the enantiodeterminating step. The results from Table 3 indicates that cycloaddition reactions of vinyloxiranes and carbodiimides are influenced not only by the ligands but also by the structure of the reaction partners. In reactions with 2-vinyloxiranes, carbodiimides provide greater steric interaction between the substituent on the nitrogen nucleophile of **7**/**8** and the substituent on the chiral phosphine ligands in comparison with reactions using isocyanates. Consequently, higher enantiomeric excesses were realized in using carbodiimides than isocyanates (see Figure 3).

Effect of Temperature on the Enantioselectivity of the Cycloaddition Reaction. It is known that the reaction temperature can have a pronounced effect on the enantioselectivity of a reaction.[4,20−23] To examine the dependence of the % ee on temperature, 2-vinyloxirane (**1a**, R = H) was reacted with

(14) (−)DIOP = (*R*,*R*)-2, 3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane. See: Kagan, H. B.; Dang, T.-P. *J. Am. Chem. Soc*. **1972**, *94*, 6429.

(15) (−)MeDUPHOS = (−)-1,2-bis((2*R*,5*R*)-2,5-dimethylphospholano)-benzene. See: Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518.

(16) (*R*,*R*)-NORPHOS = (*R*,*R*)-5,6-bis(diphenylphosphino)-2-norbornene. See: Brunner, H.; Pieronczyk, W.; Schînhammer, B.; Streng, K.; Bernal, I.; Korp, J. *Chem Ber.* **1981**, *114*, 1137.

(17) (*R*)-PROPHOS = (*R*)-1,2-bis(diphenylphosphino)propane. See: Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1978**, *100*, 5491.

(18) (*R*)-BINAP = (*R*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl. See: Miyashita, A.; Yasuda, A.; Takay, H.; Toriumi, K.; Ito, T.; Souchi, Y.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932.

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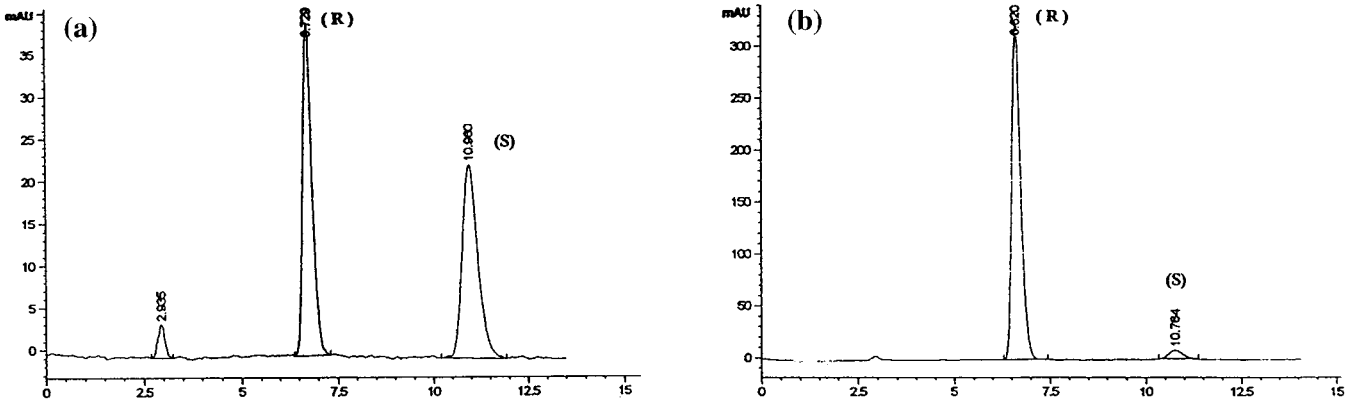


Figure 1. Chromatograms showing the resolution of (a) racemic **5b** and (b) 94% ee **5b** on chiral HPLC (Chiracel OD, 15% *i*-PrOH in hexane).

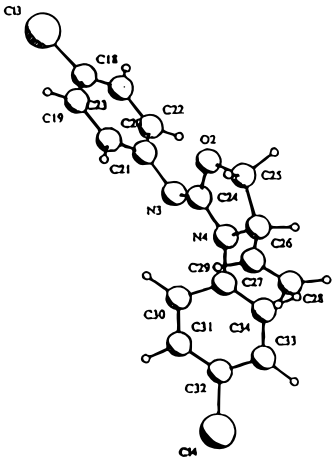


Figure 2. X-ray structure of (*R*)-**5b** obtained from the cycloaddition reaction of **1a** and **3b** in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$/(*S*)-TolBINAP.

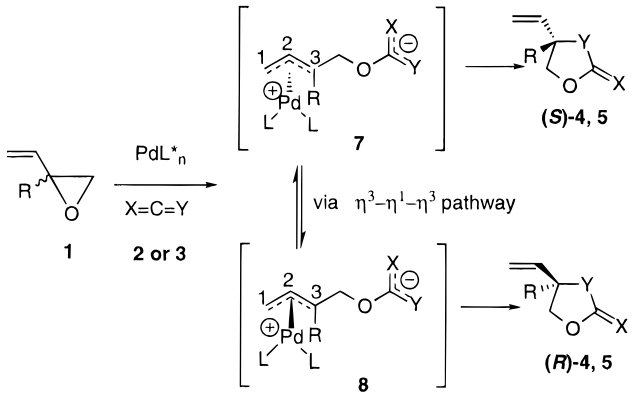
Table 3. Asymmetric Cycloaddition of 2-Vinyloxiranes **1** with Heterocumulenes **2** or **3** in the Presence of $Pd_2(dba)_3{\cdot}CHCl_3$-TolBINAP as the Catalyst[a]

entry	1	2	ligand[b]	products	yield (%)[c]	ee (%)[d]	$[\alpha]^{22}_D$ in $CHCl_3$
1	**1a**	**3a**	A	**5a**	98	93	+26.2 (*c* 5.04)
2	**1a**	**3b**	A	**5b**[e]	95	94	+38.7 (*c* 5.04)
3	**1a**	**3c**	A	**5c**	98	93	+38.5 (*c* 5.11)
4	**1a**	**3d**	A	**5d**	84	94	+34.5 (*c* 1.99)
5	**1a**	**3e**	A	**5e**	88	88	+31.7 (*c* 2.99)
6	**1a**	**3f**	A	**5f**	98	84	+32.8 (*c* 5.03)
7	**1a**	**3f**	B	**5f**	98	88	−33.5 (*c* 5.26)
8	**1a**	**3g**	B	**5g**	60	89	−31.4 (*c* 4.08)
9	**1b**	**3a**	B	**5h**[f]	87	91	−22.1 (*c* 2.80)
10	**1b**	**3b**	A	**5i**	98	69	+10.4 (*c* 5.17)
11	**1b**	**3c**	A	**5j**[g]	63	84	+18.1 (*c* 2.26)
12	**1b**	**3e**	A	**5k**	98	75	+11.6 (*c* 2.06)
13	**1a**	**2b**	B	**4b**	94	43	−1.72 (*c* 4.66)
14	**1a**	**2c**	A	**4c**	99	49	+1.43 (*c* 3.49)

[a] Reaction conditions: **1** (1 mmol); **2** or **3** (1 mmol); $Pd_2(dba)_3{\cdot}CHCl_3$ (0.03 mmol); ligand (0.06 mmol); THF (5 mL); room temperature, 15 h (unless otherwise noted), N_2 atmosphere. [b] A, (*S*)-TolBINAP; B, (*R*)-TolBINAP. [c] Yield of isolated product after silica gel TLC. [d] Determined by HPLC analysis using Chiracel OD, 15% *i*-PrOH in *n*-hexane. [e] Absolute configuration of major enantiomer is (*R*)-**5b** (see Figure 2a). [f] Reaction time was 17 h. [g] Reaction time was 3 days.

diphenylcarbodiimide (**3a**) or bis(*p*-chlorophenyl)carbodiimide (**3b**), affording the cycloadducts **5a** and **5b**, respectively. Table 4 summarizes the effect of temperature on the extent of asymmetric induction in the cycloaddition reaction.

Scheme 2



The cycloaddition of 2-vinyloxirane **(1a)** with diphenylcarbodiimide **(3a)** or bis(*p*-chlorophenyl)carbodiimide **(3b)** showed much the same temperature effects. Performing the reaction at 10 °C resulted in % ee's essentially identical to those obtained by reaction at room temperature. However, a slightly lower selectivity was observed when the reaction was carried out at 5 °C (90% ee). When these cycloaddition reactions were carried out at 80 or 100 °C a slightly lower degree of asymmetric induction was observed (90−91% ee). The same pattern was observed in the case of cycloaddition of *p*-bromophenyl isocyanate (**2c**) with 2-vinyloxirane (**1a**) (e.g., 49% ee at room temperature and 41% ee at 80 °C).

Clearly, the reaction temperature does not significantly affect the enantioselectivity of the reaction. High stereoselectivity is still maintained at a lower reaction temperature (5−22 °C), which is in contrast to the results previously reported for the preparation of vinyloxazolidin-2-one.[7] In addition, by performing the cycloaddition reactions at 10 °C for 24 h, *N*-*p*-tolyl-3-*p*-tolyl-4-vinyl-1,3-oxazolidin-2-imine **(5c)** (97% yield, 95% ee) and *N*-(*p*-bromophenyl)-3-(*p*-bromophenyl)-4-vinyl-1,3-oxazolidin-2-imine **(5d)** (84% yield, 95% ee) were obtained from the cycloaddition reactions of **1a** with **3c** and **3d**, respectively. Therefore, the optimum temperature for achieving the asymmetric cycloaddition of 2-vinyloxirane with heterocumulenes in the presence of Pd(0) and chiral phosphine ligands is in the range between 10 and 22 °C, although excellent results are also obtained at higher temperatures.

Conclusion

Palladium(0) with TolBINAP as an added chiral ligand is a useful and effective catalytic system for the enantioselective synthesis of 4-vinyl-1,3-oxazolidin-2-imines in high enantio-

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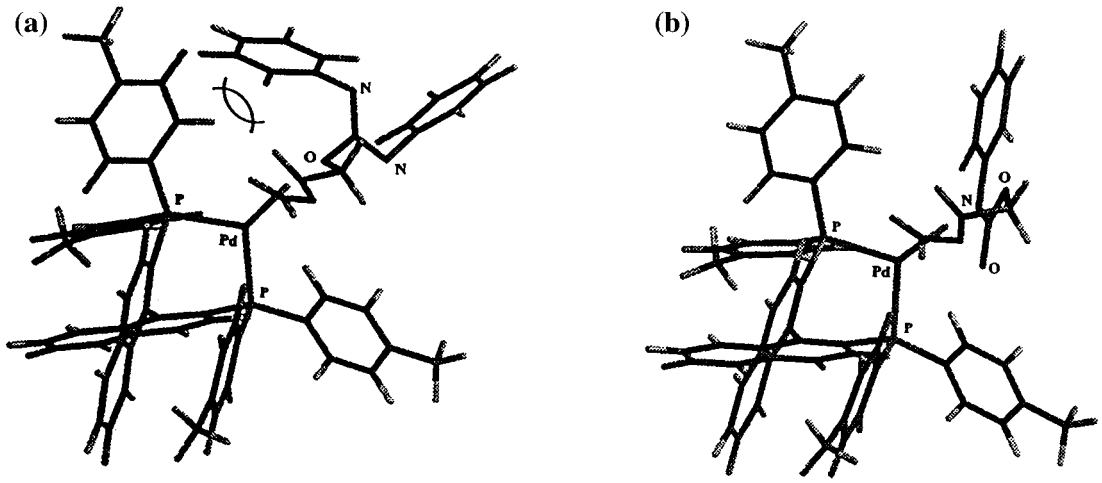

Figure 3. (a) Steric repulsion between the substituent on the nucleophilic nitrogen atom of the diphenylcarbodiimide unit and the *p*-tolyl portion of the chiral phosphine ligand. (b) This repulsion has a strong influence on the stereoselectivity compared to that of phenyl isocyanate with the same chiral phosphine ligands.

Table 4. Effect of Temperature on the Pd-Catalyzed Asymmetric Cycloaddition Reaction of 2-Vinyloxirane (**1a**) with Diphenylcarbodiimide (**3a**) or Bis(*p*-chlorophenyl)carbodiimide (**3b**) Affording **5a** and **5b**, Respectively[a]

reaction temp (°C)	reaction time (h)	**5a** yield[b] (%)	**5a** ee[c] (%)	**5a** $[\alpha]^{22}_D$ in $CHCl_3$	**5b** yield[b] (%)	**5b** ee[c] (%)	**5b** $[\alpha]^{22}_D$ in $CHCl_3$
100	1	93	90	+24.8 (*c* 5.05)	90	90	+35.0 (*c* 5.04)
80	2	95	90	+24.9 (*c* 5.01)	92	91	+35.2 (*c* 5.10)
rt[d]	15	98	93	+26.2 (*c* 5.04)	95	94	+38.7 (*c* 5.04)
10[e]	24	96	94	+26.8 (*c* 5.03)	85	94	+38.8 (*c* 5.00)
5[e]	36	98	91	+25.6 (*c* 5.04)	96	92	+ 36.0 (*c* 5.03)

[a] Refer to the Experimental Section for general procedure. [b] Isolated yield by preparative TLC. [c] Enantiomeric excess determined by HPLC using Chiracel OD column. [d] Approximately 22 °C. [e] The reaction was performed in a Schlenk tube (N_2 atmosphere) inside a cold room.

meric excess. Furthermore, the stereochemical course of the cycloaddition with chiral phosphine ligand−Pd(0) complexes was noticeably influenced by the structure of the heterocumulene substrates. Up to 95% ee was realized in the asymmetric syntheses of *N*-*p*-tolyl-3-*p*-tolyl-4-vinyl-1,3-oxazolidin-2-imine (**5c**) and *N*-(*p*-bromophenyl)-3-(*p*-bromophenyl)-4-vinyl-1,3-oxazolidin-2-imine (**5d**) in excellent yields by a proper choice of substrates and reaction temperature.

Experimental Section

General Methods. All NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard on Bruker AMX 500, Varian XL-300, and Gemini 200 spectrometers. Infrared spectra were recorded on a Bomem MB 100-C15 Fourier transform spectrometer and are reported in wavenumbers (cm^{-1}). Mass spectra were obtained on a VG 7070E spectrometer. A Fisher-Johns apparatus was used for melting point determinations. Optical rotations were measured on a Perkin-Elmer polarimeter in a 10 cm cell at 22 °C.

Enantiomeric resolutions were achieved using a Hewlett Packard HPLC Series II 1090 instrument equipped with an automatic injector and diode array detector monitoring at 220 nm. A Chiracel OD column was used with 85:15 *n*-hexane:2-propanol as the mobile phase at a flow rate of 1 mL/min (oven temperature 30 °C).

Vinyloxiranes and isocyanates were purchased from Aldrich and were used as received. Carbodiimides[24] and palladium catalysts[25] were either purchased or prepared according to literature procedures. The organic solvents were dried and distilled prior to use.

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 at room temperature for 30 min. Vinyloxirane **1** [1 mmol (up to 1.5 mmol was used occasionally with the same results)] and 1 mmol of heterocumulene **2** or **3** were added, and the mixture was stirred under nitrogen for 15 h at room temperature. The light yellow homogeneous solution was then concentrated by rotary evaporation, and the residue was purified by silica gel TLC using 1:1 pentane/ether as the developer. Melting points, IR, NMR, MS, and analytical data for **4** and **5** are as follows (except **4a** and **5a**, which have previously been reported).

***N*-Phenyl-4-vinyl-1,3-oxazolidin-2-one (4a)**[4e] (R = H, X = O, Y = C_6H_5N): oily liquid; IR (C=O) 1753 cm^{-1}; ^{1}H NMR ($CDCl_3$) 4.15 (dd, 1H, *J* = 6.0 and 8.6 Hz), 4.60 (dd, 1H, *J* = 8.6 and 8.6 Hz), 4.83 (m, 1H), 5.35 (m, 2H), 5.80 (m, 1H), 7.10−7.50 (m, 5H); ^{13}C NMR ($CDCl_3$) 59.73, 67.66, 120.84, 121.86, 125.32, 129.43, 135.25, 137.69, 156.22; MS (*m/e*) 189 $[M]^+$.

***N*-(*p*-Chlorophenyl)-4-vinyl-1,3-oxazolidin-2-one (4b)** (R = H, X = O, Y = *p*-ClC_6H_4N): mp = 45−46 °C; IR (C=O) 1754 cm^{-1}; ^{1}H NMR ($CDCl_3$) 3.98 (dd, 1H, *J* = 6.2 and 8.6 Hz), 4.47 (dd, 1H, *J* = 8.6 and 8.6 Hz), 4.77 (m, 1H), 5.25 (m, 2H), 5.72 (m, 1H), 7.15−7.40 (m, 4H); ^{13}C NMR ($CDCl_3$) 59.78, 67.70, 121.30, 122.0, 129.67, 129.43, 130.40, 134.87, 136.29, 155.98; MS (*m/e*) 223 $[M]^+$, 225 $[M + 2]^+$. Anal. Calcd for $C_{11}H_{10}ClNO_2$: C, 59.07; H, 4.51; N, 6.26. Found: C, 58.93; H, 4.18; N, 6.55.

***N*-(*p*-Bromophenyl)-4-vinyl-1,3-oxazolidin-2-one (4c)** (R = H, X = O, Y = *p*-BrC_6H_4N): mp = 68−69 °C; IR (C=O) 1753 cm^{-1}; ^{1}H NMR ($CDCl_3$) 3.99 (dd, 1H, *J* = 6.0 and 8.6 Hz), 4.49 (dd, 1H, *J* = 8.6 and 8.6 Hz), 4.78 (m, 1H), 5.26 (m, 2H), 5.68 (m, 1H), 7.20−7.40 (m, 4H); ^{13}C NMR ($CDCl_3$) 59.74, 67.71, 118.24, 121.38, 123.26, 132.41, 4.20 (dd, 2H, *J* = 8.5 and 8.5 Hz), 4.23 (d, 1H, *J* = 8.5 Hz), 5.29 (m, 2H), 6.05 (m, 1H), 134.85, 136.79, 155.92; MS (*m/e*) 267 $[M]^+$, 269 $[M + 2]^+$. Anal. Calcd for $C_{11}H_{10}BrNO_2$: C, 49.28; H, 3.76; N, 5.22. Found: C, 49.25; H, 3.57; N, 5.31.

***N*-(*p*-Chlorophenyl)-4-methyl-4-vinyl-1,3-oxazolidin-2-one (4d):** (R = CH_3, X = Y = *p*-ClC_6H_4N): mp = 75−76 °C; IR (C=O) 1752 cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.42 (s, 3H), 7.20−7.40 (m, 4H); 7.20−7.40 (m, 4H); ^{13}C NMR ($CDCl_3$) 21.73, 64.18, 74.84, 118.11, 128.57, 129.67, 133.06, 134.66, 139.75, 156.92; MS (*m/e*) 237 $[M]^+$, 239 $[M + 2]^+$.

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Anal. Calcd for $C_{12}H_{12}ClNO_2$: C, 60.64; H, 5.09; N, 5.89. Found: C, 60.32; H, 4.88; N, 6.01.

***N*-Phenyl-3-phenyl-4-vinyl-1,3-oxazolidin-2-imine (5a)**[4e] (R = H, X = C_6H_4N, Y = C_6H_4N): mp = 58−59 °C; IR (C═N) 1678 cm^{-1}; ^1H NMR ($CDCl_3$) 4.06 (dd, 1H, *J* = 5.9 and 8.2 Hz), 4.45 (dd, 1H, *J* = 8.3 and 8.3 Hz), 4.72 (m, 1H), 5.40 (m, 2H), 5.85 (m, 1H), 7.10−7.75 (m, 10H); ^{13}C NMR ($CDCl_3$) 61.07, 70.02, 120.60, 122.60, 123.22, 124.23, 124.63, 129.36, 129.44, 135.69, 139.39, 148.28, 150.65; MS (*m/e*) 264 $[M]^+$.

***N*-(*p*-Chlorophenyl)-3-(*p*-chlorophenyl)-4-vinyl-1,3-oxazolidin-2-imine (5b)** (R = H, X = *p*-ClC_6H_4N, Y = *p*-ClC_6H_4N): mp = 95−96 °C; IR (C═N) 1677 cm^{-1}; ^1H NMR ($CDCl_3$) 4.07 (dd, 1H, *J* = 6.0 and 8.3 Hz), 4.45 (dd, 1H, *J* = 8.3 and 8.3 Hz), 4.75 (m, 1H), 5.35 (m, 2H), 5.81 (m, 1H), 7.00−7.75 (m, 8H); ^{13}C NMR ($CDCl_3$) 61.17, 70.05, 121.22, 123.92, 125.40, 128.19, 129.15, 129.36, 129.92, 134.98, 137.49, 146.28, 150.62; MS (*m/e*) 332 $[M]^+$, 336 $[M + 2]^+$. Anal. Calcd for $C_{17}H_{14}Cl_2N_2O$: C, 61.28; H, 4.23; N, 8.41. Found: C, 61.43; H, 4.05; N, 8.38.

***N*-*p*-Tolyl-3-*p*-tolyl-4-methyl-4-vinyl-1,3-oxazolidin-2-imine (5j)** (R = CH_3, X = *p*-$CH_3C_6H_5N$, Y = *p*-$CH_3C_6H_5N$): mp = 136−137 °C; IR (C═N) 1672 cm^{-1}; ^1H NMR ($CDCl_3$) 1.37 (s, 3H), 2.20 (s, 3H), 2.27 (s, 3H), 4.12 (dd, 2H, *J* = 8.2 and 25.1 Hz), 5.17 (m, 2H), 6.00 (m, 1H), 6.80−7.30 (m, 8H); ^{13}C NMR ($CDCl_3$) 20.67, 20.81, 21.05, 64.05, 76.21, 116.86, 123.23, 127.91, 128.94, 129.46, 131.53, 133.77, 136.47, 139.69, 144.59, 152.09; MS (*m/e*) 306 $[M]^+$. Anal. Calcd for $C_{20}H_{22}N_2O$: C, 78.40; H, 7.24; N, 9.14. Found: C, 78.13; H, 7.26; N, 9.12.

General Procedure for the Asymmetric Palladium-Catalyzed Cycloaddition Reaction of Vinyloxiranes with Heterocumulenes. A mixture of $Pd_2(dba)_3{\cdot}CHCl_3$ (0.03 mmol), chiral phosphine ligand (0.06 mmol), and THF was stirred at room temperature for 30 min. Oxirane (1.0 mmol) and heterocumulene (1.0 mmol) were added, and the mixture was then stirred under nitrogen atmosphere at either room temperature or at 10 °C, until the conversion of the heterocumulenes was completed (as monitored by the shift of the IR-absorption band of the carbodiimide C═N group at approximately 2100 cm^{-1} was shifted to the region of 1670 cm^{-1}; the absorption band of the isocyanate unit at about 2200 cm^{-1} was replaced by one in the region of 1750 cm^{-1}). After the reaction was complete, the orange brown solution was subjected to rotary evaporation and the residue was purified by preparative silica gel TLC. The purified product was rechromatographed on preparative HPLC to eliminate the rest of the chiral phosphine ligand. The enantiomeric excess was determined by measuring the area chromatogram peaks (obtained from programming an analytical HPLC integrator). Melting points, IR, NMR, MS, and analytical data for **4** and **5** are as follows:

***N*-*p*-Tolyl-3-*p*-tolyl-4-vinyl-1,3-oxazolidin-2-imine (5c) (**R = H, X = *p*-$CH_3C_6H_5N$, Y = *p*-$CH_3C_6H_5N$): mp = 102−103 °C; IR (C═N) 1679 cm^{-1}; ^1H NMR ($CDCl_3$) 2.21 (s, 3H), 2.24 (s, 3H), 3.99 (dd, 1H, *J* = 6.4 and 8.3 Hz), 4.44 (dd, 1H, *J* = 8.3 and 8.3 Hz), 4.68 (m, 1H), 5.26 (m, 2H), 5.74 (m, 1H), 6.85−7.42 (m, 8H); ^{13}C NMR ($CDCl_3$) 21.52, 61.57, 69.89, 120.65, 123.08, 123.73, 129.73, 129.93, 132.19, 134.41, 135.79, 136.62, 145.50, 150.81; MS (*m/e*) 292 $[M]^+$. Anal. Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89; N, 9.58. Found: C, 77.86; H, 6.84; N, 9.54.

***N*-(*p*-Bromophenyl)-3-(*p*-bromophenyl)-4-vinyl-1,3-oxazolidin-2-imine (5d)** (R = H, X = *p*-BrC_6H_5N, Y = *p*-$BrCH_3C_6H_5N$): mp = 98−99 °C; IR (C═N) 1675 cm^{-1}; ^1H NMR ($CDCl_3$) 4.05 (dd, 1H, *J* = 6.3 and 8.0 Hz), 4.49 (dd, 1H, *J* = 8.0 and 8.0 Hz), 4.71 (m, 1H), 5.31 (m, 2H), 5.74 (m, 1H), 6.83−7.52 (m, 8 H); ^{13}C NMR ($CDCl_3$) 60.40, 69.36, 115.31, 117.03, 120.53, 123.49, 125.12, 131.39, 131.62, 134.29, 137.27, 145.99, 149.77; MS (*m/e*) 422 $[M]^+$, 424 $[M + 2]^+$. Anal. Calcd for $C_{17}H_{14}N_2OBr$: C, 48.37; H, 3.34; N, 6.64. Found: C, 48.38; H, 3.06; N, 6.59.

***N*-(*p*-Methoxyphenyl)-3-(*p*-methoxyphenyl)-4-vinyl-1,3-oxazolidin-2-imine (5e)** (R = H, X = *p*-$CH_3OC_6H_5N$, Y = *p*-$CH_3OC_6H_5N$): mp = 65−66 °C; IR (C═N) 1678 cm^{-1}; ^1H NMR ($CDCl_3$) 3.67 (s, 3H), 3.69 (s, 3H), 3.97 (dd, 1H, *J* = 6.6 and 8.0 Hz), 4.42 (dd, 1H, *J* = 8.0 and 8.0 Hz), 4.57 (m, 1H), 5.21 (m, 2H), 5.70 (m, 1H), 6.69−7.39 (m, 8H); ^{13}C NMR ($CDCl_3$) 55.21, 61.31, 69.09, 113.57, 113.84, 120.03, 123.98, 124.58, 131.40, 134.96, 140.51, 150.46, 154.80, 156.37; MS (*m/e*) 324 $[M]^+$. Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64. Found: C, 70.67; H, 5.99; N, 8.64.

***N*-*o*-Tolyl-3-*o*-tolyl-4-vinyl-1,3-oxazolidin-2-imine (5f)** (R = H, X = *o*-$CH_3C_6H_5N$, Y = *o*-$CH_3C_6H_5N$): mp = 68−69 °C; IR (C═N) 1688 cm^{-1}; ^1H NMR ($CDCl_3$) 2.09 (s, 3H), 2.36 (s, 3H), 4.06 (m, 1H), 4.54 (m, 2H), 5.13 (m, 2H), 5.69 (m, 1H), 6.77−7.27 (m, 8H); ^{13}C NMR ($CDCl_3$) 18.34, 63.16, 69.65, 121.06, 122.29, 122.71, 125.76, 126.66, 127.65, 129.81, 130.54, 131.16, 134.38, 136.49, 137.08, 146.66, 150.34; MS (*m/e*) 292 $[M]^+$. Anal. Calcd for $C_{20}H_{22}N_2O$: C, 78.40; H, 7.24; N, 9.14. Found: C, 78.19; H, 6.84; N, 9.54.

***N*-α-Naphthyl-3-α-naphthyl-4-vinyl-1,3-oxazolidin-2-imine (5g)** (R = H, X = 1-naphthyl, Y = 1-naphthyl): mp = 172−173 °C; IR (C═N) 1676 cm^{-1}; ^1H NMR ($CDCl_3$) 4.20 (t, 1H), 4.69 (m, 2H), 5.03 (m, 2H), 5.78 (m, 1H), 7.00−8.60 (m, 14H); ^{13}C NMR ($CDCl_3$) 63.84, 70.08, 121.24, 122.21, 123.25, 123.30, 124.39, 124.56,125.40, 125.63, 126.26, 126.48, 127.51, 128.41, 128.64, 129.33, 134.15, 134.27, 134.78, 144.0, 152.06; MS (*m/e*) 364 $[M]^+$, 365 $[M + 1]^+$. Anal. Calcd for $C_{25}H_{20}N_2O$: C, 82.39; H, 5.53; N, 7.69. Found: C, 82.03; H, 5.25; N, 7.80.

***N*-*p*-Phenyl-3-*p*-phenyl-4-methyl-4-vinyl-1,3-oxazolidin-2-imine (5h)** (R = CH_3, X = C_6H_5N, Y = C_6H_5N): mp = 82−83 °C; IR (C═N) 1677 cm^{-1}; ^1H NMR ($CDCl_3$) 1.38 (s, 3H), 4.10 (dd 2H, *J* = 8.2 and 25.4 Hz), 5.19 (m, 2H), 6.00 (m, 1H), 6.80−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) 20.72, 64.07, 76.24, 116.86, 122.23, 123.43, 126.03, 127.48, 128.37, 128.72, 136.84, 139.64, 147.52, 151.57; MS (*m/e*) 278 $[M]^+$. Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.07. Found: C, 77.60; H, 6.25; N, 10.01.

***N*-(*p*-Chlorophenyl)-3-(*p*-chlorophenyl)-4-methyl-4-vinyl-1,3-oxazolidin-2-imine (5i)** (R = CH_3, X = *p*-ClC_6H_5N, Y = *p*-ClC_6H_5N): mp = 97−98 °C; IR (C═N) 1675 cm^{-1}; ^1H NMR ($CDCl_3$) 1.39 (s, 3H), 4.14 (dd, 2H, *J* = 8.2 and 24.6 Hz), 5.22 (m, 2H), 5.98 (m, 1H), 6.90−7.27 (m, 8H), ^{13}C NMR ($CDCl_3$) 20.50, 64.17, 76.40, 117.5, 124.77, 127.44, 128.39, 128.78, 128.99, 132.02, 135.06, 139.04, 145.70, 151.70; MS (*m/e*) 346 $[M]^+$, 348 $[M + 2]^+$. Anal. Calcd for $C_{18}H_{16}N_2OCl_2$: C, 62.26; H, 4.64; N, 8.07. Found: C, 62.18; H, 4.40; N, 7.86.

***N*-(*p*-Methoxyphenyl)-3-(*p*-methoxyphenyl)-4-methyl-4-vinyl-1,3-oxazolidin-2-imine (5k)** (R = CH_3, X = *p*-$CH_3OC_6H_5N$, Y = *p*-$CH_3OC_6H_5N$): mp = 60−61 °C; IR (C═N) 1677 cm^{-1}; ^1H NMR ($CDCl_3$) 1.34 (s, 3H), 3.68 (s, 3H), 3.72 (s, 3H), 4.12 (dd, 2H, *J* = 8.2 and 26 Hz), 5.15 (m, 2H), 5.99 (m, 1H), 6.69−7.23 (m, 8H); ^{13}C NMR ($CDCl_3$) 20.62, 55.33, 63.85, 75.96, 113.61, 114.07, 116.79, 124.16, 129.23, 129.85, 139.56, 140.77, 152.12, 154.82, 158.21; MS (*m/e*) 338 $[M]^+$. Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 70.98; H, 6.55; N, 8.28. Found: C, 70.75; H, 6.35; N, 7.99.

General Procedure for the Determination of the Effect of Temperature on the Cycloaddition Reaction. A mixture of $Pd_2(dba)_3{\cdot}CHCl_3$ (0.03 mmol), (*S*)-TolBINAP (0.06 mmol), and 3 mL of THF was stirred at room temperature for 30 min. 2-Vinyloxirane (**1a**, 1 mmol) and carbodiimide **3a** or **3b** (1 mmol) were added, the mixture was then stirred under nitrogen at a given temperature (see Table 5 for the reaction time and temperature in each case). The reaction was then concentrated by rotary evaporation, and the crude product was purified by silica gel TLC using 1:1 *n*-pentane/ether as the developer. The results are summarized in Table 4.

Single-Crystal X-ray Diffraction Study Of 5b. Crystals of **5b** were obtained by purification using preparative TLC, preparative HPLC, and recrystallization from methanol. One of the crystals having proximate dimension of 0.2, 0.2, and 0.2 mm was mounted on a glass capillary. All the measurements were made on a Siemens CCD diffractometer with Mo Kα radiation. Cell constants and an orientation matrix for data collection were obtained from least-squares refinement using the setting angles of 5734 reflections in the range $3° < 2\theta < 57°$ and corresponded to a monoclinic cell with dimensions $a = 9.7465(4)$ Å, $b = 13.0803(6)$ Å, $c = 12.8570(6)$ Å, and $\beta = 103.015(1)°$. For $Z = 4$ and FW = 333.21, the calculated density is 1.386 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 $\omega-2\theta$ scan technique to a maximum 2θ value of 57°.

A total of 11377 reflections was collected. The unique set contained 7678 reflections. The data were corrected for Lorentz and polarization

effects,[26] and an absorption correction was made. The minimum and maximum transmission factors are 0.542−1.000.

The structure was solved by direct methods. All the atoms were refined anisotropically except the hydrogen atoms which were found by difference Fourier map. The final cycle of full-matrix least-squares refinement was based on 4430 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 0.450 and −0.300 e/a^3, respectively.

The absolute structure was determined by refinement of the η parameter with the Rogers Schemes, giving a value of 1.0177(0.1001), showing that we have the good hand.

All the calculations were performed using the NRCVAX crystallographic software package.[27]

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Supporting Information Available: Text giving full details of the X-ray structure determination of (*R*)-**5b** including the experimental procedure and tables of bond distances and angles and torsion angles (15 pages). See any current masthead page for ordering and Internet access instructions.

JA964335L

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