Synthesis of Optically Active Ene Carbamates from Chromium Carbene Complexes: Use in Palladium(II)-Assisted Synthesis of Relays to (+)-Thienamycin

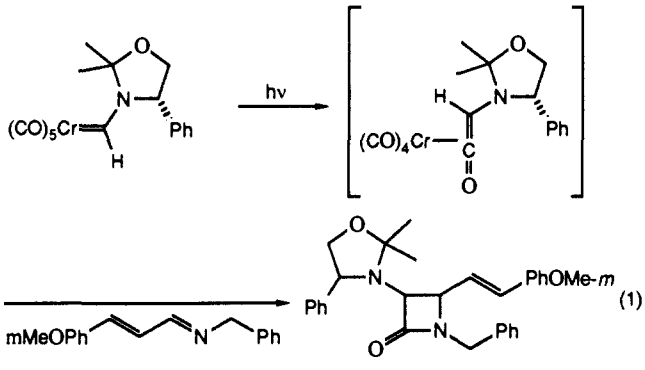
John Montgomery, Gary M. Wieber, and Louis S. Hegedus*

Contribution from the Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523. *Received December 26, 1989. Revised Manuscript Received April 5, 1990*

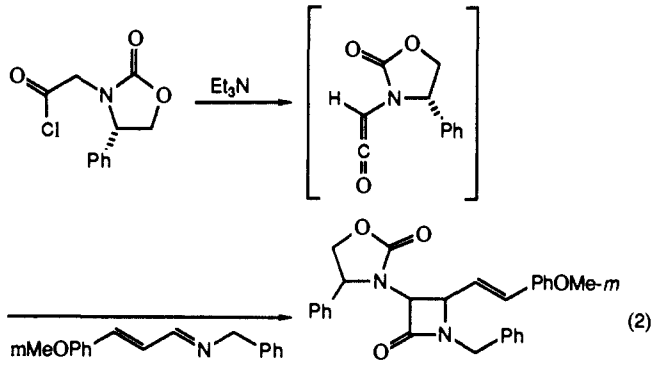
Abstract: Attempts to prepare optically active chromium carbene complexes containing the oxazolidinone moiety led instead to an efficient and general synthesis of optically active ene carbamates. One of these has been subjected to palladium(II)-assisted carboacylation, and complete control of stereochemistry was observed. This compound was converted to a key relay to (+)-thienamycin in good chemical and very high optical yield.

Introduction

An efficient synthesis of optically active β-lactams based on the photolytic reaction of optically active chromium aminocarbene complexes with imines was recently reported from these laboratories.[1] The reaction was highly stereoselective with simple aliphatic and alicyclic imines and with imidates but virtually *non*stereoselective with imines of cinnamaldehyde. Since the β-lactam-forming reaction was thought to proceed via photogenerated chromium-complexed ketenes (eq 1)[2] and since structurally related free ketenes underwent reaction with cinnamaldehyde imines with high stereoselectivity (eq 2),[3] this difference was puzzling. To discover if the difference was due to the relatively minor differences in structure of the respective chiral auxiliary (oxazolidine vs. oxazolidinone) or, instead, due to differences in behavior between metal-bound (eq 1) and free (eq 2) ketenes, the synthesis of chromium carbene complexes containing the oxazolidinone group was attempted. Herein the unexpected results of these studies are reported.



44% cis (1:1 diastereoisomer)
9% trans (single diastereoisomer)



80% cis
84% de

Results and Discussion

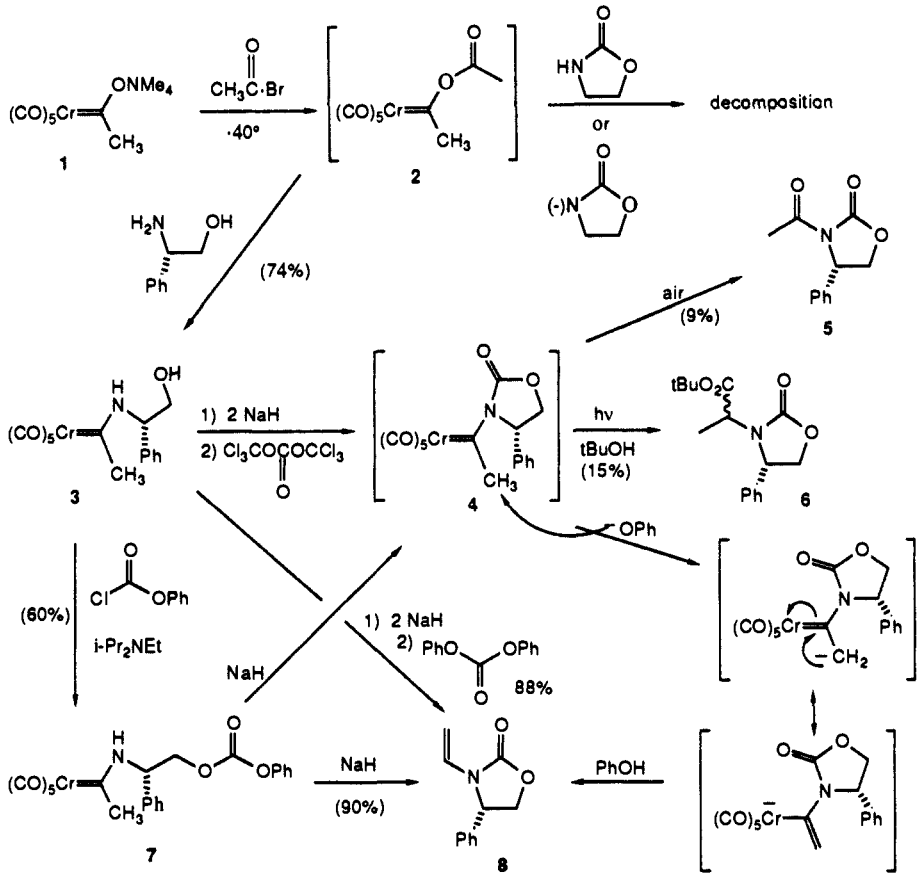
Synthesis of Optically Active Ene Carbamates. Chromium *N*-acylamino carbene complexes are potentially available by two routes: exchange reactions[4] of acetoxycarbene complexes with amides or N-acylation of aminocarbenes. Both of these processes are complicated by over-acylation and by the relative instability of *N*-acylaminocarbene complexes,[5] although *N*-(alkoxycarbonyl)aminocarbene complexes have recently been prepared by exchange and N-acylation and are relatively stable.[5] Direct introduction of the desired optically active oxazolidinone proved infeasible, since even the relatively nonhindered parent compound failed to exchange with acetoxycarbene complex **2** (Scheme I). For this reason, a two-step process was examined next.

(*S*)-Phenylglycinol readily exchanged with acetoxycarbene complex **2** to give good yields of aminocarbene complex **3**. Attempts to isolate the desired oxazolidinone carbene complex **4** from the acylation of **3** by triphosgene[6] [$(Cl_3CO)_2CO$] under a variety of conditions failed. O-Acylation occurred readily, but the relatively non-nucleophilic nitrogen of the aminocarbene failed in most cases to react to close the oxazolidinone ring. Only under one set of conditions was evidence for cyclization obtained. Treatment of **3** with 2 equivs of sodium hydride in THF followed by addition of this solution to a solution of triphosgene, followed by exposure to air and chromatographic (SiO_2) separation of the crude reaction mixture gave 54% recovery of **3** as well as 9% *N*-acetyloxazolidinone **5**, an oxidation product of the desired carbene complex **4**.[7] The above reaction was repeated, and, without exposure of the reaction mixture to air, *tert*-butyl alcohol was added and the mixture was photolyzed.[8] This led to production of α-amino ester **6** in 15% yield, as a mixture of diastereoisomers, confirming the formation of carbene complex **4** in low yield. The apparent instability of this complex was likely due to the decrease in π-overlap of the lone pair on nitrogen with the metal-carbene system caused both by the electron-withdrawing effects of N-acylation and the steric interference with coplanarity caused by the bulky side chain on nitrogen.[9]

(1) Hegedus, L. S.; Imwinkelried, R.; Alarid-Sargent, M.; Dvorak, D.; Satoh, Y. *J. Am. Chem. Soc.* **1990**, *112*, 1109.
(2) Hegedus, L. S.; deWeck, G.; D'Andrea, S. *J. Am. Chem. Soc.* **1988**, *110*, 2122.
(3) Evans, D. A.; Sjogren, E. B. *Tetrahedron Lett.* **1985**, *26*, 3783, 3787.
(4) (a) Connor, J. A.; Fischer, E. O. *J. Chem. Soc. A* **1969**, 578. (b) Connor, J. A.; Jones, E. M. *J. Chem. Soc. A* **1971**, 3368. (c) Semmelhack, M. F.; Bozell, J. J.; Sato, T.; Wulff, W.; Speiss, E.; Zask, A. *J. Am. Chem. Soc.* **1982**, *104*, 5850.
(5) (a) Aumann, R.; Althaus, S.; Krüger, C.; Betz, P. *Chem. Ber.* **1989**, *122*, 357. (b) Hegedus, L. S.; Schultze, L. M.; Montgomery, J. *Organometallics* **1989**, *8*, 2189. (c) Wulff, W. D.; Dragisich, V.; Huffman, J. C.; Kaesler, R. W.; Yang, D. C. *Organometallics* **1989**, *8*, 2196. (d) Dötz, K. H.; Grotjahn, D.; Harmas, K. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1384.
(6) Eckert, H.; Forster, B. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 894.
(7) Casey, C. P.; Boggs, R. A.; Anderson, R. L. *J. Am. Chem. Soc.* **1972**, *94*, 8947.
(8) Hegedus, L. S.; Schwindt, M. A.; DeLombaert, S.; Imwinkelried, R. *J. Am. Chem. Soc.* **1990**, *112*, 2264.

0002-7863/90/1512-6255$02.50/0

Scheme I

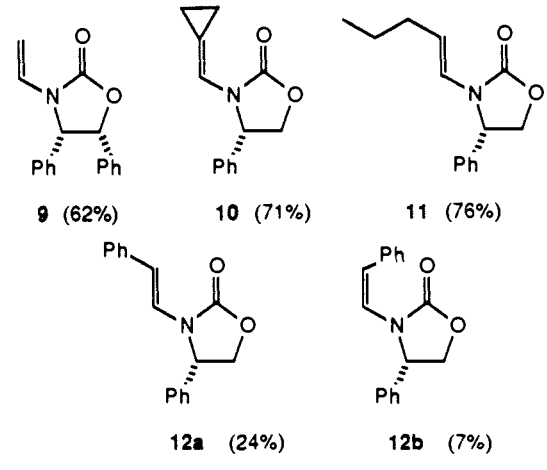


Treatment of complex **3** with phenyl chloroformate produced complex **7** in fair yield (Scheme I). Treatment of this complex with sodium hydride, in an attempt to cyclize **7** to **4**, instead produced optically active ene carbamate **8** in excellent yield. The same compound was produced in even better overall yield (65% based on commercially available **1**) by treatment of **3** with 2 equivs of NaH followed by diphenyl carbonate. Analogous tungsten carbene complexes underwent the same transformation in comparable yield.

Formation of ene carbamate **8** is likely to occur by removal of a proton from the α-carbon of complex **4** by phenoxide followed by reprotonation on chromium and reductive elimination. This process is precedented in the conversion of alkoxycarbene complexes to enol ethers and in the conversion of aminocarbene complexes to imines and/or enamines by reaction with pyridine.[10] The unexpected acidity of **4** can be attributed to the relative lack of π-overlap of the nitrogen lone pair with the metal–carbene system mentioned above.

Optically active ene carbamate **8** is, in itself, an interesting compound, with potential use in organic synthesis. There are few general approaches to this class of compounds,[11] and the reaction chemistry of *optically active* ene carbamates is virtually unexplored. Thus, a variety of optically active aminoalcohol carbenes analogous to **3** were converted to ene carbamates **9–12** in fair yield.

Ene carbamate **9** illustrates that aminoalcohols more hindered than phenylglycinol could be used. α-Branching (**10–12**) was tolerated. The *n*-butylcarbene gave a single *E* isomer (**11**), while the benzyl carbene gave a 5:1 mixture of *E* and *Z* isomers (**12a**, **12b**).



9 (62%) **10** (71%) **11** (76%)

12a (24%) **12b** (7%)

1-Acylamino-1,3-dienes (dieneamides) are better known[12] and, very recently, optically active *N*-dienyl pyroglutamates have been prepared and studied.[13] Optically active diene carbamates are potentially available from α,β-unsaturated analogues of **3** by γ-deprotonation. To determine the feasibility of this, propenylcarbene complex **13** was treated with diphenyl carbonate under standard conditions (Scheme II). Rather than the expected diene carbamate **16**, irreproducible yields of Michael adduct **15** were

(9) For a discussion of the influence of steric hindrance on π-stabilization of carbene complexes, see: Hafner, A.; Hegedus, L. S.; deWeck, G.; Hawkins, B.; Dötz, K. H. *J. Am. Chem. Soc.* **1988**, *110*, 8413 and references therein.

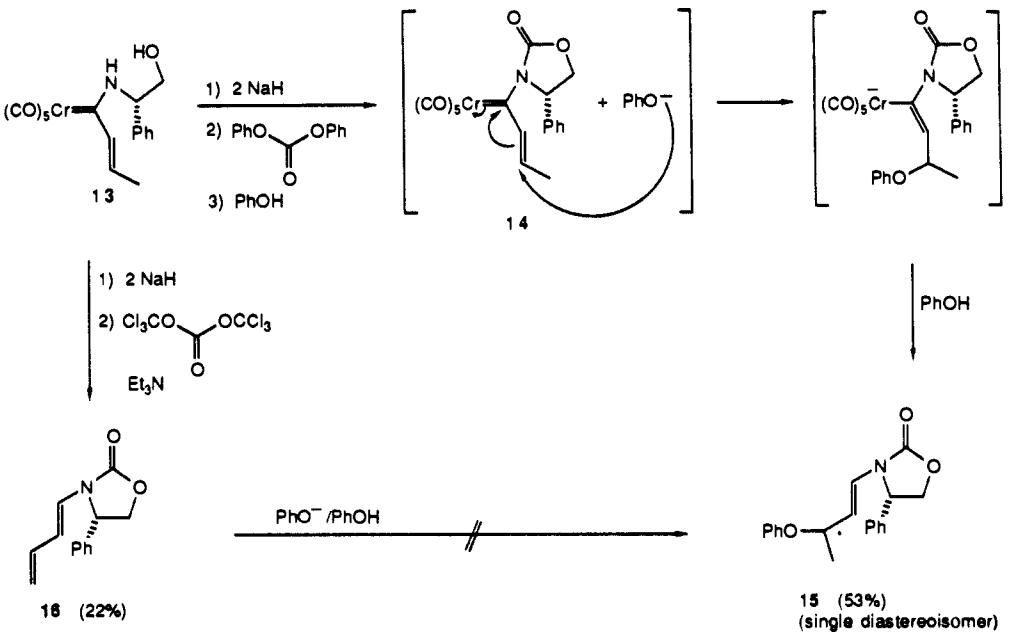
(10) (a) Fischer, E. O.; Plabst, D. *Chem. Ber.* **1974**, *107*, 3326. (b) Connor, J. A.; Rose, P. D. *J. Organomet. Chem.* **1972**, *46*, 329. (c) Casey, C. P.; Brunsvold, W. R. *Inorg. Chem.* **1977**, *16*, 391.

(11) For a review of standard synthetic approaches, see: Lenz, G. R. *Synthesis* **1978**, 489. Enamides have also been prepared by the following. (a) Metal-catalyzed rearrangement of *N*-allyl amides: Stille, J. K.; Becker, Y. *J. Org. Chem.* **1980**, *45*, 2139. Hassel, T.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 399. (b) The condensation of aryl amides with branched aldehydes: Conture, A.; Dubiez, R.; Lablanch-Combier, A. *J. Org. Chem.* **1984**, *49*, 714. (c) Electrochemical oxidation/elimination of *N*-alkyl amides: Shono, T.; Matsumura, Y.; Tsubata, K.; Sugihara, Y.; Yamane, S-i.; Kanazawa, T.; Aoki, T. *J. Am. Chem. Soc.* **1982**, *104*, 6697.

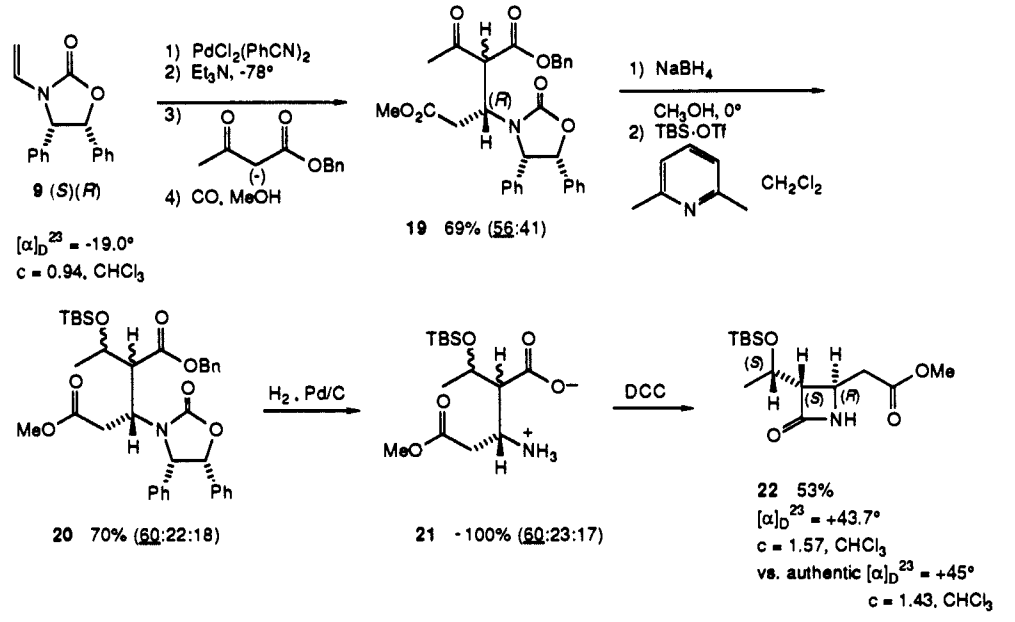
(12) (a) Overman, L. F.; Freerks, R. L.; Petty, C. B.; Clizbe, L. A.; Ono, R. K.; Taylor, G. F.; Jessup, P. J. *J. Am. Chem. Soc.* **1981**, *103*, 2816 and references therein. (b) Oppolzer, W.; Frőstl, W. *Helv. Chim. Acta* **1975**, *58*, 587.

(13) Menezes, R. F.; Zezza, C. A.; Sheu, J.; Smith, M. B. *Tetrahedron Lett.* **1989**, *30*, 3295.

Scheme II



Scheme III



obtained, as a single diastereoisomer. Carrying out the reaction in the presence of phenol, as a proton source, resulted in reproducible yields of **15** in the 50% range. This product is thought to result from *highly stereoselective* Michael addition[14] of phenoxide to the unstable carbene complex **14**, since diene carbamate **16**, made in low yield by using triethylamine in place of phenoxide, did *not* react with a 2:1 phenoxide/phenol solution to produce **15**. Conjugate addition to α,β-unsaturated *alkoxy*carbenes is a well-known phenemenon,[10c,15] although to our knowledge, asymmetric induction in the process has not been addressed. α,β-Unsaturated *amino*carbenes, being much less electrophilic, do not normally undergo Michael addition reactions. The observation that complex **14** apparently does undergo facile Michael addition again is indicative of the lack of carbene stabilization by π-overlap with the heteroatom. This phenomenon of stereoselective Michael addition to optically active conjugate carbene complexes related to **14** as well as the efficient production of dienecarbamate **16** are currently under investigation.

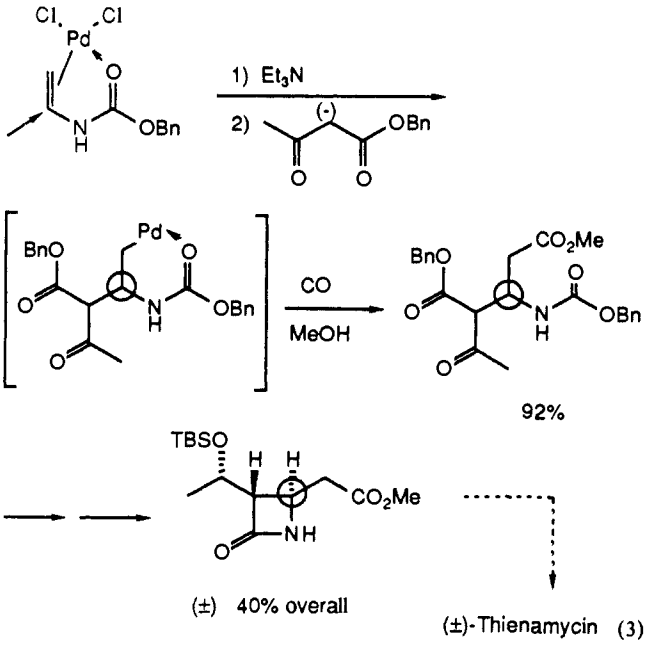
Synthesis of a Relay to (+)-Thienamycin. The development of the above synthesis of optically active ene carbamates closely followed the development in these laboratories of a synthetic approach to a relay to (±)-thienamycin, the key step of which was the palladium(II)-assisted carboacylation of an *achiral* ene carbamate (eq 3).[16] The key stereogenic center, which controlled the relative stereochemistry of the remaining stereogenic centers, was formed in the palladium-assisted alkylation reaction, a process known to occur by exclusive attack on the alkene face opposite the palladium, and for which asymmetric induction has not yet been reported.[17]

(14) Asymmetric conjugate additions to optically active α,β-unsaturated *N*-sulfonyl and *N*-acyl amides has been extensively studied. See: (a) Oppolzer, W.; Kingma, A. J. *Helv. Chim. Acta* **1989**, *72*, 1337 and references therein. (b) Tomioka, K.; Suenaga, T.; Koga, K. *Tetrahedron Lett.* **1986**, *27*, 369 and references therein. (c) Nagao, Y.; Kumagai, T.; Yamada, S.; Fujita, E.; Inoue, Y.; Nagase, Y.; Aoyagi, S.; Abe, T. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2361 and references therein.

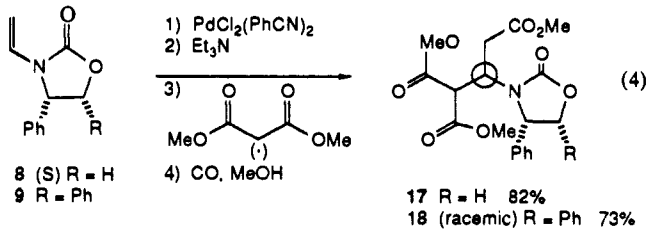
(15) Casey, C. P.; Brunsvold, W. R. *J. Organomet. Chem.* **1974**, *77*, 345.

(16) Wieber, G. M.; Hegedus, L. S.; Åkermark, B.; Michalson, E. T. *J. Org. Chem.* **1989**, *54*, 4649 and references therein.

(17) Modest asymmetric induction (60% ee) has been achieved in the related palladium(II)-assisted amination of olefins by using optically active tertiary amines as ligands and optically active secondary amines as nucleophiles: Bäckvall, J. E.; Björkman, E. E.; Byström, S. E.; Solladie-Cavallo, A. *Tetrahedron Lett.* **1982**, *23*, 943.



Optically active ene carbamates **8** and **9** appeared to be ideal substrates with which to study asymmetric induction in the palladium(II)-assisted carboacylation of olefins and, if successful, to use in a synthesis of the relay to (+)-thienamycin. Treatment of (*S*)-**8** and of racemic *syn*-**9** with dimethyl malonate under standard carboacylation conditions[16] led, in both cases, to the production of a *single* diastereoisomer of alkylation product **17** or **18** (by ^{13}C and ^{1}H NMR spectra of the crude reaction mixture) indicating virtually complete stereocontrol of the single chiral center generated (eq 4). With an eye toward the necessity of its later removal, optically active ene carbamate **9** was the starting material used in further synthetic studies.



(4)

Because it was not possible at this stage to predict which enantiomer of **9** would lead to the desired stereochemistry, parallel syntheses using both (*S*)(*R*)-**9** and (*R*)(*S*)-**9** were carried out, although the (*S*)(*R*)-enantiomer turned out to be the desired one. The approach, shown in Scheme III for the (*S*)(*R*)-enantiomer of **9**, closely paralleled the one previously developed,[16] and the methodology requires little comment, although the stereoselectivity does.

As in the model study, carboacylation of **9** was highly stereoselective giving only two diastereoisomers differing only at the epimerizable β-dicarbonyl central carbon, in a 56:44 ratio. Thus the chiral center α to the nitrogen was cleanly set in this step, and this center controlled the stereoselectivity of the remaining steps, as was observed in the racemic series. The absolute stereochemistry of the final product **22** was determined by comparison with material prepared from the O-silylation of authentic (*S*)-(*S*)(*R*)-hydroxyethylazetidinone, kindly provided by Merck, Sharp and Dohme Company.[18] The optical purity of both the synthetic sample **22** and the material from silylation of the authentic hydroxyethylazetidinone was further assessed by ^{1}H NMR spectroscopy using a chiral shift reagent under conditions for which baseline separation of several peaks for the enantiomers in the racemic mixture was obtained. Under these conditions, neither optically active sample had peaks due to the undesired enantiomer.

Chelate coordination of the ene carbamate **9** to palladium(II) can, in principle, lead to two diastereoisomeric complexes (Chart I) which differ both in the face of the olefin which is complexed, and hence the (opposite) face which is attacked, and the orientation of the olefin relative to the bulky phenyl group. The *observed* stereochemistry of alkylation corresponds to nucleophilic attack from the face opposite the metal in isomer **23a**, rather than **23b**. Complex **23a** is the less congested of the two in that a vinyl hydrogen rather than a vinyl CH_2 group is proximate to the bulky phenyl group.

Further utilization of optically active ene carbamates in palladium-assisted syntheses as well as a study of factors responsible for the high asymmetric induction observed is in progress.

Experimental Section

General Procedure. Melting points were taken on a Mel-Temp apparatus and are uncorrected. A Bruker-IBM 200-NMR spectrometer was used for the 200-MHz ^{1}H NMR spectra. The 270-MHz ^{1}H NMR and 67-MHz ^{13}C NMR spectra were obtained on a Bruker IBM-WP270SY spectrometer. The 300-MHz ^{1}H NMR and 75.5-MHz ^{13}C NMR spectra and DEPT and HETCOR-2D spectra were obtained on a Bruker ACE-300 spectrometer. NMR spectra were recorded in $CDCl_3$, and chemical shifts are given in ppm relative to Me_4Si (0 ppm, ^{1}H) or $CDCl_3$ (77 ppm, ^{13}C). IR spectra were recorded on a Perkin-Elmer 1600 Series FTIR. Electron impact and chemical ionization mass spectra were obtained on a V.G. Micromass Ltd., Model 16F spectrometer. Optical rotations were obtained on a Perkin-Elmer 24 polarimeter at a wavelength of 589 nm (sodium D line) by a 1.0-dm cell with a total volume of 1 mL. Specific rotation, $[\alpha]_D$ was reported in degrees per decimeter at 25 °C, and the concentration (*c*) was given in grams per 100 mL in the specified solvent. Radial layer chromatography was performed by using plates with silica gel 60 PF_{254} (with gypsum, E. Merck Science), and column chromatography was performed by using Alfa-70 micron silica gel as the stationary phase. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ.

Materials. Chromium hexacarbonyl (Pressure Chemicals), tetramethylammonium bromide (Aldrich), tungsten hexacarbonyl (Pressure Chemicals), sodium hydride (50% in oil, Alfa), diphenyl carbonate (Aldrich), sodium borohydride (Alfa), 5% palladium on carbon (Lancaster), carbon monoxide (Matheson), hydrogen (Liquid Air Products), methyllithium (ca. 1.4 M in diethyl ether, Aldrich), butyllithium (ca. 2.5 M in hexanes, Aldrich), cyclopropyl bromide (Aldrich), propenyl bromide (Aldrich), benzyl methyl ether (Pfaltz & Bauer), lithium wire (Aldrich), phenyl chloroformate (Aldrich), diisopropylethylamine (Aldrich), triphosgene (Aldrich), phenol (Baker), (−)-(*SR*)-1,2-diphenylethanolamine (Yamakawa Chemical Ind. Co., Ltd.), (±)-*syn*-1,2-diphenylethanolamine (Aldrich), dimethylformamide (Aldrich, stored over 3Å molecular sieves), dicyclohexylcarbodiimide (Aldrich), imidazole (Aldrich), *tert*-butyldimethylsilyl chloride (Petrarch), tris[3-(heptafluoropropyl)-hydroxymethylene]-(+)-camphorato]europium(III) (Eu(hfc)$_3$, Aldrich) were used without further purification. Literature methods were used to prepare (*S*)-phenylglycinol,[19] $PdCl_2(PhCN)_2$,[20] and *tert*-butyldimethylsilyl triflate.[21] Benzyl acetoacetate was prepared by transesterification of ethyl acetoacetate (Baker) and benzyl alcohol (Mallinckrodt). Tetrahydrofuran (Mallinckrodt) and diethyl ether (Mallinckrodt) were predried over CaH_2 and distilled from benzophenone ketyl under a nitrogen atmosphere. Methylene chloride (technical grade), ethyl acetate (Mallinckrodt), methanol (Mallinckrodt), triethylamine (Mallinckrodt), and 2,6-lutidine (Eastman) were distilled from CaH_2. Hexane (technical grade), dimethyl malonate (Aldrich), and acetyl bromide (Aldrich) were distilled at ambient pressure.

General Procedure for the Synthesis of Amino Alcohol Carbenes—Method A. An Airlessware flask was fitted with a rubber septum, magnetic stirbar, and an argon-filled balloon. The apparatus was charged with the tetramethylammonium salt of [(oxy)(alkyl)carbene]pentacarbonylchromium(0) and freshly distilled and degassed dichloromethane (0.06 M solution). The solution was saturated with argon and was then cooled to −40 °C. Acetyl bromide was slowly injected, and the mixture was stirred at −40 °C for 0.5 h. The aminoalcohol was transferred by

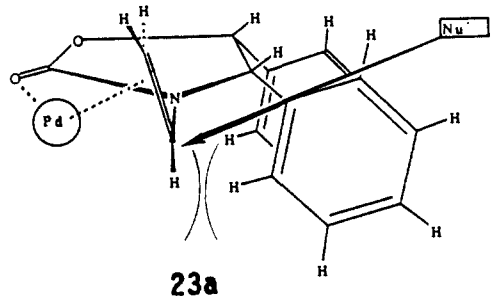
(18) We thank Dr. Paul Reider for providing authentic material for comparison purposes. The hydroxyethylazetidinone provided had $[\alpha]^{23}_D = +54.0°$, *c* 2.52, CH_3OH.

(19) Itsuno, S.; Hirao, A.; Nakahama, S.; Yamazaki, N. *J. Chem. Soc., Perkin Trans. I* **1983**, 1673. Aldrich Catalog Handbook of Fine Chemicals, 1986–1987.

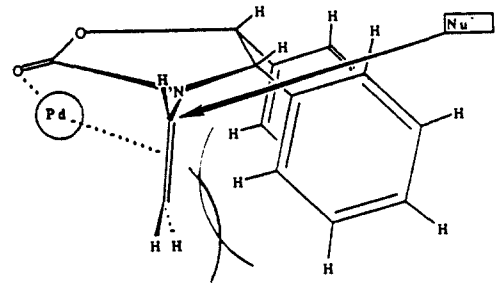
(20) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985; p 17.

(21) Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.

Chart I



23a



23b

cannula as a degassed 0.25 M dichloromethane solution to the acetoxycarbene complex. This solution was warmed to 0 °C over 4 h and then quickly to room temperature. The mixture was filtered through Celite, and the crude product was dissolved in a minimum amount of dichloromethane and was transferred onto the top of a silica column. Elution with 3:1 hexane/EtOAc gave the pure chromium complex which was collected under a gentle flow of argon. The solvent was removed by rotary evaporation, and the product was dried under vacuum and was stored at −15 °C under argon. Optical rotations were not performed due to the relative instabilities of the carbenes in solution.

Preparation of the [(2-Hydroxy-1-phenylethylamino)(methyl)carbene]pentacarbonylchromium(0) (3). The above procedure was used to produce 1.64 g (4.77 mmol, 74%) of carbene complex **3** from 2.00 g (6.48 mmol) of tetramethylammonium salt of [(oxy)(methyl)carbene]pentacarbonylchromium(0),[22] 0.800 g (6.48 mmol) of acetyl bromide, and 0.932 g (6.80 mmol) of (*S*)-phenylglycinol, as a yellow oil which was crystallized from hexane/dichloromethane: mp 53–55 °C, (R_f 0.27, 2:1 hexane/EtOAc, silica gel): ^{1}H NMR (200 MHz) δ major rotamer 1.96 (br s, 1 H, OH), 2.56 (s, 3 H, CH_3), 3.96 (dd, J = 11.5, 4.8 Hz, CH_2O), 4.10 (dd, J = 11.5, 3.7 Hz, 1 H, CH_2O), 4.95 (dt, J = 7.3, 3.8 Hz, 1 H, C*H*Ph), 7.20–7.50 (m, 5 H, Ph), 9.62 (br s, 1 H, NH); ^{13}C NMR (75 MHz) δ 36.69 (CH_3), 62.54 (*C*HPh), 65.44 (CH_2O), 126.05, 128.45, 129.29, 136.46 (Ph), 217.73 (M-CO cis), 223.01 (M-CO trans), 284.37 (*C*=Cr); ^{13}C assignments were confirmed by DEPT experiment; IR (film) ν 2050 (s), 1973 (sh), 1916 (vs) (CrCO) cm^{-1}; mass spectrum *m/e* (% rel intensity) CI(NH_3) 164 (23.4, M − Cr(CO)$_5$ + 1$^+$). Anal. Calcd for $C_{15}H_{13}NO_6Cr$: C, 50.71; H, 3.69; N, 3.94. Found: C, 50.84; H, 3.74; N, 3.99.

Preparation of the [(2-Hydroxy-1-phenylethylamino)(cyclopropyl)carbene]pentacarbonylchromium(0). The above procedure was used to produce 0.970 g (2.54 mmol, 85%) of the carbene complex from 1.00 g (2.99 mmol) of tetramethylammonium salt of [(oxy)(cyclopropyl)carbene]pentacarbonylchromium(0),[23] 0.367 g (2.99 mmol) of acetyl bromide, and 0.492 g (3.59 mmol) of (*S*)-phenylglycinol, as a yellow oil, (R_f 0.45, 2:1 hexane/EtOAc, silica gel): ^{1}H NMR (200 MHz) δ 0.82 (m, 1 H, cyclopropyl CH_2), 1.07–1.30 (m, 3 H, cyclopropyl CH_2), 1.73 (m, 1 H, C*H*-C=), 2.05 (br s, 1 H, OH), 3.96 (dd, J = 11.3, 4.6 Hz, 1 H, CH_2O), 4.10 (dd, J = 11.3, 3.2 Hz, 1 H, CH_2O), 5.15 (m, 1 H, C*H*Ph), 7.24–7.47 (m, 5 H, Ph), 9.54 (br s, 1 H, NH); ^{13}C NMR (75 MHz) δ 11.54, 12.08 (cyclopropyl CH_2's), 28.41 (*C*-C=), 62.87 (*C*HPh), 65.63 (CH_2OH), 126.10, 128.31, 129.17, 136.80 (Ph), 217.94 (M-*C*O cis), 222.38 (M-*C*O trans), 282.79 (*C*=Cr); IR (film) ν 2053 (s), 1968 (sh), 1904 (vs) (CrCO) cm^{-1}; mass spectrum *m/e* (% rel intensity) CI(NH_3) 381 (0.1, M$^+$), 399 (0.3, M + 18$^+$), 190 (100, (M − Cr(CO)$_5$ + 1$^+$). Anal. Calcd for $C_{17}H_{15}NO_6Cr$: C, 53.55; H, 3.97; N, 3.67. Found: C, 53.59; H, 4.07; N, 3.71.

Preparation of [(2-Hydroxy-1-phenylethylamino)(propenyl)carbene]pentacarbonylchromium(0) (13). The above procedure was used to produce 0.180 g (0.472 mmol, 79%) of carbene complex **13** from 0.200 g (0.597 mmol) of tetramethylammonium salt of [(oxy)(propenyl)carbene]pentacarbonylchromium(0),[24] 0.073 g (0.597 mmol) of acetyl bromide, and 0.098 g (0.716 mmol) of (*S*)-phenylglycinol as an orange oil (R_f 0.32, 3:1 hexane/EtOAc, silica gel): ^{1}H NMR (270 MHz) δ 1.84 (d, J = 6.2 Hz, 3 H, CH_3), 2.15 (br s, 1 H, OH), 3.90 (m, 2 H, CH_2O), 4.98 (m, 1 H, C*H*Ph), 6.26 (dq, J = 15.4, 6.2 Hz, 1 H, =C*H*CH$_3$), 6.45 (d, J = 15.4 Hz, 1 H, =C*H*C=Cr), 7.24–7.44 (m, 5 H, Ph), 9.37 (br s, 1 H, NH); ^{13}C NMR (75 MHz) δ 19.15 (CH_3), 63.30 (*C*HPh), 65.52 (CH_2O), 126.18, 128.38, 129.30, 137.07 (Ph), 137.17 (=*C*HC=Cr), 141.13 (*C*HCH$_3$), 218.05 (M-*C*O cis), 223.16 (M-*C*O trans), 273.79 (*C*=Cr); IR (film) ν 2053 (s), 1971 (sh), 1908 (vs) (M-CO), 1634 (m, C=C) cm^{-1}; mass spectrum *m/e* (% rel intensity) CI(NH_3) 190 (9.0, M − Cr(CO)$_5$ + 1$^+$). Anal. Calcd for $C_{17}H_{15}NO_6Cr$: C, 53.55; H, 3.97; N, 3.67. Found: C, 54.69; H, 4.55; N, 4.34.

Preparation of the [(2-Hydroxy-1-phenylethylamino)(benzyl)carbene]pentacarbonylchromium(0). The above procedure was used to produce 0.234 g (0.543 mmol, 44%) of the carbene complex from 0.475 g (1.23 mmol) of tetramethylammonium salt of [(oxy)(benzyl)carbene]pentacarbonylchromium(0),[25] 0.152 g (1.23 mmol) of acetyl bromide, and 0.202 g (1.48 mmol) of (*S*)-phenylglycinol, as an orange oil (R_f 0.23, 3:1 hexane/EtOAc, silica gel). Due to the unstable nature of this complex, a full characterization was not done, and the complex was immediately carried on to complex **12** after chromatography: IR (film) ν 2065 (w), 2054 (s), 1975 (sh), 1924 (vs) (M-CO) cm^{-1}; mass spectrum *m/e* (% rel intensity) CI(NH_3) 240 (8.3, M − Cr(CO)$_5$ + 1$^+$).

General Procedure for the Synthesis of Amino Alcohol Carbenes—Method B. A flask was fitted with a stirbar and rubber septum, and the apparatus was charged with [(methoxy)(alkyl)carbene]pentacarbonylchromium, (*S*)-phenylglycinol, and methanol (enough for 0.25 M solution in carbene). The solution was saturated with argon and was stirred at 25 °C for 24 h. The solvent was evaporated by rotary evaporation and purification and storage were done as described in method A.

Preparation of the [(2-Hydroxy-1-phenylethylamino)(butyl)carbene]pentacarbonylchromium(0). The above procedure was used to produce 0.444 g (1.12 mmol, 89%) of the carbene complex from 0.369 g (1.26 mmol) of [(methoxy)(butyl)carbene]pentacarbonylchromium[26] and 0.207 g (1.51 mmol) of (*S*)-phenylglycinol, as a yellow oil, (R_f 0.31, 3:1 hexane/EtOAc, silica gel): ^{1}H NMR (270 MHz) δ 0.86 (t, J = 7.1 Hz, 3 H, CH_3), 1.2–1.5 (m, 4 H, CH_2CH_2), 1.90 (br s, 1 H, OH), 2.75 (m, 1 H, CH_2C=), 2.91 (m, 1 H, CH_2C=), 3.97–4.20 (m, 2 H, CH_2OH), 4.92 (dt, J = 8.0, 4.0 Hz, 1 H, C*H*Ph), 7.26–7.46 (m, 5 H, Ph), 9.60 (br s, 1 H, NH); ^{13}C NMR (75 MHz) δ 13.50 (CH_3), 22.86 (CH_2CH_2), 28.34 (CH_2CH_2), 48.47 (CH_2C=), 62.00 (*C*HPh), 65.65 (CH_2OH), 126.08, 128.50, 129.29, 137.08 (Ph), 217.85 (M-*C*O cis), 222.75 (M-*C*O trans), 287.50 (*C*=Cr); IR (film) ν 2053 (s), 1972 (sh), 1908 (vs) (M-CO) cm^{-1}; mass spectrum *m/e* (% rel intensity) CI(NH_3) 204 (27.5%, M − Cr(CO)$_5$ − 1$^+$). Anal. Calcd for $C_{18}H_{19}NO_6Cr$: C, 54.41; H, 4.82; N, 3.52. Found: C, 54.48; H, 5.00; N, 3.37.

Preparation of the [(2-Hydroxy-1-phenylethylamino)(methyl)carbene]pentacarbonyltungsten. The above procedure was used to produce 1.300 g (2.67 mmol, 93%) of the carbene complex from 1.10 g (2.88 mmol) of [(methoxy)(methyl)carbene]pentacarbonyltungsten[27] and 0.473 g (3.46 mmol) of (*S*)-phenylglycinol, as a yellow oil, (R_f 0.19, 3:1 hexane/EtOAc, silica gel): ^{1}H NMR (300 MHz) δ major rotamer 2.42 (br s, 1 H, OH), 2.58 (s, 3 H, CH_3), 3.88 (dd, J = 5.0, 11.5 Hz, CH_2O), 3.99 (dd, J = 3.1, 11.5 Hz, 1 H, CH_2O), 4.86 (m, 1 H, C*H*Ph), 7.20–7.41 (m, 5 H, Ph), 9.50 (br s, 1 H, NH); ^{13}C NMR (75 MHz) δ major rotamer 38.46 (CH_3), 62.61 (*C*HPh), 65.15 (CH_2O), 126.11, 128.53, 129.32, 136.11 (Ph), 198.77 (M-*C*O cis), 203.70 (M-*C*O trans), 261.62 (*C*=Cr); IR (film) ν 2062 (s), 1972 (sh), 1900 (vs) (M-CO) cm^{-1}; mass spectrum *m/e* (% rel intensity) CI(NH_3) 484 (0.3), 485 (0.8), 486 (1.5), 487 (1.4),

(22) Fischer, E. O.; Maasböl, A. *Chem. Ber.* **1967**, *100*, 2445.
(23) Connor, J. A.; Jones, E. M. *J. Organomet. Chem.* **1973**, *60*, 77.
(24) (a) Prepared as described in Wilson, J. W.; Fischer, E. O. *J. Organomet. Chem.* **1973**, *57*, C63, substituting tetramethylammonium bromide for trimethyloxonium tetrafluoroborate and propenyllithium[24b] for vinyllithium. (b) Whitesides, G. M.; Casey, C. P.; Krieger, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 1379.
(25) Prepared as described in Fischer, E. O.; Kreiter, C. G.; Kollmeier, H. J.; Müller, J.; Fischer, R. D. *J. Organomet. Chem.* **1971**, *28*, 237, substituting tetramethylammonium bromide for trimethyloxonium tetrafluoroborate.
(26) Prepared as described in Aumann, R.; Fischer, E. O. *Chem. Ber.* **1968**, *101*, 954, substituting butyllithium for methyllithium.
(27) Prepared as described in ref 26 substituting tungsten hexacarbonyl for chromium hexacarbonyl.

488 (1.3), 489 (0.8), 490 (0.8), (^{182}W, ^{183}W, ^{184}W, ^{186}W; M + 1$^+$ and M − 1$^+$).

(±)-[(1,2-*syn*-Diphenylethanolamino)(methyl)carbene]pentacarbonylchromium(0). This material was prepared according to literature procedures[2] by using $[N(CH_3)_4][Cr(CO)_5COCH_3]$[22] (1.00 g, 3.23 mmol), acetyl bromide (240 μL, 3.25 mmol), and (±)-1,2-*syn*-diphenylethanolamine (844 mg, 3.96 mmol) and producing 1.26 g of product contaminated with 7.9% diethyl ether (83% yield). Spectroscopic data was identical with reported values.

(*SR*)-[(1,2-*syn*-Diphenylethanolamino)(methyl)carbene]pentacarbonylchromium(0). This material was prepared according to literature procedures[2] by using $[N(CH_3)_4][Cr(CO)_5COCH_3]$ (1.00 g, 3.23 mmol), acetyl bromide (240 μL, 3.25 mmol), and (−)-(*SR*)-1,2-diphenylethanolamine (760 mg, 3.56 mmol) and producing 1.22 g of product contaminated with 7% diethyl ether (82% yield). Spectroscopic data was identical with reported values.

The following ^{13}C NMR spectral data was not previously reported: ^{13}C NMR (67.9 MHz) δ 36.4 (CH_3), 66.4 (PhCHN), 75.7 (PhCHO), 126.1, 126.3, 127.4, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 135.1, 137.9 (Ph), 217.7 (CO cis), 223.0 (CO trans), 283.4 (C=Cr).

Photolysis of Oxazolidinone Carbene 4 with *tert*-Butyl Alcohol (Compound 6). A 50-mL Airlessware tube was fitted with a rubber septum, magnetic stirbar, and an argon-filled balloon. The apparatus was charged with 0.50 g (1.41 mmol) of the (phenylethanolamino)(methyl)chromium carbene and 0.068 g (2.8 mmol) of sodium hydride, and the system was placed under argon. Tetrahydrofuran (25 mL) was added by syringe, and the yellow-orange solution was stirred at 25 °C for 1 h. This solution was cooled to −25 °C, and an airless solution of 0.279 g (0.940 mmol) of triphosgene in 4 mL of tetrahydrofuran was added by cannula. The bath was removed, and stirring was continued for 5 min. The solution was cooled to −25 °C again, and 10 mL of a 1:1 tetrahydrofuran/*tert*-butyl alcohol solution was added by cannula. This red solution was stirred for 1 min to ensure solution homogeneity and was irradiated with a 200-W mercury lamp for 9 h at −25 °C. The solution was oxidized as described in the general procedure for ene carbamates. The product was purified by radial chromatography eluting with a hexane to 2:1 hexane/EtOAc gradient to yield 0.061 g (0.21 mmol, 15%) of compound **6** as a clear oil, (R_f 0.37, 2:1 hexane/EtOAc, silica gel). The diastereomeric excess of the reaction was irreproducible, ranging from moderate to high: ^{1}H NMR (300 MHz) δ major isomer 1.45 (s, 9 H, tBu), 1.54 (d, J = 7.4 Hz, 3 H, CH_3), 3.60 (q, J = 7.4 Hz, 1 H, C*H*CH_3), 4.09 (t, J = 9.0 Hz, 1 H, CH_2O, syn to Ph), 4.62 (t, J = 8.7 Hz, 1 H, CH_2O, anti to Ph), 4.93 (t, J = 9.0 Hz, 1 H, C*H*Ph), 7.37 (m, 5 H, Ph); minor isomer 1.05 (d, J = 7.5 Hz, 3 H, CH_3), 1.48 (s, 9 H, *t*Bu), 4.12 (dd, J = 6.3, 8.5 Hz, 1 H, CH_2O, syn to Ph), 4.38 (q, J = 7.5 Hz, 1 H, C*H*CH_3), 4.67 (t, J = 8.8 Hz, 1 H, CH_2O, anti to Ph), 5.03 (dd, J = 6.3, 9.1 Hz, 1 H, C*H*Ph), 7.36 (m, 5 H, Ph); ^{13}C NMR (75 MHz) δ major isomer 15.27 (CH_3), 27.95 (C(*C*H_3)$_3$), 52.76 (*C*HCH_3), 62.60 (*C*HPh), 70.34 (CH_2O), 82.17 (*C*(CH_3)$_3$), 127.47, 129.27, 137.24 (Ph), 158.23 (−NCO_2−), 169.81 (*C*O_2tBu); minor isomer 15.72 (CH_3), 27.89 (C(*C*H_3)$_3$), 52.96 (*C*HCH_3), 58.79 (*C*HPh), 70.76 (CH_2O), 82.06 (*C*(CH_3)$_3$), 158.65 (−NCO_2−), 170.32 (*C*O_2tBu); IR (film) ν 1760, 1731 (C=O) cm^{-1}; mass spectrum *m/e* (% rel intensity) EI 218 (4.9, M − tBuO$^+$), 190 (100, M − tBuO_2C^+). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 65.96; H, 7.26; N, 4.81. Found: C, 66.01; H, 7.39; N, 4.68.

O-Acylation of Carbene Complex 3 To Give Compound 7. A 25-mL Airlessware flask was fitted with a stirbar and rubber septum, and the apparatus was charged with 0.200 g (0.563 mmol) of the [(phenylethanolamino)(methyl)carbene]chromium and dichloromethane (10 mL) under argon. Phenyl chloroformate (0.265 g, 1.69 mmol) was added dropwise at 25 °C, and the color changed from yellow to yellow-green. Diisopropylethylamine (0.290 g, 2.25 mmol) was then added dropwise, and the mixture was stirred for 25 h. The mixture was filtered through Celite, and the solvent was evaporated to yield a yellow-green oil. The crude mixture was adsorbed onto silica gel and was transferred onto a silica gel column. Elution with 4:1 hexane/EtOAc yielded the chromium complex as a yellow oil contaminated with *N,N*-ethylisopropyl-*O*-phenyl carbamate. Crystallization with ether/hexane afforded the pure carbene complex **7** (0.160 g, 0.337 mmol, 60%) as cream-colored needles (R_f 0.48, 3:1 hexane/EtOAc, silica gel): ^{1}H NMR (270 MHz) δ 2.62 (s, 3 H, CH_3), 4.50 (dd, J = 12.1, 3.8 Hz, 1 H, CH_2O), 4.70 (dd, J = 12.1, 8.6 Hz, 1 H, CH_2O), 5.24 (m, 1 H, C*H*Ph), 7.14–7.49 (m, 10 H, 2 Ph), 9.5 (br s, 1 H, NH); IR (film) ν 2055 (m), 1972 (sh), 1910 (vs) (MCO), 1757 (m, C=O) cm^{-1}. Anal. Calcd for $C_{22}H_{17}NO_8Cr$: C, 55.59; H, 3.60; N, 2.95. Found: C, 55.58; H, 3.74; N, 3.12.

General Procedure for the Synthesis of Ene Carbamates. An Airlessware flask was fitted with a stirbar, rubber septum, and argon-filled balloon. The apparatus was charged with the [(phenylethanolamino)-(alkyl)carbene]chromium and sodium hydride, and the system was placed under argon. Tetrahydrofuran (enough for a 0.03 M solution in carbene) was added by syringe, H_2 was evolved for about 5 min, and the yellow-orange solution was stirred at 25 °C for 1 h. Diphenyl carbonate was added as a solid under a gentle flow of argon. More H_2 was evolved, and the color turned deep red. Stirring was continued at 25 °C for 3 h. The solvent was evaporated, and the residue was taken up in 1:1 hexane/EtOAc. This solution was saturated with air and was oxidized in a light box equipped with six 20-W Vitalite fluorescent lamps. After a few hours to 2 days, the solution was light yellow and contained a dark brown precipitate which was removed by filtration through Celite. In some cases, filtering through silica gel was necessary to separate out any remaining soluble chromium-containing species. Purification by radial chromatography eluting with 4:1 hexane/EtOAc yielded the pure ene carbamate.

Preparation of 3-Ethenyl-(*S*)-4-phenyl-2-oxazolidinone (8). From chromium complex **3**: The above procedure was used to produce 0.023 g (0.122 mmol, 88%) of compound **8** from 0.050 g (0.141 mmol) of the chromium carbene **3**, 0.007 g (0.282 mmol) of sodium hydride, and 0.151 g (0.705 mmol) of diphenyl carbonate as a clear oil (R_f 0.22, 4:1 hexane/EtOAc, silica gel).

From the corresponding tungsten complex: The above procedure was used to produce 0.047 g (0.249 mmol, 81%) compound **8** from 0.150 g (0.308 mmol) of the [(phenylethanolamino)(methyl)carbene]tungsten, 0.015 g (0.616 mmol) of sodium hydride, and 0.198 g (0.924 mmol) of diphenyl carbonate.

From carbene complex **7**: A 25-mL Airlessware flask was fitted with a stirbar, rubber septum, and argon-filled balloon, and the apparatus was charged with 0.312 g (0.657 mmol) of carbene **7** and 0.016 g (0.66 mmol) of sodium hydride. Tetrahydrofuran (20 mL) was added by syringe, H_2 was evolved for about 5 min, and the solution turned deep red upon stirring at 25 °C for 4 h. The solution was oxidized as described previously. Radial chromatography with 4:1 hexane/EtOAc yielded 0.112 g (0.592 mmol, 90%) of compound **8**: ^{1}H NMR (270 MHz) δ 4.09 (dd, J = 16.1, 1.2 Hz, 1 H, *Z*-*H*C=CN), 4.14 (dd, J = 8.7, 5.2 Hz, 1 H, CH_2O, syn to Ph), 4.32 (dd, J = 9.2, 1.2 Hz, 1 H, *E*-*H*C=CN), 4.73 (t, J = 8.9 Hz, 1 H, CH_2O, anti to Ph), 5.04 (dd, J = 9.1, 5.2 Hz, 1 H, C*H*Ph), 6.84 (dd, J = 16.1, 9.2 Hz, 1 H, NC*H*=C), 7.20–7.50 (m, 5 H, Ph); assignments were confirmed by a HETCOR 2D experiment; ^{13}C NMR (75 MHz) δ 58.13 (*C*HPh), 70.65 (*C*H_2O), 95.89 (H_2C=), 125.87, 128.72, 128.78, 129.35, 138.07 (*Ph* and =*C*HN), 155.76 (*C*=O); IR (film) ν 1761 (s, C=O), 1638 (m, C=C) cm^{-1}; mass spectrum *m/e* (% rel intensity) EI 189 (0.3, M$^+$). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.71; H, 6.00; N, 7.63; $[\alpha]_D$ +113° (*c* 1.25, CH_2Cl_2).

Preparation of 3-(2-Methylenecyclopropyl)-(*S*)-4-phenyl-2-oxazolidinone (10). The above procedure was used to produce 0.032 g (0.15 mmol, 71%) of compound **10** from 0.080 g (0.21 mmol) of the [(phenylethanolamino)(cyclopropyl)carbene]chromium, 0.010 g (0.42 mmol) of sodium hydride, and 0.180 g (0.84 mmol) of diphenyl carbonate as white crystals which was recrystallized from ether/hexane: mp 66–67 °C, (R_f 0.18, 3:1 hexane/EtOAc, silica gel): ^{1}H NMR (300 MHz) δ 0.30 (m, 1 H, cyclopropyl CH_2), 0.91–1.06 (m, 3 H, cyclopropyl CH_2), 4.11 (dd, J = 5.0, 8.6 Hz, 1 H, CH_2O, syn to Ph), 4.69 (t, J = 8.8 Hz, 1 H, CH_2O, anti to Ph), 5.23 (dd, J = 5.0, 9.0 Hz, 1 H, C*H*Ph), 6.97 (t, J = 1.9 Hz, 1 H, NC*H*=C), 7.21–7.40 (m, 5 H, Ph); ^{13}C NMR (75 MHz) δ 1.79, 4.54 (cyclopropyl *C*H_2's), 58.63 (*C*HPh), 70.52 (*C*H_2O), 105.06 (*C*=CHN), 113.01 (=*C*HN), 125.55, 128.40, 129.13, 140.04 (Ph), 156.17 (*C*=O); IR (film) ν 1755 (C=O, C=C) cm^{-1}; mass spectrum *m/e* (% rel intensity) EI 215 (21.7, M$^+$); $[\alpha]_D$ +129° (*c* 1.33, CH_2Cl_2). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.50; H, 6.15; N, 6.34.

Preparation of 3-(*E*)-1-Pentenyl-(*S*)-4-phenyl-2-oxazolidinone (11). The above procedure was used to produce 0.186 g (0.805 mmol, 76%) of compound **11** from 0.420 g (1.057 mmol) of the [(phenylethanolamino)(butyl)carbene]chromium, 0.051 g (2.12 mmol) of sodium hydride, and 0.679 g (3.17 mmol) of diphenyl carbonate as a fluffy white solid: mp 34–35.5 °C (R_f 0.32, 3:1 hexane/EtOAc, silica gel); ^{1}H NMR (300 MHz) δ 0.72 (t, J = 7.3 Hz, 3 H, CH_3), 1.20 (hex, J = 7.3 Hz, 2 H, C$H_2$$CH_3$), 1.86 (m, 2 H, C$H_2$C=), 4.10 (dd, J = 5.3, 8.6 Hz, 1 H, CH_2O, syn to Ph), 4.61 (dt, J = 7.2, 14.5 Hz, 1 H, *H*C=CN), 4.70 (t, J = 8.9 Hz, 1 H, CH_2O, anti to Ph), 5.01 (dd, J = 5.3, 9.0 Hz, 1 H, C*H*Ph), 6.57 (d, J = 14.5 Hz, 1 H, NC*H*=C), 7.23–7.42 (m, 5 H, Ph); ^{13}C NMR (75 MHz) δ 13.13 (*C*H_3), 22.79 (*C*$H_2$$CH_3$), 31.86 (*C*$H_2$C-H=), 58.59 (*C*HPh), 70.41 (*C*H_2O), 113.55 (*C*H=CHN), 122.52 (NCH=C), 125.83, 128.57, 129.17, 138.26 (Ph), 155.77 (*C*=O); IR (film) ν 1760 (C=O), 1672 (C=C) cm^{-1}; mass spectrum *m/e* (% rel intensity) EI 231 (14.9, M$^+$); $[\alpha]_D$ +107° (*c* 1.26, CH_2Cl_2). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.59; H, 7.51; N, 6.17.

Preparation of 3-(*E*+*Z*)-Styryl-(*S*)-4-phenyl-2-oxazolidinone (12a and 12b). The above procedure (extending the final reaction time from

3 h to overnight) was used to produce 0.034 g (0.13 mmol, 24%) of compound **12a** (trans) and 0.010 g (0.04 mmol, 7%) of compound **12b** (cis) from 0.234 g (0.543 mmol) of the [(phenylethanolamino)(methyl)carbene]chromium, 0.026 g (1.1 mmol) of sodium hydride, and 0.465 g (2.17 mmol) of diphenyl carbonate. Crude ^{1}H NMR indicated a 5:1 ratio of **12a**:**12b**. Compound **12a** was isolated as a white crystalline solid which was recrystallized from ether/hexane, mp 120–123 °C (R_f 0.19, 3:1 hexane/EtOAc, silica gel); ^{1}H NMR (300 MHz) δ 4.18 (dd, J = 5.1, 8.7 Hz, 1 H, CH_2O, syn to Ph), 4.77 (t, J = 8.9 Hz, 1 H, CH_2O, anti to Ph), 5.15 (dd, J = 5.1, 9.0 Hz, 1 H, C*H*Ph), 5.58 (d, J = 14.9 Hz, 1 H, C*H*=CHN), 7.12–7.45 (m, 11 H, NC*H*=C, 2Ph); ^{13}C NMR (75 MHz) δ 58.57 (*C*HPh), 70.70 (*C*H_2O), 112.96 (*C*H=CHN), 122.93 (N*C*H=C), 125.39, 125.80, 126.60, 128.55, 128.91, 129.47, 135.79, 137.93 (2Ph), 155.76 (*C*=O); IR (film) ν 1746 (C=O), 1655 (C=C) cm^{-1}; mass spectrum m/e (% rel intensity) EI 265 (6.5%, M$^+$); $[\alpha]_D$ +113° (c 0.68, CH_2Cl_2). Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.00; H, 6.00; N, 5.51.

Compound **12b** was isolated as a white solid which was recrystallized from ether/hexane: mp 103–107 °C, (R_f 0.24, 3:1 hexane/EtOAc, silica gel); ^{1}H NMR (270 MHz) δ 4.11 (dd, J = 4.1, 8.7 Hz, 1 H, CH_2O, syn to Ph), 4.61 (t, J = 8.7 Hz, 1 H, CH_2O, anti to Ph), 4.89 (dd, J = 4.1, 8.7 Hz, 1 H, C*H*Ph), 5.88 (d, J = 9.6 Hz, 1 H, C*H*=CHN), 6.49 (d, J = 9.6 Hz, 1 H, NC*H*=C), 6.62, 7.00, 7.10–7.30 (m, 10 H, 2Ph); ^{13}C NMR (75 MHz) δ 58.81 (*C*HPh), 70.32 (*C*H_2O), 116.30 (*C*H=CHN), 122.20 (N*C*H=C), 126.10, 127.18, 127.93, 128.50, 128.68, 129.10, 135.68, 138.14 (2 Ph), 157.08 (*C*=O); IR (film) ν 1760 (C=O), 1652 (C=C) cm^{-1}; mass spectrum m/e (% rel intensity) EI 265 (72.4%, M$^+$).

(±)-*syn*-4,5-Diphenyl-3-vinyl-2-oxazolidinone [(±)-9]. (±)-[(1,2-*syn*-(Diphenylethanolamino)(methyl)carbene]pentacarbonylchromium(0) (248 mg, 0.58 mmol) was dissolved in THF (100 mL). A 50% mineral oil suspension of sodium hydride (55 mg, 1.4 mmol) was added, causing significant bubbling and a gradual darkening of the mixture's color to deep red. The mixture was stirred 1 h at room temperature before diphenyl carbonate (617 mg, 2.90 mmol) was added as a THF solution (5 mL), causing the color to darken further. The solution was stirred 3.5 h at room temperature under argon before exposing to air for 15 min. Filtration through silica gel, concentration by rotary evaporation, and purification by radial chromatography (1 mm silica gel plate, eluting with 9:1 hexane/diethyl ether, R_f 0.41 with 2:1 hexane/ethyl acetate) gave 94 mg (62%) of product, mp 162.5–164.5 °C.

(−)-(*SR*)-4,5-Diphenyl-3-vinyl-2-oxazolidinone [(−)-9]. This material was prepared as described for the racemic material [(±)-9] by using (*SR*)-[(1,2-diphenylethanolamino)(methyl)carbene]pentacarbonylchromium(0) (1.03 g, 2.39 mmol), 50% sodium hydride (239 mg, 4.98 mmol), and diphenyl carbonate (2.59 g, 12.1 mmol) producing 319 mg (50%) product whose spectroscopic data was identical with that of the racemic material: $[\alpha]_D$ = 22.1° (c 1.99, $CHCl_3$); ^{1}H NMR (200 MHz) δ 4.09 (dd, J = 16.1, 1.2 Hz, 1 H, *Z*-H_2C=), 4.37 (dd, J = 9.2, 1.1 Hz, 1 H, *E*-H_2C=), 5.26 (d, J = 8.2 Hz, 1 H, PhC*H*N), 5.92 (d, J = 8.2 Hz, 1 H, PhC*H*O), 6.80–7.11 (m, 11 H, Ph, =CHN); ^{13}C NMR (67.9 MHz) δ 63.1 (PhCHN), 80.4 (PhCHO), 96.1 (H_2C=), 126.2, 127.0, 127.8, 128.1, 128.2, 128.6, 133.3, 133.7 (Ph, =CHN), 155.2 (CO); IR (film) ν 1734 (CO), 1640 cm^{-1}; mass spectrum m/e EI 265 (M$^+$). Anal. Calcd for $C_{17}H_{15}O_2N$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.98; H, 5.77; N, 5.30.

Michael Addition of Phenoxide to Carbene Complex 14 To Give Compound 15. An Airlessware flask was fitted with a stirbar, rubber septum, and argon-filled balloon. The apparatus was charged with 0.100 g (0.263 mmol) of the [(phenylethanolamino)(propenyl)carbene]chromium and 0.013 g (0.525 mmol) of sodium hydride, and the system was placed under argon. Tetrahydrofuran (8 mL) was added by syringe, H_2 was evolved for about 5 min, and the orange solution was stirred at 25 °C for 1 h. Diphenyl carbonate (0.225 g, 1.052 mmol) was dissolved in THF (3 mL) under argon, and this solution was transferred by cannula to the carbene solution. This deep red solution was stirred at 25 °C for 5 min, and a solution of 0.030 g (0.316 mmol) of phenol in THF (2 mL) under argon was added by cannula, followed by stirring at 25 °C for 4 h. The THF was evaporated, and the residue was oxidized under the standard conditions described previously. The product was purified by radial chromatography eluting with 4:1 hexane/EtOAc to yield 0.043 g (0.139 mmol, 53%) of compound **15** as white crystals which was recrystallized from ether/hexane: mp 107–110 °C (R_f 0.40, 2:1 hexane/EtOAc); ^{1}H NMR (300 MHz) δ 1.21 (d, J = 6.0 Hz, 3 H, CH_3), 4.12 (dd, J = 8.7, 5.2 Hz, 1 H, CH_2O, syn to Ph), 4.69 (m, 3 H, CH_2O, anti to Ph, C*H*=CN, C*H*CH_3), 4.99 (dd, J = 9.0, 5.2 Hz, 1 H, C*H*Ph), 6.74–6.93 (m, 4 H, NC*H*=C, Ph), 7.25, 7.38 (m, 7 H, *Ph*); ^{13}C NMR (75 MHz) δ 22.05 (CH_3), 58.41 (*C*HPh), 70.53 (*C*H_2O), 72.80 (*C*HCH_3), 113.91 (*C*H=CHN), 116.16, 120.84, 125.89, 128.84, 129.31, 129.34, 137.60, 157.50 (2 Ph), 124.58 (N*C*H=C), 155.67 (*C*=O); IR (film) ν 1760 (C=O), 1672 (C=C) cm^{-1}; mass spectrum m/e (% rel intensity) CI (NH_3) 310 (4.8, M + 1$^+$), 327 (2.9, M + 18$^+$); $[\alpha]_D$ +166° (c 1.24, CH_2Cl_2). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.57; H, 6.34; N, 4.54.

Preparation of 3-(1,3-Dienyl)-4-phenyl-2-oxazolidinone (16). A 25-mL Airlessware flask was fitted with a rubber septum, magnetic stirbar, and an argon-filled balloon. The apparatus was charged with 0.200 g (0.525 mmol) of the [(phenylethanolamino)(propenyl)carbene]chromium and 0.025 g (1.1 mmol) of sodium hydride under argon. Tetrahydrofuran (10 mL) was added by syringe, and the orange solution was stirred at 25 °C for 1 h. This solution was cooled to −78 °C, and 0.027 g (0.26 mmol) of triethylamine was added by syringe followed by a solution of 0.057 g (0.19 mmol) of triphosgene in 3 mL of tetrahydrofuran added slowly by cannula. The color changed to deep red quickly, and, after 5 min, the cooling bath was removed and stirring was continued for 3.5 h. The solution was oxidized as described previously for only 3 h, for compound **16** decomposes slowly under these conditions. The product was purified by radial chromatography eluting with 4:1 hexane/EtOAc to yield 0.025 g (0.12 mmol, 22%) of compound **6** as a clear oil which was crystallized with ether/hexane: mp 100–102 °C (R_f 0.25, 3:1 hexane/EtOAc); ^{1}H NMR (300 MHz) δ 4.14 (dd, J = 5.1, 8.6 Hz, 1 H, CH_2O, syn to Ph), 4.73 (t, J = 8.8 Hz, 1 H, CH_2O, anti to Ph), 4.87 (d, J = 9.2 Hz, 1 H, *E*-H_2C=CH), 4.88 (d, J = 18.6 Hz, 1 H, *Z*-H_2C=CH), 5.04 (dd, J = 5.1, 8.9 Hz, 1 H, C*H*Ph), 5.31 (dd, J = 10.6, 14.3 Hz, 1 H, C*H*=CHN), 6.19 (dt, J = 16.8, 10.4 Hz, 1 H, C*H*=CH_2), 6.85 (d, J = 14.4 Hz, 1 H, NC*H*=CH), 7.25–7.44 (m, 5 H, Ph); ^{13}C NMR (75 MHz) δ 58.53 (*C*HPh), 70.65 (*C*H_2O), 113.96 (H_2*C*=), 114.68 (*C*H=CHN), 125.75, 128.92, 129.47, 137.89 (Ph), 126.01 (C=*C*HN), 134.29 (*C*H=CH_2), 155.56 (*C*=O); IR (film) ν 1760 (s), 1651 (s), 1606 (w) cm^{-1}; mass spectrum m/e (% rel intensity) EI 215 (38.3, M$^+$); $[\alpha]_D$ +248° (c 0.47, CH_2Cl_2). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.31; H, 5.86; N, 6.34.

Carboacylation of Ene Carbamate (±)-9 with Dimethyl Malonate (Compound (±)-18). A solution of (±)-*syn*-4,5-diphenyl-3-vinyl-2-oxazolidinone (167 mg, 0.629 mmol) in 10 mL of THF was stirred as $PdCl_2(PhCN)_2$ (241 mg, 0.628 mmol) was added, turning the solution a deep burgundy-orange color. After stirring 10 min at room temperature, the solution was cooled to −78 °C. Triethylamine (175 μL, 1.26 mmol) was added dropwise over 10 min, and then the mixture stirred at −78 °C for 10 min. A THF solution (2 mL) containing 0.63 mmol of sodium dimethyl malonate (prepared from sodium hydride) was added dropwise over 5 min. The mixture was stirred 5 h at −78 °C. Precooled methanol (−78 °C, 10 mL) was added, and a carbon monoxide atmosphere was placed over the mixture. The temperature was allowed to slowly rise to room temperature over 15 h and then stirred at room temperature another 4 h. Filtration of the black slurry through Celite, concentration by rotary evaporation, and purification by radial chromatography (1 mm silica gel plate, eluting with a 5:1 hexane/diethyl ether to diethyl ether gradient, R_f 0.17 with 2:1 hexane/ethyl acetate) gave 211 mg (73%) of product as a single diastereomer: ^{1}H NMR (300 MHz) δ 2.92 (dd, J = 16.5, 6.2 Hz, 1 H, C$H_2$$CO_2$Me), 2.99 (dd, J = 16.4, 6.1 Hz, 1 H, C$H_2$$CO_2$Me), 3.45 (s, 3 H, C$H_3O_2CCH_2$), 3.67 (s, 3 H, C$H_3O_2$C), 3.81 (s, 3 H, C$H_3O_2$C), 4.22 (d, J = 8.8 Hz, 1 H, C*H*-(CO_2CH_3)$_2$), 4.41 (ddd, J = 8.7, 6.3, 6.3 Hz, 1 H, C*H*CH_2), 5.21 (d, J = 8.2 Hz, 1 H, PhCHN), 5.81 (d, J = 8.2 Hz, 1 H, PhCHO), 7.00 (m, 4 H, Ph), 7.10 (m, 6 H, Ph); ^{13}C NMR (75.5 MHz) δ 36.0 (*C*$H_2$$CO_2$-$CH_3$), 51.0, 51.8, 52.8, 53.0, 53.7 (3*C*H_3O_2C, Ph*C*HN, *C*HCH_2), 67.0 (*C*H(CO_2CH_3)$_2$), 80.4 (Ph*C*HO), 125.7, 127.7, 127.8, 128.2, 128.4, 134.3, 134.8 (Ph), 157.0 (NCO_2), 167.6, 167.9 ((CH_3O_2C)$_2$CH), 170.6 (CH_3O_2*C*CH_2); IR (film) 3035, 1748 (s, CO) cm^{-1}; mass spectrum m/e CI (NH_3) 456 (M + 1$^+$). Anal. Calcd for $C_{24}H_{25}NO_8$: C, 63.29; H, 5.53; N, 3.08. Found: C, 63.51; H, 5.56; N, 2.86.

Carboacylation of (−)-(*S*)-Ene Carbamate 8 with Dimethyl Malonate (Compound 17). A solution of (−)-(*S*)-4-phenyl-3-vinyl-2-oxazolidinone (154 mg, 0.814 mmol) in 20 mL of THF was stirred as $PdCl_2(PhCN)_2$ (312 mg, 0.813 mmol) was added, turning the solution's color to a deep burgundy-orange. After stirring 10 min at room temperature, the solution was cooled to −78 °C. Triethylamine (227 μL, 1.63 mmol) was added dropwise over 3 min, and then the mixture was stirred at −78 °C for 15 min. A THF solution (5 mL) containing 0.8 mmol of sodium dimethyl malonate (prepared from sodium hydride) was added dropwise over 3 min. The mixture was stirred 50 min at −78 °C. Precooled methanol (15 mL) was added, and a carbon monoxide atmosphere was placed over the mixture. The temperature was allowed to slowly rise to room temperature over 15 h. Filtration of the black slurry through Celite, concentration by rotary evaporation, and purification by radial chromatography (2 mm silica gel plate, eluting with a 10% diethyl ether in hexane to diethyl ether gradient, followed by a second run with a 1 mm plate and 25% ethyl acetate in hexane, R_f 0.33 in 2:1 hexane/ethyl acetate) gave 249 mg (82%) of the product as a single diastereomer: ^{1}H NMR (200 MHz) δ 2.81 (d, J = 6.4 Hz, 2 H, $CH_3O_2CCH_2$), 3.47 (s,

3 H, $CH_3O_2CCH_2$), 3.67, 3.77 (2s, 6 H, $(CH_3O_2C)_2CH$), 4.13 (d, J = 9.2 Hz, 1 H, $(CH_3O_2C)_2CH$), 4.20 (dd, J = 6.4, 8.8 Hz, 1 H, CH_2O syn to Ph), 4.27 (dt, J = 9.2, 6.3 Hz, 1 H, $CHCH(CO_2CH_3)_2$), 4.58 (t, J = 8.8 Hz, 1 H, CH_2O anti to Ph), 4.93 (dd, J = 8.8, 6.3 Hz, 1 H, PhCH), 7.41 (s, 5 H, Ph); ^{13}C NMR (67.9 MHz) δ 35.9 ($CH_2CO_2CH_3$), 50.0, 51.5, 52.5, 52.6, 53.1 ($3CH_3O$, $CHCH_2CO_2CH_3$, PhCHN), 61.3 ($CH(CO_2CH_3)_2$), 70.1 (PhCHO), 127.5, 129.0, 137.9 (Ph), 156.9 (NCO), 167.2, 167.5 ($(CH_3O_2C)_2CH$), 170.2 ($CH_3O_2CCH_2$); IR (film) ν 1754 (CO) cm^{-1}; mass spectrum m/e CI (NH_3) 380 (M + 1^+). Anal. Calcd for $C_{18}H_{21}NO_8$: C, 56.99; H, 5.58; N, 3.69. Found: C, 56.83; H, 5.48; N, 3.80.

Carboacylation of Ene Carbamate (±)-9 with Benzyl Acetoacetate (Compound (±)-19). This material was prepared as described for the chiral material below using (±)-*syn*-4,5-diphenyl-3-vinyl-2-oxazolidinone (±)-**9** (150 mg, 0.57 mmol), $PdCl_2(PhCN)_2$ (108 mg, 0.28 mmol), triethylamine (79 μL, 0.57 mmol), sodium benzylacetoacetate (0.42 mmol), and methanol (7 mL) to give 84.9 mg (59%) of product. Spectroscopic data were identical with that of the optically active material.

Carboacylation of (−)-(*S*)(*R*)-Ene Carbamate 9 with Benzyl Acetoacetate (Compound 19). A solution of (*S*,*R*)-4,5-diphenyl-3-vinyl-2-oxazolidinone (264 mg, 0.995 mmol) in 15 mL of THF was stirred as $PdCl_2(PhCN)_2$ (258 mg, 0.673 mmol) was added, turning the solution to a deep burgundy color. After stirring 15 min at room temperature, the solution was cooled to −78 °C. Triethylamine (185 μL, 1.3 mmol) was added dropwise, and then the mixture was stirred for 15 min. A THF solution (2 mL) of sodium benzyl acetoacetate (1.3 mmol, prepared from sodium hydride) was added dropwise over 20 min. The mixture was stirred for 5 h at −78 °C. Precooled methanol (7 mL) was added, and a carbon monoxide atmosphere was placed over the mixture. The temperature was allowed to slowly rise to room temperature over 15 h and then warmed to 40 °C for 1 h. The black slurry was filtered through Celite to remove the palladium metal, and the filtrate was concentrated. Purification by radial chromatography (2 mm silica gel plate, eluting with a 9:1 hexane/diethyl ether to diethyl ether gradient, R_f 0.31 with 2:1 hexane/ethyl acetate) gave 238 mg (69%) of product as a 56:44 mixture of diastereomers and 127 mg of recovered vinyl oxazolidinone: ^1H NMR (270 MHz) δ major isomer 2.26 (s, 3 H, CH_3CO), 2.60 (dd, J = 15.7, 5.5 Hz, 1 H, $CH_2CO_2CH_3$), 2.69 (dd, J = 15.7, 5.9 Hz, 1 H, $CH_2CO_2CH_3$), 3.47 (s, 3 H, CH_3O_2C), 4.26 (ddd, J = 9.8, 5.7, 5.5 Hz, 1 H, $CHCH_2$), 4.76 (d, J = 9.7 Hz, 1 H, $CHCO_2Bn$), 4.87 (d, J = 8.2 Hz, 1 H, PhCHN), 5.0–5.3 (m, 3 H, CH_2Ph, PhCHO), 6.8–7.5 (m, 15 H, Ph); minor isomer 2.26 (s, 3 H, CH_3CO), 2.58 (dd, J = 15.8, 4.8 Hz, 1 H, $CH_2CO_2CH_3$), 2.86 (dd, J = 15.9, 7.0 Hz, 1 H, $CH_2CO_2CH_3$), 3.37 (s, 3 H, CH_3O_2C), 4.48 (ddd, J = 10.2, 6.9, 4.7 Hz, 1 H, $CHCH_2$), 4.70 (d, J = 10.2 Hz, 1 H, $CHCO_2Bn$), 5.0–5.3 (m, 3 H, CH_2Ph, PhCHN), 5.76 (d, J = 8.2 Hz, 1 H, PhCHO), 6.8–7.5 (m, 15 H, Ph); ^{13}C NMR (75.5 MHz) δ 30.2, 30.9 (CH_3CO), 36.0, 36.4 ($CH_2CO_2CH_3$), 50.0, 50.9, 50.9, 51.8 (CH_3O, $CHCH_2$), 60.7, 60.9 ($CHCO$), 67.1, 67.3, 67.7, 67.9 (CH_2Ph, PhCHN), 80.0, 80.6 (PhCHO), 125.7, 125.8, 127.6, 127.7, 127.8, 128.2, 128.3, 128.4, 128.5, 128.7, 128.8, 134.2, 134.3, 134.8, 134.9, 135.1, 135.2 (Ph), 157.1, 157.2 (NCO), 167.4 (BnO_2C), 170.4, 170.8 (CH_3O_2C), 200.7, 201.4 (CH_3CO); IR (film) ν 1754 (CO), 1718 (sh, CO) cm^{-1}; mass spectrum m/e CI (NH_3) 324 (M + 1 − $CH_3COCH_2CO_2Bn^+$). Anal. Calcd for $C_{30}H_{29}NO_7$: C, 69.89; H, 5.67; N, 2.72. Found: C, 70.00, H, 5.87; N, 2.72.

Reduction of (±)-19. A solution of (±)-**19** (265 mg, 0.51 mmol) in 6 mL of methanol was cooled in an ice bath. Sodium borohydride (20.2 mg, 0.53 mmol) was added, and the mixture was stirred at 0 °C for 4.5 h. Twelve drops of 5% aqueous HCl were required to bring the solution to pH 4–5. The solvent was removed by rotary evaporation, dissolved in CH_2Cl_2, and washed with distilled water. The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Radial chromatography (1 mm silica gel plate, 1:1 hexane/diethyl ether) gave 232 mg (89%) of product as a mixture of four diastereomers in the ratio 65:16:10:8.

Reduction of Optically Active 19. This material was reduced as above for the racemic material by using chiral compound **19** (118 mg, 0.23 mmol) and sodium borohydride (9.2 mg, 0.24 mmol) giving 104 mg (88%) of product as a mixture of diastereomers. Spectroscopic data were identical with those of the racemic material: ^1H NMR (200 MHz) δ major isomer 1.24 (d, J = 6.5 Hz, 3 H, CH_3CH), 2.77 (dd, J = 16.9, 4.9 Hz, 1 H, $CH_2CO_2CH_3$), 2.95 (dd, J = 16.9, 6.4 Hz, 1 H, $CH_2CO_2CH_3$), 3.39 (dd, J = 10.3, 2.9 Hz, 1 H, $CHCO_2Bn$), 3.44 (s, 3 H, CH_3O), 3.92 (br s, 1 H, OH), 4.03 (ddd, J = 10.5, 5.5, 4.7 Hz, 1 H, $CHCH_2$), 4.72 (d, J = 8.2 Hz, 1 H, PhCHN), 5.03 (d, J = 8.2 Hz, 1 H, PhCHO), 5.19 (d, J = 12.0 Hz, 1 H, CH_2Ph), 5.36 (d, J = 12.0 Hz, 1 H, CH_2Ph), 6.88 (m, 4 H, Ph), 7.04 (m, 6 H, Ph), 7.40 (m, 5 H, Ph); ^{13}C NMR (75.5 MHz, major peak in italics) δ 17.5, 21.1, 21.2, *21.7* (CH_3CH), 32.6, 35.0, *36.4*, 36.5 (CH_2CH), 47.3, 48.2, 50.1, 51.0, 51.3, *51.7*, *51.9* (CH_3O, $CHCH_2$), 53.6, *54.0*, 55.0 (CHOH), 65.3, 65.5, *65.8*, 65.9, 66.1, 66.5, *66.9*, 67.1, 67.4, *67.7* ($CHCO_2Bn$, CH_2Ph, PhCHN), 79.1, *79.5*, 79.8, 80.1 (PhCHO), 125.6, 125.8, 127.5, 127.7, 127.8, 127.9, 127.9, 128.0, 128.2, 128.3, 128.4, 128.4, 128.5, 128.6, 128.7, 128.7, 128.9, 129.1, 134.2, 134.4, 134.6, 134.9, 135.0, 135.6 (Ph), *156.9*, 157.9 (NCO), 170.6, *172.0*, *172.7* (CO_2Bn, CO_2CH_3); IR (film) ν 3458 (OH), 1748 (CO) cm^{-1}; mass spectrum m/e CI (NH_3) 502 (M − CH_3^+). Anal. Calcd for $C_{30}H_{31}NO_7$: C, 69.62; H, 6.04; N, 2.71. Found: C, 69.49; H, 6.13; N, 2.70.

Silylation of Racemic Alcohol To Give Compound (±)-20. The racemic alcohol from above (91 mg, 0.18 mmol) was dissolved in 10 mL of CH_2Cl_2 followed by addition of 2,6-lutidine (41 μL, 0.35 mmol) and *tert*-butyldimethylsilyl triflate (61 μL, 0.27 mmol). The mixture was stirred at room temperature for 90 min and then concentrated by rotary evaporation. Radial chromatography (1 mm silica gel plate, eluting with a 9:1 hexane/diethyl ether to diethyl ether gradient) gave 81 mg (73%) of product as a mixture of diastereomers in the ratio 54:20:16:10.

Silylation of Optically Active Alcohol To Give Compound 20. This material was prepared as described above for the racemic material by using chiral alcohol from above (104 mg, 0.20 mmol), 2,6-lutidine (47 μL, 0.40 mmol), and *tert*-butyldimethylsilyl triflate (69 μL, 0.30 mmol) to give 101 mg (79%) of product as a mixture of diastereomers. Spectroscopic data were identical with those of the racemic material: ^1H NMR (300 MHz) δ −0.11, 0.05, 0.07, 0.08, 0.14 (5s, 6 H, $(CH_3)_2Si$), 0.69, 0.89, 0.90, 0.91 (4s, 9 H, $(CH_3)_3C$), 0.97, 1.02, 1.20, 1.25, 1.26 (5d, J = 6.2, 6.5, 6.1, 6.4, 5.9 Hz, 3 H, CH_3CH), 2.72 (dd, J = 3.4, 15.8 Hz, CH_2CH), 2.83 (m, CH_2CH), 2.83 (dd, J = 3.4, 16.3 Hz, CH_2CH), 3.08 (dd, J = 8.0, 16.3 Hz, CH_2CH), 3.37, 3.64, 3.69 (3s, 3 H, CH_3O), 3.47 (dd, J = 3.2, 10.3 Hz, 1 H, $CHCO_2Bn$), 4.18 (m, 2 H, $CHOSi$, $CHCH_2$), 4.89 (d, J = 12.1 Hz, CH_2Ph), 4.96 (d, J = 8.2 Hz, 1 H, PhCHN), 4.98 (d, J = 12.1Hz, CH_2Ph), 5.10 (d, J = 12.1 Hz, CH_2Ph), 5.17 (d, J = 12.1 Hz, CH_2Ph), 5.19 (d, J = 8.2 Hz, PhCHO), 5.20 (d, J = 8.2 Hz, PhCHO), 5.26 (m, CH_2Ph), 5.71 (d, J = 7.7 Hz, PhCHO), 5.73 (d, J = 7.8 Hz, PhCHO), 6.93 (m, 4 H, Ph), 7.08 (m, 6 H, Ph), 7.40 (m, 5 H, Ph); ^{13}C NMR (75.5 MHz) δ −5.4, −5.3, −5.1, −4.2, −4.0 ($(CH_3)_2Si$), 17.5, 17.9 ($(CH_3)_3C$), 21.3, 21.7, 22.2, 22.6 (CH_3CH), 25.5, 25.7, 25.7 ($(CH_3)_3C$), 31.5, 32.6, 34.1, 35.7 (CH_2CH), 50.3, 51.3, 51.4, 51.6, 51.7, 51.8 (CH_3O, $CHCH_2$), 54.2, 54.5, 54.9 ($CHCH_3$), 64.3, 64.7, 66.5, 66.9, 67.0, 67.1 (PhCHN, CH_2Ph, $CHCO_2Bn$), 79.8, 79.8 (PhCHO), 125.7, 125.9, 126.1, 127.4, 127.6, 127.7, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 128.8, 134.0, 134.3, 134.5, 134.6, 134.7, 135.3, 135.5, 135.9 (Ph), 157.0, 157.5, 157.9 (NCO), 170.5, 171.0, 171.1, 171.3, 171.5, 171.6 (CO_2Bn, CO_2CH_3); IR (film) ν 1757 (CO) cm^{-1}; mass spectrum m/e CI (NH_3) 632 (M + 1^+). Anal. Calcd for $C_{36}H_{45}NO_3Si$: C, 68.43; H, 7.18; N, 2.22. Found: C, 68.20; H, 7.24; N, 2.19.

Hydrogenolysis of Racemic Compound (±)-20 To Give Compound 21. Starting material (63.4 mg, 0.10 mmol) was dissolved in 5 mL of methanol. Palladium (5%) on carbon (34 mg, 0.016 mmol) was added, and the mixture was placed under a hydrogen gas atmosphere. After stirring 16 h at room temperature, the mixture was filtered through Celite and concentrated by rotary evaporation, giving 52.7 mg of crude product containing a quantitative yield of desired product as a mixture of diastereomers in the ratio 60:24:17 and bibenzyl. This mixture was used in the subsequent step without purification. Spectroscopic data were identical with those previously reported.[16]

Hydrogenolysis of Optically Active Compound 20 To Give Compound 21. This material was prepared as described above for the racemic material by using chiral compound **20** (192 mg, 0.30 mmol), 5% palladium on carbon (109 mg, 0.051 mmol), and hydrogen to give 153.6 mg of crude material containing a quantitative yield of compound **21** and bibenzyl which was carried on without purification. Spectroscopic data were identical with those previously reported for the racemic material.[16]

Ring Closure of Racemic Amino Acid (±)-21 To Give β-Lactam (±)-22. The ring closure was performed as described in a previous paper by using amino acid (±)-**21** (32 mg, 0.10 mmol) and dicyclohexylcarbodiimide (40 mg, 0.19 mmol) to give, upon chromatography, 15.9 mg (53%) of the desired isomer of compound (±)-**22**. Spectroscopic data were identical with those previously reported.[16]

Ring Closure of Optically Active Amino Acid 21 To Give (+)-22. This material was prepared as described previously using optically active amino acid **22** (96 mg, 0.30 mmol) and dicyclohexylcarbodiimide (125 mg, 0.61 mmol) to give, after chromatography, 32.1 mg (36%) of the desired isomer of (+)-(*SSR*)-**22**. Spectroscopic data were identical with those previously reported[16] and to authentic material prepared below: $[\alpha]_D$ +43.7° (*c* 1.57, $CHCl_3$).

(+)-(*SSR*)-22 (from Authentic Hydroxyethylazetidinone). (−)-(*SSR*)-3-(1-Hydroxyethyl)-4-(carbomethoxymethyl)-2-azetidinone (204 mg, 1.09 mmol) was dissolved in 2 mL of dimethylformamide. Imidazole (147 mg, 2.16 mmol) and *tert*-butyldimethylsilyl chloride (164 mg, 1.09 mmol) were added, and the mixture was stirred for 27 h at room temperature. Diethyl ether (25 mL) was added, and the solution was washed with distilled water (20 mL). The organic portion was dried ($MgSO_4$)

and concentrated by rotary evaporation. Radial chromatography (1 mm silica gel plate, eluting with a 3:1 hexane/ethyl acetate to ethyl acetate gradient), gave 205 mg (63%) of product: $[\alpha]_D$ +45.0° (*c* 1.43, $CHCl_3$).

Determination of Enantiomeric Purities Using a Chiral NMR Shift Reagent. Racemic β-lactam (±)-**22** (10.8 mg, 0.0358 mmol) and Eu(hfc)$_3$ (12.7 mg, 0.0106 mmol) were dissolved in 0.7 mL of $CDCl_3$/TMS. Baseline resolution was obtained for the *tert*-butyl (δ 1.34, 1.45 ppm) and methyl ester (δ 3.75, 3.77 ppm) peaks in a 300-MHz ^{1}H NMR spectrum.

(+)-(*SSR*)-**22** (23.4 mg, 0.0776 mmol) and Eu(hfc)$_3$ (25.7 mg, 0.0215 mmol) were dissolved in 0.7 mL of $CDCl_3$/TMS. Exclusively one peak was observed each for the *tert*-butyl (δ 1.26 ppm) and methyl ester (δ 3.73 ppm) peaks in the 300-MHz ^{1}H NMR spectrum.

Authentic (+)-(*SSR*)-**22** (18.3 mg, 0.0607 mmol) and Eu(hfc)$_3$ (20.9 mg, 0.0175 mmol) were dissolved in 0.7 mL of $CDCl_3$/TMS. Exclusively one peak was observed each for the *tert*-butyl (δ 1.40 ppm) and methyl ester (δ 3.75 ppm) in the 300-MHz ^{1}H NMR spectrum.

Acknowledgment. Support for this research by National Science Foundation Grant CHE-870152 is gratefully acknowledged. G.W. thanks Dow Corning Corporation for support in the form of a scholarship. The authors thank Yamakawa Chemical Ind. Co. Ltd. for the kind gift of (+)- and (−)-2-amino-1,2-diphenylethanol. Professor William Scott is acknowledged for helpful discussions.

Synthesis of Medium-Sized Ring Ethers from Thionolactones. Applications to Polyether Synthesis†

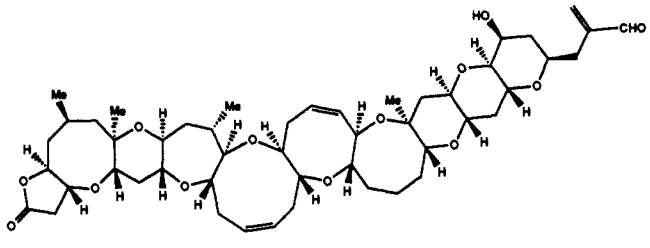
K. C. Nicolaou,* D. G. McGarry, P. K. Somers, B. H. Kim, W. W. Ogilvie, G. Yiannikouros, C. V. C. Prasad, C. A. Veale, and R. R. Hark

Contribution from the Department of Chemistry, Research Institute of Scripps Clinic, 10666 North Torrey Pines Road, La Jolla, California 92037, and Department of Chemistry, University of California, San Diego, La Jolla, California 92093. *Received January 3, 1990. Revised Manuscript Received April 9, 1990*

Abstract: A variety of medium-sized thionolactones have been prepared and condensed with nucleophiles giving alkylated thioacetals upon quenching with methyl iodide. Reductive desulfurization using triphenyltin hydride under radical conditions afforded the corresponding cyclic ethers rapidly and efficiently and, in most cases, with complete stereocontrol. This methodology has been proven through the construction of model systems of rings B and D of brevetoxin A (**1**) and a synthesis of (±)-lauthisan (**44**).

Introduction

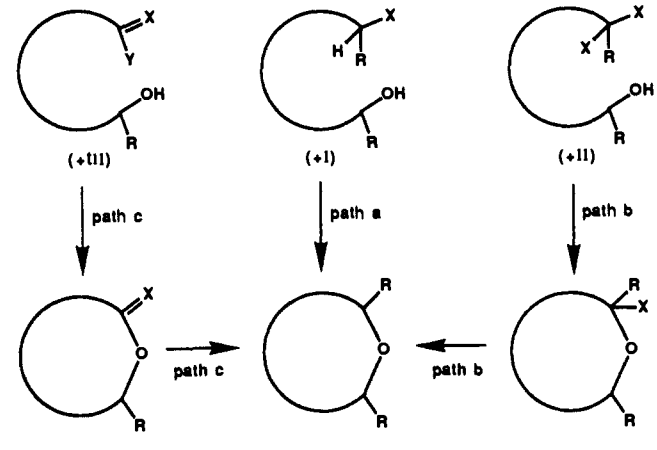
Medium-sized ring ethers occur widely in nature, particularly in marine natural products[1] such as brevetoxins A (**1**)[2a,b] and B,[2c]



1: Brevetoxin A

laurencin,[3] isolaurallene,[4] and ciguatoxin.[5] The construction of such systems is complicated by the difficulties in effecting ring closure due to unfavorable entropy factors[6] as well as nonbonding interactions inherent in the medium ring structures themselves.[7] A number of elegant approaches to these problems have recently been reported that utilize both carbon–carbon and carbon–oxygen bond-forming processes to effect cyclization.[8] In connection with the total synthesis of brevetoxins A (**1**) and B, currently in progress in these laboratories, we have sought general methods for the synthesis of seven-, eight-, and nine-membered ring ethers. Clearly, ring closure by carbon–oxygen bond formation provides the most flexible approach to these systems, allowing, in principle, the use of a variety of carbon-centered electrophilic groups at either the I, II, or III oxidation states (Scheme I). This would lead to either

Scheme I



the cyclic ether directly (path a) or, in the case of the aldehyde or carboxylic acid oxidation states, to cyclic intermediates, which

* Address correspondence to this author at the Research Institute of Scripps Clinic.

† This work was partially carried out at the University of Pennsylvania.

(1) Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 251.

(2) (a) Shimizu, Y.; Chou, H. N.; Bando, H.; Van Duyne, G.; Clardy, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 514. (b) Pawlak, M.; Tempesta, M. S.; Golik, J.; Zagorski, M. G.; Lee, M. S.; Nakanishi, K.; Iwashita, T.; Gross, M. L.; Tomer, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 1144. (c) Lin, Y.; Risk, M.; Ray, S. M.; Van Engen, D.; Clardy, J.; Golik, J.; James, J. C.; Nakanishi, K. *J. Am. Chem. Soc.* **1981**, *103*, 6773.

(3) Irie, T.; Suzuki, M.; Masamune, T. *Tetrahedron* **1968**, *24*, 4193.

(4) Kurata, K.; Furusaki, A.; Suehiro, K.; Katayama, C.; Suzuki, T. *Chem. Lett.* **1982**, 1031.

(5) Murata, M.; Legrand, A. M.; Ishibashi, Y.; Yasumoto, T. *J. Am. Chem. Soc.* **1989**, *111*, 8929.

(6) Winnik, M. L. *Chem. Rev.* **1981**, *81*, 491.

0002-7863/90/1512-6263$02.50/0