Synthesis of Optically Active β-Lactams by the Photolytic Reaction of Imines with Optically Active Chromium Carbene Complexes

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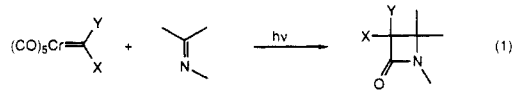
Abstract: Optically active chromium carbene complexes utilizing (*S*)-valine- and (*R*)-phenylglycine-derived chiral auxillaries were synthesized and subjected to photolytic reaction with a number of imines. Optically active β-lactams were produced in good to excellent chemical yield and with high diastereoisomeric excess. Procedures for removal of the chiral auxilliary to produce the optically active free amino β-lactams were developed.

Recent research in these laboratories has centered on the development of efficient approaches to β-lactams of biological interest utilizing the photolytic reaction between chromium carbene complexes and imines (eq 1) developed several years ago.[1] Initial



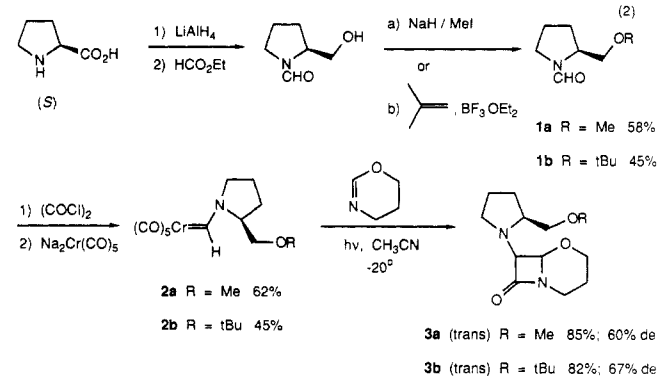
(1)

studies involved alkoxycarbene complexes (X = Me, Ph; Y = OMe), and although a large number of β-lactams were prepared by this method, they all lacked the substituents required for biological activity (X = H; Y = NHCOR).[2] Subsequently, an efficient synthesis of aminocarbenes (X = H; Y = NR_2) was developed,[3] and these complexes were successfully used in the synthesis of the desired classes of β-lactams.[4] However, most biologically active β-lactams are also optically active, and asymmetric induction in this new β-lactam synthesis is the problem addressed in this paper.

Previous studies[1a] using imines derived from optically active benzylamines as substrates resulted in only low to modest (15–60% de) asymmetric induction with the (methoxy)(methyl)carbene complex, and none at all with the (*N*,*N*-dibenzylamino)(methylene)chromium complex.[5] In contrast, when the rigid, chiral, cyclic optically active thiazoline (*S*)(+)-methyl-5,5-dimethyl-4*H*-1,3-thiazoline was used as the imine substrate, the process was virtually diastereospecific, with both alkoxy[1] and amino[4] carbene complexes. Since chiral centers on the imine substrate were not *generally* effective in inducing asymmetry in this process, other sites for the introduction of a chiral auxilliary were sought. The synthesis of optically active pentacarbonyl(aminocarbene)chromium complexes and their reactions with imines to produce optically active β-lactams are described below.

Results and Discussion

Readily available optically active α-amino acids are commonly used as sources of chiral auxilliaries in asymmetric synthesis.[6] Optically active formamides were required to produce the desired chromium aminocarbene complexes, and these were accessible by conventional methods. Initial studies used proline-derived formamides, and the results of these studies are summarized in eq 2.



Carbenes **2a** and **2b** were prepared in reasonable (unoptimized) yield by reaction of the chromium pentacarbonyl dianion with the appropriate Vilsmeier's salt of the proline-derived formamide.[4,7] Photolytic reaction of these carbenes with 5,6-dihydro-4*H*-1,3-oxazine gave the corresponding bicyclic β-lactams **3a** and **3b** in good chemical yield, as a single trans geometrical isomer. However, the diastereoselectivity of this process was not only unacceptably low, it was remarkably insensitive to the steric bulk of the chiral auxilliary. This, coupled with the fact that chemical transformation of the prolinol fragment to the requisite free amino group would be difficult, led to the search for a more effective chiral auxilliary.

The next system examined was that based on *N*-formyl acetonides of (*R*)-phenylglycinol and (*S*)-valinol. The requisite optically active carbene complexes **4a** and **4b** were readily prepared in high yield by a previously developed procedure[3] from the formamides, $Na_2Cr(CO)_5$, and trimethylsilyl chloride. The results of the reactions of these two carbene complexes with a variety of representative simple imines are summarized in eq 3 and 4 and Tables I and II. Several important features were noted. The chemical yields obtained with complex **4a** were uniformly better than those with **4b**, and with the exception of **5e**, imines that exist as cyclic trimers in solution (**5a**, **5d**, **5e**) did not convert to β-lactams with **4b**, while the reactions of **4a** with those substrates proceeded in good yield. The *geometry* (e.g., cis, trans) of the

(1) (a) Hegedus, L. S.; McGuire, M. A.; Schultze, L. M.; Yijun, C.; Anderson, O. P. *J. Am. Chem. Soc.* **1984**, *106*, 2680. (b) Hegedus, L. S.; Schultze, L. M.; Toro, J.; Yijun, C. *Tetrahedron* **1985**, *41*, 5833.

(2) Durkheimer, W.; Blumbach, J.; Lattrell, R.; Scheunemann, K. H. J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 180.

(3) Imwinkelreid, R.; Hegedus, L. S. *Organometallics* **1988**, *7*, 702.

(4) Borel, C.; Hegedus, L. S.; Krebs, J.; Satoh, Y. *J. Am. Chem. Soc.* **1987**, *109*, 1101.

(5) Hegedus, L. S.; D'Andrea, S. *J. Org. Chem.* **1988**, *53*, 3113.

(6) Copola, G. M.; Schuster, H. F. *Asymmetric Synthesis—Construction of Chiral Molecules using Amino Acids*; John Wiley & Sons: New York, 1987.

(7) These preliminary studies were carried out prior to development of the more efficient trimethylsilyl chloride route to amino carbene complexes reported in ref 3.

(8) Floyd, D. M.; Fritz, A. W.; Phisec, V.; Weaver, E. R.; Cimarusti, C. M. *J. Org. Chem.* **1982**, *47*, 5160. The value for the cis compound reported in this paper, +34°, was erroneous. We thank Dr. Floyd for providing the correct value and samples of authentic cis and trans compounds for direct comparison with those synthesized herein.

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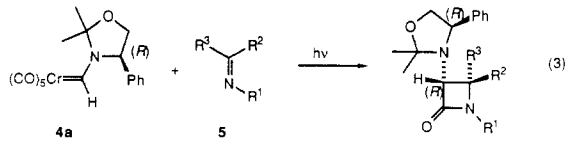
Table I. Reaction of Complex **4a** with Imines (Equation 3)

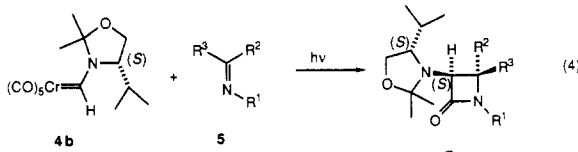


(3)

5	R^1	R^2	R^3	6	R^1	R^2	R^3	yield,[a] %	de,[b] %
a	Bn	H	H	a	Bn	H	H	74	70
b	Bn	Me	Me	b	Bn	Me	Me	79	70
c	Bn	Me, H		c	Bn	Me	H (trans)	41	≥97
				c′	Bn	H	Me(cis)	20	≥97
d	$-(CH_2)_3-$		H	d	$-(CH_2)_3-$		H	75	≥97
e	$-(CH_2)_4-$		H	e	$-(CH_2)_4-$		H	91	≥97
f	Bn	OMe	H	f	Bn	OMe	H	91	≥97
g	$-(CH_2)_3O$		H	g	$-(CH_2)_3O$		H	95	≥97

[a] Reported yields are those of isolated, purified material. [b] Diastereoisomeric excess (de) are those for crude reaction products, as assessed by high-field proton and carbon NMR spectroscopy and analytical HPLC.

Table II. Reaction of Complex **4b** with Imines (Equation 4)



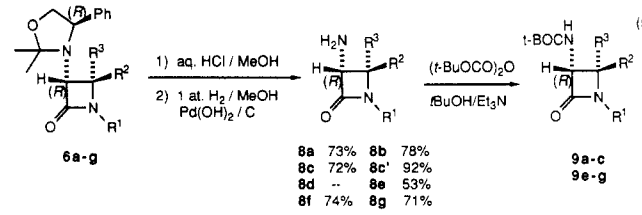
(4)

5	R^1	R^2	R^3	7	R^1	R^2	R^3	yield,[a] %	de,[b] %
a	Bn	H	H						
b	Bn	Me	Me	b	Bn	Me	Me	59	70
c	Bn	Me,H		c	Bn	Me	H (trans)	40	≥97
				c′	BN	H	Me(cis)	14	≥97
d	$-(CH_2)_3-$		H						
e	$-(CH_2)_4-$		H	e	$-(CH_2)_4-$		H	55	≥97
f	Bn	OMe	H	f	Bn	OMe	H	76	≥97
g	$-(CH_2)_3O$		H	g	$-(CH_2)_3O$		H	70	≥97

[a] Reported yields are those of isolated, purified material. [b] Diastereoisomeric excess (de) are those for crude reaction products, as assessed by high-field proton and carbon NMR spectroscopy and analytical HPLC.

β-lactams formed from both complexes strictly paralleled that observed with achiral carbenes,[4,5] with cyclic imines and imidates giving exclusively trans β-lactams, and the *N*-benzylimine of acetaldehyde giving a cis/trans mixture in which trans predominated. The *diastereoselectivity* observed with both complexes was comparable and excellent. The worst cases were those with symmetrically substituted imines **5a** and **5b** ($R^2 = R^3$ = H or Me) for which an easily separated 85:15 mixture of diastereoisomers was obtained. With **5c**, a mixture of cis and trans geometrical isomers was obtained, but each of these was a *single* diastereoisomer, indicating that stereocontrol at the position adjacent to the chiral auxilliary was virtually complete. With imines **5d–5g**, only a single diastereoisomer, as determined by high-field ^1H and ^{13}C NMR spectroscopy and analytical HPLC of the crude reaction mixtures, was obtained with both complexes **4a** and **4b**. Thus, with all unsymmetrically substituted imines studied, complexes **4a** and **4b** produced good to excellent chemical yields with very high diastereoselectivity. Further, the absolute configuration of the newly formed chiral center adjacent to the β-lactam carbonyl group was the same as that of the chiral auxilliary (*R* → *R*, *S* → *S*) (see proof below), while the absolute configuration of the β-carbon was set by the intrinsic cis/trans specificity of the β-lactam-forming process.

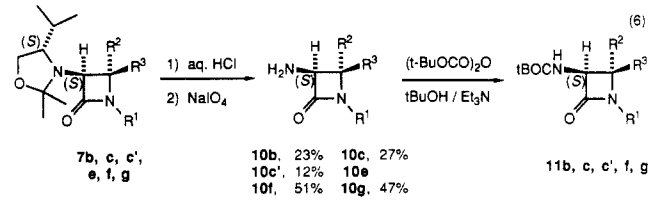
Removal of the chiral auxilliary from β-lactams **6** was efficiently accomplished by a two-step process involving hydrolysis of the acetonide and hydrogenolysis of the benzylamine (eq 5). In this



(5)

manner good yields of free amino β-lactams **8** were obtained. Since these were relatively unstable, they were immediately converted to their *t*-BOC derivatives for further characterization and storage. Only carbapenam **6d**, which decomposed during removal of the chiral auxilliary, was unavailable by this procedure. Since diastereoisomerically pure β-lactams **6a–g** were used, enantiomerically pure β-lactams **8a–c**, **e–g** and **9a–c**, **e–g** were obtained (see below).

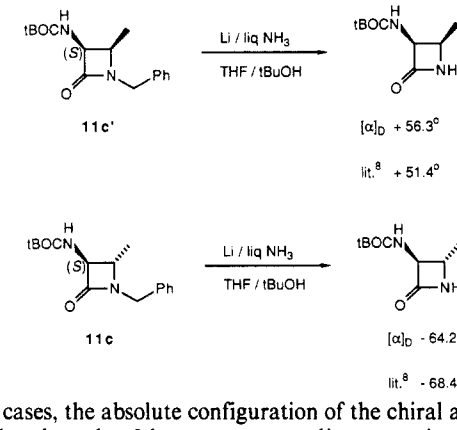
Cleavage of the isopropyl-derived chiral auxilliary involved hydrolysis followed by oxidative cleavage of the amino alcohol (eq 6). This cleavage was less efficient than the hydrogenolytic



(6)

cleavage (eq 5) in that the yields were lower and the cleavage products more difficult to purify. Thus, the phenylglycine-derived chiral carbene complex **4a** was the complex of choice for the synthesis of simple optically active β-lactams in high chemical and optical yield.

The absolute stereochemistry of the β-lactam-forming reaction (eq 3 and 4) was determined by the conversion of **11c** and **11c′** to compounds of known absolute configuration (eq 7 and 8). In

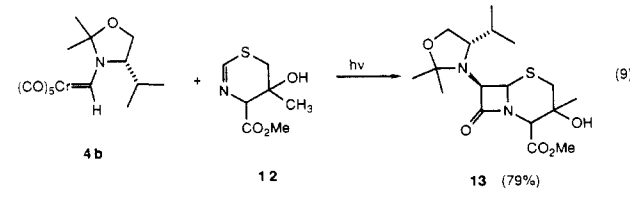


(7)

(8)

these cases, the absolute configuration of the chiral auxilliary was translated to the β-lactam center adjacent to it. Further, all compounds **9** had equal but opposite rotations to the corresponding compounds **11**, as expected from the enantiomeric relationship of the chiral auxilliaries used in their synthesis.

In a preliminary effort to extend this methodology to more complex systems, thiazine **12**[10] (racemic, single diastereoisomer) was allowed to react with complex **4b** to give cepham **13** in good yield (eq 9). High asymmetric induction was again observed as



(9)

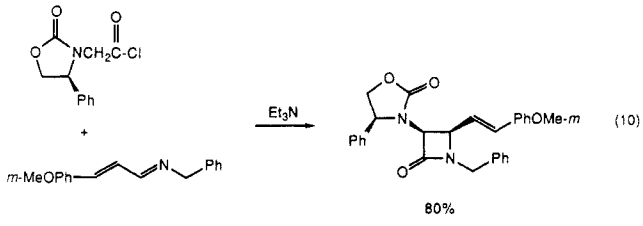
evidenced by **13** being a 1:1 mixture of only two diastereoisomers,

(9) Mattingly, P. G.; Miller, M. J. *J. Org. Chem.* **1980**, *45*, 410.

(10) Hashimoto, T.; Watanabe, T.; Kawano, Y.; Tanaka, T.; Miyadera, T. *Heterocycles* **1978**, *11*, 207.

due to the use of racemic **12**. (Had asymmetric induction been poor, additional diastereoisomers would have been formed.) Studies with more complex systems are continuing using chiral carbene **4a** and its enantiomer, because of the ease of removal of that chiral auxilliary.

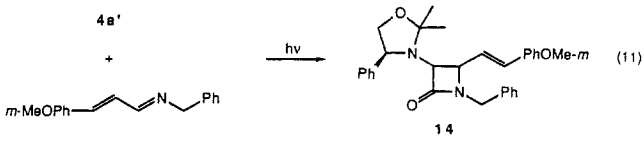
Recent mechanistic studies[11] of the photoreaction between imines and chromium carbene complexes have suggested that the reaction involves the photogeneration of metal-bound ketenes, which then react with imines to give β-lactams, analogous to the Staudinger reaction.[12] Recently, the reactions of optically active amidoketenes generated in situ from the corresponding α-amido acid chlorides and triethylamine, with imines[13-15] and with optically active imines,[16,17] have been used to produce optically active β-lactams, with excellent asymmetric induction in most cases. In contrast to the studies reported here, these studies have uniformly utilized imines of aryl or cinnamyl aldehydes as substrates, and in all but one case[15] very high cis selectivity was observed, along with good to excellent diastereoselectivity. The most efficient of these systems was based on an optically active oxazolidone,[14] which added to the *N*-benzyl aldimine of *m*-methoxycinnamaldehyde to give *only* the cis β-lactam, with a diastereoselectivity of 92:8 (eq 10). For comparison, this same aldimine was subjected to



(10)

80%

photolytic reaction with chromium carbene complex **4a'** (*S* enantiomer of **4a**) (eq 11). *This* process was remarkably *non*specific,



(11)

14

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

particularly in light of the selectivity observed above with nonconjugated imines. Although the cis β-lactam was the major product, it was formed *nonselectively*, while a single diastereoisomer of the minor trans compound was obtained.[18] If free ketenes are involved in both of these processes, and if the origins of asymmetric induction in ketene–imine reactions are indeed those recently advanced,[13] the small differences in structure between the putative ketenes in eq 10 and 11 have a profound effect on the stereoselectivity of the process. Alternatively, the chromium carbene derived ketene is likely to be metal-bound, not free, which may account for the large differences in stereoselectivity observed. Studies addressing the role of ketenes in these processes and directed toward increasing the selectivity of reactions with conjugated imines are 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 the 67-MHz ^{13}C NMR spectra were obtained on a Bruker IBM-270 NMR 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) unless otherwise specified. IR spectra were recorded on a Beckmann 4240 spectrophotometer. Electron impact (EI) and chemical ionization (CI) 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 the specified temperature and the concentration (*c*) given in grams per 100 mL in the specified solvent. Ultraviolet irradiation of the reaction mixtures was carried out in 20-mL Pyrex test tubes or 100-mL Pyrex pressure tubes placed at a distance of 10 cm from a Conrad-Hanovia 7825 medium-pressure mercury lamp operating at 450 W, which was placed in a water-cooled immersion well. A Conrad-Hanovia 7830-C power supply was used.

For the purification of crude reaction mixtures, radial-layer (Chromatotron Model 7924) and column chromatographic techniques were applied in most cases. Merck silica gel 60 PF (for radial-layer chromatography) and Merck silica gel (230–400 mesh) or Alfa activated, neutral aluminum oxide (for column chromatography) were used as stationary phases.

High-performance liquid chromatograms were obtained on a Waters RCM-100 radial compression column [Waters Radial Pak liquid chromatography cartridge, silica gel (8-mm i.d.)] equipped with Model 6000A solvent delivery system and Model R-400 refractive index detector.

Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ.

Materials. Tetrahydrofuran (Fisher, reagent grade) and diethyl ether (ASP, analytical reagent) were predried over CaH_2 and distilled from benzophenone ketyl under a nitrogen atmosphere just prior to use. Hexane (technical grade) was distilled at atmospheric pressure. Ethyl acetate (technical grade) was distilled over CaH_2. Methylene chloride was distilled over CaH_2 or filtered through aluminum oxide (Baker Analyzed, 5 g/100 mL). Acetonitrile (Fisher) was distilled over CaH_2 and stored over 4-Å molecular sieves. Methanol (Fisher) was dried over Mg and distilled.

Chromium hexacarbonyl (Pressure Chemical), (*S*)-proline (Sigma), (*S*)-2,3-diaminopropionic acid (Calbiochem), (*R*)- and (*S*)-phenylglycine (Aldrich), and (*S*)-valine (Aldrich) were obtained from commercial suppliers and used without further purification. (2*S*)-*N*-formyl-2-(methoxymethyl)pyrrolidine (**1a**)[19] and (5*S*)- and (5*R*)-*N*-formyl-2,2-dimethyl-5-phenyl-1,3-oxazolidine[3] were prepared by literature procedures.

(2*S*)-*N*-Formyl-2-(*tert*-butoxymethyl)pyrrolidine (1b). *N*-Formylprolinol[19] (3.38 g, 26.0 mmol) was taken in a 300-mL glass pressure vessel equipped with a magnetic stirring bar and a rubber stopper and dissolved in 50 mL of dry *p*-dioxane. To this was added a few drops of concentrated H_2SO_4 and ca. 20 mL of isobutene; the top of the flask was then secured by a rubber stopper and copper wires. Boron trifluoride etherate (9.7 mL, 79 mmol) was forcibly introduced via a syringe by inserting the needle through the gap between the rim of the bottle and the rubber stopper. The plunger should be held tightly since the internal pressure of the vessel can be very high. The reaction was allowed to proceed for 3 h at room temperature. After the internal pressure of the bottle had been released by forcing a syringe needle through the same gap, contents of the flask was poured into 50 mL of water. The organic phase was separated, and the aqueous layer was extracted three times with ether. The organic layer was washed with aqueous $NaHCO_3$ and then with saturated aqueous NaCl and dried over magnesium sulfate. Removal of the solvent and subsequent distillation of the remaining liquid gave 2.20 g (45%) of pure *tert*-butyl ether **1b** as a colorless oil: bp 140 °C (1 mmHg) (bath temperature); ^{1}H NMR (60 MHz) δ 1.15 (s, 9, O-*t*-Bu), 1.6–2.5 (m, 4), 3.1–3.8 (m, 5), 8.15 (s, C*H*O, the minor rotamer), 8.26 (s, C*H*O, the major rotamer). This material was used without further purification.

Pentacarbonyl[(2*S*)-2-(methoxymethyl)pyrrolidyl]carbene]chromium (2a). The formamide **1a** (0.54 g, 3.50 mmol) was dissolved in 40 mL of dry THF and treated with 0.98 g (7.70 mmol) of oxalyl chloride. Instantaneous evolution of a gas was observed. After 2 h, the resultant mixture was evaporated first at water aspirator pressure through a calcium chloride tube (to protect from moisture) and then under an oil pump vacuum. This was redissolved in 30 mL of THF and cooled to −78 °C. Disodium pentacarbonylchromium (48 mL, 0.093 mL in THF, 4.60 mmol) was then introduced by means of a cannula. The cooling bath was removed and the mixture was stirred at room temperature for 2 h. Silica gel (3 g) was added and the mixture was evaporated to dryness. The

(11) Hegedus, L. S.; deWeck, G.; D'Andrea, S. *J. Am. Chem. Soc.* **1988**, *110*, 2122.
(12) For a review of ketene–imine cycloadditions to produce β-lactams, see: Holden, K. G. Total Synthesis of Penicillans, Cephalosporins, and Their Nuclear Analogs. In *Chemistry and Biology of β-Lactam Antibiotics*; Morin, R. B., Gorman, M., Eds.; Academic: New York, 1982; Vol. 2, pp 114–131.
(13) Cooper, R. D. G.; Daugherty, B. W.; Boyd, D. B. *Pure Appl. Chem.* **1987**, *59*, 485.
(14) Evans, D. A.; Sjogren, E. B. *Tetrahedron Lett.* **1985**, *26*, 3783, 3787.
(15) Ikota, N.; Hanaki, A. *Heterocycles* **1984**, *22*, 2227.
(16) Evans, D. A.; Williams, J. M. *Tetrahedron Lett.* **1988**, *29*, 5065.
(17) Ojima, I.; Chen, H.-C.; Qiu, X. *Tetrahedron* **1988**, *44*, 5307.
(18) The minor trans isomer in the studies described in ref 15 was also obtained as a single diastereoisomer, while the major cis isomer was formed with 70–90% de.
(19) Enders, E.; Fey, P.; Kipphardt, H. *Org. Synth.* **1987**, *65*, 173.

silica-impregnated sample thus obtained was purified by column chromatography (silica gel, hexane/methylene chloride) to give 0.60 g of a yellow oil, which solidified upon storage in a freezer: mp 40–41 °C (open capillary); ^{1}H NMR (270 MHz, $CDCl_3$, Me_4Si) δ 1.9–2.3 (m, 4), 3.2–3.5 (m, 2), 3.35 (s, 3, OCH_3), 3.81 (m, 1, NC*H*), 4.08 (m, 2, NCH_2), 11.54 (s, 1, carbene proton); IR ($CHCl_3$) ν 2055, 1975, 1925 cm^{-1}. Anal. Calcd for $C_{12}H_{13}CrNO_6$: C, 45.15; H, 4.10; N, 4.39. Found: C, 45.30; H, 4.26; N, 4.22.

Pentacarbonyl [[(2*S*)-2-(*tert*-Butoxymethyl)pyrrolidyl]carbene]chromium (2b). In a manner similar to that used for **2a**, the title compound was obtained in 45% yield: mp 52–53 °C; ^{1}H NMR (270 MHz) δ 1.16 (s, 9, O-*t*-Bu), 1.9–2.4 (m, 4), 3.3–3.5 (m, 2), 3.78 (m, 1, NC*H*), 4.06 (m, 2), 11.00 (s, 1, carbene proton); IR ($CHCl_3$) ν 2060, 1980, 1930 cm^{-1}. Anal. Calcd for $C_{15}H_{19}CrNO_6$: C, 49.86; H, 5.30; N, 3.88. Found: C, 49.99; H, 5.25; N, 3.93.

7-[2′-(*tert*-Butoxymethyl)pyrrolidyl]oxacepham (3b). The carbene complex **1b** (87 mg, 0.22 mmol) was placed in a Pyrex test tube and dissolved in 10 mL of dry acetonitrile. This was degassed by evacuation–refilling cycles (three times). After the atmosphere was secured under argon, 18 mg (0.22 mmol) of the 1,3-oxazine[20] was added and the reaction mixture was placed in a constant-temperature bath kept at −20 °C and irradiated for 16 h. Acetonitrile was removed under reduced pressure, and the residue was dissolved in a hexane/ether mixture. The mixture was irradiated with direct sunlight while exposed to air in order to remove chromium-containing organic materials. After the supernatant became colorless, the solids were removed by filtration, and the filtrate was concentrated. A crude ^{1}H NMR spectrum showed that two diastereoisomeric β-lactams were formed in a ratio of 83:17 (67% de). This was purified by column chromatography (silica gel, hexane/ether) to give a colorless oil (50 mg, 82%). Separation of these two diastereomers was unsuccessful. ^{1}H NMR (270 MHz) δ 1.14 (s, 9, O-*t*-Bu), 1.4, 1.7, 1.8, 2.6, 3.0, 3.1, 3.3, 3.6, 3.9, 4.1 (m, 14), 4.87 (s, NC*H*O, minor isomer), 4.99 (s, NC*H*O, major isomer); IR 1755 cm^{-1}. Anal. Calcd for $C_{15}H_{26}N_2O_3$: C, 63.80; H, 9.28; N, 9.20. Found: C, 63.67; H, 9.36; N, 9.18.

Pentacarbonyl[(5*R*)-2,2-Dimethyl-5-phenyl-1,3-azoxacyclopentyl)-methylene]chromium (4a). This complex was prepared by the previously reported[3] procedure on a 20-mmol scale in 80–90% yield, using 1.2 equiv of $Na_2Cr(CO)_5$ rather than the reported 2 equiv of this reagent.

General Procedure for the Preparation of β-Azetidinones 6b, 6c, 6c′, 6f, and 6g. The chromium carbene complex (1.00 mmol) and the corresponding imine or imidate (1.05 mmol) were added to a CO-saturated solution of Et_2O (~22 mL) in a 25-mL pressure tube equipped with a Matheson/Whitey Brand 100 psi pressure head and a pressure release valve. The solution was pressurized with CO to ~90 psi and then the pressure was released, three times. Finally, the solution was pressurized to 60 psi CO and carefully transported, using a protective shield, to an irradiation box and exposed to a 450-W UV lamp for 24 h. The reaction mixture turned from bright yellow to pale yellow with a white solid at the bottom of the tube. The progress of the reaction was monitored by use of analytical TLC (silica gel). After complete consumption of the carbene, the solvent was evaporated. This mixture was taken up in ~20 mL of MeOH and placed in the freezer overnight. The following day, the solvent and crude product were removed by decanting or pipeting and then rinsing (MeOH) them away from the $Cr(CO)_6$. Normal recovery of the $Cr(CO)_6$ ranged from 0.58 to 0.62 mmol (127–136 mg = 58–62%). The solvent was removed from the crude product to leave a yellow to green to brown oil (0.95–1.00 mmol = 95–100% crude yield). This change in color was attributed to the oxidation of residual chromium species. The crude product was purified by chromatography [silica gel, hexane/EtOAc (4:1)] to yield 60–90% of the pure β-azetidinone product (a clear, colorless oil).

Synthesis of 1-Benzyl-4,4-dimethyl-β-azetidinone (6b). The reaction of carbene complex **4a** (381 mg, 1.00 mmol) and the *N*-benzyl acetone imine **5b** (155 mg, 1.05 mmol) in 22 mL of diethyl ether at 60 psi CO gave 310 mg (85%) of a green oil after 24 h of irradiation. Analysis of the crude product by ^{1}H and ^{13}C NMR spectroscopy and analytical HPLC revealed an 85:15 mixture of diastereoisomers. The crude product was purified by preparative layer chromatography (silica gel) eluting with hexane/EtOAc (1:1) to yield 248 mg (0.68 mmol = 68%) of the major diastereoisomer (a white solid) and 40 mg (0.11 mmol = 11%) of the minor diastereoisomer (a colorless oil) for a total yield of 288 mg (0.79 mmol = 79%). Major diastereoisomer **6b**: ^{1}H NMR (270 MHz) δ 0.59 (s, 3, CH_3), 1.17 (s, 3, CH_3), 1.37 (s, 3, CH_3), 1.39 (s, 3, CH_3), 3.81 (s, 1, C*H*C=O), 3.81 (d, J = 15.5 Hz, 1, C*H*Ph), 3.85 (m, 1, OCH_2CHN), 4.34 (m, 1, OCH_2CHN), 4.40 (d, J = 15.5 Hz, 1, C*H*Ph), 4.89 (dd, J = 4.7, 8.2 Hz, 1, OCH_2CHN), 6.82 (m, 2, ArH), 7.14 (m, 3, ArH), 7.28 (m, 3, ArH), 7.46 (m, 2, ArH); ^{13}C NMR (67 MHz, $CDCl_3$) δ 21.0, 21.8, 24.5, 28.3, 42.5, 61.4, 62.4, 72.6, 73.0, 95.9, 126.9, 127.1, 127.9, 128.0, 128.3, 128.7, 136.8, 144.4, 165.5; IR (neat) ν 1744 (s, C=O) cm^{-1}. Minor diastereoisomer: ^{1}H NMR (270 MHz) δ 0.63 (s, 3, CH_3), 0.68 (s, 3, CH_3), 1.59 (s, 3, CH_3), 1.68 (s, 3, CH_3), 3.77 (s, 1, C*H*C=O), 3.84 (dd, J = 5.8, 8.1 Hz, 1, OCH_2CHN), 3.98 (t, J = 6.9 Hz, 1, OCH_2CHN), 4.07 (d, J = 15.3 Hz, 1, C*H*Ph), 4.27 (d, J = 15.3 Hz, 1, C*H*Ph), 4.32 (t, J = 8.1 Hz, 1, OCH_2CHN), 7.16–7.38 (m, 10, ArH); ^{13}C NMR (67 MHz, $CDCl_3$) δ 21.2, 22.1, 23.9, 27.9, 42.5, 62.6, 68.8, 71.8, 75.8, 96.7, 127.4, 127.5, 127.8, 128.0, 128.1, 128.2, 128.4, 128.5, 128.8, 137.4, 142.2, 165.0.

Synthesis of 1-Benzyl-4-methyl-β-azetidinone (6c). The reaction of carbene complex **4a** (191 mg, 0.50 mmol) and the benzylethylideneamine **5c** (73.3 mg, 0.55 mmol) in 22 mL of diethyl ether at 60 psi carbon monoxide gave 167 mg (0.50 mmol, 100%) of a gold oil after 24 h of irradiation. Analysis of the crude product by ^{1}H and ^{13}C NMR spectroscopy showed the product to be a 3:2 mixture of trans and cis azetidinones, *each* of which was a single diastereoisomer. The product was purified by preparative layer chromatography (silica gel) eluting with hexane/EtOAc (1:1) to yield 68 mg (0.20 mmol, 41%) of *trans*-**6c** and 34 mg (0.10 mmol, 20%) of *cis*-**6c′** for a total yield of 102 mg (0.31 mmol, 61%). *trans*-**6c**: ^{1}H NMR (270 MHz) δ 1.00 (d, J = 6.1 Hz, 3, CH_3), 1.45 (s, 3, CH_3), 1.46 (s, 3, CH_3), 2.88 (dq, J = 2.3, 6.1 Hz, 1, C*H*CHC=O), 3.67 (dd, J = 5.3, 7.8 Hz, 1, OCH_2CHN), 3.71 (d, J = 2.3 Hz, 1, C*H*C=O), 3.90 (d, J = 15.2 Hz, 1, C*H*Ph), 4.27 (t, J = 7.8 Hz, 1, OCH_2CHN), 4.33 (dd, J = 5.3, 7.8 Hz, 1, OCH_2CHN), 4.42 (d, J = 15.2 Hz, 1, C*H*Ph), 6.97 (m, 2, ArH), 7.18–7.31 (m, 8, ArH); ^{13}C NMR (67 MHz, $CDCl_3$) δ 16.7, 23.5, 27.8, 43.8, 54.2, 61.9, 71.9, 72.6, 96.0, 127.3, 127.41, 128.2, 128.4, 128.6, 135.8, 143.0, 167.8; IR ($CHCl_3$) ν 1738 (s, C=O) cm^{-1}. *cis*-**6c′**: ^{1}H NMR (270 MHz) δ 0.63 (d, J = 6.4 Hz, 3, CH_3), 1.36 (s, 3, CH_3), 1.41 (s, 3, CH_3), 3.45 (dq, J = 4.7, 6.4 Hz, 1, C*H*CHC=O), 3.84 (dd, J = 4.7, 8.3 Hz, 1, OCH_2CHN), 4.10 (d, J = 15.2 Hz, 1, C*H*Ph), 4.23 (d, J = 15.2 Hz, 1, C*H*Ph), 4.25 (d, J = 4.7 Hz, 1, C*H*C=O), 4.35 (t, J = 8.3 Hz, 1, OCH_2CHN), 4.81 (dd, J = 4.7, 8.3 Hz, 1, OCH_2CHN), 6.96 (m, 2, ArH), 7.19–7.38 (m, 6, ArH), 7.44 (m, 2, ArH); ^{13}C NMR (67 MHz, $CDCl_3$) δ 14.6, 21.5, 28.1, 44.4, 55.1, 61.9, 66.0, 72.4, 96.3, 127.1, 127.5, 128.1, 128.1, 128.5, 144.4, 166.6; IR ($CHCl_3$) ν 1738 (s, C=O) cm^{-1}.

Synthesis of *trans*-1-Benzyl-4-methoxy-β-azetidinone (6f). The reaction of carbene complex **4a** (381 mg, 1.00 mmol) and methyl *N*-benzylformimidate **5f** (156 mg, 1.05 mmol) in 22 mL of Et_2O at 60 psi CO gave 400 mg (>100%) of a yellow oil after 24 h of irradiation. Analysis of the crude reaction mixture by ^{1}H and ^{13}C NMR spectroscopy and by analytical HPLC showed a single diastereoisomer, indicating a de of ≥97%. The crude product was purified by radial-layer chromatography (Chromatotron, 2 mm, silica gel) using hexane/EtOAc (4:1) to yield 332 mg (0.91 mmol, 91%) of a colorless oil: ^{1}H NMR (270 MHz) δ 1.35 (s, 3, CH_3), 1.38 (s, 3, CH_3), 2.97 (s, 3, OCH_3), 3.58 (dd, J = 4.5, 6.5 Hz, 1, OCH_2CHN), 3.81 (d, J = 1.0 Hz, 1, C*H*C=O), 3.86 (d, J = 15.1 Hz, 1, C*H*Ph), 3.91 (d, J = 1.0 Hz, 1, C*H*CHC=O), 4.16 (m, 2, OCH_2CHN), 4.29 (d, J = 15.1 Hz, 1, C*H*Ph), 6.9 (m, 2, ArH), 7.1 (m, 8, ArH); ^{13}C NMR (67 MHz) δ 23.2, 27.2, 43.5, 54.8, 61.3, 71.0, 71.9, 87.1, 95.7, 127.0, 127.1, 127.2, 127.8, 128.0, 128.1, 135.2, 142.0, 165.6; IR (neat) ν 1752 (s, C=O) cm^{-1}.

Synthesis of *trans*-Oxacepham 6g. The reaction of carbene complex **4a** (381 mg, 1.00 mmol) and 5,6-dihydro-4*H*-1,3-oxazine (**5g**; 90 mg, 1.05 mmol) in 22 mL of Et_2O at 60 psi CO gave ~360 mg (>100%) of a yellow oil after 24 h of irradiation. Analysis of the crude reaction mixture by ^{1}H and ^{13}C NMR spectroscopy and by analytical HPLC showed a single diastereoisomer, indicating a de of ≥97%. The crude product was purified by radial-layer chromatography (Chromatotron, 2 mm, silica gel) using hexane/EtOAc (4:1) to yield 288 mg (0.95 mmol, 95%) of a colorless oil: ^{1}H NMR (270 MHz) δ 1.34 (m, 1, ring CH), 1.43 (s, 3, CH_3), 1.47 (s, 3, CH_3), 1.64 (m, 1, ring CH), 2.71 (ddd, J = 4.7, 13.2, 17 Hz, 1, NC*H*CHCHO), 3.32 (ddd, J = 2.0, 12.2, 13.7 Hz, 1, OC*H*CHCHN), 3.76 (m, 2, ring CH and OCH_2CHN), 3.95 (m, 1, OC*H*CHCHN), 4.01 (s, 1, C*H*C=O), 4.06 (s, 1, C*H*CHC=O), 4.25 (m, 2, OCH_2CHN), 7.26–7.43 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 23.2, 23.3, 27.2, 36.8, 62.2, 64.6, 71.7, 73.2, 83.0, 95.6, 127.3, 127.9, 128.0, 141.9, 165.4; IR (neat) ν 1750 (s, C=O) cm^{-1}.

General Procedure for the Preparation of β-Azetidinones 6a, 6d, and 6e. The chromium carbene complex **4a** (381 mg, 1.00 mmol) and the corresponding imine trimer (0.35 mmol) were placed in a test tube (Pyrex test tube no. 9800) which was sealed with a rubber septum. The vessel was evacuated and purged with argon (four cycles) and ~22 mL of dry CH_3CN was then introduced via a cannula. The mixture was gently shaken until all of the contents were dissolved. The vessel was evacuated again and then purged with argon (four cycles). The tube was then placed into an irradiation box and exposed to a 450-W UV lamp for 24 h. The reaction mixture turned from bright yellow to green or brown as

(20) Ito, Y.; Inubishi, Y.; Zenbayashi, M.; Tomita, S.; Saegusa, T. *J. Am. Chem. Soc.* **1973**, *95*, 4448.

the reaction proceeded. The progress of the reaction was monitored by use of analytical TLC (silica gel). After complete consumption of the carbene, the solvent was evaporated and the residue was taken up in EtOAc. The mixture would then be placed on the roof top (sunlight), or placed in a light box, equipped with six 20-W Vitalite fluorescent lamps to air oxidize the chromium-containing byproduct(s). To accelerate the oxidation, after 2 or 3 h the mixture was filtered through Celite and from there on approximately once every 12 h until the oxidation was complete. The end point of the oxidation was indicated by a clear solution. Removal of the solvent on a rotatory evaporator gave the crude β-azetidinone, which was purified by chromatography [silica gel, hexane/EtOAc (4:1)].

Note: This second procedure for the preparation of β-azetidinones had to be used in the cases where the imine or imidate existed as a trimer. The trimers formed an imine–chromium complex when allowed to react in Et_2O under a CO pressure.

Synthesis of 1-Benzyl-β-azetidinone (6a). The reaction of carbene complex **4a** (191 mg, 0.50 mmol) and 1,3,5-tribenzylhexahydro-*s*-triazine (64 mg, 0.18 mmol) in 22 mL of CH_3CN gave 150 mg (0.46 mmol, 92%) of a gold oil after 24 h of irradiation. Analysis of the crude reaction mixture by ^1H and ^{13}C NMR spectroscopy and by analytical HPLC show the product to be an 85:15 mixture of diastereoisomers. The crude product was purified by preparative-layer chromatography [silica gel, hexane/EtOAc (1:1)] to yield 94 mg (0.29 mmol, 58%) of the major diastereoisomer (a white solid) and 25 mg (0.08 mmol, 16%) of the minor diastereoisomer (a colorless oil) for a total yield of 119 mg (0.37 mg, 74%). Major diastereoisomer **6a**: ^1H NMR (270 MHz) δ 1.38 (s, 3, CH_3), 1.41 (s, 3, CH_3), 2.37 (dd, J = 2.8, 5.7 Hz, 1, CHCHC=O), 2.90 (t, J = 5.7 Hz, 1, CHCHC=O), 3.63 (dd, J = 4.4, 6.9 Hz, 1, NCHCH_2O), 4.11 (s, 2, CHPh), 4.22 (m, 3), 6.95 (m, 2, ArH), 7.11 (m, 8, ArH); ^{13}C NMR (67 MHz) δ 23.8, 27.7, 45.6, 45.9, 61.9, 64.8, 72.4, 96.2, 127.4, 127.5, 128.1, 128.4, 128.6, 135.4, 142.9, 168.6; IR (neat) ν 1742 (s, C=O) cm^{-1}. Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.05; H, 7.46; N, 8.64. Found: C, 74.24; H, 7.18; N, 8.40. Minor diastereoisomer **6a**: ^1H NMR (270 MHz) δ 1.32 (s, 3, CH_3), 1.54 (s, 3, CH_3), 2.94 (t, J = 5.5 Hz, 1, CHCHC=O), 3.17 (dd, J = 2.6, 5.5 Hz, 1, CHCHC=O), 3.74 (t, J = 7.4 Hz, 1), 4.05–4.24 (m, 4), 4.27 (dd, J = 2.6, 5.5 Hz, 1, CHC=O), 7.18 (m, 2, ArH), 7.30 (m, 8, ArH); ^{13}C NMR (67 MHz) δ 22.7, 28.1, 43.8, 45.7, 64.2, 64.9, 72.4, 96.3, 127.7, 127.9, 128.0, 128.2, 128.3, 128.7, 135.5, 139.7, 167.3.

Synthesis of *trans*-β-Azetidinone (6d). The reaction of carbene complex **4a** (381 mg, 1.00 mmol) and 4,5-dihydro-3*H*-pyrrole (**5d**; 80 mg, 0.35 mmol) in 22 mL of acetonitrile gave 213 mg (0.90 mmol, 90%) of a brown oil after 24 h of irradiation. Analysis of the crude reaction mixture by ^1H and ^{13}C NMR spectroscopy and by analytical HPLC showed a single diastereoisomer, de ≥97%. The product was purified by radial-layer chromatography (Chromatotron, 2 mm, silica gel) using hexane/EtOAc (4:1) to yield 213 mg (0.75 mmol, 75%) of a colorless solid: mp 90–91 °C; $[\alpha]_D$ +10.93° (c 1.5, CH_2Cl_2); ^1H NMR (270 MHz) δ 1.29 (m, 1, ring CH), 1.35 (s, 3, CH_3), 1.39 (s, 3, CH_3), 1.79 (m, 3, ring CH), 2.57 (m, 1, NCH), 2.97 (dt, J = 2.2, 6.2 Hz, 1, CHCHC=O), 3.43 (m, 1, NCH), 3.63 (m, 1, NCHCH_2O), 3.69 (d, J = 2.2 Hz, 1, CHC=O), 4.20 (m, 2, NCHCH_2O), 7.16–7.36 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 23.6, 27.6, 28.7, 29.1, 44.9, 59.3, 63.1, 71.1, 72.1, 95.9, 127.2, 127.3, 128.2, 142.9, 176.3; IR ($CHCl_3$) ν 1741 (s, C=O) cm^{-1}. Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.33; H, 7.69; N, 9.79. Found: C, 71.10; H, 7.42; N, 9.98.

Synthesis of *trans*-β-Azetidinone (6e). The reaction of carbene complex **4a** (381 mg, 1.00 mmol) and 2,3,4,5-tetrahydropyridine (**5e**; 87 mg, 0.35 mmol) in 22 mL of acetonitrile gave 300 mg (1.00 mmol, 100%) of a brown oil after 24 h of irradiation. Analysis of the crude reaction mixture by ^1H and ^{13}C NMR spectroscopy and by analytical HPLC showed a single diastereoisomer, de ≥97%. The product was purified by radial-layer chromatography (Chromatotron, 2 mm, silica gel) using hexane/EtOAc (4:1) to yield 272 mg (0.91 mmol, 91%) of a colorless oil: ^1H NMR (270 MHz) δ 0.98 (m, 1, ring CH), 1.18 (m, 1, ring CH), 1.37 (s, 6, CH_3), 1.40 (m, 2, ring CH), 1.63 (m, 1, ring CH), 1.75 (m, 1, ring CH), 2.34 (dt, J = 5.2, 12 Hz, 1, NCH), 2.48 (ddd, J = 1.7, 4.4, 10 Hz, 1, CHCHC=O), 3.61 (br d, J = 5.2 Hz, 1, NCH), 3.67 (dd, J = 5.0, 7.2 Hz, 1, NCHCH_2O), 3.74 (d, J = 1.7 Hz, 1, CHC=O), 4.21 (m, 2, NCHCH_2O), 7.17–7.34 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 22.1, 23.6, 24.2, 27.2, 29.4, 38.4, 54.8, 62.4, 72.2, 73.4, 95.9, 127.5, 128.2, 142.8, 165.6; IR ($CHCl_3$) ν 1727 (s, C=O) cm^{-1}.

(5*S*)-*N*-Formyl-2,2-dimethyl-5-isopropyl-1,3-oxazolidine. To a solution of 9.1 g (88 mmol) of l-valinol and 63 mL (85.8 mmol) of acetone in 300 mL of methylene chloride was added 34 g (282 mmol) of anhydrous $MgSO_4$, and the mixture was stirred overnight at room temperature. Filtration and removal of the solvent in vacuum gave the crude product: ^1H NMR (270 MHz) δ 0.91 (d, J = 6.6 Hz, 3, CH(CH_3)$_2$), 1.04 (d, J = 6.6 Hz, 3, CH(CH_3)$_2$), 1.31 (s, 3, C(CH_3)$_2$), 1.44 (s, 3, C(CH_3)$_2$), 1.57 (m, 1, CH(CH_3)$_2$), 3.10 (m, 1, NCHCH_2O), 3.33 (t, J = 8 Hz, 1, NCHCH_2O), 3.93 (t, J = 7.3 Hz, 1, NCHCH_2O). Crude (5*S*)-*N*-formyl-2,2-dimethyl-5-isopropyl-1,3-oxazolidine can be purified by distillation [bp 52–54 °C (12 mmHg)], but purification did not influence the yield of the next step.

Crude product was dissolved in 300 mL of methylene chloride, and after cooling to 0 °C, 14 mL (100 mmol) of the mixed anhydride of formic and pivalic acids was added dropwise. The cooling bath was removed and the reaction mixture was stirred overnight at room temperature. Methylene chloride was evaporated in vacuo and the residue was stirred with 150 mL of ether and 200 mL of 0.25 M NaOH for 1 h. Separation of the ether layer followed by drying over $MgSO_4$, solvent removal, and distillation gave 8.06 g (65%) of the product [bp 74–76 °C (0.2 mmHg)] (mixture of two rotamers): ^1H NMR (270 MHz) δ 0.89–0.98 (m, 6, CH(CH_3)$_2$), 1.50 (s, 1.5, C(CH_3)$_2$), 1.56 (s, 1.5, C(CH_3)$_2$), 1.58 (s, 1.5, C(CH_3)$_2$), 1.62 (s, 1.5, C(CH_3)$_2$), 1.92 (m, 0.5, CH(CH_3)$_2$), 2.27 (m, 0.5, CH(CH_3)$_2$), 3.58 (m, 0.5, NCHCH_2O), 3.85–4.05 (m, 2.5, OCH_2CHN), 8.27 (s, 0.5 CHO), 8.29 (s, 0.5, CHO); ^{13}C NMR (67 MHz) δ 17.2, 18.0, 19.0, 19.3, 23.2, 25.4, 27.6, 28.1, 29.2, 31.5, 60.4, 62.7, 64.9, 65.6, 92.4, 93.9, 158.9, 159.2; $[\alpha]_D$ = +1.38° (c = 11.02, CH_2Cl_2). Anal. Calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.01; N, 8.18. Found: C, 62.90; H, 10.21; N, 8.08.

Preparation of Pentacarbonyl[5(*S*)-2,2-dimethyl-5-isopropyl-1,3-azoxacyclopentyl)methylene]chromium (4b). The published procedure using 24.1 mmol of $Na_2Cr(CO)_5$ and 3.44 g (20.1 mmol) of the oxazolidine gave, after crystallization from 30 mL of *n*-hexane (cooling by dry ice/2-propanol mixture), 6.05 g (86.8%) of pure product: mp 84–85 °C; ^1H NMR (270 MHz) δ 0.95 (d, J = 6.8 Hz, 3, CH(CH_3)$_2$), 1.08 (d, J = 6.9 Hz, 3, CH(CH_3)$_2$), 1.35 (s, C(CH_3)$_2$), 1.49 (s, 3, C(CH_3)$_2$), 2.75 (m, 1, CH(CH_3)$_2$), 4.16–4.31 (m, 3, OCH_2CHN), 11.24 (d, J = 1 Hz, 1, Cr=CH); ^{13}C NMR (67 MHz) δ 15.8, 19.3, 25.7, 26.8, 30.1, 63.4, 67.8, 100.9, 217.3, 223.8, 253.6; IR (CH_2Cl_2) ν 2040 (m), 1960 (m), 1935 (s), 1910 (s) (Cr–CO) cm^{-1}; $[\alpha]_D$ = −161.3° (c = 1.24, CH_2Cl_2). Anal. Calcd for $C_{14}H_{17}CrNO_6$: C, 48.42; H, 4.93; N, 4.03. Found: C, 48.60; H, 5.12; N, 3.99.

Preparation of 1-Benzyl-4,4-dimethyl-β-azetidinone (7b). The same procedure as was used for **6b** was followed; starting with 1.042 g (3.00 mmol) of the carbene complex **4b** and 0.464 g (3.16 mmol) of imine **5b** gave, after 36 h of irradiation of the usual isolation, 0.790 g of a crude product. Pure compound (0.584 g, 59%) was obtained for after chromatography [Chromatotron, silica gel, *n*-hexane/ether (2:1)] as an ~85:15 mixture of diastereoisomers. Crystallization from *n*-hexane gave pure major isomer. Attempts to separate the minor diastereoisomer from the mixture by chromatography failed. The diastereoisomer **7b**: mp 72–73 °C (*n*-hexane); ^1H NMR (270 MHz) δ 0.88 (d, J = 6.8 Hz, 3, CH(CH_3)$_2$), 0.89 (d, J = 6.6 Hz, 3, CH(CH_3)$_2$), 1.07 (s, 3, CH_3), 1.21 (s, 3, CH_3), 1.23 (s, 3, CH_3), 1.26 (s, 3, CH_3), 1.62 (m, 1, CH(CH_3)$_2$), 3.71–3.92 (m, 3, NCHCH_2O), 3.80 (s, 1, CHC=O), 4.18 (d, J = 15.2 Hz, CH_2Ph), 4.42 (d, J = 15.2 Hz, 1, CH_2Ph), 7.32 (br s, 5, ArH); ^{13}C NMR (67 MHz) δ 15.5 (q, CH_3), 19.7 (q, CH_3), 20.9 (q, CH_3), 21.7 (q, CH_3), 24.6 (q, CH_3), 28.4 (q, CH_3), 32.1 (d, CH(CH_3)$_2$), 42.9 (t, NCHCH_2O), 62.6 (s, CONC(CH_3)$_2$), 62.6 (d, NCHCH_2O), 64.2 (t, CH_2Ph), 73.3 (d, COCH), 95.0 (s, C(CH_3)$_2$), 127.5 (d, Ph), 128.3 (d, Ph), 137.4 (s, Ph), 165.9 (s, CO); IR (film) ν 1740 (C=O) cm^{-1}; $[\alpha]_D$ = −37.9° (c = 1.14, CH_2Cl_2). Anal. Calcd for $C_{20}H_{30}N_2O_2$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.86; H, 8.95; N, 8.54.

Preparation of 1-Benzyl-4-methyl-β-azetidinone (7c, 7c'). The above procedure was followed, using 1.080 g (3.11 mmol) of the carbene complex **4b** and 0.507 g (3.81 mmol) of imine **5c**. After irradiation in 30 mL of ether and the usual isolation, chromatography purification [Chromatotron, silica gel, *n*-hexane/ether (2:1)] gave 0.539 g (55%) of the pure β-lactam as a 25:75 mixture of cis and trans isomers. Crystallization from *n*-hexane gave 0.175 g of pure trans isomer. At this stage, the cis and trans isomers were inseparable by chromatography.

Trans isomer **7c**: mp 90–91 °C (*n*-hexane); ^1H NMR (270 MHz) δ 0.75 (d, J = 6.9 Hz, 3, CH(CH_3)$_2$), 0.77 (d, J = 6.7 Hz, 3, CH(CH_3)$_2$), 1.23 (d, J = 6.1 Hz, CHCH_3), 1.28 (s, 3, C(CH_3)$_2$), 1.33 (s, 3, C(CH_3)$_2$), 1.49 (m, 1, CH(CH_3)$_2$), 3.26 (m, 1, NCHCH$_2$O), 3.35 (dq, J = 2.4, 6.1 Hz, 1, NCHCH$_3$), 3.68 (d, J = 2.4 Hz, 1, COCH), 3.69 (m, 1, NCHCH_2O), 3.85 (dd, J = 8.4, 7.7 Hz, 1, NCHCH_2O), 3.93 (d, J = 15.0 Hz, 1, CH_2Ph), 4.76 (d, J = 15.0 Hz, 1, CH_2Ph), 7.30 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 15.5 (q, CH_3), 16.7 (q, CH_3), 19.6 (q, CH_3), 22.9 (q, CH_3), 28.2 (q, CH_3), 30.9 (d, CH(CH_3)$_2$), 44.0 (t, NCHCH_2O), 55.8 (d, NCHCH$_3$), 63.1 (d, NCHCH$_2$O), 64.3 (t, CH_2Ph), 72.5 (d, COCH), 95.4 (s, C(CH_3)$_2$), 127.7 (d, Ph), 128.4 (d, Ph), 128.7 (d, Ph), 136.3 (s, Ph), 167.9 (s, CO); IR (film) ν 1728 (C=O) cm^{-1}; $[\alpha]_D$ = −123.3 ° (c = 1.03, CH_2Cl_2). Anal. Calcd for $C_{19}H_{28}N_2O_2$: C, 72.12; H, 8.92; N, 8.85. Found: C, 72.31; H, 8.65; N, 8.99.

Cis isomer **7c'**: ^1H NMR (from mixture) (270 MHz) δ 0.90 (d, J = 7.0 Hz, 3, CH(CH_3)$_2$), 0.91 (d, J = 6.7 Hz, 3, CH(CH_3)$_2$), 1.14 (d, J

= 6.3 Hz, $CHCH_3$), 1.22 (s, 3, $C(CH_3)_2$), 1.25 (s, 3, $C(CH_3)_2$), 1.66 (m, 1, $CH(CH_3)_2$), 3.49 (m, 1), 4.08 (d, J = 15.0 Hz, 1, CH_2Ph), 4.19 (d, J = 4.4 Hz, 1, COCH), 4.59 (d, J = 15.0 Hz, 1, CH_2Ph).

Preparation of *trans*-1-Benzyl-4-methoxy-β-azetidinone (7f). The procedure above using carbene complex **4b** (2.123 g, 6.11 mmol) and imidate **5f** (0.914 g, 6.13 mmol) gave 1.64 g of crude β-lactam, as a single diastereoisomer by ^1H and ^{13}C NMR spectroscopy. Purification by chromatography [Chromatotron, silica gel, hexane/Et_2O (2:1)] gave 1.522 g (76%) of a white crystalline solid: mp 44–44.5 °C (hexane); ^1H NMR (270 MHz) δ 0.74 (d, J = 6.9 Hz, 3, $CH(CH_3)_2$), 0.78 (d, J = 6.8 Hz, $CH(CH_3)_2$), 1.32 (s, 6, $C(CH_3)_2$), 1.32 (m, 1, $CH(CH_3)_2$), 3.18 (m, 1, $NCHCH_2O$), 3.35 (s, 3, OCH_3), 3.68 (dd, J = 4.2, 8.6 Hz, 1, $NCHCH_2O$), 3.83 (dd, J = 8.6 Hz, 1, $NCHCH_2O$), 3.98 (s, 1, COCHN), 4.03 (d, J = 15.1 Hz, 1, CH_2Ph), 4.50 (s, 1, $CHOCH_3$), 4.75 (d, J = 15.1 Hz, 1, CH_2Ph), 7.30 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 15.0 (q, CH_3), 19.2 (q, CH_3), 22.6 (q, CH_3), 27.6 (q, CH_3), 30.3 (d, $CH(CH_3)_2$), 43.8 (t, OCH_2), 55.1 (q, OCH_3), 62.4 (d, $NCHCH(CH_3)_2$), 63.8 (t, CH_2Ph), 71.4 (d, COCHN), 88.9 (d, $CHOCH_3$), 95.3 (s, $C(CH_3)_2$), 127.5 (d, Ph), 128.1 (d, Ph), 128.4 (d, Ph), 135.6 (s, Ph), 166.1 (s, CO); IR (film) ν 1760 (C=O) cm^{-1}; $[\alpha]_D$ = −80.2° (c = 1.05, CH_2Cl_2). Anal. Calcd for $C_{19}H_{28}N_2O_3$: C, 68.65; H, 8.49; N, 8.43. Found: C, 68.63; H, 8.44; N, 8.55.

Preparation of *trans*-Oxacepham 7g. The procedure above using carbene complex **4b** (1.051 g, 3.03 mmol) and oxazine **5g** (0.330 g, 3.88 mmol) gave 0.786 g of crude β-lactam **7g**, a single diastereoisomer by ^1H and ^{13}C NMR spectroscopy. Pure product (0.571 g, 70.3%) was obtained after chromatography [Chromatotron, silica gel, n-hexane/ether (2:1)] as a colorless oil: ^1H NMR (270 MHz) δ 0.84 (d, J = 6.9 Hz, 3, $CH(CH_3)_2$), 0.90 (d, J = 6.8 Hz, 3, $CH(CH_3)_2$), 1.31 (s, 3, $C(CH_3)_2$), 1.33 (s, 3, $C(CH_3)_2$), 1.51 (br d, J = 13.0 Hz, 1, $NCH_2CH_2CH_2O$), 1.65 (m, 1, $CH(CH_3)_2$), 1.87 (m, 1, $NCH_2CH_2CH_2O$), 3.06 (dt, J = 4.6, 13 Hz, 1, $NCH_2CH_2CH_2O$), 3.21 (m, 1, $NCHCH_2O$), 3.64 (dd, J = 12, 1.5 Hz, 1, $NCH_2CH_2CH_2O$), 3.70 (dd, J = 4.4, 8.6 Hz, 1, $NCHCH_2O$), 3.84 (dd, J = 8.6, 7.9 Hz, 1, $NCHCH_2O$), 3.91 (dd, J = 5.9, 13 Hz, 1, $NCH_2CH_2CH_2O$), 4.03 (s, 1, COCH), 4.12 (br d, J = 12 Hz, 1, $NCH_2CH_2CH_2O$), 4.77 (s, 1, $NCHOCH_2$); ^{13}C NMR (67 MHz) δ 15.5 (q, CH_3), 19.5 (q, CH_3), 22.6 (q, CH_3), 23.9 (t, $NCH_2CH_2CH_2O$), 27.9 (q, CH_3), 31.0 (d, $CH(CH_3)_2$), 37.6 (t, OCH_2), 63.4 (d, $NCHCH_2O$), 64.1 and 65.2 (t, $NCH_2CH_2CH_2O$), 74.0 (d, COCH), 85.1 (d, NCHO), 95.5 (s, $C(CH_3)_2$), 166.1 (s, CO); IR (film) ν 1763 (C=O) cm^{-1}; $[\alpha]_D$ = −40.8° (c = 1.20, CH_2Cl_2). Anal. Calcd for $C_{11}H_{18}N_2O_4$: C, 62.66; H, 9.01; N, 10.44. Found: C, 62.43; H; 8.88; N, 10.63.

Preparation of *trans*-β-Azetidinone 7e. The procedure described for the synthesis of **6e** was followed by starting with 1.051 g (3.03 mmol) of complex **4b** and 0.272 g (3.28 mmol) of imine **5e**, to give 0.672 g (84.6%) of almost pure product **7e**, as a single diastereoisomer by ^1H and ^{13}C NMR spectroscopy. Chromatography [Chromatotron, silica gel, n-hexane/ether (2:1)] yielded 0.435 g (54.5%) of the pure β-lactam **7e** as a white solid: mp 62–65 °C (n-hexane); ^1H NMR (270 MHz) δ 0.86 (d, J = 7.0 Hz, 3, $CH(CH_3)_2$), 0.90 (d, J = 6.8 Hz, 3, $CH(CH_3)_2$), 1.31 (s, 6, $C(CH_3)_2$), 1.38 (m, 3, ring CH), 1.65 (m, 1, $CH(CH_3)_2$), 1.75 (m, 1, ring CH), 1.90 (m, 1, ring CH), 2.07 (m, 1, ring CH), 2.75 (dt, J = 4.5, 12.4 Hz, 1, $NCH_2(CH_2)_3CH$), 3.26 (m, 2, (CONCH) and $NCHCH_2O$), 3.71 (dd, J = 8.6, 4.2 Hz, 1, $NCHCH_2O$), 3.77 (d, J = 1.5 Hz, 1, COCH), 3.84 (dd, J = 8.5, 7.8 Hz, 1, $NCHCH_2O$), 3.85 (br d, J = 8.7 Hz, 1, $NCH_2(CH_2)_3CH$); ^{13}C NMR (67 MHz) δ 15.7 (q, CH_3), 19.4 (q, CH_3), 22.1 (t, ring CH_2), 22.5 (q, CH_3), 24.3 (t, ring CH_2), 28.1 (q, CH_3), 29.4 (t, ring CH_2), 31.0 (d, $CH(CH_3)_2$), 38.6 (t, $NCHCH_2O$), 56.9 (d, CONCH), 63.7 (d, $NCHCH_2O$), 64.2 (t, $NCH_2(CH_2)_3CH$), 73.7 (d, COCH), 95.3 (s, $C(CH_3)_2$), 165.7 (s, CO); IR (film) ν 1741 (C=O) cm^{-1}; $[\alpha]_D$ = −33.2° (c = 1.125, CH_2Cl_2). Anal. Calcd for $C_{15}H_{26}N_2O_2$: C, 67.63; H, 9.84; N, 10.52. Found: C, 67.53; H, 9.67; N, 10.44.

General Procedure for the Removal of the Chiral Auxilliary Group of the β-Azetidinones 6a–g. Hydrolysis of the Oxazolidine Group. A methanol solution of the β-azetidinone was treated with 0.2 N HCl at room temperature and stirred for 3 h. The reaction was monitored by TLC [hexane/EtOAc (1:1)]. Upon complete hydrolysis the MeOH was removed on a rotatory evaporator and the aqueous solution was brought to pH 7.0 with aqueous sodium bicarbonate. The product was then extracted with CH_2Cl_2 and dried with $MgSO_4$. After removal of the solvent, a white solid (the hydrolysis product) was present in yields ranging from 70 to 100%.

Hydrogenolysis of the *N*-Benzyl Group. A MeOH solution (10 mL) of the β-azetidinone hydrolysis product was treated with 0.10 equiv of 20% $Pd(OH)_2/C$. The reaction mixture was evacuated and purged several times by use of a H_2 balloon. It was stirred under a hydrogen atmosphere for 12 h. The $Pd(OH)_2/C$ catalyst was removed by centrifugation followed by decantation. The methanol was removed on the rotatory evaporator to leave a mixture of the free amino product and 2-phenylethanol. The mixture was taken up in aqueous HCl and extracted four times with CH_2Cl_2 to remove the 2-phenylethanol formed. The aqueous phase was brought to pH 7.0 by the addition of aqueous sodium bicarbonate solution. The product was extracted with CH_2Cl_2 and dried with $MgSO_4$. Removal of the solvent resulted in the free amino β-azetidinone (a colorless oil). These compounds were relatively unstable and were directly converted to their t-BOC derivatives for full characterization.

Synthesis of 1-Benzyl-3-amino-β-azetidinone (8a). By the above procedure, 1-benzyl-β-azetidinone **6a** (65 mg, 0.20 mmol), 5 mL of MeOH, and 5 mL of 0.2 N HCl were stirred for 3 h in a round-bottomed flask. After isolation, 54 mg (0.18 mmol, 91%) of the solid hydrolysis product was recovered: ^1H NMR (270 MHz) δ 2.84 (dd, J = 2.1, 5.5 Hz, 1, $CHCHC{=}O$), 3.10 (dd, J = 4.7, 5.5 Hz, 1, $CHCHC{=}O$), 3.52 (dd, J = 9.0, 11 Hz, 1, CH_2OH), 3.64 (dd, J = 4.1, 11 Hz, CH_2OH), 3.75 (dd, J = 4.1, 9.0 Hz, PhCHNH), 4.04 (dd, J = 2.1, 4.7 Hz, 1, $CHC{=}O$), 4.21 (d, J = 15 Hz, 1, CHPh), 4.30 (d, J = 15 Hz, 1, CHPh), 7.10 (m, 2, ArH), 7.20 (m, 8, ArH). The hydrolysis product was then subjected to hydrogenolysis and separation by extraction to give 22 mg (74%) of **8a** as a colorless oil: ^1H NMR (270 MHz) δ 1.80 (br s, 2, NH_2), 2.91 (dd, J = 2.0, 5.5 Hz, 1, $CHCHC{=}O$), 3.44 (t, J = 5.5 Hz, 1, $CHCHC{=}O$), 4.21 (dd, J = 2.0, 5.5 Hz, 1, $CHC{=}O$), 4.38 (s, 2, CHPh), 7.23–7.39 (m, 5, ArH). This material was difficult to purify further and was immediately converted to its t-BOC derivative for complete characterization.

Synthesis of 1-Benzyl-3-amino-4,4-dimethyl-β-azetidinone (8b). By the above procedure, **6b** (250 mg, 0.69 mmol), 5 mL of MeOH, and 5 mL of 0.2 N HCl were stirred for 3 h in a round-bottomed flask. After isolation, 208 mg (0.64 mmol, 94%) of the solid hydrolysis product was recovered: ^1H NMR (200 MHz) δ 0.99 (s, 3, CH_3), 1.14 (s, 3, CH_3), 3.53 (s, 1, $CHC{=}O$), 3.48–3.67 (m, 2, CH_2OH), 3.75 (dd, J = 4.0, 9.0 Hz, PhCHNH), 4.10 (d, J = 15.3 Hz, 1, CHPh), 4.20 (d, J = 15.3 Hz, 1, CHPh), 7.13–7.28 (m, 5, ArH). The hydrolysis product was then subjected to hydrogenolysis and separation by extraction to give 108 mg (82%) of **8b** as a colorless oil: ^1H NMR (270 MHz) δ 1.02 (s, 3, CH_3), 1.12 (s, 3, CH_3), 1.51 (br s, 2, NH_2), 3.74 (s, 1, $CHC{=}O$), 4.18 (d, J = 15.3 Hz, 1, CHPh), 4.25 (d, J = 15.3 Hz, 1, CHPh), 7.18 (m, 5, ArH). This material was immediately converted to its t-BOC derivative for complete characterization.

Synthesis of *trans*-1-Benzyl-3-amino-4-methyl-β-azetidinone (8c). By the above procedure, **6c** (91 mg, 0.27 mmol), 5 mL of MeOH, and 5 mL of 0.2 N HCl were stirred for 3 h in a round-bottomed flask. After isolation, 84 mg (0.27 mmol, 100%) of the solid hydrolysis product was recovered: ^1H NMR (270 MHz) δ 1.06 (d, J = 6.2 Hz, 3, CH_3), 2.93 (br s, 2, OH and NH), 3.34 (dq, J = 1.6, 6.2 Hz, 1, $CHCHC{=}O$), 3.58 (dd, J = 8.9, 11 Hz, 1, CH_2OH), 3.62 (s, 1, $CHC{=}O$), 3.70 (dd, J = 4.1, 11 Hz, 1, CH_2OH), 3.84 (dd, J = 4.1, 8.9 Hz, 1, PhCHNH), 4.07 (d, J = 15.2 Hz, 1, CHPh), 4.54 (d, J = 15.2 Hz, 1, CHPh), 7.27 (m, 10, ArH). The hydrolysis product was then subjected to hydrogenolysis and separation as above to give 39 mg (76%) of **8c** as a colorless oil: ^1H NMR (270 MHz) δ 1.23 (d, J = 6.2 Hz, 3, CH_3), 1.74 (br s, 2, NH_2), 3.28 (dq, J = 1.8, 6.2 Hz, 1, $CHCHC{=}O$), 3.70 (d, J = 1.8 Hz, 1, $CHC{=}O$), 4.09 (d, J = 15.2 Hz, 1, CHPh), 4.59 (d, J = 15.2 Hz, 1, CHPh), 7.31 (m, 5, ArH). This material was immediately converted to its t-BOC derivative for complete characterization.

Synthesis of *cis*-1-Benzyl-3-amino-4-methyl-β-azetidinone (8c′). By the above procedure, **6c′** (82 mg, 0.24 mmol), 5 mL of MeOH, and 5 mL of 0.2 N HCl were stirred for 3 h in a round-bottomed flask. After workup, 76 mg (0.24 mmol, 100%) of the solid hydrolysis product was recovered: ^1H NMR (270 MHz) δ 1.22 (d, J = 6.2 Hz, 3, CH_3), 2.83 (br s, 2, OH and NH), 3.53–3.62 (m, 1, $CHCHC{=}O$), 3.64 (dd, J = 9.0, 11 Hz, 1, CH_2OH), 3.76 (dd, J = 4.1, 11 Hz, CH_2OH), 3.83 (dd, J = 4.1, 9.0 Hz, PhCHNH), 4.00 (d, J = 4.8 Hz, 1, $CHC{=}O$), 4.05 (d, J = 15.2 Hz, 1, CHPh), 4.60 (d, J = 15.2 Hz, 1, CHPh), 7.11–7.49 (m, 10, ArH). The hydrolysis product was then subjected to hydrogenolysis and separation by extraction to give 44 mg (94%) of **8c′** as a colorless oil: ^1H NMR (270 MHz) δ 1.05 (d, J = 6.3 Hz, 3, CH_3), 1.61 (br s, 2, NH_2), 3.61 (dq, J = 5.0, 6.3 Hz, 1, $CHCHC{=}O$), 4.03 (d, J = 15.1 Hz, 1, CHPh), 4.13 (d, J = 5.0 Hz, 1, $CHC{=}O$), 4.51 (d, J = 15.1 Hz, 1, CHPh), 7.15–7.31 (m, 5, ArH). This material was immediately converted to its t-BOC derivative for further characterization.

Attempted Synthesis of Carbapenam 8d. All attempts to remove the chiral auxiliary from **6d** led to complete decomposition of the β-lactam product.

Synthesis of *trans*-3-Amino-β-carbacepham (8e). By the above procedure, *trans*-β-azetidinone **7** (50 mg, 0.17 mmol), 5 mL of MeOH, and 5 mL of 0.2 N HCl were stirred for 3 h in a round-bottomed flask. After isolation, 42 mg (0.16 mmol, 96%) of the solid hydrolysis product was recovered: ^1H NMR (270 MHz) δ 1.05 (m, 1, ring CH), 1.29 (m, 2, ring CH), 1.60 (m, 1, ring CH), 1.77 (m, 1, ring CH), 1.88 (m, 1, ring CH),

2.68 (ddd, J = 4.6, 13, 15 Hz, 1, NCH), 3.16 (dd, J = 4.4, 10 Hz, 1, C*H*CHC=O), 3.27 (br s, 2, OH and NH), 3.62 (dd, J = 8.8, 10 Hz, 1, CH_2OH), 3.66 (s, 1, C*H*C=O), 3.71 (dd, J = 4.1, 10 Hz, 1, CH_2OH), 3.80 (dd, J = 4.6, 13 Hz, 1, NCH), 3.85 (dd, J = 4.1, 8.8 Hz, 1, PhC*H*NH), 7.23–7.36 (m, 5, ArH). The hydrolysis product was then subjected to hydrogenolysis and separation by extraction to give 12 mg (53%) of **8e** as a colorless oil: ^{1}H NMR (270 MHz) δ 1.18–1.43 (m, 3, ring CH), 1.65 (m, 1, ring CH), 1.88 (m, 1, ring CH), 2.12 (m, 1, ring CH), 2.28 (br s, 2, NH_2), 2.77 (dt, J = 4.5, 12 Hz, 1, NCH), 3.17 (ddd, J = 1.1, 5.4, 11 Hz, 1, C*H*CHC=O), 3.80 (s, 1, C*H*C=O), 3.82 (dd, J = 4.5, 13 Hz, 1, NCH). This material was immediately converted to its t-BOC derivative for further characterization.

Synthesis of *trans*-1-Benzyl-3-amino-4-methoxy-β-azetidinone (8f). By the above procedure, **6f** (321 mg, 0.88 mmol), 5 mL of MeOH, and 5 mL of 0.2 N HCl were stirred for 3 h in a round-bottomed flask. After isolation, 272 mg (0.88 mmol, 100%) of the solid hydrolysis product was recovered: ^{1}H NMR (270 MHz) δ 2.83 (br s, 2, OH and NH), 3.15 (s, 3, OMe), 3.56 (dd, J = 9.0, 11 Hz, 1, CH_2OH), 3.70 (dd, J = 4.1, 11 Hz, 1, CH_2OH), 3.85 (dd, J = 4.1, 9.0 Hz, 1, PhC*H*NH), 3.88 (s, 1, C*H*C=O), 4.13 (d, J = 15.2 Hz, 1, C*H*Ph), 4.42 (s, 1, C*H*CHC=O), 4.55 (d, J = 15.2 Hz, 1, C*H*Ph), 7.26 (m, 5, ArH). The hydrolysis product was then subjected to hydrogenolysis and isolation by extraction to give 130 mg (71%) of **8f** as a colorless oil: ^{1}H NMR (270 MHz) δ 1.62 (br s, 2, NH_2), 3.31 (s, 3, OMe), 4.00 (s, 1, C*H*C=O), 4.18 (d, J = 15.1 Hz, 1, C*H*Ph), 4.47 (s, 1, C*H*CHC=O), 4.60 (d, J = 15.1 Hz, 1, C*H*Ph), 7.33 (m, 5, ArH). This material was immediately converted to its t-BOC derivative for further characterization.

Synthesis of *trans*-3-Amino-β-oxacepham (8g). Compound **6g** (273 mg, 0.90 mmol), 5 mL of MeOH, and 5 mL of 0.2 N HCl were stirred for 3 h in a round-bottomed flask. After isolation, 206 mg (0.79 mmol, 88%) of the solid hydrolysis product was recovered: ^{1}H NMR (270 MHz) δ 1.40 (br d, J = 10 Hz, 1, ring CH), 1.70 (m, 1, ring CH), 2.96 (dt, J = 5, 12 Hz, 1, NCH), 3.02 (br s, 2, OH and NH), 3.48–3.58 (m, 2, CH_2OH and OCH), 3.70 (dd, J = 4.0, 11 Hz, 1, CH_2OH), 3.83 (dd, J = 5, 12 Hz, 1, NCH), 3.88 (s, 1, C*H*C=O), 3.91 (dd, J = 4.0, 11 Hz, 1, PhC*H*NH), 3.99 (dd, J = 1.6, 10 Hz, 1, OCH), 4.64 (s, 1, C*H*CHC=O), 7.31 (m, 5, ArH). The hydrolysis product was then subjected to hydrogenolysis and isolation by extraction to give 82 mg (74%) of **8g** as a colorless oil: ^{1}H NMR (270 MHz) δ 1.51 (br d, J = 12 Hz, 1, ring CH), 1.82 (m, 1, ring CH), 1.82 (br s, 2, NH_2), 3.06 (ddd, J = 4.6, 12, 13 Hz, 1, NCH), 3.65 (dt, J = 1.9, 12 Hz, 1, OCH), 3.89 (dd, J = 6.0, 13 Hz, 1, NCH), 4.02 (s, 1, C*H*C=O), 4.09 (br d, J = 12 Hz, 1, OCH), 4.69 (s, 1, C*H*CHC=O). This material was immediately converted to its t-BOC derivative for further characterization.

General Procedure for the Preparation of 3-[[(*tert*-Butyloxy)carbonyl]amino]-β-azetidinone Derivatives. The 3-amino-β-azetidinones were placed in a round-bottomed flask equipped with a stir bar. *tert*-Butyl alcohol (10 mL) was added, followed by the addition of di-*tert*-butyl dicarbonate (1.1 equiv) and triethylamine (1.1 equiv). The reaction mixture was stirred for 6 h. At this time, the solvent was removed on a rotatory evaporator and the product was purified by chromatography (preparative TLC, 5% MeOH/CH_2Cl_2) to give the 3-[[(*tert*-butyloxy)carbonyl]amino]-β-azetidinone derivatives. These products could be crystallized from hexane/EtOAc.

Synthesized of 1-Benzyl-3-[[(*tert*-butyloxy)carbonyl]amino]-β-azetidinone (9a). By the above procedure, 78 mg (0.24 mmol) of free amino compound **8a** was converted to 15 mg (24%) of the pure **9a**: mp 133–134 °C; $[\alpha]_D$ = +2.89° (c 1.35, CH_2Cl_2); ^{1}H NMR (270 MHz) δ 1.43 (s, 9, CH_3), 3.12 (dd, J = 2.4, 5.6 Hz, 1, C*H*CHC=O), 3.45 (t, J = 5.3 Hz, 1, C*H*CHC=O), 4.40 (d, J = 15 Hz, 1, C*H*Ph), 4.41 (d, J = 15 Hz, 1, C*H*Ph), 4.82 (br s, 1, C*H*C=O), 5.15 (br s, 1, NH), 7.31 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 28.3, 46.0, 48.7, 57.4, 80.4, 127.9, 128.2, 128.9, 135.1, 154.8, 166.7; IR ($CHCl_3$) ν 1713, 1751 (s, C=O) cm^{-1}. Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.20; H, 7.30; N, 10.14. Found: C, 64.95; H, 7.59; N, 9.82.

Synthesis of 1-Benzyl-3-[[(*tert*-butyloxy)carbonyl]amino]-4,4-dimethyl-β-azetidinone (9b). By the above procedure, 87 mg (0.43 mmol) of free amino compound **8a** was converted to 129 mg (99%) of the pure **9b**: mp 160–161 °C; $[\alpha]_D$ = −6.60° (c = 2.0, CH_2Cl_2). The spectra of this compound were identical with those of its enantiomer **11b** reported below.

Synthesis of *trans*-1-Benzyl-3-[[(*tert*-butyloxy)carbonyl]amino]-4-methyl-β-azetidinone (9c). By the above procedure, 39 mg (0.21 mmol) of free amino compound **8c** was converted to 45 mg (76%) of the pure **9c**: mp 129–130 °C; $[\alpha]_D$ = +54.31° (c 1.00, CH_2Cl_2). The spectra of this compound were identical with those of its enantiomer **11c** reported below.

Synthesis of *cis*-1-Benzyl-3-[[(*tert*-butyloxy)carbonyl]amino]-4-methyl-β-azetidinone (9c′). By the above procedure, 44 mg (0.23 mmol) of free amino compound **8c′** was converted to 43 mg (64%) of the pure **9c′**: mp 171–172 °C; $[\alpha]_D$ = −40.74° (c = 0.54, CH_2Cl_2). The spectra of this compound were identical with those of its enantiomer **11c′** reported below.

Synthesis of *trans*-1-Benzyl-3-[[(*tert*-butyloxy)carbonyl]amino]-β-azetidinone (9e). By the above procedure, 12 mg (0.086 mmol) of free amino compound **8e** was converted to 17 mg (83%) of the desired product.

Synthesis of *trans*-1-Benzyl-3-[[(*tert*-butyloxy)carbonyl]amino]-4-methoxy-β-azetidinone (9f). By the above procedure, 43 mg (0.21 mmol) of free amino compound **8f** was converted to 42 mg (66%) of the pure **9f**: mp 107–108 °C; $[\alpha]_D$ = +24.56° (c 1.8, CH_2Cl_2). The spectra of this compound were identical with those of its enantiomer **11f** reported below.

Synthesis of *trans*-3-[[(*tert*-Butyloxy)carbonyl]amino]-β-oxacepham (9g). By the above procedure, 82 mg (0.58 mmol) of free amino compound **8g** was converted to 44 mg (32%) of the pure **9g**: mp 157–158 °C; $[\alpha]_D$ = +32.58° (c 1.2, CH_2Cl_2). The spectra of this compound were identical with those of its enantiomer **11g** reported below.

General Procedure for Removal of the Chiral Auxiliary Group from β-Azetidinone 7. Hydrolysis of the Oxazolidine Group. The azetidinone was stirred in an appropriate amount (~5 mL/mmol) of 0.2 N HCl until it dissolved (~6–8 h). The aqueous solution was washed with 3 × 5 mL of CH_2Cl_2, and excess acid was neutralized with solid $NaHCO_3$. Extraction with 5 × 5 mL of CH_2Cl_2, drying over anhydrous $MgSO_4$, and removal of solvent gave relatively pure amino alcohol. In some cases, the amino alcohol was directly oxidized without isolation.

Oxidative Cleavage of the Amino Alcohols to Free Amino β-Azetidinones 8. The amino alcohol was dissolved in 5–10 mL of 0.2 N HCl and $NaIO_4$ (1 equiv) in H_2O was slowly added. After being stirred for 30 min at room temperature the solution was extracted with CH_2Cl_2 (5 mL), the combined acidic portion was neutralized with $NaHCO_3$ and extracted with CH_2Cl_2 (5 × 5 mL), and the CH_2Cl_2 portions were dried over anhydrous $MgSO_4$. Removal of the solvent under vacuum gave the free amino β-lactam, which was unstable and was immediately converted to its t-BOC derivative.

Synthesis of 1-Benzyl-3-amino-4,4-dimethyl-β-azetidinone (10b). Starting from 2.00 g (6.07 mmol) of **7b** (85:15 mixture of diastereoisomers) and 32 mL 0.2 N HCl gave 1.02 g (52.5%) of the product amino alcohol as a mixture of isomers. The major isomer was separated by preparative TLC chromatography (silica gel, four 25 × 25 cm plates, 5% 2-propanol in CH_2Cl_2, R_f minor > R_f major) to yield 0.572 g the pure major isomer. The minor isomer could not be isolated pure. Major isomer: ^{1}H NMR (300 MHz) δ 0.92 (d, J = 6.8 Hz, 3, CH(CH_3)$_2$), 0.97 (d, J = 6.8 Hz, 3, CH(CH_3)$_2$), 1.12 (s, 3, CH_3), 1.19 (s, 3, CH_3), 1.75 (m, 2, C*H*(CH$_3$)$_2$) + NH), 2.48 (m, 1, NC*H*CH$_2$O), 3.41 (m, 1, NCHCH_2O), 3.61 (m, 2, NCHCH_2O + OH), 3.69 (s, 1, C*H*C=O), 4.26 (d, J = 15.2 Hz, 1, CH_2Ph), 4.31 (d, J = 15.2 Hz, 1, CH_2Ph), 7.29 (m, 5, ArH). A 0.510-g (1.76-mmol) portion of the amino alcohol was used as a starting material. After dissolving in 13 mL of 0.2 N HCl, a solution of 0.382 g (1.78 mmol) of $NaIO_4$ in 4 mL of H_2O was slowly added. After 30 min, the reaction mixture was treated as above: yield 0.152 g (42%); ^{1}H NMR (270 MHz) δ 1.10 (s, 3, CH_3), 1.21 (s, 3, CH_3), 1.65 (bs 2, NH_2), 3.83 (s, 1, COC*H*NH$_2$), 4.30 (m, 2, CH_2Ph), 7.31 (m, 5, ArH).

Synthesis of *trans*- and *cis*-1-Benzyl-3-amino-4-methyl-β-azetidinones (10c and 10c′). A 1:1 mixture of cis and trans oxazolidine derivatives (1.14 g, 3.60 mmol) (mother liquors after crystallization of the trans isomer) and 20 mL of 0.2 N HCl was used. The usual procedure gave 0.686 g (69%) of the mixture of isomeric amino alcohols. The isomers were separated by preparative TLC (silica gel, three 25 × 25 cm plates, 5% 2-propanol in CH_2Cl_2, R_f cis > R_f trans); 0.289 g of the pure cis and 0.275 g of the pure trans isomers were obtained as oils. Trans isomer: ^{1}H NMR (270 MHz) δ 0.91 (d, J = 6.8 Hz, 3, CH(CH_3)$_2$), 0.96 (d, J = 6.8 Hz, 3, CH(CH_3)$_2$), 1.22 (d, J = 6.1 Hz, 3, CHCH_3), 1.77 (m, 1, C*H*(CH$_3$)$_2$), 2.45 (m, 1, NC*H*CH$_2$O), 3.37 (dq, J = 6.1, 1.7 Hz, 1, C*H*CH$_3$), 3.41 (dd, J = 11, 7.7 Hz, 1, NCHCH_2O), 3.61 (dd, J = 11, 3.9 Hz, 1, NCHCH_2O), 3.68 (d, J = 1.7 Hz, 1, C*H*C=O), 4.11 (d, J = 15.1 Hz, 1, CH_2Ph), 4.60 (d, J = 15.1 Hz, 1, CH_2Ph), 7.30 (m, 5, ArH). Cis isomer: ^{1}H NMR (270 MHz) δ 0.93 (d, J = 6.8 Hz, 3, CH(CH_3)$_2$), 0.98 (d, J = 6.8 Hz, 3, CH(CH_3)$_2$), 1.16 (d, J = 6.2 Hz, CHCH_3), 1.84 (m, 1, C*H*(CH$_3$)$_2$), 2.54 (m, 1, NC*H*CH$_2$O), 3.43 (dd, J = 12, 8.4 Hz, 1, NCHCH_2O), 3.64 (dd, J = 12, 3.9 Hz, 1, NCHCH_2O), 3.69 (dq, J = 6.3, 5.0 Hz, 1, C*H*CH$_3$), 4.10 (d, J = 15.1 Hz, 1, CH_2Ph), 4.11 (d, J = 5.0 Hz, 1, C*H*C=O), 4.59 (d, J = 15.1 Hz, 1, CH_2Ph), 7.30 (m, 5, ArH).

***cis*-3-Amino-4-methyl Derivative 10c′.** Reaction of 0.269 g (0.975 mmol) of cis amino alcohol with 0.222 g (1.04 mmol) of $NaIO_4$ in 15 mL 0.2 N HCl gave 0.126 g (66%) of **10c′**: ^{1}H NMR (270 MHz) δ 1.15 (d, J = 6.3 Hz, 3, CH_3), 2.00 (br s, 2, NH_2), 3.69 (dq, J = 6.1, 5.2 Hz, 1, NC*H*CH$_3$), 4.11 (d, J = 15.1 Hz, 1, CH_2Ph), 4.23 (d, J = 5.2 Hz,

1, COC*H*NH_2), 4.58 (d, J = 15.1 Hz, 1, CH_2Ph), 7.20 (m, 5, ArH).

***trans*-3-Amino-4-methyl Derivative 10c.** HIO_4 was used in this case. The procedure was the same as that used for 4-methoxy derivative (see below). Reaction of 0.653 g (2.07 mmol) of *trans*-oxazolidine derivative **7c** with 0.518 g (2.27 mmol) of periodic acid in 13 mL of 0.2 N HCl gave 0.199 g (50.6%) of *trans*-3-amino-4-methyl derivative: ^{1}H NMR (270 MHz) δ 1.24 (d, J = 6.2 Hz, 3, CH_3), 2.10 (br s, 2, NH_2), 3.28 (dq, J = 1.8, 6.2 Hz, 1, NC*H*CH_3), 3.71 (s, 1, COC*H*NH_2), 4.10 (d, J = 15.1 Hz, 1, CH_2Ph), 4.59 (d, J = 15.1 Hz, 1, CH_2Ph), 7.31 (m, 5, ArH).

Attempted Synthesis of *trans*-3-Aminocarbacepham 10e. From 0.325 g (1.22 mmol) of **7e** in 10 mL of 0.2 N HCl was obtained 0.244 g (88.3%) of the product amino alcohol as an oil: ^{1}H NMR (270 MHz) δ 0.85 (d, J = 6.8 Hz, 3, CH(C*H*$_3$)$_2$), 0.91 (d, J = 6.8 Hz, 3, CH(C*H*$_3$)$_2$), 1.14–1.36 (m, 2, ring CH), 1.56–1.84 (m, 3, ring CH and C*H*$(CH_3)_2$), 1.99 (m, 1, ring CH), 2.39 (m, 1, PhC*H*N), 2.72 (dt, J = 12.5, 4.5 Hz, 1, NC*H*$(CH_2)_3$), 3.12 (ddd, J = 1.3, 4.3, 11 Hz, 1, C*H*CHC=O), 3.35 (dd, J = 11, 7.2 Hz, 1, C*H*$_2$OH), 3.54 (dd, J = 4.0, 11 Hz, 1, C*H*$_2$OH), 3.69 (d, J = 1.3 Hz, 1, C*H*C=O), 3.75 (dd, J = 13.2, 4.7 Hz, 1, NC*H*$(CH_2)_3$). All attempts to oxidatively cleave this amino alcohol led to decomposition of the β-lactam product.

Synthesis of *trans*-3-Benzyl-3-amino-4-methoxy-β-azetidinone (10f). a. Hydrolysis. From 0.613 g of **7f**, was obtained 0.400 g (74%) of the amino alcohol hydrolysis product as a colorless oil: ^{1}H NMR (270 MHz) δ 0.92 (d, J = 6.8 Hz, 3, CH(C*H*$_3$)$_2$), 0.98 (d, J = 6.8 Hz, 3, CH(C*H*$_3$)$_2$), 1.79 (m, 1, C*H*$(CH_3)_2$), 2.48 (m, 1, NC*H*CH_2O), 3.31 (s, 3, OCH_3), 3.40 (dd, J = 11, 7.9 Hz, 1, NCHC*H*$_2$O), 3.63 (dd, J = 11, 3.9 Hz, 1, NCHC*H*$_2$O), 3.95 (s, 1, COC*H*NH), 4.19 (d, J = 15.1 Hz, 1, CH_2Ph), 4.51 (s, 1, C*H*OCH_3), 4.63 (d, J = 15.1 Hz, 1, CH_2Ph), 7.30 (m, 5, ArH).

b. Direct Oxidation. β-Lactam **7f** (0.168 g, 0.51 mmol) was dissolved in 5 mL of 0.2 N HCl (3/4 hr), and a solution of 0.115 g (0.54 mmol) of $NaIO_4$ in 2 mL of H_2O was slowly added. After 30 min of stirring at room temperature, the acidic solution was extracted twice with 5-mL portions of CH_2Cl_2, the CH_2Cl_2 layer was washed with 5 mL of 0.2 N HCl, and the combined acidic portions were neutralized with an excess of solid $NaHCO_3$ and were extracted with five portions of CH_2Cl_2. The methylene chloride extract was washed twice with 10 mL of 0.2 N HCl and this acidic extract gave, after neutralization with solid $NaHCO_3$ and extraction to CH_2Cl_2, drying by $MgSO_4$ and evaporation of the solvent, 0.052 g (50.5%) of the free amino compound: ^{1}H NMR (270 MHz) δ 1.62 (br s, 2, NH_2), 3.31 (s, 3, OCH_3), 4.0 (s, 1, COC*H*NH_2), 4.18 (d, J = 15.1 Hz, 1, CH_2Ph), 4.46 (s, 1, C*H*OCH_3), 4.61 (d, J = 15.1 Hz, 1, CH_2Ph), 7.33 (m, 5, ArH).

Synthesis of *trans*-3-Aminooxacepham *t*-BOC Derivative 11g. a. Hydrolysis. A 0.571-g (2.13-mmol) portion of **7g** and 15 mL of 0.2 N HCl were mixed for 20 min and the resulting solution was worked up as above: yield. 0.410 g (84.4%) of an almost colorless oil; ^{1}H NMR (270 MHz) δ 0.92 (d, J = 6.9 Hz, 3, CH(C*H*$_3$)$_2$), 0.98 (d, J = 6.9 Hz, 3, CH(C*H*$_3$)$_2$), 1.50 (m, 1, ring CH), 1.60 (m, 1, ring CH), 1.80 (m, 2, ring CH and C*H*$(CH_3)_2$), 2.48 (dt, J = 7.0, 4.0 Hz, 1), 2.64 (br s, 1), 3.07 (dt, J = 12.1, 4.5 Hz, 1, NC*H*$(CH_2)_2$O), 3.43 (m, 1), 3.65 (dt, J = 12.2, 1.9 Hz, 1), 3.65 (m, 1), 3.90 (dd, J = 13.5, 5.7 Hz, 1), 3.97 (s, 1, C*H*C=O), 4.09 (br d, J = 12 Hz, 1), 4.71 (s, 1, NC*H*OCH_2).

b. Oxidation and Conversion to *t*-BOC Derivative 11g. The amino alcohol (0.400 g, 1.75 mmol) was dissolved in 20 mL of *tert*-butyl alcohol and a solution of 0.992 g (1.83 mmol) of $NaIO_4$ in a mixture of 1.2 mL of 2 N HCl and 1 mL of H_2O was added dropwise. The mixture was stirred 30 min at room temperature and then made basic by addition of triethylamine. Di-*tert*-butyl dicarbonate (0.764 g, 3.50 mmol) and *tert*-butyl alcohol were added and the reaction mixture was stirred overnight. The *tert*-butyl alcohol was evaporated and the residue was partitioned between water and ether. After drying with $MgSO_4$ and evaporation of the solvent, 0.504 g of an oil was obtained. Crystallization from *n*-hexane/ethyl acetate mixture gave 0.065 g (16%) of the desired product. The analytical sample was prepared by second crystallization: mp 157–158 °C (EtOAc/hexane); ^{1}H NMR (270 MHz) δ 1.44 (s, 9, C(C*H*$_3$)$_3$), 1.55 (m, 1), 1.86 (m, 1), 3.12 (br dt, J = 12.6, 4.4 Hz, 1, NC*H*), 3.67 (dt, J = 12.2, 1.8 Hz, 1, OC*H*), 3.92 (dd, J = 13.5, 6.0 Hz, 1, NCH), 4.11 (m, 1), 4.43 (d, J = 7.1 Hz, 1, COC*H*NH), 4.95 (s, 1, NC*H*OCH_2), 5.04 (br s, 1, NH); ^{13}C NMR (67 MHz) δ 23.8, 28.2, 37.9, 65.3, 66.0, 80.7, 84.6, 154.7, 163.9; IR (CH_2Cl_2) ν 1713, 1765 cm^{-1}; $[\alpha]_D$ = −32.64° (c = 1.40, CH_2Cl_2). Anal. Calcd for $C_{11}H_{28}N_2O_4$: C, 54.53; H, 7.49; N, 11.56. Found: C, 54.94; H, 7.33; N, 11.62.

Synthesis of 11b. Compound **10b** (0.141 g, 0.686 mmol), 0.178 g (0.816 mmol) of di-*tert*-butyl dicarbonate, and 0.1 g (1 mmol) of triethylamine in 7 mL of *tert*-butyl alcohol were allowed to react overnight. *tert*-Butyl alcohol was evaporated and the residue purified by preparative TLC chromatography (silica gel, two 25 × 25 cm plates, 5% of 2-propanol in CH_2Cl_2): yield 0.164 g (78%): mp 160–161 °C (EtOAc/hexane); ^{1}H NMR (270 MHz) δ 1.06 (s, 3, CH_3), 1.30 (s, 3, CH_3), 1.43 (s, 9, $(CH_3)_3$), 4.25 (d, J = 15.3 Hz, 1, CH_2Ph), 4.36 (d, J = 15.3 Hz, 1, CH_2Ph), 4.54 (d, J = 7.1 Hz, 1, COC*H*NH), 5.20 (br s, 1, NH), 7.30 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 20.5, 24.3, 28.2, 43.2, 62.7, 66.4, 80.2, 127.7, 128.4, 128.7, 136.6, 155.3, 165.3; IR (CH_2Cl_2) ν 1715, 1750 cm^{-1}; $[\alpha]_D$ = +6.64° (c = 1.05, CH_2Cl_2). Anal. Calcd for $C_{17}H_{24}N_2O_3$: C, 67.08; H, 7.95; N, 9.20. Found: C, 66.92; H, 7.69; N, 9.15.

Synthesis of 11c. The reaction of 0.164 g (0.86 mmol) of the free amino compound **10c** with 0.221 g (1.01 mmol) of di-*tert*-butyl dicarbonate and 0.120 g (1.2 mmol) of triethylamine in 5 mL of *tert*-butyl alcohol gave 0.185 g (74%) of the product after chromatography: mp 129–130 °C (EtOAc/hexane); ^{1}H NMR (270 MHz) δ 1.28 (d, J = 6.1 Hz, 3, CH_3), 1.43 (s, 9, C(C*H*$_3$)$_3$), 3.45 (dq, J = 6.1, 1.8 Hz, 1, NC*H*CH_3), 4.12 (d, J = 15.1 Hz, 1, CH_2Ph), 4.32 (d, J = 5.9 Hz, 1, COC*H*NH), 4.63 (d, J = 15.1 Hz, 1, CH_2Ph), 5.14 (br s, 1, NH), 7.30 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 16.8, 28.3, 44.3, 57.8, 64.3, 80.4, 127.8, 128.3, 128.8, 135.6, 155.0, 165.7; IR (CH_2Cl_2) ν 1710, 1750 cm^{-1}; $[\alpha]_D$ = −54.27° (c 1.10, CH_2Cl_2). Anal. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.19; H, 7.64; N, 9.65. Found: C, 66.17; H, 7.53; N, 9.76.

Synthesis of 11c′. From 0.126 g (0.663 mmol) of the free amino compound **10c′** (0.178 g, 0.816 mmol) of di-*tert*-butyl dicarbonate, and 0.81 mmol of triethylamine in 5 mL of *tert*-butyl alcohol was obtained after chromatography 0.110 g (57.2%) of the product: mp 171–172 °C (EtOAc/hexane); ^{1}H NMR (270 MHz) δ 1.06 (d, J = 6.2 Hz, 3, CH_3), 1.43 (s, 9, C(C*H*$_3$)$_3$), 3.77 (m, 1, NC*H*CH_3), 4.17 (d, J = 15.1 Hz, 1, CH_2Ph), 4.54 (d, J = 15.1 Hz, 1, CH_2Ph), 4.97 (m, 1, COC*H*NH), 5.04 (br s, 1, NH), 7.30 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 13.5, 28.3, 44.4, 54.0, 60.1, 80.3, 127.9, 128.3, 128.9, 135.5, 155.1, 166.3; IR (CH_2Cl_2) ν 1712, 1749 cm^{-1}; $[\alpha]_D$ = +40.52° (c 1.15, CH_2Cl_2). Anal. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.19; H, 7.64; N, 9.65. Found: C, 66.31; H, 7.51; N, 9.72.

Synthesis of 11f. Free amino compound **10f** (0.155 g, 0.752 mmol) was dissolved in 5 mL of *tert*-butyl alcohol, and 0.206 g (0.99 mmol) of di-*tert*-butyl dicarbonate was added followed by 0.1 g (1 mmol) of triethylamine. After 3 h the *tert*-butyl alcohol evaporated; the residue was dissolved in 25 mL of ether, washed twice 10 mL of 0.2 N HCl, and dried by $MgSO_4$. The yield was 0.210 g (91%) of a crude product. Crystallization from *n*-hexane/ethyl acetate mixture gave 0.110 g of a pure compound: mp 108–109 °C (EtOAc/hexane); ^{1}H NMR (270 MHz) δ 1.43 (s, 9, C(C*H*$_3$)$_3$), 3.35 (s, 3, OCH_3), 4.20 (d, J = 15.1 Hz, 1, CH_2Ph), 4.48 (d, J = 7.1 Hz, 1, COC*H*NH), 4.62 (s, 1, C*H*OCH_3), 4.64 (d, J = 15.1 Hz, 1, CH_2Ph), 5.20 (br s, 1, NH), 7.32 (m, 5, ArH); ^{13}C NMR (67 MHz) δ 28.3 (q, C(*C*H$_3$)$_3$), 44.5 (t, *C*H$_2$Ph), 55.3 (q, OCH_3), 64.1 (d, CHNH), 80.6 (s, O*C*(CH$_3$)$_3$), 89.6 (d, *C*HOCH$_3$), 127.8 (d, Ph), 128.4 (d, Ph), 128.8 (d, Ph), 135.4 (s, Ph), 154.7 (s, NHCO), 164.5 (s, NCOCH); IR (CH_2Cl_2) ν 1715, 1768 cm^{-1}; $[\alpha]_D$ = −24.96° (c 1.15, CH_2Cl_2). Anal. Calcd for $C_{16}H_{22}N_2O_4$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.81; H, 7.18; N, 9.19.

Debenzylation of the *cis*-3-*t*-BOC-4-methyl Derivative 11c′. A solution of 0.075 g (0.258 mmol) of **11c′** in 2 mL of a mixture of THF and *tert*-butyl alcohol (9:1) was added dropwise to a solution of 0.018 g (2.6 mmol) of Li in 3 mL of ammonia at −78 °C. After 2 min, 0.45 g of NH_4Cl was added and the ammonia was allowed to evaporate at room temperature. After removal of solvents in vacuo the residue was acidified with diluted hydrochloric acid to pH ~3. After several minutes this solution was neutralized with an excess of $NaHCO_3$ and was extracted with five 5-mL portions of CH_2Cl_2. Pure compound was obtained after crystallization from *n*-hexane/ethyl acetate mixture: mp 185–186 °C; $[\alpha]_D$ = +55.6° (c 1.68, CH_3OH). Product after the second crystallization (mp 185.5–186 °C) had rotation $[\alpha]_D$ = +56.3° (c 2.14, CH_3OH). It was identical in all respects with authentic material.[8]

Debenzylation of the *trans*-3-*t*-BOC-4-methyl Derivative 11c. The same procedure as for the cis isomer was used, starting with 0.148 g (0.51 mmol) of *t*-BOC derivative and 0.032 g (4.60 mmol) of lithium. Purification by crystallization gave material identical in all respects with authentic material:[8] mp 134–136 °C; $[\alpha]_D$ = −64.2° (c 0.85, MeOH).

Methyl *N*-(Thioformyl)glycinate. To an ice-cooled solution of 12.57 g (0.10 mmol) of glycine methyl ester hydrochloride and 14 mL of triethylamine in 100 mL of methanol was added slowly 10.6 g (0.12 mmol) of ethyl thioformate. The reaction mixture was allowed to warm to room temperature, the methanol was evaporated in vacuo, and the residue was mixed with 100 mL of water and 100 mL of ethyl acetate. The organic layer was washed with 5 × 50 mL of water and dried over $MgSO_4$. Evaporation of the solvent gave 9.42 g of a crude product, which was purified by crystallization from CCl_4: yield 8.21 g (62%); mp 45–48 °C; (lit.[21] mp 46–48 °C); ^{1}H NMR (270 MHz) δ 3.84 (s, 3, CO_2CH_3), 4.45 (d, J = 4.7 Hz, 2, CH_2), 7.90 (br s, 1, NH), 9.52 (d, J = 5.8 Hz, 1, CHS).

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Preparation of Thiazine 12.[10] To an ice-cooled solution of 3.28 g (24.7 mmol) of methyl *N*-(thioformyl)glycinate in 50 mL of THF was added 1.38 g (34.5 mmol) of 60% dispersion of NaH. After $^1/_2$ h, 3.28 g (34.3 mmol) of chloroacetone was added. The reaction was monitored by TLC chromatography (silica gel, 5% of 2-propanol in CH_2Cl_2). After 1 h at 0 °C, THF was evaporated, the residue decomposed by addition of 50 mL of cold 10% aqueous solution of K_2HPO_4, and the product extracted into ethyl acetate. Evaporation of the solvent gave 5.81 g of a crude product consisting of two isomers of the product and unreacted starting material. Dissolving in 10 mL of diethyl ether and cooling to −15 °C overnight gave 1.167 g (27%) of a crystalline main isomer. The analytical sample was obtained by crystallization from benzene: mp 100–101.5 °C (benzene); ^{1}H NMR (270 MHz) δ 1.41 (s, 3, CH_3), 2.91 (d, J = 12.6 Hz, 1, SCH_2), 3.06 (d, J = 12.6 Hz, 1, SCH_2), 3.42 (s, 1, OH), 3.84 (s, 3, CO_2CH_3), 4.20 (s, 1, $CHCO_2CH_3$), 8.30 (d, J = 2.2 Hz, 1, N=CHS); ^{13}C NMR (67 MHz) δ 26.7, 34.0, 52.3, 62.8, 66.0, 152.9, 171.5; IR (CH_2Cl_2) ν 1730 (s, C=O), 1604 (s, C=N) cm^{-1}. Anal. Calcd for $C_7H_{11}NO_3S$: C, 44.43; H, 5.86; N, 7.40; S, 16.94. Found: C, 44.52; H, 5.75; N, 7.42; S, 16.76.

Preparation of Cepham 13. The procedure for **4b**, starting from 1.054 g (3.03 mmol) of the carbene complex and 0.604 g (3.19 mmol) thiazine **12** in 30 mL of ether, gave, after 24-h irradiation, 1.016 g of crude product after the usual isolation. Pure β-lactam **13** (0.893 g, 79%) was obtained after chromatography [Chromatotron, silica gel, *n*-hexane/ether (1:1)] as a yellowish oil. The product was ~1:1 mixture of diastereoisomers (because of the racemic starting thiazine): ^{1}H NMR (270 MHz) δ 0.88 (m, 6, $CH(CH_3)_2$), 1.33 (m, 5, $C(CH_3)_2$), 1.59 (s, 1, $C(CH_3)_2$), 1.62–1.80 (m, 1, $CH(CH_3)_2$), 2.63 (d, J = 13.8 Hz, 1, SCH_{2a}), 2.81 (d, J = 14.4 Hz, 1, SCH_{2b}), 2.92 (d, J = 14.8 Hz, 1, SCH_{2b}), 3.04 (d, J = 13.8 Hz, 1, SCH_{2a}), 3.23 (m, 1, $NCHCH_2O$), 3.36 (br s, 1, OH_a), 3.67 (s, 1, $CHCO_2CH_{3b}$), 3.73 (dd, J = 8.7, 4.3 Hz, 1, $NCHCH_2O$), 3.80 (s, 3, OCH_{3a}), 3.82 (dd, J = 7.8, 10.2 Hz, 1, $NCHCH_2O$), 3.88 (s, 3, OCH_{3b}), 4.07 (s, 1, OH_b), 4.22 (d, J = 1.4 Hz, 1, $COCH_a$), 4.27 (d, J = 1.6 Hz, 1, $COCH_b$), 4.47 (s, 1, $CHCO_2CH_{3b}$), 4.55 (br s, 1, $NCHS_b$), 4.78 (d, J = 1.4 Hz, 1, $NCHS_a$); IR (film) ν 1734 (s, C=O), 1760 (s, C=O) cm^{-1}. Anal. Calcd for $C_{17}H_{28}N_2SO_5$: C, 54.82; H, 7.58; N, 7.52; S, 8.61. Found: C, 54.72; H, 7.46; N, 7.40; S, 8.83.

Synthesis of 14. The reaction of carbene complex **4a** (191 mg, 0.500 mmol) and the *N*-benzyl imine of *m*-methoxybenzaldehyde (138 mg, 0.550 mmol) in acetonitrile (22 mL) gave 262 mg of an orange oil after 24 h of irradiation. The product was purified by chromatography [preparative TLC, hexane/EtOAc (1:1)] to yield 21 mg (0.045 mmol, 9%) of a trans (**14a**) isomer and 97 mg (0.21 mmol, 41%) of a 1:1 mixture of two cis (**14b**) isomers. *trans*-**14a**: ^{1}H NMR (270 MHz, $CDCl_3$, Me_4Si) δ 1.41 (s, 3, CH_3), 1.46 (s, 3, CH_3), 3.38 (dd, J = 2.3, 8.6 Hz, 1, $CHCHC$=O), 3.71 (dd, J = 4.1, 6.9 Hz, 1, OCH_2CHN), 3.80 (s, 3, OCH_3), 3.90 (d, J = 14.9 Hz, 1, $CHPh$), 3.99 (d, J = 2.3 Hz, 1, CHC=O), 4.30 (m, 2, OCH_2CHN), 4.45 (d, J = 14.9 Hz, 1, $CHPh$), 5.88 (dd, J = 8.6, 15.8 Hz, 1, CH=CHPh), 6.13 (d, J = 15.8 Hz, 1, CH=CHPh), 6.8 (m, 2, ArH), 7.0 (m, 2, ArH), 7.3 (m, 10, ArH). *cis*-**14b**: ^{1}H NMR (270 MHz, $CDCl_3$, Me_4Si) δ 1.29 (s, 3, CH_3), 1.39 (s, 3, CH_3), 1.46 (s, 3, CH_3), 1.55 (s, 3, CH_3), 3.64–3.79 (m, 4), 3.80 (s, 3, OCH_3), 3.82 (s, 3, OCH_3), 3.91 (dd, J = 4.6, 9.2 Hz, 1, $CHCHC$=O), 3.97 (d, J = 4.4 Hz, 1, CHC=O), 4.02 (d, J = 4.6 Hz, 1, CHC=O), 4.10 (m, 2), 4.24–4.41 (m, 4), 4.44 (dd, J = 4.4, 8.3 Hz, 1, $CHCHC$=O), 5.48 (dd, J = 9.2, 15.9 Hz, 1, CH=CHPh), 5.95 (dd, J = 8.3, 16.0 Hz, 1, CH=CHPh), 6.15 (d, J = 16.0 Hz, 1, CH=CHPh), 6.25 (d, J = 15.9 Hz, 1, CH=CHPh), 6.61–7.51 (m, 28, ArH). These compounds were not further purified.

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Intersystem Crossing to both Ligand-Localized and Charge-Transfer Excited States in Mononuclear and Dinuclear Ruthenium(II) Diimine Complexes

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Abstract: The unsaturated bridging ligand 1,4-bis[2-(4′-methyl-2,2′-bipyrid-4-yl)ethenyl]benzene (dstyb) was prepared in a simple two-step sequence. The ruthenium complexes $\{[(dmb)_2Ru]_n(dstyb)\}^{2n+}$ (n = 1,2; dmb = 4,4-dimethyl-2,2′-bipyridine) were prepared, and their redox and photophysical properties were examined. Both complexes have a single oxidation in cyclic voltammetry at 1.10 V vs SSCE, for the dinuclear complex n = 2. The first one-electron reductions are localized on the dstyb ligand and occur at −1.32 and −1.26 V for the mononuclear and dinuclear complexes, respectively. The emission maximum in room-temperature CH_3CN is 680 nm for $[(dmb)_2Ru(dstyb)]^{2+}$ and 720 nm for $\{[(dmb)_2Ru]_2(dstyb)\}^{4+}$. For both complexes emission quantum yields are <0.005, and luminescence lifetimes are 622 ns for the monomer and 2.02 μs for the dimer at room temperature. The very low radiative decay rates (ϕ_{em}/τ) observed result from low intersystem crossing efficiencies for population of the emitting ^{3}MLCT state. Transient absorption spectra of the two complexes provide evidence for the presence of a $^3(\pi \rightarrow \pi^*)$ state. In the mononuclear complex the lifetime of the $T_1 \rightarrow T_2$ absorbance of the $^3(\pi \rightarrow \pi^*)$ state is 1.6 μs, much longer than the emission lifetime. The ^{3}MLCT emission and the $^3(\pi \rightarrow \pi^*)$ absorption lifetimes of the dinuclear complex are within experimental error, indicating the states are equilibrated. Quenching of the transient absorbance with a series of triplet quenchers provides a measure of the triplet energy of the $^3(\pi \rightarrow \pi^*)$ state of the complexes.

There has been considerable recent interest in the photochemical and photophysical properties of binuclear and multinuclear transition-metal complexes having bridging ligands that allow varying degrees of electronic interaction between the coupled metal centers.[1-11] Complexes of this type are of interest as potential chromophores for multielectron photoredox processes. Studies of coupled ruthenium(II) diimine complexes have shown that the

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