# Enantiospecific and Stereospecific Rhodium(I)-Catalyzed Carbonylation and Ring Expansion of Aziridines. Asymmetric Synthesis of β-Lactams and the Kinetic Resolution of Aziridines

Serge Calet, Fabio Urso, and Howard Alper*,[1]

Contribution from the Ottawa-Carleton Chemistry Institute, Department of Chemistry, University of Ottawa, Ottawa, Ontario, Canada K1N 6N5. Received April 18, 1988

Abstract: Rhodium(I) complexes catalyze the regiospecific ring expansion–carbonylation reaction of aziridines to β-lactams. This process is both stereospecific and enantiospecific, occurring with retention of configuration [e.g., (*S*)-1-*tert*-butyl-2-phenylaziridine is converted to (*S*)-1-*tert*-butyl-3-phenylazetidin-2-one]. The synthesis of β-lactams in high optical purity, from racemic aziridines, can be realized by using the dimer of chloro(1,5-cyclooctadiene)rhodium(I) as the catalyst and *d*- or *l*-menthol as an added chiral agent. The recovered aziridine is also obtained in fine optical yield.

Inorganic and transition-metal organometallic complexes have been utilized as reagents and catalysts for the preparation and reactivity of heterocyclic nitrogen compounds.[2–5] The synthesis of β-lactams has attracted widespread interest for many years.[6,7] In addition to conventional organic methodology, transition metal complex mediated routes to β-lactams have been the subject of a number of recent investigations. Unfortunately nearly all of the chemistry developed, while elegant, relies on the use of *stoichiometric* quantities of the metal complex.[8,9] An example of a catalytic process leading to bicyclic β-lactams is the tetra-kis(triphenylphosphine)palladium(0) induced carbonylation of azirines at 40 °C and 1 atm (eq 1).[10] The latter reaction is not applicable to the synthesis of monocyclic β-lactams.
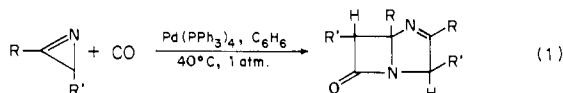

It seemed conceivable to us that saturated three-membered-ring heterocycles could undergo incorporation of carbon monoxide in the presence of an appropriate metal catalyst. Indeed, in 1983, we reported, in communication form, the first examples of a direct, regiospecific, rhodium(I)-catalyzed carbonylation and ring expansion of aziridines to β-lactams.[11] The present paper provides full details on the process. Furthermore, it is important to know the stereoselectivity and enantioselectivity of the reaction. The results described herein clearly show that the conversion of aziridines to β-lactams is stereo- and enantiospecific. In addition, one can realize the synthesis of β-lactams in high optical purity by conducting the metal-catalyzed carbonylation reaction of racemic aziridines in the presence of a suitable added chiral ligand.

When *N-tert*-butyl-2-phenylaziridine (**1**: R = Ph; R′ = C(CH₃)₃) was exposed to carbon monoxide and a catalytic quantity

Scheme I
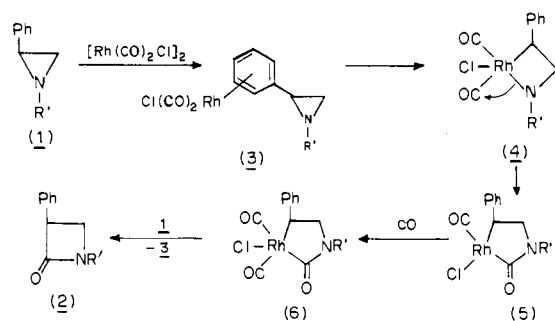
of the dimer of chlorodicarbonylrhodium(I) [20/1 ratio of **1**/Rh(I)] in benzene at 90 °C and 20 atm for 48 h, monocyclic β-lactam **2** (R = Ph; R′ = C(CH₃)₃) was formed in quantitative yield. Analytical and spectral data supported **2** as the assigned structure. A molecular ion peak was observed in the mass spectrum at *m/e* 203, and the intense infrared carbonyl stretching
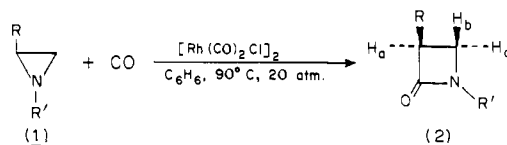
band at 1740 cm⁻¹ is consistent with the presence of a β-lactam unit. In the proton magnetic resonance spectrum, a 12-line AMX pattern for the three heterocyclic ring protons is also in accord with the assigned structure, as are the carbon magnetic resonance data (see Table I for pertinent spectral data).

Insertion of carbon monoxide occurs exclusively into the nitrogen–carbon bond of **1** (R = Ph; R′ = C(CH₃)₃) bearing the phenyl substituent. This regiospecific process is general as demonstrated by the results for a series of aziridines **1** (R = Ph, *p*-BrC₆H₄, *p*-PhC₆H₄; R′ = C(CH₃)₃ or 1-adamantyl) as reactants, all of which afford the corresponding β-lactams in 97–100% yields [see Table I for NMR and mass spectral results (all compounds gave ν_CO 1740–1745 cm⁻¹)].

In contrast to aryl-substituted aziridines, 2-alkylaziridines such as *N-tert*-butyl-2-methylaziridine are recovered unchanged on attempted carbonylation with Rh(I), even at 75 atm and 90 °C. In Scheme I is outlined a possible mechanism for the formation of β-lactams (illustrated for **1**, R = Ph). It is conceivable that the arene ring of **1** initially coordinates to rhodium (**3**), facilitating insertion into the more substituted of the two carbon–nitrogen bonds, to give rhodium(III) complex **4**. Ligand migration from the N–Rh bond of **4** to a carbonyl carbon may form **5**. Such a formal carbonyl insertion, rather than that involving the rhodi-
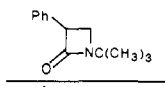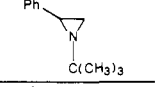
(1) Killam Research Fellow, 1986–88.
(2) Alper, H. *Isr. J. Chem.* **1981**, *21*, 203.
(3) Davidson, J. L.; Preston, P. N. *Adv. Heterocycl. Chem.* **1982**, *30*, 319.
(4) Newkome, G. R.; Paudler, W. W. *Contemporary Heterocyclic Chemistry*; Wiley-Interscience: New York, 1982.
(5) Alper, H.; Mahatantila, C. P.; Einstein, F. W. B.; Willis, A. C. *J. Am. Chem. Soc.* **1984**, *106*, 2708.
(6) Nagahara, T.; Kametani, T. *Heterocycles* **1987**, *25*, 729.
(7) Hassner, A. *Small Ring Heterocycles*; Wiley Interscience: New York, 1983; Volume 42, Part 2.
(8) Hegedus, L. S.; Schultze, L. M.; Toro, J., Yuun, C. *Tetrahedron* **1985**, *41*, 5833 and references cited therein. Borel, C.; Hegedus, L. S.; Krebs, J.; Satoh, Y. *J. Am. Chem. Soc.* **1987**, *109*, 1101.
(9) Barrett, A. G. M.; Brock, C. P.; Sturgess, M. A. *Organometallics* **1985**, *4*, 1903. Barrett, A. G. M.; Sturgess, M. A. *Tetrahedron Lett.* **1986**, *27*, 3811.
(10) Alper, H.; Perera, C. P.; Ahmed, F. R. *J. Am. Chem. Soc.* **1981**, *103*, 1289.
(11) Alper, H.; Urso, F.; Smith, D. J. H. *J. Am. Chem. Soc.* **1983**, *105*, 6737.

932 *J. Am. Chem. Soc., Vol. 111, No. 3, 1989*

Calet et al.

Table I. β-Lactams (**2**) Obtained by the Rhodium(I)-Catalyzed Carbonylation of Aziridines (**1**)

2: R, R′	**^{1}H NMR, ppm^a**	**^{13}C NMR, ppm^{a,b}**	**MS, m/e**
Ph, C(CH$_3$)$_3$	1.36 (s, 9 H, C(CH$_3$)$_3$), 3.07 (dd, 1 H, H$_b$, J_{AB} = 2, J_{BC} = 6 Hz), 3.52 (dd, 1 H, H$_c$, J_{ac} = 5 Hz), 4.06 (dd, 1 H, H$_a$), 7.23 (s, 5 H, Ph)	27.78 (q, CH$_3$), 44.70 (t, CH$_2$), 52.28 (s, C(CH$_3$)$_3$), 53.24 (d, CHPh), 128.79, 127.26 (d each, CH of Ph), 136.39 (s, quaternary carbon of Ph), 167.14 (s, CO)	203, [M]$^+$
Ph, 1-adamantyl	1.68–2.05 (m, 15 H, adamantyl protons), 3.11 (dd, 1 H, H$_b$, J_{ab} = 2, J_{bc} = 5.5 Hz) 3.55 (dd, 1 H, H$_c$, J_{ac} = 5.0 Hz), 4.06 (dd, 1 H, H$_a$), 7.23 (s, 5 H, Ph)	29.06 (d), 36.21 (t), 40.83 (t) (secondary and tertiary adamantyl carbons), 43.75 (t, CH$_2$), 52.06 (d, CHPh), 53.97 (s, quaternary C of adamantane group), 127.29, 128.75 (d each, CH of Ph), 136.45 (s, quaternary carbon of Ph), 167.12 (s, CO)	281, [M]$^+$
p-PhC$_6$H$_4$, C(CH$_3$)$_3$	1.33 (s, 9 H, C(CH$_3$)$_3$), 3.13 (dd, 1 H, H$_b$, J_{ab} = 2, J_{bc} = 5.5 Hz), 3.53 (dd, 1 H, H$_c$, J_{ac} = 6 Hz), 4.10 (dd, 1 H, H$_a$), 7.16–7.56 (m, 9 H, aromatic ring protons)	27.77 (q, CH$_3$), 44.63 (t, CH$_2$), 51.94 (d, CHPh), 53.28 (s, C(CH$_3$)$_3$), 127.01, 127.26, 127.51, 127.66, 128.76 (d each, aromatic CH), 135.31, 140.26, 140.78 (s each, quaternary carbons of p-PhC$_6$H$_4$), 167.05 (s, CO)	
p-PhC$_6$H$_4$, 1-adamantyl	1.70–2.05 (m, 15 H, adamantyl protons), 3.15 (dd, 1 H, H$_b$, J_{ab} = 2, J_{bc} = 5.5 Hz), 3.56 (dd, 1 H, H$_c$, J_{ac} = 5 Hz), 4.10 (dd, 1 H, H$_a$), 7.15–7.65 (m, 9 H, aromatic ring protons)	29.04 (d), 36.19 (t), 40.82 (t) (secondary and tertiary adamantyl carbons), 43.63 (t, CH$_2$), 51.72 (d, CHPh), 54.00 (s, quaternary C of adamantane group), 127.01, 127.25, 127.50, 127.68, 128.75 (d each, aromatic CH), 135.44, 140.25, 140.81 (s each, quaternary carbons of p-PhC$_6$H$_4$), 167.03	357, [M]$^+$
p-BrC$_6$H$_4$, C(CH$_3$)$_3$	1.38 (s, 9 H, C(CH$_3$)$_3$), 3.06 (dd, 1 H, H$_b$, J_{ab} = 2, J_{bc} = 5.5 Hz), 3.53 (dd, 1 H, H$_c$, J_{ac} = 5.0 Hz), 4.05 (dd, 1 H, H$_a$), 7.00–7.60 (m, 4 H, aromatic protons)		283, 281, [M]$^+$

^{a} CDCl$_3$ with tetramethylsilane as internal standard. ^{b} Multiplicity of signals observed when C-13 spectra were recorded in the partially decoupled mode.

Table II. Carbonylation of 1-*tert*-Butyl-2-phenylaziridine^a

reaction time, h	menthol	i.y.,^{b} %	o.y., %	i.y.,^{b} %	o.y., %
24	d	21	97 (R)	65	77 (S)
72	d	44	87 (R)	28	85 (S)
24	l	25	99.5 (S)	56	85 (R)
48	l	30	98 (S)	43	81 (R)

^{a} Conditions: aziridine [0.35 g, 2.0 mmol], menthol [0.94 g, 6.0 mmol], [1,5-CODRhCl]$_2$ [0.049 g, 0.10 mmol], C$_6$H$_6$ (15 mL), 20 atm, 90 °C. ^{b} i.y. = isolated yields. Yields are of pure materials.

um–carbon bond of the 2-azametallacyclobutane, is based on the findings by Bryndza and co-workers[12] in organoplatinum systems where the facility for carbonyl insertion is Pt–N > Pt–C. Carbonylation of **5** to **6** followed by reductive elimination, with or without the participation of another molecule of aziridine, would afford β-lactam **2**.

The stereochemistry of the ring-expansion process was examined by the use of *cis*-1-isopropyl-3-methyl-2-phenylaziridine (**7**), which was prepared according to literature methods.[13] When the aziridine was subjected to [Rh(CO)$_2$Cl]$_2$-catalyzed carbonylation in benzene the *cis*-3,4-disubstituted β-lactam, **8**, was isolated as the only product in 81% yield. Therefore, carbonylation occurs with retention of stereochemistry of the substituent groups.
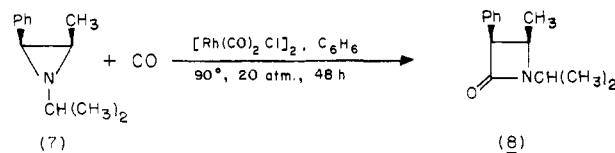
In order to determine the enantioselectivity of the carbonylation reaction, several optically pure aziridines were readily prepared from the commercially available enantiomers of phenyloxirane [i.e., styrene oxide]. Treatment of (R)-phenyloxirane with

tert-butylamine afforded (R)-2-(*tert*-butylamino)-1-phenylethanol ([α]$^{23}_D$ −78.8° (c 1.00, CHCl$_3$))[14] in 77% yield. Cyclization of the latter with bromine and triphenylphosphine in acetonitrile[15] gave (S)-1-*tert*-butyl-2-phenylaziridine (**9**: R = C(CH$_3$)$_3$) ([α]$^{23}_D$ +129.7° (c 2.57, CHCl$_3$)) in 58% yield. R enantiomer **11** (R = C(CH$_3$)$_3$) ([α]$^{23}_D$ −128° (c 4.47, CHCl$_3$)) was synthesized in the same manner from (S)-phenyloxirane. This two-step sequence was also applied to the preparation of the N-adamantyl-substituted
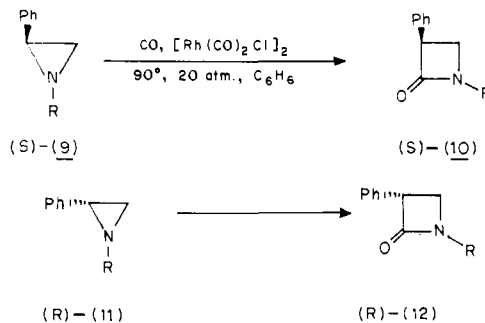
(S)-(**9**), (R = C$_{10}$H$_{15}$)([α]$^{23}_D$ +108.9° (c 4.32, CHCl$_3$)) and (R)-(**11**) (R = C$_{10}$H$_{15}$) ([α]$^{23}_D$ −109.2° (c 4.56, CHCl$_3$)) aziridines. The rhodium(I)-catalyzed carbonylation of **9** (R = C-(CH$_3$)$_3$) gave pure (S)-β-lactam **10** ([α]$^{23}_D$ −40.5° (c 1.67, CHCl$_3$)) in 93% yield. Likewise, R enantiomer **12** (R = C(CH$_3$)$_3$) ([α]$^{23}_D$ +41.0° (c 1.60, CHCl$_3$)) was obtained in quantitative yield when (R)-1-*tert*-butyl-2-phenylaziridine (**11**: R = C(CH$_3$)$_3$) was used as the reactant. In an analogous fashion, enantiomeric adamantyl-substituted β-lactam **10** (R = C$_{10}$H$_{15}$) ([α]$^{23}_D$ −14.8° (c 0.30, CHCl$_3$); [α]$^{23}_D$ −15.0° (c 1.60, CHCl$_3$)) and **12** (R = C$_{10}$H$_{15}$) ([α]$^{23}_D$ +15.0° (c 2.70, CHCl$_3$))[16] were formed in 89% and 81% yields, respectively, from the corresponding aziridines. These results convincingly demonstrate the enantiospecificity of the rhodium-catalyzed ring-expansion process.

The remarkable regio-, stereo-, and enantiospecificity of the β-lactam synthesis suggested that it might be possible to achieve

(12) Bryndza, H. E.; Fultz, W. C.; Tam, W. *Organometallics* **1985**, *4*, 939.
(13) (a) Weingarten, H.; Chupp, J. P.; White, W. A. *J. Org. Chem.* **1967**, *32*, 3246. (b) de Kimpe, N.; Verhè, R.; de Buyck, L.; Tukiman, S.; Schamp, N. *Tetrahedron* **1979**, *35*, 789. (c) de Kimpe, N.; Verhè, R.; de Buyck, L.; Schamp, N. *J. Org. Chem.* **1980**, *45*, 5319.

(14) Farbenfabriken Bayer, A. G., Brit. Pat. 1,043,510 (21 Sept. 1966); *Chem. Abstr.* **1967**, *66*, 2336y.
(15) Okada, I.; Ichimura, K.; Sudo, R. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1185.
(16) An X-ray determination of **12** (R = C$_{10}$H$_{15}$) will be published separately.

Synthesis of β-Lactams

J. Am. Chem. Soc., Vol. 111, No. 3, 1989 933

asymmetric synthesis by effecting the carbonylation of racemic aziridines in the presence of an appropriate chiral ligand. The carbonylation of 2.0 mmol of racemic 1-*tert*-butyl-2-phenylaziridine was carried out with 0.1 mmol of [Rh(CO)$_2$Cl]$_2$ and an added chiral agent. Commonly used chiral ligands[17] such as (+)-diethyl tartrate [12% optical yield with 0.1 mmol; 10% o.y. with 2.0 mmol], (+)-DIOP [0% o.y., 0.2 mmol], (S)-BINAP [0% o.y., 0.2 mmol], and β-cyclodextrin (0% o.y., 0.1 mmol) were essentially useless in this regard. More promising was the finding that the presence of 0.1 mmol of 1-menthol gave (S)-β-lactam **10** (R = C(CH$_3$)$_3$) in 25% o.y. The optical yield increased to 39% with 2.0 mmol of 1-menthol and to 48% with 6.0 mmol of the added chiral agent [43% o.y. with 20 mmol of 1-menthol].

Several other rhodium(I) catalysts were used for the reaction (2 mmol of racemic aziridine, 6 mmol of 1-menthol, and 0.1 mmol of metal complex). The optical yield of **10** (R = C(CH$_3$)$_3$) increased to 88% with chloro(1,5-hexadiene)rhodium(I) dimer as the catalyst, and we were gratified to observe the formation of nearly optically pure (S)-β-lactam (i.e., >99.5% o.y.) when the dimer of chloro(1,5-cyclooctadiene)rhodium(I) was used as the catalyst. The optical yield assessment was made by determination of the specific rotation and was corroborated by the use of Chiralplate (Mackerey-Nagel). We found that Chiralplate is capable of detecting 0.5% of one enantiomer in a mixture of the two β-lactam stereoisomers. With *d*-menthol, (R)-β-lactam **12** (R = C(CH$_3$)$_3$) was obtained in 96% o.y. Note that one can use less catalyst, as the (S)-β-lactam was formed in 99% o.y. with 1-menthol and one-third the concentration (i.e., 0.033 mmol) of [1,5-CODRhCl]$_2$. Excellent results were also obtained with racemic 1-adamantyl-2-phenylaziridine (1.0 mmol), [1,5-CODRhCl]$_2$ (0.02 mmol), and 1.0 mmol of *l*- or *d*-menthol affording **10** (R = 1-ad) (98% o.y.) and **12** (R = 1-ad) (96%, o.y.), respectively.

The carbonylation reaction does not result in the creation of a new chiral center, but rather it is a kinetic resolution. Consequently, the β-lactam can be produced in a maximum yield of 50%. The degree of asymmetric induction is a function, to some extent, of the degree of conversion. Consider the results in Table II regarding the [1,5-CODRhCl]$_2$-catalyzed carbonylation of 1-*tert*-butyl-2-phenylaziridine in the presence of *d*- or *l*-menthol. With either menthol, one can isolate the β-lactams in 21-25% yield after 24 h, but in high optical purity. The isolated yield increases with reaction time, but at the expense of optical yield. Another attractive feature of the carbonylation reaction is that the recovered aziridine can also be obtained in high optical purity (Table I).

Much needs to be learned concerning the reasons for the exceptional chiral discrimination exhibited by the [1,5-CODRhCl]$_2$/menthol system. Nevertheless, these results show that one can attain high degrees of asymmetric induction in a ring expansion-carbonylation reaction and indicate considerable potential of the process, both as a chiral route to β-lactams as well as for the resolution of aziridines.

Experimental Section

General. Melting point determinations were made on a Fisher-Johns apparatus. Elemental analyses were carried out by MHW Laboratories, Phoenix, Arizona, and by Guelph Chemical Laboratories, Guelph, Ontario.

Infrared spectra were recorded on a Perkin-Elmer 783 or Nicolet MX-1 FT spectrometer. Nuclear magnetic resonance spectra were recorded on Varian XL-300 or EM-360 spectrometers, and a VG7070E spectrometer was used for mass spectral determinations. A Perkin-Elmer 241 polarimeter was used for the measurement of rotations. Chiralplate, which was purchased from Mackerey-Nagel (Duren), consists of a plate coated with a reversed phase silica gel and impregnated with a chiral selector (a proline derivative) and copper(II) ions. All organic solvents were dried and distilled by standard methods prior to use. The metal catalysts and added chiral ligands were commercial materials. The aziridines, **1**, were prepared from the corresponding epoxides following the procedure of Okada and co-workers.[15]

(17) Kagan, H. B. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, pp 1-39.

General Procedure for the [Rh(CO)$_2$Cl]$_2$-Catalyzed Carbonylation of 1. In a 50-mL autoclave was placed 5.71 mmol of **1**, 0.110 g (0.28 mmol) of [Rh(CO)$_2$Cl]$_2$, and 30 mL of freshly distilled benzene. The autoclave was purged twice with nitrogen and then charged with 20 atm of carbon monoxide. The mixture was stirred at 90 °C for 2 days, cooled to room temperature, and filtered through Celite, and the filtrate was concentrated by rotary evaporation. Analytically pure β-lactam (**2**) was isolated by chromatography of the resulting oil on a silica gel column or by preparative thin-layer chromatography, using 10:1 hexane-ethyl acetate as the eluant or developer, respectively. The NMR and mass spectral data for **2** are listed in Table I. Yield and analytical data for **2** are as follows. **2** (R = Ph; R' = C(CH$_3$)$_3$) 99% yield. Anal. Calcd for C$_{13}$H$_{17}$NO: C, 76.81; H, 8.43; N, 6.89. Found: C, 77.08; H, 8.44; N, 6.95. **2** (R = Ph; R' = 1-adamantyl) 97%. Anal. Calcd for C$_{19}$H$_{23}$NO: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.22; H, 8.27; N, 4.91. **2** (R = *p*-PhC$_6$H$_4$; R' = C(CH$_3$)$_3$) 99%. Anal. Calcd for C$_{19}$H$_{21}$NO: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.62; H, 7.58; N, 5.33. **2** (R = *p*-PhC$_6$H$_4$; R' = 1-adamantyl) 100%. Anal. Calcd for C$_{25}$H$_{27}$NO: C, 83.99; H, 7.61; N, 3.92. Found: C, 84.11; H, 7.84; N, 3.88. **2** (R = *p*-BrC$_6$H$_4$; R' = C(CH$_3$)$_3$) 97%. Anal. Calcd for C$_{13}$H$_{16}$BrNO: C, 55.33; H, 5.72; N, 4.96. Found: C, 55.08; H, 5.77; N, 5.01.

cis-1-Isopropyl-3-methyl-2-phenylaziridine (**7**). This compound was prepared from propiophenone by using known methodology: (i) propiophenone was reacted with isopropylamine and a catalytic amount of titanium tetrachloride[13a] affording the Schiff base PhC(C$_2$H$_5$)=NCH(CH$_3$)$_2$ in 76% yield, bp 115-119 °C (10 (mmHg)); (ii) treatment of the latter with *N*-chlorosuccinimide in carbon tetrachloride[13b] gave PhC-(CCl$_2$CH$_3$)=NCH(CH$_3$)$_2$ as an oil in quantitative yield; (c) reductive cyclization of the α,α-dichloroimine with LiAlH$_4$ in ether[13c] gave **7** in 68% yield, bp 54-56 °C (0.4 (mmHg)). Anal. Calcd for C$_{12}$H$_{17}$N: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.14; H, 9.69; N, 8.01.

Carbonylation of 7. A mixture of 0.80 g (4.57 mmol) of **7**, 0.088 g (0.22 mmol) of [Rh(CO$_2$Cl]$_2$, and 30 mL of benzene was reacted in exactly the same manner as described for **1**. Workup by preparative thin-layer chromatography with 10/1 hexane-ethyl acetate as the developer afforded *cis*-β-lactam **8** in 81% yield: IR (neat) ν_{CO} 1740 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.90 (d, 3 H, CH$_3$), 1.15 (d, 6 H, (CH$_3$)$_2$CH), 1.62 (m, 1 H, (CH$_3$)$_2$CH), 3.42 (dq, 1 H, CHCH$_3$), 4.03 (d, 1 H, J_{H3-H4} = 6.0 Hz, PhCH), 7.20 (s, 5 H, Ph); MS (*m/e*) 203 [M]$^+$, 175 [M-CO]$^+$. Anal. Calcd for C$_{13}$H$_{17}$NO: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.82; H, 8.47; N, 6.92.

(S)-1-*tert*-Butyl-2-phenylaziridine (9, R = C(CH$_3$)$_3$). (a) Conversion of (R)-Phenyloxirane to (R)-1-Phenyl-2-(*tert*-butylamino)-1-ethanol. A mixture of 10 mL (87.4 mmol) of (R)-phenyloxirane (Fluka) and 37.2 mL (350 mmol) of *tert*-butylamine was stirred in an autoclave for 60 h at 95 °C. After evaporation of excess *tert*-butylamine, the residual solid was crystallized from hexane to give 12.9 g (77%) of the white amino alcohol, mp 85-86 °C; [α]^{23}$_D$ -78.8 (c 1.00, CHCl$_3$); IR (CHCl$_3$) $\nu_{OH,NH}$ 3600, 3400-3300 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.11 (s, 9 H, C(CH$_3$)$_3$), 2.70 (d, 3 H, CH$_2$ and NH), 4.55 (1 H, CHOH), 7.28 (s, 5 H, Ph); MS (*m/e*) 193 [M]$^+$.

(b) Cyclization of (R)-1-Phenyl-2-(*tert*-butylamino)-1-ethanol. To an ice-cold solution of 4.42 g (16.8 mmol) of triphenylphosphine in 25 mL of acetonitrile (N$_2$ atmosphere) was added, drop-by-drop, an ice-cold solution of 2.7 g (16.8 mmol) of bromine in 10 mL of acetonitrile. To the resulting red solution was slowly added 3.25 g (16.8 mmol) of the β-amino alcohol, followed by drop-by-drop addition of 5.11 g (50.5 mmol) of distilled triethylamine in 10 mL of acetonitrile (all done at 0 °C). The reaction mixture was then stirred at ambient temperature for 20 min, triethylamine hydrobromide (7.07 g, 77%) was filtered, and the filtrate was concentrated by rotary evaporation. The residue was treated with hexane (5 × 20 mL), concentrated to 10 mL, and then filtered to remove triphenylphosphine oxide, and the filtrate was evaporated. Aziridine **9** (R = C(CH$_3$)$_3$) was obtained by distillation at 40 °C (0.5 (mmHg)): yield 58%; [α]^{23}$_D$ +129.7° (c 2.57, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 1.10 (s, 9 H, C(CH$_3$)$_3$), 1.52 (d, 1 H, J = 2 Hz), 1.90 (d, 1 H, J = 6 Hz), 2.61 (dd, 1 H, CHPh, J = 2, 6 Hz), 7.28 (s, 5 H, Ph); MS (*m/e*) 175 [M]$^+$. Anal. Calcd for C$_{12}$H$_{17}$N: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.22; H, 9.84; N, 7.84.

(R)-1-*tert*-Butyl-2-phenylaziridine (11, R = C(CH$_3$)$_3$). Aziridine **11** (R = C(CH$_3$)$_3$) was prepared by treatment of (S)-phenyloxirane (Fluka) with *tert*-butylamine, followed by reaction of the resultant amino alcohol with bromine and triphenylphosphine. Both reactions were run in an identical manner to that described for the preparation of **9** (R = C(CH$_3$)$_3$) and gave **11** (R = C(CH$_3$)$_3$) in 71% overall yield, [α]^{23}$_D$ -128° (c 4.47, CHCl$_3$).

(S)-1-Adamantyl-2-phenylaziridine (9, R = 1-Adamantyl). (a) Conversion of (R)-Phenyloxirane to (R)-1-Phenyl-2-((1-adamantyl)-amino)-1-ethanol. A mixture of 5 mL (43.7 mmol) of (R)-phenyloxirane and 6.60 g (43.7 mmol) of 1-aminoadamantane in methanol (30 mL) was

refluxed for 5 h. The cooled solution was filtered, the filtrate was evaporated, and the crude product was crystallized from hexane affording the amino alcohol in 65% yield, mp 108–110 °C; $[\alpha]^{23}_D$ –57.0° (c 1.22, CHCl₃); IR (CHCl₃) $\nu_{OH,NH}$ 3600, 3400–3300 cm⁻¹; ¹H NMR (CDCl₃) δ 1.62–2.03 (m, 15 H, adamantyl protons), 2.40–2.81 (m, 4 H, CH₂, NH, OH), 4.52 (1 H, CHOH), 7.25 (s, 5 H, Ph); MS (m/e) 271 [M]⁺.

(b) Cyclization of (R)-1-Phenyl-2-((1-adamantyl)amino)-1-ethanol. The reaction was effected in the same manner as that described for the preparation of **9** (R = C(CH₃)₃) with the following modification of the workup procedure: instead of distilling the product, it was crystallized from ether/ethanol affording **9** (R = 1-adamantyl), mp 161–162 °C, in 94% yield. $[\alpha]^{23}_D$ +108.9° (c 4.32, CHCl₃); H NMR (CDCl₃) δ 1.51–2.22 (m, 17 H, adamantyl and CH₂), 2.72 (dd, 1 H, CHPh), 7.14 (s, 5 H, Ph); MS (m/e) 253 [M]⁺. Anal. Calcd for C₁₈H₂₃N: C, 85.33; H, 9.13; N, 5.53. Found: C, 85.20; H, 9.27; N, 5.51.

(R)-1-Adamantyl-2-phenylaziridine (11, R = 1-Adamantyl). Aziridine **11** (R = C(CH₃)₃) was prepared by treatment of (S)-phenyloxirane with 1-aminoadamantane, followed by reaction of the formed amino alcohol with bromine and triphenylphosphine. The two-step sequence, identical with that described for the preparation of **9** (R = 1-adamantyl) from (R)-phenyloxirane, afforded **11** (R = 1-adamantyl) in 66% overall yield, $[\alpha]^{23}_D$ –109.2° (c 4.56, CHCl₃). Anal. Calcd for C₁₈H₂₃N: C, 85.33; H, 9.13; N, 5.53. Found: C, 85.28; H, 9.07; N, 5.62.

Carbonylation of (S)-1-tert-Butyl-2-phenylaziridine (9, R = C(CH₃)₃). The reaction was effected in the same manner as that described for **1** (R = C(CH₃)₃) [i.e., using 1.00 g (5.71 mmol) of **9** (R = C(CH₃)₃) and 0.11 g (0.28 mmol) of (Rh(CO)₂Cl)₂]. Workup with preparative thin-layer chromatography (10/1 hexane–ethyl acetate) gave 93% of pure (S)-1-*tert*-butyl-3-phenylazetidin-2-one (**10** (R = C(CH₃)₃)); $[\alpha]^{23}_D$ –40.5° (c 1.67, CHCl₃). None of the R-enantiomer was detected by the use of Chiralplate. The IR, NMR, and mass spectral results are in accord with data obtained for the racemate (see Table I). Anal. Calcd for C₁₃H₁₇NO: C, 76.81; H, 8.43; N, 6.89. Found: C, 77.20; H, 8.47; N, 7.02.

Carbonylation of (R)-1-tert-Butyl-2-phenylaziridine (11, R = C(CH₃)₃). Reaction execution and workup, as described for **9** (R = C(CH₃)₃), afforded 98% pure (R)-1-*tert*-butyl-3-phenylazetidin-2-one (**12**, R = C(CH₃)₃), $[\alpha]^{23}_D$ +41.0 (c 1.60, CHCl₃). Anal. Calcd for C₁₃H₁₇NO: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.77; H, 8.51; N, 6.92.

Carbonylation of (S)-1-Adamantyl-2-phenylaziridine (9, R = 1-Adamantyl). The reaction was run in the same manner as that described for **1** (R = 1-adamantyl) [i.e., using 0.40 g (1.58 mmol) of **9** (R = 1-adamantyl) and 0.028 g (0.07 mmol) of [Rh(CO)₂Cl]₂ in 25 mL of C₆H₆]. Workup by preparative thin-layer chromatography (10/1 hexane–ethyl acetate) gave 89% pure (S)-1-adamantyl-3-phenylazetidin-2-one (**10**, R = 1-adamantyl), $[\alpha]^{23}_D$ –14.8 (c 0.30, CHCl₃); $[\alpha]^{23}_D$ –15.0° (c 1.60, CHCl₃). The spectral data were in good agreement with results obtained for **2** (R = Ph; R′ = 1-adamantyl) (Table I). Anal. Calcd for

C₁₉H₂₃NO: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.49; H, 8.13; N, 4.89.

Carbonylation of (R)-1-Adamantyl-2-phenylaziridine (11, R = 1-Adamantyl). The reaction, which was run and worked up in the same manner as that described for **9** (R = 1-adamantyl) gave 81% pure (R)-1-adamantyl-3-phenylazetidin-2-one (**12**, R = 1-adamantyl); $[\alpha]^{23}_D$ +15.0° (c 2.70, CHCl₃). Anal. Calcd for C₁₉H₂₃NO: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.14; H, 8.22; N, 5.17.

Asymmetric Carbonylation of 1-tert-Butyl-2-phenylaziridine. A mixture of 0.350 g (2.0 mmol) of racemic **1** (R = Ph; R′ = C(CH₃)₃), 0.937 g (6.0 mmol) of *l*-menthol, and 49.2 mg (0.1 mmol) of chloro(1,5-cyclooctadiene)rhodium(I) dimer in 15 mL of freshly distilled benzene was reacted and worked up in the same manner as that described for the reaction carried out in the absence of *l*-menthol. The optical yields of the β-lactam and the recovered aziridine were determined by specific rotation measurements, and the presence of 0.5% of one enantiomer in a mixture of the two stereoisomers could be detected by the use of Chiralplate. Note that Chiralplate is also an excellent method for the separation of the enantiomeric β-lactams with 10:1 hexane–ethyl acetate. In Table II are listed results obtained with *d*- or *l*-menthol as a function of reaction time.

Other added chiral ligands such as (S)-BINAP, β-cyclodextrin, (+)-diethyl tartrate, and (+)-DIOP could be substituted for *d*- or *l*-menthol, but with inferior results (see text).