the mesogen (100 mg) in dichloromethane (2 mL), evaporating the volatile solvent on the rotary evaporator, and then pumping on the residue under high vacuum for 1–2 h. Three portions of the resulting mixture (ca. 25 mg) were placed in tubes constructed from 7-mm Pyrex tubing which had been soaked overnight in 5% aqueous sodium hydroxide, washed repeatedly with distilled water, and oven-dried. The tubes were vacuum-sealed after three freeze–pump–melt degassing cycles. They were placed in the constant-temperature bath for 2 or 4 h (6 or 12 h for **1** + **2c** in S1544), cooled, and then opened. The contents were dissolved in dichloromethane (ca. 1 mL) and analyzed by HPLC. Product yields were determined from the HPLC peak areas (calculated by triangulation), assuming identical detector responses for each set of adducts, and are the averages of three runs each analyzed in triplicate. The isolation and identification of **3**–**6** from the reaction of **1** and **2a**–**c** in benzene solution and analytical procedures for their separation and detection have been reported elsewhere.[22]

Acknowledgment. We thank E. Merck (Darmstadt) for the generous gifts of S1409 and S1544. Financial support of this work was provided by the Natural Sciences and Engineering Council of Canada and the Research Corporation.

Registry No. 1, 1059-86-5; **2a**, 941-69-5; **2b**, 58609-75-9; **2c**, 141171-23-5; **3a**, 141197-50-4; **3b**, 112575-19-6; **3c**, 141171-24-6; **4a**, 141171-25-7; **4b**, 112575-18-5; **4c**, 141171-26-8; **5a**, 141171-27-9; **5b**, 112575-20-9; **5c**, 141171-28-0; **6a**, 141171-29-1; **6b**, 141269-54-7; **6c**, 141171-30-4; CnP, 141269-55-8; CnB, 141269-56-9; CnT, 141269-57-0; ChCB, 22575-27-5; S1409, 79709-85-6; S1544, 80955-71-1.

Synthesis of Azapenams, Diazepinones, and Dioxocyclams via the Photolytic Reaction of Chromium Alkoxycarbene Complexes with Imidazolines

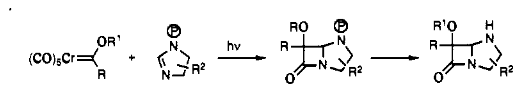
Claudia Betschart and Louis S. Hegedus*

Contribution from the Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523. *Received December 27, 1991*

Abstract: Photolysis of chromium alkoxycarbene complexes with *N*-(benzyloxycarbonyl)imidazolines produced protected azapenams. Hydrogenolysis gave free azapenams which were stable, one of which was characterized by X-ray crystallography. Hydrogenolysis under acidic conditions produced hexahydro-1,4-diazepin-5-ones. Treatment of the free azapenams with camphorsulfonic acid produced unsaturated 14-membered tetraazamacrocycles in excellent yield. These were reduced to dioxocyclams.

Introduction

The photolytic reaction of chromium carbene complexes with imines to produce β-lactams has been developed[1] and extensively studied in these laboratories,[2] and a wide range of β-lactam types has been synthesized by this methodology. These include monocyclic β-lactams,[1,3] cephams,[4] oxacephams,[4] carbacephams,[5,6] penams,[5] carbapenams,[5] and (in low yield) oxapenams,[4] many in both the racemic and optically active[7] forms. Noticably absent from this list are azapenams, a relatively rare class of compounds. Although azapen*ems*, having an sp^2 center in the 5-membered ring, have been synthesized by a variety of methods,[8-14] azapen*ams*, from the reaction of azidoketene with imidazolines, have only been detected as intermediates, but not isolated.[15] Because of the mild reaction conditions (visible light, almost any solvent, no other reagents) and the broad scope of the photolytic reaction of chromium carbene complexes with imines to produce β-lactams, azapenams were chosen as suitable targets to test the limits of this methodology (eq 1). Below, the results of studies addressing this issue are reported.


(Eq. 1)

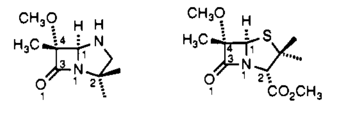
Results and Discussion

Synthesis of Protected Imidazolines. Imidazolines are available by a number of routes,[16] but the reaction of a 1,2-diamine with *tert*-butyl isocyanide with silver cyanide as catalyst[17] proved most

(1) Hegedus, L. S.; McGuire, M. A.; Schultze, L. M.; Yijun, C.; Anderson, O. P. *J. Am. Chem. Soc.* **1984**, *106*, 2680.
(2) (a) Hegedus, L. S.; deWeck, G.; D'Andrea, S. *J. Am. Chem. Soc.* **1988**, *110*, 2122. (b) Hegedus, L. S.; Montgomery, J.; Narukawa, Y.; Snustad, D. C. *J. Am. Chem. Soc.* **1991**, *113*, 5784.
(3) Hegedus, L. S.; D'Andrea, S. *J. Org. Chem.* **1988**, *53*, 3113.
(4) Hegedus, L. S.; Schultze, L. M.; Toro, J.; Yijun, C. *Tetrahedron* **1985**, *41*, 5833.
(5) Borel, C.; Hegedus, L. S.; Krebs, J.; Satoh, Y. *J. Am. Chem. Soc.* **1987**, *109*, 1101.
(6) Narukawa, Y.; Juneau, K.; Snustad, D. C.; Miller, D. B.; Hegedus, L. S. *J. Org. Chem.*, submitted for publication.
(7) Hegedus, L. S.; Imwinkelried, R.; Alarid-Sargent, M.; Dvorak, D.; Satoh, Y. *J. Am. Chem. Soc.* **1990**, *112*, 1109.
(8) Nagakura, I. *Heterocycles* **1981**, *16*, 1495.
(9) Davies, D.; Pearson, M. J. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2539.
(10) Johnson, G.; Rees, P. M.; Ross, B. C. *J. Chem. Soc., Chem. Commun.* **1984**, 970.
(11) (a) Alper, H.; Perera, Ch. P.; Ahmed, F. R. *J. Am. Chem. Soc.* **1981**, *103*, 1289. (b) Alper, H.; Perera, C. *Organometallics* **1982**, *1*, 70.
(12) Johnson, G.; Rosse, B. C. *J. Chem. Soc., Chem. Commun.* **1981**, 1269.
(13) Shibata, T.; Sugimura, Y.; Sato, S.; Kawazoe, K. *Heterocycles* **1985**, *23*, 3069.
(14) Pacansky, J.; Chang, J. S.; Brown, D. W.; Schwarz, W. *J. Org. Chem.* **1982**, *47*, 2233.
(15) Bose, A. K.; Kapin, J. E.; Fakey, J. L.; Mankas, M. S. *J. Org. Chem.* **1973**, *38*, 3437.
(16) (a) Bieräugel, H.; Plemp, R.; Hiemstra, H. C.; Pandit, U. K. *Tetrahedron* **1983**, *39*, 3971. (b) Grundmann, C.; Krentzberger, A. *J. Am. Chem. Soc.* **1955**, *77*, 6559. (c) Jentzsch, W.; Seefelder, M. *Chem. Ber.* **1965**, *98*, 1342.
(17) Ito, Y.; Inubushi, Y.; Zenbayashi, M.; Tomita, S.; Saegusa, T. *J. Am. Chem. Soc.* **1973**, *95*, 4447.

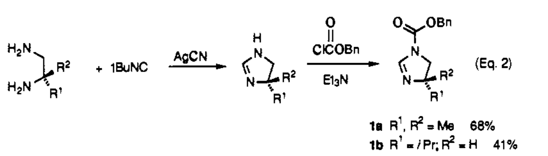
0002-7863/92/1514-5010$03.00/0

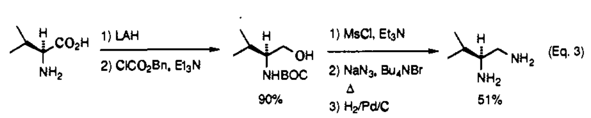
Table I. Selected Structural Features of Azapanam **4aa**



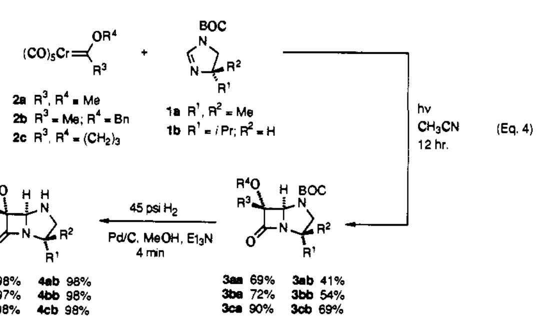
	4aa		
Bond Lengths, Å			
N_1–C_3	1.394 (6)		1.375 (4)
N_1–C_1	1.473 (6)		1.447 (4)
C_3–O_1	1.210 (6)		1.210 (4)
C_3–C_4	1.550 (7)		1.546 (5)
C_1–C_4	1.591 (8)		1.579 (4)
Bond Angles, °			
$C_3N_1C_2$	129.6 (4)		131.2 (3)
$C_1N_1C_2$	110.2 (4)		117.2 (3)
$C_1N_1C_3$	94.1 (4)		95.3 (3)
Σ	333.3	(Pyramidal = 328.5)	343.7
ν_{CO}	1745cm^{-1}		1780cm^{-1}

useful. Protection of the free NH group was deemed essential to prevent its reaction with the photogenerated ketene, so the easily removed BOC (benzyloxycarbonyl) group was appended directly to the crude imidazoline. Two N-protected imidazolines were prepared by this method: the achiral 4,4-dimethylimidazoline **1a** and the optically active 4-(*S*)-isopropylimidazoline **1b** (eq 2). These compounds existed as mixtures of two rotamers about the amide bond. The requisite optically active diamine for **1b** was synthesized from (*S*)-valine by conventional, although not previously reported, methodology (eq 3).





Synthesis of Azapenams. Photolysis of chromium alkoxycarbene complexes **2a–c** with imidazolines **1a,b** produced protected azapenams **3aa–cb** in fair to excellent yields (eq 4). In all cases only a single diastereoisomer was detected in the crude reaction mixtures although these were a mixture of two rotamers about the BOC amide bond. Removal of the BOC group was fast and efficient, giving free azapenams **4aa–cb** in virtually quantitative yield. From achiral imidazoline **1a**, single racemic diastereoisomers were obtained that had the relative stereochemistry shown. From optically active imidazoline **1b**, single, optically active diastereoisomers were obtained. Their absolute stereochemistry was assigned by analogy to closely related thiazoline systems[1,18] and confirmed by an X-ray crystal structure of a subsequent product.



Because azapenams of this type have, to our knowledge, not been previously structurally characterized, an X-ray crystallographic structure determination on compound **4aa** was carried out. Pertinent structural features, along with those of a closely

(18) Thompson, D. K.; Suzuki, N.; Hegedus, L. S.; Satoh, Y. *J. Org. Chem.*, in press.

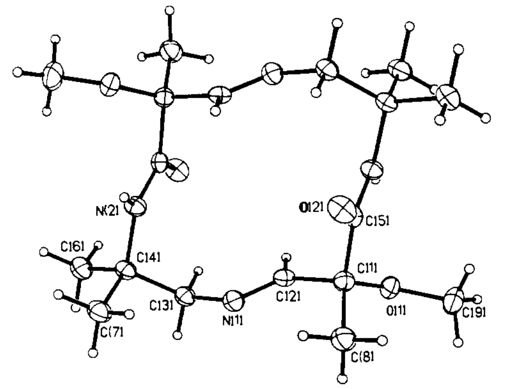
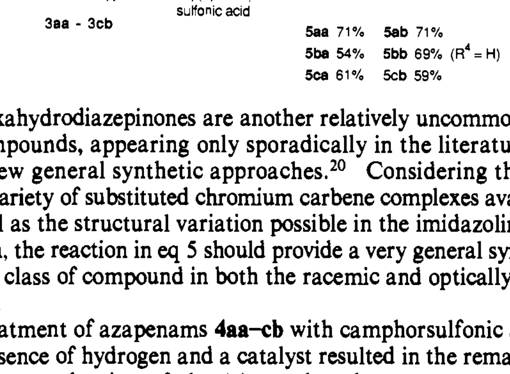


Figure 1. Compound **6aa**.

related penam system,[1] are collected in Table I. Full structural details will be reported elsewhere. Of note are the long amide C–N bond (N_1C_3), the long N_1C_1 bond, and the identical carbonyl C–O bond length, notwithstanding the large difference in CO stretching frequency in the infrared spectrum. From the sum of the angles about the lactam nitrogen (Σ), the azapenam is considerably more pyramidal[19] than the penam.

When the deprotection of BOC-azapenams **3aa–cb** was carried out under acidic conditions, the reaction took a completely different course, producing hexahydrodiazepinones **5aa–cb** in fair to good yields (eq 5). This reaction is likely to proceed by acid-catalyzed cleavage of the strained β-lactam ring of the deprotected azapenam, followed by hydrogenation of the resulting 7-membered imine (see below for details). Most characteristic for this transformation was the change in γ_{CO} from ~1745 cm^{-1} for the azapenam to ~1640 cm^{-1} for the caprolactam. Since the chiral centers were not involved in this transformation, no change in relative or absolute stereochemistry was expected, and single racemic (**5aa–ca**) or optically active (**5ab–cb**) diastereoisomers were obtained.



Hexahydrodiazepinones are another relatively uncommon class of compounds, appearing only sporadically in the literature and with few general synthetic approaches.[20] Considering the very wide variety of substituted chromium carbene complexes available, as well as the structural variation possible in the imidazoline ring system, the reaction in eq 5 should provide a very general synthesis of this class of compound in both the racemic and optically active forms.

Treatment of azapenams **4aa–cb** with camphorsulfonic acid in the absence of hydrogen and a catalyst resulted in the remarkably efficient production of the 14-membered tetraazamacrocyclic compounds **6aa–cb**, which were easily reduced to dioxocyclams **7aa–cb** (eqs 6 and 7). There are a number of extraordinary features of this process. The first feature is its efficiency. In spite of the number of bonds being broken and formed, the fact that some kind of intermolecular dimerization must occur, and the fact

(19) Attempts have been made to correlate biological activity with the degree of pyramidalization of the amide nitrogen: Glidewell, C.; Mollison, G. S. M. *J. Mol. Struct.* **1981**, *72*, 203.

(20) For examples of syntheses of specific hexahydrodiazepinones, see: (a) Crombie, L.; Jones, R. C. F.; Haigh, D. *Tetrahedron Lett.* **1986**, *27*, 5151. (b) Crombie, L.; Jones, R. C. F.; Osborne, S.; Hat-Zin, A. R. *J. Chem. Soc., Chem. Commun.* **1983**, 959. (c) Ueda, T.; Kato, Y.; Sakakibara, J.; Murata, M. *Chem. Pharm. Bull.* **1988**, *36*, 2902. (d) Takechi, H.; Machida, M.; Kanaoka, Y. *Liebigs Ann. Chem.* **1986**, 859. (e) Pinnen, F.; Zanotti, G.; Lucente, G. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1311. (f) Tatee, T.; Narita, K.; Kurashige, S.; Ito, S.; Miyazaki, H.; Yamanaka, H.; Mizugaki, M.; Sakamoto, T.; Fukuda, H. *Chem. Pharm. Bull.* **1987**, *35*, 3676.

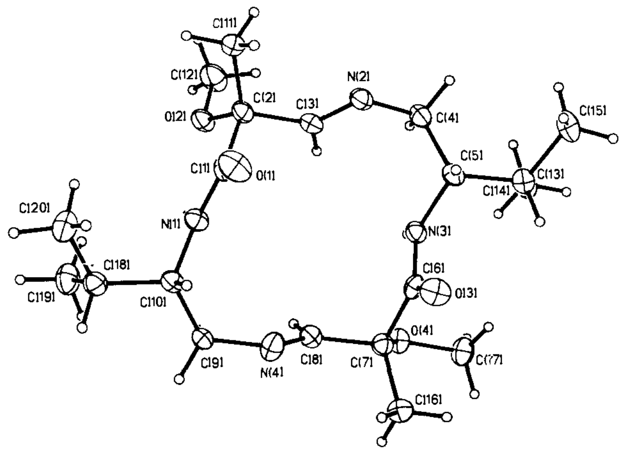
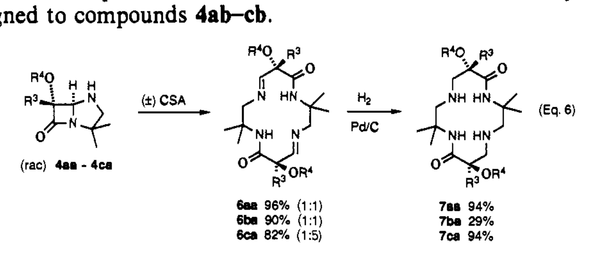
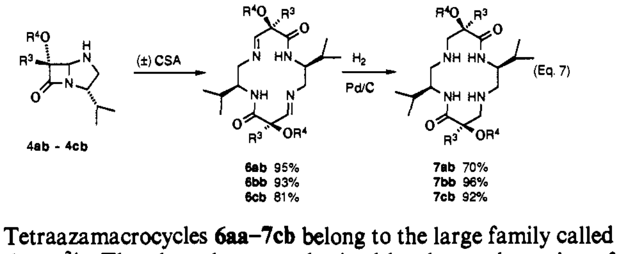


Figure 2. Compound **6ab**.

that a 14-membered ring is formed directly from a [3.2.0] bicyclic system, virtually quantitative yields are obtained. For the racemic compounds **4aa–ca**, macrocycles **6aa–ca** are exclusively centrosymmetric, such that dimerization occurs only between complementary (*R*) and (*S*) enantiomers, with *no* (*S*,*S*) or (*R*,*R*) combinations being formed. This was confirmed by X-ray crystallography (Figure 1). As formed in solution, **6aa–ca** exist as two distinct conformers, as evidenced by doubling of all peaks in the ^{1}H and ^{13}C NMR spectra. Crystallization leads to a single conformation, which can reequilibrate with the other one in solution under acid catalysis. Crystallization of this mixture again gave quantitative recovery of a single conformer. With optically active compounds **6ab–cb**, a single, optically active compound was present both in the solid state and in solution, and no evidence for other conformers was obtained. The X-ray crystal structure (Figure 2) confirms the structure and absolute stereochemistry of these compounds, as well as the absolute stereochemistry assigned to compounds **4ab–cb**.





Tetraazamacrocycles **6aa–7cb** belong to the large family called cyclams.[21] They have been synthesized by the condensation of ethylenediamine with ketones[22] and the reaction of tetraamines with dihalides,[23] ditosylates,[24] or diesters.[25] They have been synthesized with pendent functional groups,[26] with sulfur replacing some of the nitrogen groups,[27] with fluorine on the periphery,[28] and recently with optically active centers on the periphery (in 8–12% yield).[29] Cyclams are particularly effective in coordinating first row transition metals[30] and stabilizing unusual oxidation states and geometries (e.g., copper(0),[31] copper(III),[32] nickel(III),[33] and monovalent palladium(II)[34]), although other metals such as aluminum,[35] zinc, cadmium,[36] and technicium[37] also form complexes with these ligands. Metal cyclam complexes catalyze a number of classes of reactions,[38] including the epoxidation of olefins[39] and the oxidative cleavage of DNA.[40] Given this very wide variety of chromium carbene complexes available,[41] as well as the ease of synthesis of substituted imidazolines, the reactions reported in eqs 6 and 7 should make a very wide range of functionalized racemic and optically active dioxocyclams readily available in good yield for complexation and catalysis studies.

A reasonable hypothesis for the facile conversion of azapenams **4aa–cb** to dioxocyclams **6aa–cb** under acidic conditions is shown in eq 8. The ring strain of the bicyclo[3.2.0] system along with the pyramidalized (and thus more basic) amide nitrogen could result in a facile acid-catalyzed cleavage of the β-lactam C–N bond. If this occurred without rearrangement, a highly strained *trans*-cycloheptylimine **8** would be formed.[42] Under reducing conditions, conversion to hexahydrodiazepinones **5aa–cb** results. In the absence of hydrogen, this strained imine could undergo a head-to-tail cyclodimerization (**9**) followed by a cycloreversion to generate the observed 14-membered ring system. In the racemic series (**4aa–ca**), the dimerization *must* occur *only* between (*R*) and (*S*) enantiomers to account for exclusive formation of the centrosymmetric macrocycles **6aa–ca**.[43] Experimental confor-

(21) For reviews, see: (a) Busch, D. H. *Acc. Chem. Res.* **1978**, *11*, 392. (b) Ito, T.; Kato, M.; Yamashita, M.; Ito, H. *J. Coord. Chem.* **1986**, *15*, 29. (c) Bhallacharya, S.; Mukheijee, R.; Chakraworthy, A. *Inorg. Chem.* **1986**, *25*, 3448.

(22) (a) Caulkett, P. W. R.; Greatbanks, D.; Turner, R. W.; Jarvis, J. A. J. *Heterocycles* **1978**, *9*, 1003. (b) Ferguson, G.; Roberts, P. J.; Lloyd, D.; Hideg, K.; Hay, R. W.; Pipiani, D. P. *J. Chem. Res.* **1978**, 314. (c) Hankovszky, O. H.; Hideg, K.; Lloyd, D. C.; McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1345. (d) Miyamura, K.; Kohzuki, M.; Narushima, R.; Sabwi, M.; Gohshi, Y.; Tsuboyama, S.; Tsuboyama, K.; Sakurai, T. *J. Chem. Soc., Dalton Trans.* **1987**, 3093.

(23) Kobiro, K.; Nakayama, A.; Hiro, T.; Swiva, M.; Kakiuchi, K.; Toke, Y.; Odaira, Y. *Chem. Lett.* **1990**, 1979.

(24) (a) Stetter, H.; Frank, W.; Mertens, R. *Tetrahedron* **1981**, *37*, 1967. (b) Benabdallah, T.; Guglielmetti, R. *Helv. Chim. Acta* **1988**, *71*, 602.

(25) Tabushi, I.; Taniguchi, Y.; Kato, H. *Tetrahedron Lett.* **1977**, *18*, 1049.

(26) (a) Kimura, E.; Koike, T.; Uenishi, K.; Hediger, M.; Kuramoto, M.; Joko, S.; Arai, Y.; Kodama, M.; Iitaka, Y. *Inorg. Chem.* **1987**, *26*, 2975. (b) Kimura, E. *Pure Appl. Chem.* **1989**, *61*, 823. (c) Kimura, E.; Wada, S.; Shinonoya, M.; Takahashi, T.; Iitaka, Y. *J. Chem. Soc., Chem. Commun.* **1990**, 397.

(27) Kimura, E.; Kurogi, Y.; Tojo, T.; Shionoya, M.; Shiro, M. *J. Am. Chem. Soc.* **1991**, *113*, 4857.

(28) Shionoya, M.; Kimura, E.; Iitaka, Y. *J. Am. Chem. Soc.* **1990**, *112*, 9237.

(29) Wagler, T. R.; Fang, Y.; Burrows, C. J. *J. Org. Chem.* **1989**, *54*, 1584.

(30) For an old review, see: Curtis, N. F. *Coord. Chem. Rev.* **1968**, *3*, 3.

(31) Bond, A. M.; Khalifa, A. *Inorg. Chem.* **1987**, *26*, 413.

(32) (a) Buttafava, A.; Fabbrizzi, L.; Perotti, A.; Poggi, A.; Seghi, B. *Inorg. Chem.* **1984**, *23*, 3917. (b) Fabbrizzi, L.; Forlini, F.; Perotti, A.; Seghi, B. *Inorg. Chem.* **1984**, *23*, 807.

(33) Calligaris, M.; Carngo, O.; Crippa, G.; DeSantis, G.; DiCasa, M.; Fabbrizzi, L.; Poggi, A.; Seghi, B. *Inorg. Chem.* **1990**, *29*, 2964.

(34) Blake, A. J.; Gould, R. O.; Hyde, T. I.; Schröder, M. *J. Chem. Soc., Chem. Commun.* **1987**, 431.

(35) Robinson, G. H.; Sangokoya, S. A.; Pennington, W. T.; Self, M. F. *J. Coord. Chem.* **1989**, *19*, 287.

(36) Kimura, E.; Koike, T.; Shiota, T.; Iitaka, Y. *Inorg. Chem.* **1990**, *29*, 4621.

(37) Marchi, A.; Rossi, R.; Magon, L.; Duatti, A.; Casellato, U.; Graziani, R.; Vidal, M.; Riche, F. *J. Chem. Soc., Dalton Trans.* **1990**, 1935.

(38) Yatsimirskii, K. B. *Russ. Chem. Rev.* **1990**, *59*, 1960.

(39) (a) Koola, J. D.; Kochi, J. K. *Inorg. Chem.* **1987**, *26*, 908. (b) Kinneary, J. F.; Alkert, J. S.; Burrows, C. J. *J. Am. Chem. Soc.* **1988**, *110*, 6124. (c) Nam, W.; Ho, R.; Valentine, J. S. *J. Am. Chem. Soc.* **1991**, *113*, 7052.

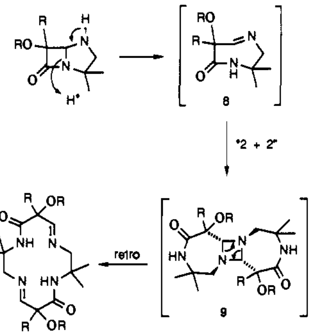
(40) Chen, X.; Rokita, S. E.; Burrows, C. J. *J. Am. Chem. Soc.* **1991**, *113*, 5884.

(41) Seyferth, D., Ed. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1983.

(42) We thank Professor Jules Rebec for suggesting that the imine formed should be trans.

(43) The reason for this stereoselective dimerization is not clear, but does find precedent in the exclusive production of meso cyclams from the condensation of 1,2-propanediamine with acetone. See: Bembi, R.; Sondhi, S. M.; Singh, A. K.; Jhanji, N. K.; Roy, T. G.; Lown, J. W.; Ball, R. G. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3701.

mation of this sequence of steps must await further experimental results.



(Eq. 8)

Experimental Section

General. If not otherwise stated, all NMR spectra were recorded in $CDCl_3$. Chemical shifts are given in δ ppm relative to Me_4Si (δ 0, ^1H) or $CDCl_3$ (δ 77, ^{13}C). Optical rotations were measured on a Perkin-Elmer 24 polarimeter at 589 nm (sodium D line) in a 1.0-dm cell with a total volume of 1 mL. Specific rotations ($[\alpha]_D$) are reported in degrees per decimeter at room temperature, and the concentration (c) is given in grams per 100 mL in the specified solvent.

The following chemicals were prepared according to literature procedures: (*S*)-valinol[44] (in analogy to (*S*)-phenylglycinol), pentacarbonyl[(methoxy)(methyl)carbene]chromium(0) (**19**),[45] and pentacarbonyl[(benzyloxy)(methyl)carbene]chromium(0) (**2b**).[46]

Pentacarbonyl[(tetrahydrofuran-2-yl)carbene]chromium(0) (2c). Graphite (6.49 g, 540 mmol) was heated under vacuum at 150 °C for 15 min. After it was cooled to room temperature, 2.35 g (60 mmol) of potassium in small pieces was added. The mixture was heated under argon at 150–190 °C for 1 h to obtain the potassium laminate as a solid of bronze color. After the laminate was cooled to room temperature, 100 mL of THF was added and the suspension was cooled in a dry ice/acetone bath. Chromium hexacarbonyl (6.60 g, 30 mmol) was added, and the suspension was stirred for 1 h at −70 °C followed by 50 min at 0 °C. The greenish gray suspension was cooled again to −70 °C, and 3.36 mL (4.23 g, 30 mmol) of 4-chlorobutyryl chloride was added dropwise via syringe. After 10 min the reaction was allowed to warm to room temperature. After 1 h, silica gel was added, and the solvents were evaporated on a rotary evaporator. The residue was put on a short column of silica gel. Elution with 3/1 hexane/EtOAc gave, after evaporation of the solvents, the crude product which was recrystallized from hexane to give 4.75 g (18.1 mmol, 60%) of **2c** as yellow crystals (physical data in accordance with literature[46]): ^1H NMR δ 4.91 (t, J = 7.7 Hz, 2 H, OCH_2), 3.63 (t, J = 7.9 Hz, 2 H, $H_2C(3)$), 1.92 (quin, J = 7.8 Hz, 2 H, $H_2C(4)$).

4,4-Dimethyl-Δ^2-imidazoline. 2-Methyl-1,2-propanediamine (5.0 mL, 47.7 mmol), *tert*-butyl isocyanide (6.5 mL, 57 mmol), and silver cyanide (350 mg, 2.6 mmol) were heated in a sealed tube at 85–90 °C. After 6 h, argon was bubbled through the reaction mixture, which was then kept at 85–90 °C overnight. The product was distilled with a pump vacuum at about 60 °C to yield 4.17 g of a colorless oil (42.5 mmol, 89%): ^1H NMR δ 6.94 (s, 1 H, CH=N), 4.39 (br s, 1 H, NH), 3.28 (s, 2 H, CH_2), 1.25 (s, 6 H, CH_3); ^{13}C NMR δ 152.1 (C=N), 76.4 (CMe_2), 60.9 (CH_2), 28.2 (CH_3); IR (neat) ν 1600 (C=N) cm^{-1}; MS 98 (M^+). This material was converted to **1a** without further purification or characterization.

1-(Benzyloxycarbonyl)-4,4-dimethyl-Δ^2-imidazoline (1a). The imidazoline (1.37 g, 14 mmol) and 2.09 mL (15 mmol) of triethylamine were dissolved in methylene chloride, and 2.07 mL (14.5 mmol) of benzyl chloroformate was added (exothermic reaction). After 1.5 h at room temperature, the mixture was washed with 5% aqueous $NaHCO_3$ and water and dried over $MgSO_4$, and the solvent was evaporated to yield an oil which was chromatographed on silica gel (1/1 ethyl acetate/hexane) to give 2.49 g (10.7 mmol, 76%) of a colorless oil: ^1H NMR (two rotamers, a/b $\approx$ 10/1) δ 7.48(b)/7.40(a) (s, 1 H, CH=N), 7.37–7.28 (m, 5 H, ArH), 5.20(a)/5.19(b) (s, 2 H, CH_2Ph), 3.72(b)/3.40(a) (s, 2 H, CH_2N), 1.44(b)/1.28(a) (s, 6 H, CH_3); ^{13}C NMR (50 °C, at room temperature the signals marked * appeared as two broad signals) δ 151.2* (CO), 144.9* (C=N), 135.5, 128.4, 128.3, 128.0 (Ar), 68.5* (CMe_2), 67.6 (CH_2Ph), 55.7 (CH_2N), 28.7 (CH_3); IR (neat) ν 1721 (CO), 1621 (C=N) cm^{-1}. Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 66.89; H, 7.01; N, 12.02.

(*S*)-*N*-(Benzyloxycarbonyl)valinol. (*S*)-Valinol (10.4 g, 100.8 mmol) was dissolved in 70 mL of methylene chloride and 150 mL of a 5% aqueous solution of $NaHCO_3$. Benzyl chloroformate (14.4 mL, 100.8 mmol) was added (exothermic reaction), and the mixture was stirred for 2 h at room temperature. The layers were separated, and the water layer was extracted with methylene chloride. The combined organic fractions were dried over $MgSO_4$, and the solvent was evaporated to give 23.7 g (99.9 mmol, 99%) of a white solid. The crude product was used for the next step. A small portion was recrystallized from hexane and a small amount of ethyl acetate to give very fine, white needles: mp 58.5–59 °C; $[\alpha]^{22}_D$ −16.9° (c = 2.0, MeOH); ^1H NMR δ 7.37–7.26 (m, 5 H, Ar), 5.14 (br s, 1 H, CONH), 5.08 (s, 2 H, $PhCH_2$), 3.66 (dd, J_1 = 11.2 Hz, J_2 = 4.0 Hz, 1 H, CH_2OH), 3.59 (dd, J_1 = 11.2 Hz, J_2 = 6.0 Hz, 1 H, CH_2OH), 3.50–3.40 (m, 1 H, CHN), 2.9 (br s, 1 H, OH), 1.83 (oct, J = 6.8 Hz, 1 H, $CHMe_2$), 0.93 (d, J = 6.8 Hz, 3 H, CH_3), 0.90 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR δ 157.1 (CO), 136.4, 128.4, 128.0 (Ar), 66.8 (CH_2Ph), 63.5 (CH_2OH), 58.5 (CHN), 29.1 ($CHMe_2$), 19.4 (CH_3), 18.4 (CH_3); IR (KBr) 1686 (CO), 1552 cm^{-1}; MS (NH_3, CI) 238 (M^+ + 1).

(*S*)-3-Methyl-2-[(benzyloxycarbonyl)amino]butyl Azide. The protected valinol from above (22.6 g, 95.2 mmol) was dissolved in 160 mL of toluene and 13.3 mL (95.2 mmol) of triethylamine. Mesyl chloride (7.4 mL, 95.2 mmol) was added (exothermic reaction), and after 10 min, a solution of 47.9 g of NaN_3 in 180 mL of water and 2.7 g of Bu_4NBr were added. The mixture was heated overnight at 80–95 °C. After the mixture was cooled to room temperature, ether was added, the layers were separated, and the organic layer was washed with phosphate buffer (pH ~5.4, 0.5 M), brine, and water and dried over $MgSO_4$. The solvents were evaporated to give 24.5 g (93.4 mmol, 98%) of a yellow oil. The azide-containing aqueous layer was treated with aqueous ceric ammonium nitrate[47] to decompose the azide for safe disposal. The crude product was used for the next step. A small portion was chromatographed on silica (hexane/EtOAc, 8/1): $[\alpha]^{22}_D$ −40.8° (c = 2.20, MeOH); ^1H NMR δ 7.3–7.2 (m, 5 H, ArH), 5.06 (s, 2 H, CH_2Ph), 4.97 (d, J = 8.9 Hz, 1 H, NH), 3.6–3.5 (m, 1 H, CHN), 3.35 (d, J = 4.9 Hz, 2 H, CH_2N_3), 1.75 (oct, J = 6.8 Hz, 1 H, $CHMe_2$), 0.89 (d, J = 6.5 Hz, 3 H, CH_3), 0.86 (d, J = 6.5 Hz, 3 H, CH_3); ^{13}C NMR δ 156.1 (CO), 136.3, 128.4, 128.0, 127.9 (Ar), 66.7 (CH_2Ph), 56.0 (CHN), 52.8 ($C-H_2N_3$), 29.6 ($CHMe_2$), 19.3 (CH_3), 18.2 (CH_3); IR (neat) ν 2100 (N_3), 1700 (CO), 1534 cm^{-1}; MS (NH_3, CI) 263 (M^+ + 1).

(*S*)-3-Methyl-1,2-butanediamine. The azide (9.60 g, 37 mmol) was hydrogenated in 140 mL of methanol at 40 psi of H_2 with 1.0 g of 10% Pd/C over 6 days. The catalyst was renewed three times in this period. The catalyst was then removed by filtration, and the solvent was evaporated. The residue was distilled by water pump vacuum at ~66 °C to give 1.92 g (18.8 mmol, 51%) of a colorless oil that crystallized on standing: $[\alpha]^{22}_D$ +19.6° (neat); ^1H NMR (methanol-d_4) δ 4.55 (s, 4 H, NH_2), 2.78–2.70 (m, 1 H, $CHNH_2$), 2.49–2.41 (m, 2 H, CH_2NH_2), 1.66 (d of hept, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 1 H, $CHMe_2$), 0.93 (d, J = 6.9 Hz, 3 H, CH_3), 0.92 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR (methanol-d_4) δ 60.0 (CHN), 46.2 (CH_2N), 32.7 ($CHMe_2$), 19.8 (CH_3), 18.4 (CH_3); IR (neat) ν 3350, 3285, 3176 (NH), 1591 cm^{-1}.

(*S*)-4-(1′-Methylethyl)-Δ^2-imidazoline. The diamine (0.76 g, 7.4 mmol), 1.5 mL (13 mmol) of *tert*-butyl isocyanide, and 55 mg (0.4 mmol) of silver cyanide were heated overnight in a sealed tube at ~85 °C. Distillation of the mixture by pump vacuum at ~66 °C gave 0.87 g of a colorless oil. Although the NMR spectrum showed that the product was not pure, this oil was used directly for the next step: ^1H NMR δ 7.02 (s, 1 H, CH=N), 4.35 (s, broad, 1 H, NH), 3.68–3.53 (m, 2 H, CHN), 3.31–3.25 (m, 1 H, CHN), 1.66 (oct, J = 6.7 Hz, 1 H, $CHMe_2$), 0.94 (d, J = 6.7 Hz, 3 H, CH_3), 0.87 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR δ 153.8 (C=N), 65.9 (CHN), 52.9 (CH_2N), 32.9 ($CHMe_2$), 18.7 (CH_3), 18.2 (CH_3).

(*S*)-1-(Benzyloxycarbonyl)-4-(1′-methylethyl)-Δ^2-imidazoline (1b). The crude imidazoline (0.869 g) was dissolved in 25 mL of tetrahydrofuran and 1.25 mL (9 mmol) of triethylamine. Benzyl chloroformate (1.14 mL, 8 mmol) was added, and the mixture was stirred for 4 h at room temperature. Aqueous $NaHCO_3$ (5%) was then added, the layers were separated, and the organic layer was washed with brine and then dried over $MgSO_4$. Evaporation of the solvent gave a yellow oil which was chromatographed on silica (hexane/EtOAc, 1/1) to give 0.75 g (3.0 mmol, 41% from diamine) of a colorless oil: $[\alpha]^{22}_D$ −96.5° (c = 3.0, CH_2Cl_2); ^1H NMR δ 7.53 (br s, 1 H, CH=N), 7.39–7.32 (m, 5 H, ArH), 5.21 (s, 2 H, CH_2Ph), 3.99 (br q, J = 8 Hz, 1 H, HC(4)), 3.67 (t, J = 10.4 Hz, 1 H, CH_2N), 3.37 (br t, J = 9 Hz, 1 H, CH_2N), 1.80

(44) Imwinkelried, R.; Hegedus, L. S. *Organometallics* **1988**, *7*, 702.
(45) Aumann, R.; Fischer, E. O. *Chem. Ber.* **1968**, *101*, 954.
(46) Hafner, A.; Hegedus, L. S.; deWeck, G.; Hawkins, B.; Dötz, K. H. *J. Am. Chem. Soc.* **1988**, *110*, 8413.
(47) Lunn, G.; Sansone, E. B. *Destruction of Hazardous Chemicals in the Laboratory*; Wiley-Interscience: New York, 1990; p 44.

(oct, J = 6.7 Hz, 1 H, CHMe$_2$), 0.97 (d, J = 6.7 Hz, 3 H, CH$_3$), 0.90 (d, J = 6.7 Hz, 3 H, CH$_3$); ^{13}C NMR (at 50 °C, at room temperature the signals marked * appeared as two broad signals) δ 151.0 (CO), 146.7* (C=N), 135.5, 128.4, 128.2, 128.0 (Ar), 73.4* (CHMe), 67.6 (CH$_2$Ph), 45.9 (CH$_2$N), 32.5 (CHMe$_2$), 18.3 (CH$_3$), 17.9 (CH$_3$); IR (neat) ν 1724 (CO), 1623 (C=N) cm^{-1}. Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.00; H, 7.22; N, 11.26.

General Procedure for the Photoreaction of Pentacarbonylchromium Carbene Complexes with Imidazolines To Form Azapenams. The chromium carbene complex (1 mmol) and the imidazoline (1 mmol) were dissolved in acetonitrile (70 mL), and the resulting dark yellow solution was irradiated in a Pyrex tube under argon (450-W Conrad-Hanovia 7825 medium-pressure mercury lamp, Pyrex well). The reaction was followed by TLC (silica, hexane/EtOAc, 1/1). After 12 h, the solvent was evaporated, and the residue was dissolved in 140 mL of a 2/1 mixture of hexane/EtOAc and exposed to air and either sunlight or 6–20-W Vitalites. The oxidation was complete when the supernatant solution was colorless and there were no signals at 2000–1800 cm^{-1} in the IR spectrum. Filtration through Celite and evaporation of the solvents gave an oil which was chromatographed on silica (hexane/EtOAc, 2/1).

(5*R,6*R**)-4-(Benzyloxycarbonyl)-6-methoxy-2,2,6-trimethyl-1,4-diazabicyclo[3.2.0]heptan-7-one (3aa).** Carbene complex **2a** and imidazoline **1a** were allowed to react according to the general procedure to give a 69% yield of product **3aa** as a mixture of two rotamers: ^{1}H NMR (two rotamers a/b ≈ 7/4) δ 7.4–7.3 (m, 5 H, ArH), 5.27–5.10 (m, 3 H, CH$_2$Ph, CH), 3.77(a) (d, J = 10.5 Hz)/3.71(b) (d, J = 10.4 Hz) (1 H, HC(3)), 3.47(b)/3.34(a) (s, 3 H, OCH$_3$), 3.14(a+b) (d, J = 10.4 Hz, HC(3)), 1.60 (s, 3 H, CH$_3$), 1.29(b)/1.19(a) (s, 3 H, C(6)CH$_3$), 1.17 (s, 3 H, CH$_3$); ^{1}H NMR (50 °C) δ 7.36–7.28 (m, 5 H, ArH), 5.20 (d, J = 12.5 Hz, 1 H, PhCH$_2$), 5.14 (d, J = 12.5 Hz, 1 H, PhCH$_2$), 5.11 (s, 1 H, CH), 3.73 (d, J = 10.4 Hz, HC(3)), 3.40 (s, 3 H, OCH$_3$), 3.13 (d, J = 10.4 Hz, HC(3)), 1.59 (s, 3 H, CH$_3$), 1.22 (s, 3 H, C(6)*C*H$_3$), 1.16 (s, 3 H, CH$_3$); ^{13}C NMR δ 173.6(b)/173.2(a) (CO lactam), 153.8(b)/153.3(a) (CO carbamate), 135.9(b)/135.7(a), 128.4, 128.2, 128.0, 127.8 (Ar), 90.4 (C$_6$), 74.3(b)/73.8(a) (C$_5$), 67.4 (CH$_2$Ph), 61.0(b)/60.5(a) (C$_2$), 60.3 (C$_3$), 53.3 (OCH$_3$), 25.7 (CH$_3$), 21.8 (CH$_3$), 13.6(a)/13.4(b) (C$_6$*C*H$_3$); ^{13}C NMR (50 °C) δ 173.2 (CO lactam), 153.6 (CO), 136.1, 128.4, 128.1, 127.9 (Ar), 90.6 (C$_6$), 74.4 (C$_5$), 67.4 (CH$_2$Ph), 60.6 (C$_2$), 60.5 (C$_3$), 53.2 (OCH$_3$), 25.8 (CH$_3$), 21.7 (CH$_3$), 13.4 (C$_6$*C*H$_3$); IR (neat) ν 1770 (CO lactam), 1713 (CO carbamate) cm^{-1}. Anal. Calcd for $C_{17}H_{22}N_2O_4$: C, 64.13; H, 6.96; N, 8.80. Found: C, 63.88; H, 6.80; N, 8.81.

(5*R,6*R**)-4-(Benzyloxycarbonyl)-6-(benzyloxy)-2,2,6-trimethyl-1,4-diazabicyclo[3.2.0]heptan-7-one (3ba).** Carbene complex **2b** and imidazoline **1a** were allowed to react according to the general procedure to give a 72% yield of product as a mixture of two rotamers: ^{1}H NMR (two rotamers a/b ≈ 2.5/1) δ 7.36–7.23 (m, 10 H, ArH), 5.28–5.11 (m, 3 H, CH$_2$Ph, CH), 4.77(b) (d, J = 11.3 Hz, 1 H, CH$_2$Ph), 4.71(b) (d, J = 11.3 Hz, 1 H, CH$_2$Ph), 4.61(a) (d, J = 11.4 Hz, 1 H, CH$_2$Ph), 4.56(a) (d, J = 11.4 Hz, 1 H, CH$_2$Ph), 3.79(a)/3.72(b) (d, J = 10.4 Hz, 1 H, HC(3)), 3.18(a+b) (d, J = 10.4 Hz, 1 H, HC(3)), 1.64(a)/1.62(b) (s, 3 H, C(2)CH$_3$), 1.40(b)/1.32(a) (s, 3 H, C(6)CH$_3$), 1.19 (s, 3 H, C-(2)CH$_3$); ^{1}H NMR (50 °C) δ 7.35–7.21 (m, 10 H, ArH), 5.20 (d, J = 12.4 Hz, 1 H, PhCH$_2$O), 5.13 (d, J = 12.4 Hz, 1 H, PhCH$_2$O), 5.15 (s, 1 H, CH), 4.63 (br s, 2 H, PhCH$_2$), 3.73 (d, J = 10.3 Hz, 1 H, HC(3)), 3.13 (d, J = 10.4 Hz, 1 H, HC(3)), 1.59 (s, 3 H, CH$_3$), 1.31 (s, 3 H, C(6)CH$_3$), 1.14 (s, 3 H, CH$_3$); ^{13}C NMR δ 173.3 (CO, lactam), 153.4 (CO), 137.6, 135.7, 128.6, 128.3, 128.0, 127.7, 127.5, 127.4 (Ar), 90.6-(b)/90.5(a) (C$_6$), 74.9(b)/74.5(a) (C$_5$), 68.1 (CH$_2$Ph), 67.6(a)/67.5(b) (CH$_2$Ph), 60.7 (C$_2$), 60.4 (C$_3$), 25.9 (CH$_3$), 21.9 (CH$_3$), 14.5(a)/14.1(b) (CH$_3$); ^{13}C NMR (50 °C) δ 173.1 (CO lactam), 153.4 (CO), 137.8, 135.9, 128.4, 128.1, 127.8, 127.4, 127.2 (Ar), 90.5 (C$_6$), 74.8 (C$_5$), 67.9 (CH$_2$Ph), 67.3 (CH$_2$Ph), 60.6 (C$_2$), 60.4 (C$_3$), 25.7 (CH$_3$), 21.7 (CH$_3$), 14.1 (CH$_3$); IR (neat) ν 1773 (CO, lactam), 1713 (CO, carbamate) cm^{-1}. Anal. Calcd for $C_{23}H_{26}N_2O_4$: C, 70.03; H, 6.64; N, 7.10. Found: C, 69.89; H, 6.45; N, 7.07.

(5*R,6*R**)-4-(Benzyloxycarbonyl)-2,2-dimethyl-1,4-diazabicyclo-[3.2.0]heptan-7-one-6-spiro-2′-tetrahydrofuran (3ca).** Carbene complex **2c** and imidazoline **1a** were allowed to react according to the general procedure to give a 90% yield of product as a mixture of two rotamers: ^{1}H NMR (two rotamers) δ 7.4–7.3 (m, 5 H, Ar), 5.3–5.0 (m, 3 H, CH$_2$Ph, CH), 4.0–3.6 (m, 3 H, 2CH$_2$O, CH$_2$N), 3.09 (d, J = 10.4 Hz, 1 H, CH$_2$N), 2.1–1.6 (m, 4 H, CH$_2$CH$_2$), 1.58 (s, 3 H, CH$_3$), 1.15 (s, 3 H, CH$_3$); ^{1}H NMR (50 °C) δ 7.34–7.28 (m, 5 H, ArH), 5.20 (d, J = 12.2 Hz, 1 H, PhCH$_2$), 5.10 (d, J = 12.3 Hz, 1 H, PhCH$_2$), 5.01 (s, 1 H, CH), 3.90 (br d, J = 9.0 Hz, 1 H, CHO), 3.72 (br d, J = 9.0 Hz, 1 H, CHO), 3.08 (d, J = 10.4 Hz, 1 H, CH$_2$N), 2.0–1.8 (m, 4 H, CH$_2$CH$_2$), 1.57 (s, 3 H, CH$_3$), 1.14 (s, 3 H, CH$_3$); ^{13}C NMR δ 174.7-(b)/174.3(a) (CO, lactam), 153.6(b)/153.1(a) (CO), 135.7(b)/135.4(a), 128.3, 128.1, 127.9, 127.6 (Ar), 93.7(b)/93.6(a) (C$_6$), 77.1(b)/76.6(a) (C$_5$), 70.3 (CH$_2$O), 67.2(a)/67.1(b) (CH$_2$Ph), 60.8(b)/60.4(a) (C$_2$), 60.0 (C$_3$), 27.0 (C$_{3'}$), 25.5(b)/25.4(a) (CH$_3$), 25.0 (C$_{4'}$), 21.5 (CH$_3$); ^{13}C NMR (50 °C) δ 174.4 (CO, lactam), 153.4 (CO), 135.9, 128.2, 128.0, 127.7 (Ar), 93.9 (C$_6$), 76.9 (C$_5$), 70.2 (CH$_2$O), 67.2 (CH$_2$Ph), 60.5 (C$_2$), 60.2 (C$_3$), 27.0 (C$_{3'}$), 25.5 (CH$_3$), 25.1 (C$_{4'}$), 21.5 (CH$_3$); IR (neat) ν 1770 (CO, lactam), 1714 (CO, carbamate) cm^{-1}. Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.31; H, 6.98; N, 8.43.

(2*S*,5*R*,6*R*)-4-(Benzyloxycarbonyl)-6-methoxy-6-methyl-2-(1′-methylethyl)-1,4-diazabicyclo[3.2.0]heptan-7-one (3ab). Carbene complex **2a** and imidazoline **1b** were allowed to react according to the general procedure to give a 41% yield of product as a mixture of two rotamers: ^{1}H NMR (two rotamers a/b ≈ 2/1) δ 7.4–7.3 (m, 5 H, ArH), 5.27–5.03 (m, 3 H, CH$_2$Ph, CH), 3.9–3.65 (m, 2 H, CHN, CH$_2$N), 3.53(a+b) (dd, J_1 = 7.5 Hz, J_2 = 10.9 Hz, 1 H, CH$_2$N), 3.50(b)/3.34(a) (s, 3 H, OCH$_3$), 1.67 (oct, J = 6.7 Hz, 1 H, CHMe$_2$), 1.31(b)/1.20(a) (s, 3 H, CH$_3$), 0.94 (d, J = 6.7 Hz, 3 H, CH$_3$), 0.93 (d, J = 6.7 Hz, 3 H, CH$_3$); ^{1}H NMR (50 °C) δ 7.35–7.30 (m, 5 H, ArH), 5.21 (d, J = 12.3 Hz, 1 H, CH$_2$Ph), 5.15 (d, J = 12.3 Hz, 1 H, CH$_2$Ph), 5.04 (s, 1 H, CH), 3.80 (ddd, J_1 = J_2 = 7.2 Hz, J_3 = 2.3 Hz, 1 H, HC(2)), 3.74 (br d, J = 11.1 Hz, 1 H, HC(3)), 3.52 (dd, J_1 = 7.5 Hz, J_2 = 11.0 Hz, 1 H, HC(3)), 3.42 (s, 3 H, OCH$_3$), 1.66 (oct, J = 6.7 Hz, 1 H, CHMe$_2$), 1.23 (s, 3 H, CH$_3$), 0.93 (d, J = 6.7 Hz, 3 H, CH$_3$), 0.92 (d, J = 6.7 Hz, 3 H, CH$_3$); ^{13}C NMR δ 176.8(b)/176.5(a) (CO, lactam), 153.4 (CO), 135.8, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0 (Ar), 91.1 (C$_6$), 75.7(b)/75.1(a) (C$_5$), 69.1 (CH$_2$Ph), 61.7(b)/61.1(a) (C$_2$), 53.6 (OCH$_3$), 50.9(a)/50.6(b) (C$_3$), 31.1 (CHMe$_2$), 19.1 (CH$_3$), 18.3 (CH$_3$), 13.8(a)/13.6(b) (CH$_3$); ^{13}C NMR (50 °C) δ 176.5 (CO, lactam), 153.7 (CO), 136.1, 128.5, 128.2, 128.0 (Ar), 91.3 (C$_6$), 75.5 (C$_5$), 67.5 (CH$_2$Ph), 61.5 (C$_2$), 53.4 (OCH$_3$), 50.8 (C$_3$), 31.1 (CHMe$_2$), 18.9 (CH$_3$), 18.2 (CH$_3$), 13.7 (CH$_3$); IR (neat) ν 1777 (CO, lactam), 1713 (CO, carbamate) cm^{-1}. Anal. Calcd for $C_{18}H_{24}N_2O_4$: C, 65.04; H, 7.28; N, 8.43. Found: C, 64.89; H, 7.17; N, 8.50.

(2*S*,5*R*,6*R*)-4-(Benzyloxycarbonyl)-6-(benzyloxy)-6-methyl-2-(1′-methylethyl)-1,4-diazabicyclo[3.2.0]heptan-7-one (3bb). Carbene complex **2b** and imidazoline **1b** were allowed to react according to the general procedure to give a 54% yield of product as a mixture of two rotamers: ^{1}H NMR (two rotamers a/b ≈ 3/1) δ 7.38–7.27 (m, 10 H, ArH), 5.26–5.06 (m, 3 H, CH$_2$Ph, CH), 4.78–4.55 (m, 2 H, CH$_2$Ph), 3.85 (ddd, J_1 = J_2 = 7.2 Hz, J_3 = 2.3 Hz, 1 H, CHN), 3.83–3.68 (m, 1 H, CH$_2$N), 3.55 (dd, J_1 = 7.4 Hz, J_2 = 10.9 Hz, 1 H, CH$_2$N), 1.66 (oct, J = 6.7 Hz, 1 H, CHMe$_2$), 1.40(b)/1.31(a) (s, 3 H, CH$_3$), 0.94 (d, J = 6.3 Hz, 3 H, CH$_3$), 0.92 (d, J = 6.3 Hz, 3 H, CH$_3$); ^{1}H NMR (50 °C) δ 7.36–7.20 (m, 10 H, ArH), 5.20 (d, J = 12.3 Hz, 1 H, CH$_2$Ph), 5.14 (d, J = 12.3 Hz, 1 H, CH$_2$Ph), 5.08 (s, 1 H, CH), 4.66 (br s, 2 H, CH$_2$Ph), 3.82 (ddd, J_1 = J_2 = 7.2 Hz, J_3 = 2.4 Hz, 1 H, HC(2)), 3.74 (br d, J = 11.0 Hz, 1 H, HC(3)), 3.52 (dd, J_1 = 7.5 Hz, J_2 = 11.0 Hz, 1 H, HC(3)), 1.64 (oct, J = 6.7 Hz, 1 H, CHMe$_2$), 1.32 (s, 3 H, CH$_3$), 0.92 (d, J = 6.7 Hz, 3 H, CH$_3$), 0.90 (d, J = 6.7 Hz, 3 H, CH$_3$); ^{13}C NMR δ 176.8(b)/176.4(a) (CO, lactam), 153.3 (CO), 137.5, 135.9(b)/135.6(a), 128.5, 128.3, 128.0, 127.7, 127.4, 127.0 (Ar), 91.0 (C$_6$), 76.1(b)/75.5(a) (C$_5$), 68.2 (CH$_2$Ph), 67.6 (CH$_2$Ph), 61.7(b)/61.2(a) (C$_2$), 50.8(a)/50.6(b) (C$_3$), 31.1 (CHMe$_2$), 19.0 (CH$_3$), 18.3 (CH$_3$), 14.7(a)/14.3(b) (CH$_3$); ^{13}C NMR (50 °C) δ 176.3 (CO, lactam), 153.5 (CO), 137.8, 135.9, 128.5, 128.2, 127.9, 127.6, 127.3 (Ar), 91.2 (C$_6$), 75.9 (C$_5$), 68.3 (CH$_2$Ph), 67.5 (CH$_2$Ph), 61.5 (C$_2$), 50.7 (C$_3$), 31.1 (CHMe$_2$), 18.9 (CH$_3$), 18.2 (CH$_3$), 14.5 (CH$_3$); IR (neat) ν 1778 (CO, lactam), 1715 (CO, carbamate) cm^{-1}. Anal. Calcd for $C_{24}H_{28}N_2O_4$: C, 70.57; H, 6.91; N, 6.86. Found: C, 70.40; H, 6.82; N, 6.85.

(2*S*,5*R*,6*R*)-4-(Benzyloxycarbonyl)-2-(1′-methylethyl)-1,4-diazabicyclo[3.2.0]heptan-7-one-6-spiro-2′-tetrahydrofuran (3cb). Carbene complex **2c** and imidazoline **1b** were allowed to react according to the general procedure to give a 69% yield of product as a mixture of two rotamers: ^{1}H NMR (two rotamers a/b ≈ 5/1) δ 7.36 (m, 5 H, ArH), 5.30–4.96 (m, 3 H, CH$_2$Ph, CH), 4.07–3.46 (m, 5 H, CH$_2$O, HC(2), H$_2$C(3)), 2.05–1.75 (m, 4 H, CH$_2$CH$_2$), 1.64 (oct, J = 6.6 Hz, 1 H, CHMe$_2$), 0.93 (d, J = 6.6 Hz, 3 H, CH$_3$), 0.92 (d, J = 6.6 Hz, 3 H, CH$_3$); ^{1}H NMR (50 °C) 7.35–7.30 (m, 5 H, ArH), 5.21 (d, J = 12.2 Hz, 1 H, CH$_2$Ph), 5.12 (d, J = 12.2 Hz, 1 H, CH$_2$Ph), 4.96 (s, 1 H, CH), 3.95–3.85 (m, 1 H, CH$_2$O), 3.8–3.7 (m, 3 H, 1CH$_2$O, 1CH$_2$N, CHN), 3.48 (dd, J_1 = 7.5 Hz, J_2 = 10.9 Hz, 1 H, CH$_2$N), 1.95–1.80 (m, 4 H, CH$_2$CH$_2$), 1.64 (oct, J = 6.7 Hz, 1 H, CHMe$_2$), 0.92 (d, J = 6.7 Hz, 3 H, CH$_3$), 0.91 (d, J = 6.7 Hz, 3 H, CH$_3$); ^{13}C NMR δ 178.1-(b)/177.7(a) (CO, lactam), 153.9(b)/153.3(a) (CO), 135.9(b)/135.5(a), 128.5, 128.4, 128.2, 127.8 (Ar), 94.2 (C$_6$), 78.4(b)/77.7(a) (C$_5$), 70.6 (CH$_2$O), 67.5 (CH$_2$Ph), 61.7(b)/61.1(a) (C$_2$), 50.8(a)/50.6(b) (C$_3$), 31.0 (CHMe$_2$), 27.5 (C$_{3'}$), 25.6(b)/25.3(a) (C$_{4'}$), 19.0 (CH$_3$), 18.1 (CH$_3$); ^{13}C NMR (50 °C) δ 177.7 (CO, lactam), 153.6 (CO), 135.9, 128.4, 128.2, 127.9 (Ar), 94.5 (C$_6$), 78.0 (C$_5$), 70.4 (CH$_2$O), 67.4 (CH$_2$Ph), 61.5 (C$_2$), 50.7 (C$_3$), 31.0 (CHMe$_2$), 27.5 (C$_{3'}$), 25.3 (C$_{4'}$), 18.8 (CH$_3$), 18.1 (CH$_3$);

IR (neat) ν 1781 (CO, lactam), 1714 (CO, carbamate) cm^{-1}. Anal. Calcd for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 66.51; H, 6.98; N, 8.40.

General Procedure for the Deprotection of the *N*-Benzyloxycarbonyl Azapenams. The azapenam was dissolved in methanol, and a few drops of triethylamine were added. Hydrogenation with palladium on carbon at 45 psi of H_2 for 4 min, filtration through Celite, and evaporation of the solvent gave the product. If necessary, it was purified by chromatography on silica gel (EtOAc). Crude yields were, in general, quantitative, and after chromatography about 75–95%. (Note: Hydrogenation times varied with the specific bottle of catalyst used, with older, previously opened bottles giving slower reaction.)

(5*S,6*R**)-6-Methoxy-2,2,6-trimethyl-1,4-diazabicyclo[3.2.0]heptan-7-one (4aa).** Azapenam **3aa** (103 mg, 0.31 mmol) and 50 mg of 5% Pd/C were allowed to react according to the general procedure to give 56 mg (0.30 mmol, 98%) of product: mp 85–87 °C (hexane/CH_2Cl_2); ^1H NMR δ 4.75 (s, 1 H, CH), 3.46 (s, 3 H, OCH_3), 3.07 (d, J = 11.2 Hz, 1 H, CH_2N), 2.63 (d, J = 11.2 Hz, 1 H, CH_2N), 2.28 (br s, 1 H, NH), 1.58 (s, 3 H, CH_3), 1.31 (s, 3 H, C_6-CH_3), 1.11 (s, 3 H, CH_3); ^{13}C NMR δ 175.6 (CO), 90.0 (C_6), 77.3 (C_5), 61.9 (C_3), 60.9 (C_2), 53.4 (OCH_3), 24.8 (CH_3), 21.7 (CH_3), 14.4 (C_6-CH_3); IR (KBr) ν 3363 (NH), 1745 (CO) cm^{-1}. Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.21. Found: C, 58.72; H, 8.92; N, 15.20.

(5*S,6*R**)-6-(Benzyloxy)-2,2,6-trimethyl-1,4-diazabicyclo[3.2.0]heptan-7-one (4ba).** Azapenam **3ba** (291 mg, 0.73 mmol) and 145 mg of 5% Pd/C were allowed to react according to the general procedure to give 184 mg (0.71 mmol, 97%) of product: mp 87–88 °C (hexane/CH_2Cl_2); ^1H NMR δ 7.38–7.25 (m, 5 H, ArH), 4.77 (s, 1 H, CH), 4.73 (d, J = 11.2 Hz, 1 H, CH_2Ph), 4.67 (d, J = 11.2 Hz, 1 H, CH_2Ph), 3.07 (d, J = 11.2 Hz, 1 H, CH_2N), 2.65 (d, J = 11.2 Hz, 1 H, CH_2N), 2.29 (br s, 1 H, NH), 1.59 (s, 3 H, CH_3), 1.40 (s, 3 H, C(6)-CH_3), 1.11 (s, 3 H, CH_3); ^{13}C NMR δ 175.6 (CO), 137.9, 128.4, 127.7 (Ar), 89.9 (C_6), 78.1 (C_5), 68.2 (CH_2Ph), 62.0 (C_3), 61.0 (C_2), 24.9 (CH_3), 21.7 (CH_3), 14.9 (C_6-CH_3); IR (KBr) ν 3340 (NH), 1738 (CO) cm^{-1}. Anal. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.21; H, 7.74; N, 10.76. Found: C, 69.30; H, 7.71; N, 10.71.

(5*S,6*R**)-2,2-Dimethyl-1,4-diazabicyclo[3.2.0]heptan-7-one-6-spiro-2′-tetrahydrofuran (4ca).** Azapenam **3ca** (322 mg, 0.97 mmol) and 160 mg of 5% Pd/C were allowed to react according to the general procedure to give 188 mg (0.96 mmol, 99%) of product: mp 76–78 °C (hexane/CH_2Cl_2); ^1H NMR δ 4.66 (s, 1 H, CH), 4.05–3.85 (m, 2 H, CH_2O), 3.04 (d, J = 11.3 Hz, 1 H, CH_2N), 2.52 (d, J = 11.3 Hz, 1 H, CH_2N), 2.50–2.35 (m, 2 H, NH and $1CH_2$), 2.10–1.85 (m, 3 H, CH_2CH_2), 1.55 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3); ^{13}C NMR δ 177.3 (CO), 93.4 (C_6), 80.0 (C_5), 70.4 (CH_2O), 61.8 (C_3), 61.2 (C_2), 27.0 (CH_2), 25.6 (CH_2), 24.6 (CH_3), 21.6 (CH_3); IR (KBr) 3345 (NH), 1748 (CO) cm^{-1}. Anal. Calcd for $C_{10}H_{16}N_2O_2$: C, 61.20; H, 8.22; N, 14.27. Found: C, 61.13; H, 8.42; N, 14.26.

(2*S*,5*R*,6*R*)-6-Methoxy-6-methyl-2-(1′-methylethyl)-1,4-diazabicyclo[3.2.0]heptan-7-one (4ab). Azapenam **3ab** (143 mg, 0.43 mmol) and 70 mg of 5% Pd/C were allowed to react according to the general procedure to give 89 mg (0.43 mmol, 98%) of product: $[\alpha]^{25}{}_D$ +125.6° (c = 2.9, CH_2Cl_2); ^1H NMR δ 4.66 (s, 1 H, CH), 3.54 (ddd, J_1 = 3.7 Hz, J_2 = 6.5 Hz, J_3 = 8.1 Hz, CHN), 3.49 (s, 3 H, OCH_3), 3.15 (dd, J_1 = 3.7 Hz, J_2 = 11.0 Hz, 1 H, CH_2N), 3.07 (dd, J_1 = 8.1 Hz, J_2 = 11.0 Hz, 1 H, CH_2N), 1.95 (br s, 1 H, NH), 1.55 (d of hept, J_1 = 7.9 Hz, J_2 = 6.7 Hz, 1 H, $CHMe_2$), 1.31 (s, 3 H, CH_3), 0.99 (d, J = 6.7 Hz, 3 H, CH_3), 0.92 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR δ 178.5 (CO), 89.8 (C_6), 77.7 (C_5), 63.1 (C_2), 53.6 (OCH_3), 52.1 (C_3), 30.3 (CMe_2), 19.6 (CH_3), 19.3 (CH_3), 14.4 (C_6-CH_3); IR (neat) ν 3354 (NH), 1756 (CO) cm^{-1}. Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.40; H, 9.11; N, 13.97.

(2*S*,5*R*,6*R*)-6-(Benzyloxy)-6-methyl-2-(1′-methylethyl)-1,4-diazabicyclo[3.2.0]heptan-7-one (4bb). Azapenam **3bb** (207 mg, 0.51 mmol) and 110 mg of 5% Pd/C were allowed to react according to the general procedure to give 139 mg (0.51 mmol, >98%) of product: $[\alpha]^{25}{}_D$ +99.8° (c = 3.1, CH_2Cl_2); ^1H NMR (270 MHz) δ 7.39–7.26 (m, 5 H, ArH), 4.76 (d, J = 11.2 Hz, 1 H, CH_2Ph), 4.70 (d, J = 11.2 Hz, 1 H, CH_2Ph), 4.70 (s, 1 H, CH), 3.57 (ddd, J_1 = 3.7 Hz, J_2 = 6.4 Hz, J_3 = 7.9 Hz, CHN), 3.16 (dd, J_1 = 3.7 Hz, J_2 = 11.1 Hz, 1 H, CH_2N), 3.08 (dd, J_1 = 6.4 Hz, J_2 = 11.1 Hz, 1 H, CH_2N), 1.87 (br s, 1 H, NH), 1.55 (oct, J = 6.8 Hz, 1 H, $CHMe_2$), 1.40 (s, 3 H, CH_3), 0.99 (d, J = 6.7 Hz, 3 H, CH_3), 0.92 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR δ 178.5 (CO), 137.9, 128.4, 127.7 (Ar), 89.7 (C_6), 78.3 (C_5), 68.4 (CH_2Ph), 63.1 (C_2), 52.2 (C_3), 30.4 (CMe_2), 19.6 (CH_3), 19.4 (CH_3), 15.1 (C_6-CH_3); IR (neat) ν 3354 (NH), 1760 (CO) cm^{-1}. Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.82; H, 8.10; N, 10.05.

(2*S*,5*R*,6*R*)-2-(1′-Methylethyl)-1,4-diazabicyclo[3.2.0]heptan-7-one-6-spiro-2′-tetrahydrofuran (4cb). Azapenam **3cb** (227 mg, 0.66 mmol) and 112 mg of 5% Pd/C were allowed to react according to the general procedure to give 142 mg (0.66 mmol, >98%) of product: $[\alpha]^{25}{}_D$ +125.9° (c = 3.25, CH_2Cl_2); ^1H NMR δ 4.61 (s, 1 H, CH), 4.03–3.88 (m, 2 H, CH_2O), 3.52 (ddd, J_1 = 3.5 Hz, J_2 = 6.5 Hz, J_3 = 8.1 Hz, CHN), 3.13 (dd, J_1 = 3.5 Hz, J_2 = 11.2 Hz, 1 H, CH_2N), 2.98 (dd, J_1 = 6.5 Hz, J_2 = 11.2 Hz, 1 H, CH_2N), 2.27–2.16 (m, 1 H, $1CH_2$), 2.06–1.83 (m, 4 H, $3CH_2CH_2$ and NH), 1.53 (d of hept, J_1 = 6.7 Hz, J_2 = 8.1 Hz, 1 H, $CHMe_2$), 0.98 (d, J = 6.7 Hz, 3 H, CH_3), 0.91 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR δ 180.1 (CO), 93.3 (C_6), 80.0 (C_5), 70.4 (CH_2O), 63.5 (C_2), 52.0 (C_3), 30.3 (CMe_2), 27.5 ($C_{3'}$), 25.7 ($C_{4'}$), 19.5 (CH_3), 19.4 (CH_3); IR (neat) ν 3346 (NH), 1760 (CO) cm^{-1}. Anal. Calcd for $C_{11}H_{18}N_2O_2$: C, 62.83; H, 8.63; N, 13.32. Found: C, 62.69; H, 8.53; N, 13.13.

General Procedure for the Transformation of Azapenams to Hexahydrodiazepinones. The *N*-benzyloxycarbonyl azapenams and 1.1 equiv of racemic camphorsulfonic acid were dissolved in THF and hydrogenated at 45 psi of H_2 with palladium on carbon at the specified temperature and reaction time. The reaction mixture was filtered through Celite, and the solvent was evaporated. The residue was dissolved in CH_2Cl_2, and the solution was washed with 5% aqueous $NaHCO_3$. Drying over $MgSO_4$ and evaporation of the solvent gave the product. If necessary, they were purified by chromatography on silica gel with 4/1 CH_2Cl_2/MeOH or 2/1 EtOAc/MeOH.

Hexahydro-3,3,6-trimethyl-6-methoxy-5*H*-1,4-diazepin-5-one (5aa). *N*-Benzyloxycarbonyl azapenam **3aa** (53 mg, 0.16 mmol), 40 mg of (±)-camphorsulfonic acid, and 5% Pd/C (26 mg) were allowed to react according to the general procedure at room temperature for 4.5 h to give 22 mg (0.12 mmol, 71%) of the product: mp 153–154 °C (hexane, CH_2Cl_2); ^1H NMR δ 5.64 (br s, 1 H, CONH), 3.27 (s, 3 H, OCH_3), 3.04 (d, J = 15.0 Hz, 1 H, CH_2N), 2.88 (d, J = 14.4 Hz, 1 H, CH_2N), 2.81 (d, J = 15.0 Hz, 1 H, CH_2N), 2.75 (d, J = 14.5 Hz, 1 H, CH_2N), 1.82 (br s, 1 H, NH), 1.47 (s, 3 H, CH_3), 1.24 (s, 3 H, CH_3), 1.15 (s, 3 H, CH_3); ^{13}C NMR δ 174.0 (CO), 80.7 (C_6), 60.5 (CH_2), 55.9 (CH_2), 54.3 (C_3), 51.2 (OCH_3), 30.2 (CH_3), 24.8 (CH_3), 19.7 (CH_3); IR (KBr) ν 1643 (CO) cm^{-1}; MS 186 (M^+). Anal. Calcd for $C_9H_{18}N_2O_2$: C, 58.04; H, 9.74; N, 15.04. Found: C, 58.14; H, 9.86; N, 14.97.

Hexahydro-3,3,6-trimethyl-6-(phenylmethoxy)-5*H*-1,4-diazepin-5-one (5ba). *N*-Benzyloxycarbonyl azapenam **3ba** (67 mg, 0.17 mmol), 43 mg of CSA, and 5% Pd/C (30 mg) were allowed to react according to the general procedure at 100 °C for 10 min to give 24 mg (0.09 mmol, 54%) of the product: mp 117–120 °C (hexane/CH_2Cl_2); ^1H NMR δ 7.35–7.25 (m, 5 H, ArH), 5.84 (br s, 1 H, CONH), 4.65 (d, J = 11.1 Hz, 1 H, $PhCH_2$), 4.31 (d, J = 11.1 Hz, 1 H, $PhCH_2$), 3.17 (d, J = 15.0 Hz, 1 H, CH_2N), 2.86 (d, J = 14.9 Hz, 1 H, CH_2N), 2.82 (d, J = 14.6 Hz, 1 H, CH_2N), 2.77 (d, J = 14.6 Hz, 1 H, CH_2N), 2.36 (br s, 1 H, NH), 1.40 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.15 (s, 3 H, CH_3); ^{13}C NMR δ 173.9 (CO), 138.1, 128.3, 127.7, 127.5 (Ar), 80.9 (C_6), 65.8 (CH_2Ph), 60.4 (CH_2N), 56.1 (CH_2N), 54.6 (C_3), 30.1 (CH_3), 25.4 (CH_3), 20.6 (CH_3); IR (KBr) ν 1644 (CO) cm^{-1}; MS 171 (M^+ − 91, M^+ − CH_2Ph). Anal. Calcd for $C_{15}H_{22}N_2O_2$: C, 68.67; H, 8.45; N, 10.68. Found: C, 68.47; H, 8.34; N, 10.58.

Hexahydro-3,3-dimethyl-5*H*-1,4-diazepin-5-one-6-spiro-2′-tetrahydrofuran (5ca). *N*-Benzyloxycarbonyl azapenam **3ca** (55 mg, 0.17 mmol), 40 mg of CSA, and 5% Pd/C (26 mg) were allowed to react according to the general procedure at room temperature for 1.25 h to give 20 mg (0.10 mmol, 61%) of the product: mp 102–103 °C (hexane, CH_2Cl_2); ^1H NMR δ 6.23 (br s, 1 H, CONH), 4.85 (br s, 1 H, NH), 4.0–3.8 (m, 2 H, CH_2O), 3.05–2.8 (m, 4 H, CH_2NCH_2), 2.7–2.6 (m, 1 H, CH_2CH_2), 2.1–1.8 (m, 2 H, CH_2CH_2), 1.66–1.57 (m, 1 H, CH_2CH_2), 1.46 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3); ^{13}C NMR δ 174.2 (CO), 86.0 (C_6), 68.9 (CH_2O), 59.3 (CH_2N), 54.1 (CH_2N), 53.9 (C_3), 33.4 ($C_{3'}$), 29.2 (CH_3), 26.7 (CH_3), 25.7 ($C_{4'}$); IR (KBr) ν 1642 (CO) cm^{-1}; MS 198 (M^+). Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.38; H, 9.17; N, 14.07.

(3*S*,6*R*)-Hexahydro-6-methyl-3-(1′-methylethyl)-6-methoxy-5*H*-1,4-diazepin-5-one (5ab). *N*-Benzyloxycarbonyl azapenam **3ab** (103 mg, 0.31 mmol), 79 mg of CSA, and 10% Pd/C (25 mg) were allowed to react according to the general procedure at room temperature overnight and at 70 °C for 0.5 h to give 44 mg (0.22 mmol, 71%) of the product as a waxy solid: $[\alpha]^{25}{}_D$ −11.0° (c = 2.0, CH_2Cl_2); ^1H NMR δ 6.36 (br s, 1 H, CONH), 3.32 (s, 3 H, OCH_3), 3.12 (dd, J_1 = 5.6 Hz, J_2 = 14.3 Hz, 1 H, HC_2), 3.05 (d, J = 14.5 Hz, 1 H, HC_7), 2.90 (dd, J_1 = 2.4 Hz, J_2 = 14.3 Hz, 1 H, HC_2), 2.80 (d, J = 14.5 Hz, 1 H, HC_7), 2.77 (ddd, J_1 = 2.4 Hz, J_2 = 5.6 Hz, J_3 = 8.3 Hz, 1 H, HC_3), 2.58 (br s, 1 H, NH), 2.29 (d of hept, J_1 = 6.7 Hz, J_2 = 8.3 Hz, 1 H, $CHMe_2$), 1.33 (s, 3 H, CH_3), 1.01 (d, J = 6.7 Hz, 3 H, CH_3), 0.94 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR δ 175.7 (CO), 80.6 (C_6), 60.5 (CHN), 54.8 (CH_2N), 51.7 (OCH_3), 50.7 (CH_2N), 29.4 ($CHMe_2$), 20.0 (CH_3), 19.8 (CH_3), 19.4 (CH_3); IR (KBr) ν 1656 (CO) cm^{-1}; MS 200 (M^+). Anal. Calcd for $C_{10}H_{20}N_2O_2$: C, 59.97; H, 10.06; N, 13.99. Found: C, 59.95; H, 9.89; N, 13.76.

(3S,6R)-Hexahydro-6-methyl-3-(1'-methylethyl)-6-hydroxy-5H-1,4-diazepin-5-one (5bb). N-Benzyloxycarbonyl azapenam **3bb** (78 mg, 0.19 mmol), 49 mg of CSA, and 10% Pd/C (20 mg) were allowed to react according to the general procedure at room temperature for 2.5 days to give 25 mg (0.13 mmol, 69%) of the product as a waxy solid: $[\alpha]^{25}_D$ +6.0° (c = 1.2, CH_2Cl_2); ^1H NMR δ 5.90 (br s, 1 H, CONH), 4.53 (br s, 1 H, OH), 3.42–3.36 (m, 1 H, HC_3), 3.10 (d, J = 13.3 Hz, 1 H, HC_2), 2.94 (d, J = 13.5 Hz, 1 H, HC_7), 2.79 (d, J = 13.5 Hz, 1 H, HC_7), 2.55 (dd, J_1 = 13.3 Hz, J_2 = 9.7 Hz, 1 H, HC_2), 1.82 (d of hept, J_1 = 6.9 Hz, J_2 = 4.4 Hz, 1 H, $CHMe_2$), 1.8 (br s, 1 H, NH), 1.49 (s, 3 H, CH_3), 0.99 (d, J = 6.9 Hz, 3 H, CH_3), 0.98 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR δ 179.6 (CO), 74.2 (C_6), 60.6 (CHN), 55.7 (CH_2N), 52.4 (CH_2N), 31.5 ($CHMe_2$), 23.0 (CH_3), 18.2 (CH_3), 18.0 (CH_3); IR (KBr) ν 1646 (CO) cm^{-1}; MS 186 (M^+). Anal. Calcd for $C_9H_{18}N_2O_2$: C, 58.04; H, 9.74; N, 15.04. Found: C, 58.28; H, 9.60; N, 14.94.

(3S,6R)-Hexahydro-3-(1'-methylethyl)-5H-1,4-diazepin-5-one-6-spiro-2'-tetrahydrofuran (5cb). N-Benzyloxycarbonyl azapenam **3cb** (248 mg, 0.72 mmol), 186 mg of CSA, and 10% Pd/C (60 mg) were allowed to react according to the general procedure at room temperature overnight at 60 °C for 0.5 h to give 90 mg (0.42 mmol, 59%) of the product as a waxy solid: $[\alpha]^{25}_D$ +28.8° (c = 1.79, CH_2Cl_2); ^1H NMR δ 5.82 (d, J = 3.1 Hz, 1 H, CONH), 4.05 (ddd, J_1 = J_2 = 6.9 Hz, J_3 = 8.1 Hz, 1 H, CH_2O), 3.94 (ddd, J_1 = J_2 = 6.5 Hz, J_3 = 8.1 Hz, 1 H, CH_2O), 3.25–3.18 (m, 1 H, HC_3), 3.03 (d, J = 13.6 Hz, 1 H, HC_7), 3.02 (dd, J_1 = 13.3 Hz, J_2 = 1.4 Hz, 1 H, HC_2), 2.83 (d, J = 13.6 Hz, 1 H, HC_7), 2.63 (dd, J_1 = 13.3 Hz, J_2 = 9.0 Hz, 1 H, HC_2), 2.38 (br s, 1 H, NH), 2.22–2.17 (m, 2 H, CH_2 furan), 2.00–1.82 (m, 3 H, CH_2 furan and $CHMe_2$), 0.97 (d, J = 6.8 Hz, 3 H, CH_3), 0.96 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR δ 177.2 (CO), 86.5 (C_6), 68.7 (CH_2O), 59.9 (CHN), 53.8 (CH_2N), 51.9 (CH_2N), 32.3 ($C_{3'}$), 31.0 ($CHMe_2$), 25.2 ($C_{4'}$), 18.4 (CH_3), 18.1 (CH_3); IR (KBr) ν 1660 (CO) cm^{-1}; MS 212 (M^+). Anal. Calcd for $C_{11}H_{20}N_2O_2$: C, 62.24; H, 9.50; N, 13.20. Found: C, 62.08; H, 9.60; N, 12.92.

General Procedure for the Dimerization of Azapenams to Dioxocyclams. The azapenam and a catalytic amount (about 25 mg) of racemic camphorsulfonic acid in CH_2Cl_2 were stirred at the specified temperature for the reaction time. The solution was washed with aqueous 5% $NaHCO_3$ and dried over $MgSO_4$, and the solvent was evaporated.

(6R*,13S*)-3,3,6,10,10,13-Hexamethyl-6,13-dimethoxy-1,4,8,11-tetraazacyclotetradeca-7(E),14(E)-diene-5,12-dione (6aa). Azapenam **4aa** (56 mg, 0.30 mmol) was allowed to react according to the general procedure for 2.5 h at room temperature to give 54 mg (96%) of product as one single diastereoisomer (meso compound) but as two conformers in solution, a/b ≈ 1/1; mp 222–223 °C (CH_2Cl_2/hexane). Conformer a: ^1H NMR δ 7.57 (t, J = 1.2 Hz, 1 H, HCN), 7.48 (s, 1 H, CONH), 3.98 (d, J = 11.9 Hz, 1 H, CH_2N), 3.30 (dd, J_1 = 1.4 Hz, J_2 = 11.9 Hz, 1 H, CH_2N), 3.33 (s, 3 H, OCH_3), 1.50 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3); ^{13}C NMR δ 169.6 (CO), 166.9 (C=N), 81.1 ($C_{6,13}$), 67.8 (CH_2), 53.8 ($C_{3,10}$), 52.7, 26.0 (CH_3), 24.9 (CH_3), 20.6 (CH_3). Conformer b: ^1H NMR δ 7.54 (br s, 1 H, HC=N), 7.12 (s, 1 H, CONH), 4.00 (d, J = 11.7 Hz, 1 H, CH_2N), 3.45 (dd, J_1 = 1.5 Hz, J_2 = 11.7 Hz, 1 H, CH_2N), 3.27 (s, 3 H, OCH_3), 1.47 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3); ^{13}C NMR δ 169.2 (CO), 167.2 (C=N), 81.6 ($C_{6,13}$), 66.7 (CH_2), 54.2 ($C_{3,10}$), 52.2 (OCH_3), 26.6 (CH_3), 25.3 (CH_3), 19.2 (CH_3); IR (KBr) ν 1686 (CO), 1663 (C=N), 1524 cm^{-1}; MS 368 (M^+). Anal. Calcd for $C_{18}H_{32}N_4O_4$: C, 58.67; H, 8.75; N, 15.21. Found: C, 58.46; H, 8.50; N, 15.14.

(6R*,13S*)-3,3,6,10,10,13-Hexamethyl-6,13-bis(phenylmethoxy)-1,4,8,11-tetraazacyclotetradeca-7(E),14(E)-diene-5,12-dione (6ba). Azapenam **4ba** (56 mg, 0.30 mmol) was allowed to react in a sealed tube at 80 °C for 2 h according to the general procedure to give 95 mg (90%) of product as a single diastereoisomer (meso compound) but as two conformers in solution, a/b ≈ 1/1, mp 201–202 °C (CH_2Cl_2/hexane). Conformer a: ^1H NMR δ 7.85 (s, 1 H, CH=N), 7.72 (s, 1 H, CONH), 7.4–7.2 (m, 5 H, ArH), 4.75 (d, J = 11.8 Hz, 1 H, $PhCH_2$), 4.39 (d, J = 11.8 Hz, 1 H, $PhCH_2$), 3.93 (d, J = 11.9 Hz, 1 H, CH_2N), 3.26 (dd, J_1 = 0.6 Hz, J_2 = 12.0 Hz, 1 H, CH_2N), 1.61 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3); ^{13}C NMR δ 169.8 (CO), 167.5 (C=N), 138.3, 128.3, 127.7 (Ar), 81.1 ($C_{6,13}$), 68.3, 67.5 (CH_2N and CH_2Ph), 53.7 ($C_{3,10}$), 25.6 (CH_3), 24.9 (CH_3), 22.6 (CH_3). Conformer b: ^1H NMR δ 7.63 (s, 1 H, CHN), 7.18 (s, 1 H, COHN), 7.42–7.2 (ArH), 4.57 (d, J = 11.2 Hz, 1 H, $PhCH_2$), 4.35 (d, J = 11.2 Hz, 1 H, $PhCH_2$), 4.02 (d, J = 11.8 Hz, 1 H, CH_2N), 3.40 (dd, J_1 = 1.5 Hz, J_2 = 11.8 Hz, 1 H, CH_2N), 1.59 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3); ^{13}C NMR δ 169.4 (CO), 166.8 (C=N), 137.9, 128.4, 127.5 (Ar), 82.1 ($C_{6,13}$), 66.9, 66.8 (CH_2N and CH_2Ph), 54.2 ($C_{3,10}$), 26.5 (CH_3), 25.2, 19.7 (CH_3); IR (KBr) ν 1694 (CO), 1657 (C=N), 1512 cm^{-1}; MS 520 (M^+). Anal. Calcd for $C_{30}H_{40}N_4O_4$: C, 69.21; H, 7.74; N, 10.76. Found: C, 69.09; H, 7.51; N, 10.82.

(6R*,13S*)-3,3,10,10-Tetramethyl-6,13-bis(oxypropylene)-1,4,8,11-tetraazacyclotetradeca-7(E),14(E)-diene-5,12-dione (6ca). Azapenam **4ca** (157 mg, 0.80 mmol) was allowed to react according to the general procedure at room temperature overnight to give 129 mg (82%) of product as a single diastereoisomer (meso compound) but as two conformers in solution, a/b ≈ 5/1, mp 246–247 °C ($CHCl_3$/CH_2Cl_2). Conformer a: ^1H NMR δ 7.68 (d, J = 1.6 Hz, 1 H, CH=N), 6.61 (s, 1 H, CONH), 4.2–3.8 (m, 3 H, CH_2O and $1CH_2N$), 3.34 (dd, J_1 = 1.7 Hz, J_2 = 11.3 Hz, 1 H, CH_2N), 2.5–2.4 (m, 1 H, CH_2CH_2), 2.0–1.8 (m, 3 H, CH_2CH_2), 1.43 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3); ^{13}C NMR δ 170.5 (CO), 165.0 (C=N), 87.9 ($C_{6,13}$), 69.6 (CH_2), 66.2 (CH_2), 53.8 ($C_{3,10}$), 34.6 ($OCH_2CH_2CH_2$), 27.3 (CH_3), 25.0 (CH_3), 24.4 ($OCH_2CH_2CH_2$). Conformer b: ^1H NMR δ 7.64 (s, 1 H, HC=N), 6.88 (s, 1 H, CONH), 4.2–3.8 (m, 3 H), 3.41 (dd, J_1 = 1.1 Hz, J_2 = 12.0 Hz, 1 H, CH_2N), 2.5–2.4 (m, 1 H, CH_2CH_2), 2.0–1.8 (m, 3 H, CH_2CH_2), 1.43 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3); ^{13}C NMR δ 170.1 (CO), 166.4 (C=N), 87.4 ($C_{6,13}$), 69.2 (CH_2), 66.8 (CH_2), 53.9 ($C_{3,10}$), 33.6 ($OCH_2CH_2CH_2$), 26.4 (CH_3), 25.6, 25.3 (CH_3); IR (KBr) ν 1684 (CO), 1659 (C=N), 1535 cm^{-1}; MS 392 (M^+). Anal. Calcd for $C_{20}H_{32}N_4O_4$: C, 61.20; H, 8.22; N, 14.27. Found: C, 61.46; H, 7.96; N, 14.44.

(3S,6R,10S,13R)-6,13-Dimethyl-3,10-bis(1'-methylethyl)-6,13-dimethoxy-1,4,8,11-tetraazacyclotetradeca-7(E),14(E)-diene-5,12-dione (6ab). Azapenam **4ab** (60 mg, 0.30 mmol) was allowed to react according to the general procedure at 80–100 °C for 1.5 h to give 57 mg (95%) of product: mp 161–163 °C (CH_2Cl_2/hexane); $[\alpha]^{25}_D$ −38.8° (c = 1.62, CH_2Cl_2); ^1H NMR δ 8.00 (d, J = 9.7 Hz, 1 H, CONH), 7.62 (s, 1 H, CH=N), 3.97–3.88 (m, 1 H, CHN), 3.80 (ddd, J_1 = 1.4 Hz, J_2 = 6.3 Hz, J_3 = 11.8 Hz, 1 H, CH_2N), 3.36 (dd, J_1 = 3.7 Hz, J_2 = 11.8 Hz, 1 H, CH_2N), 3.33 (s, 3 H, OCH_3), 1.90 (oct, J = 6.8 Hz, 1 H, $CHMe_2$), 1.51 (s, 3 H, CH_3), 1.02 (d, J = 6.7 Hz, 3 H, CH_3), 0.95 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR δ 169.8 (CO), 167.2 (C=N), 81.0 ($C_{6,13}$), 61.7 (CH_2), 54.6 (CHN), 53.1 (OCH_3), 30.7 ($C_{3,10}$), 21.2 (CH_3), 19.6 (CH_3), 19.1 (CH_3); IR (KBr) ν 1684 (CO), 1659 (C=N), 1522 cm^{-1}; MS 396 (M^+). Anal. Calcd for $C_{20}H_{36}N_4O_4$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.33; H, 8.98; N, 13.92.

(3S,6R,10S,13R)-6,13-Dimethyl-3,10-bis(1'-methylethyl)-6,13-bis(phenylmethoxy)-1,4,8,11-tetraazacyclotetradeca-7(E),14(E)-diene-5,12-dione (6bb). Azapenam **4bb** (114 mg, 0.42 mmol) was allowed to react according to the general procedure at 100 °C for 1 h to give 106 mg (93%) of product: mp 207–208 °C (CH_2Cl_2/hexane); $[\alpha]^{25}_D$ −33.4° (c = 1.89, CH_2Cl_2); ^1H NMR δ 8.10 (d, J = 9.8 Hz, 1 H, CONH), 7.70 (s, 1 H, CH=N), 7.45–7.25 (m, 5 H, ArH), 4.73 (d, J = 10.9 Hz, 1 H, $PhCH_2$), 4.34 (d, J = 10.9 Hz, 1 H, $PhCH_2$), 4.0–3.9 (m, 1 H, CHN), 3.77 (ddd, J_1 = 11.8 Hz, J_2 = 6.5 Hz, J_3 = 0.8 Hz, 1 H, CH_2N), 3.34 (dd, J_1 = 11.8 Hz, J_2 = 3.6 Hz, 1 H, CH_2N), 1.87 (oct, J = 6.7 Hz, 1 H, $CHMe_2$), 1.61 (s, 3 H, CH_3), 0.99 (d, J = 6.7 Hz, 3 H, CH_3), 0.93 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR δ 169.9 (CO), 167.2 (C=N), 138.2, 128.3, 127.6 (Ar), 81.0 ($C_{6,13}$), 67.6 (CH_2Ph), 61.8 (CH_2N), 54.6 (CHN), 30.8 ($C_{3,10}$), 21.9 (CH_3), 19.5 (CH_3), 19.1 (CH_3); IR (KBr) ν 1678 (CO), 1657 (C=N), 1533 cm^{-1}; MS 457 ($M^+ - 91$, $M^+ - CH_2Ph$). Anal. Calcd for $C_{32}H_{44}N_4O_4$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.14; H, 8.14; N, 10.47.

(3S,6R,10S,13R)-3,10-Bis(1'-methylethyl)-6,13-bis(oxypropylene)-1,4,8,11-tetraazacyclotetradeca-7(E),14(E)-diene-5,12-dione (6cb). Azapenam **4cb** (102 mg, 0.49 mmol) was allowed to react according to the general procedure at 100 °C for 1 h to give 81 mg (82%) of product: mp 195–198 °C (CH_2Cl_2/hexane); $[\alpha]^{25}_D$ −99.1° (c = 1.83, CH_2Cl_2); ^1H NMR δ 7.69 (s, 1 H, CH=N), 7.14 (d, J = 9.8 Hz, 1 H, NH), 4.10–3.90 (m, 3 H, CHN and CH_2O), 3.56 (dd, J_1 = 12.0 Hz, J_2 = 11.6 Hz, 1 H, CH_2N), 3.48 (dd, J_1 = 12.1 Hz, J_2 = 3.9 Hz, 1 H, CH_2N), 2.57, 2.12–1.81 (m, 5 H, CH_2CH_2 and $CHMe_2$), 0.98 (d, J = 6.7 Hz, 3 H, CH_3), 0.91 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR δ 170.7 (CO), 165.5 (C=N), 87.5 ($C_{6,13}$), 70.1 (CH_2O), 61.2 (CH_2N), 54.2 (CHN), 34.7 ($OCH_2CH_2CH_2$), 30.9 ($C_{3,10}$), 25.4 ($OCH_2CH_2CH_2$), 19.6 (CH_3), 18.8 (CH_3); IR (KBr) ν 1676 (CO), 1656 (C=N), 1542, 1535 cm^{-1}; MS 420 (M^+). Anal. Calcd for $C_{22}H_{36}N_4O_4$: C, 62.83; H, 8.63; N, 13.32. Found: C, 62.77; H, 8.44; N, 13.13.

(6R*,13S*)-3,3,6,10,10,13-Hexamethyl-6,13-dimethoxy-1,4,8,11-tetraazacyclotetradecane-5,12-dione (7aa). Dioxocyclam **6aa** (91 mg, 0.25 mmol) was hydrogenated in MeOH at 45 psi of H_2 with 25 mg of 10% Pd/C at room temperature for 2 days. Filtration through Celite and evaporation of the solvent gave 86 mg (94%) of product as a 1/1 mixture of two conformers: mp ~170 °C dec (hexane/CH_2Cl_2); ^1H NMR (two conformers a/b ≈ 1/1, NH not visible) δ 7.84/7.38 (br s, CONH), 3.70(a) (d, J = 11.3 Hz, 1 H, CH_2N), 3.32/3.27 (s, 3 H, OCH_3), 3.02(b) (d, J = 12.0 Hz, 1 H, CH_2N), 2.95(a+b) (d, J = 12.1 Hz, 1 H, CH_2N), 2.82(b) (d, J = 12.5 Hz, 1 H, CH_2N), 2.76(a) (d, J = 12.1 Hz, 1 H, CH_2N), 2.48(b) (d, J = 12.1 Hz, 1 H, CH_2N), 2.35(a) (d, J = 11.3 Hz, 1 H, CH_2N), 1.50 (br)/1.42/1.41/1.37/1.33/1.31 (6 s, 9 H, 3 CH_3); ^1H NMR (50 °C, generally broad signals) δ 7.78 (s, 1 H, CONH), 3.25 (s, 3 H, OCH_3), 3.03 (d, J = 11.8 Hz, 1 H, CH_2N), 2.86 (d, J = 12.0 Hz, 1 H, CH_2N), 2.76 (d, J = 12.2 Hz, 1 H, CH_2N), 2.37 (d, J = 11.9 Hz, 1 H, CH_2N), 1.40 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3); ^{13}C NMR (two conformers) δ 172.3/171.8 (CO), 79.4/79.3 ($C_{6,13}$), 59.4/56.8/56.1/56.0 (2 CH_2), 53.1/52.4 ($C_{3,10}$) 50.9/50.6 (OCH_3), 27.3/26.5/25.3/23.4 (2 CH_3), 18.6/18.2 ($C_{6,13}$-CH_3); IR (KBr) ν 1664 (CO), 1541 cm^{-1}. Anal. Calcd for $C_{18}H_{36}N_4O_4$: C, 58.04; H, 9.74; N, 15.04. Found: C, 57.93; H, 9.86; N, 14.88.

3,3,6,10,10,13-Hexamethyl-6,13-bis(phenylmethoxy)-1,4,8,11-tetraazacyclotetradecane-5,12-dione (7ba). Dioxocyclam **6ba** (76 mg, 0.15 mmol) and racemic CSA (0.3 mmol, 68 mg) were hydrogenated in CH_2Cl_2 at 45 psi of H_2 with 20 mg of 10% Pd/C at 90 °C for 6 h. Filtration through Celite, washing with 5% aqueous $NaHCO_3$, drying over $MgSO_4$, and evaporation of the solvent gave the product as a mixture of two conformers. Chromatography on silica gel (EtOAc/MeOH, 2/1) gave the two conformers I (11.0 mg) and II (7.5 mg) in a total yield of 24%. Conformer I: mp 163–166 °C (hexane/CH_2Cl_2); ^1H NMR δ 8.69 (s, 1 H, CONH), 7.38–7.26 (m, 5 H, ArH), 4.55 (d, J = 11.4 Hz, 1 H, $PhCH_2$), 4.36 (d, J = 11.4 Hz, 1 H, benzylic), 2.96 (d, J = 12.1 Hz, 1 H, CH_2N), 2.71 (d, J = 11.9 Hz, 2 H, 1 H of each CH_2N), 2.37 (d, J = 11.7 Hz, 1 H, CH_2N), 1.78 (br s, 1 H, NH), 1.41 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3); ^{13}C NMR δ 171.9 (CO), 138.6, 128.4, 127.5, 127.1 (Ar), 79.4 ($C_{6,13}$), 65.9 (CH_2Ph), 60.8 (CH_2), 57.7 (CH_2), 52.8 ($C_{3,10}$), 25.6 (CH_3), 23.1 (CH_3), 19.6 ($C_{6,13}$-CH_3); IR (KBr) ν 1666 (CO), 1533 cm^{-1}. Conformer II: ^1H NMR δ 7.32–7.25 (m, 5 H, ArH), 7.16 (s, 1 H, CONH), 4.58 (d, J = 11.1 Hz, 1 H, $PhCH_2$), 4.45 (d, J = 11.1 Hz, 1 H, $PhCH_2$), 3.40 (d, J = 11.4 Hz, 1 H, CH_2N), 2.90 (d, J = 12.2 Hz, 1 H, CH_2N), 2.76 (d, J = 12.2 Hz, 1 H, CH_2N), 2.14 (d, J = 11.4 Hz, 1 H, CH_2N), 1.6 (br s, 1 H, NH), 1.41 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.14 (s, 3 H, CH_3); ^{13}C NMR δ 172.0 (CO), 138.7, 128.5, 127.6, 127.2 (Ar), 80.4 ($C_{6,13}$), 65.1 (CH_2Ph), 56.9 (CH_2), 56.1 (CH_2), 52.8 ($C_{3,10}$), 26.5 (CH_3), 25.2 (CH_3), 19.6 ($C_{6,13}$-CH_3); IR (KBr) ν 1666 (CO), 1522 cm^{-1}. Anal. Calcd for $C_{30}H_{44}N_4O_4$: C, 68.67; H, 8.45; N, 10.68. Found: C, 68.43; H, 8.30; N, 10.71 (mixture of conformers).

(6*R,13*S**)-3,3,10,10-Tetramethyl-6,13-bis(oxypropylene)-1,4,8,11-tetraazacyclotetradecane-5,12-dione (7ca).** Dioxocyclam **6ca** (62 mg, 0.16 mmol) was hydrogenated in CH_2Cl_2 at 45 psi of H_2 with 10% Pd/C (21 mg) at 90–100 °C for 22 h. Filtration through Celite, washing with 5% aqueous $NaHCO_3$, drying over $MgSO_4$, and evaporation of the solvent gave the product (54 mg, 86%) as a mixture of two conformers, a/b $\approx$ 1/3. Crystallization from hexane/CH_2Cl_2 gave one conformer: mp ~170 °C dec; ^1H NMR δ 6.86 (s, 1 H, CONH), 3.97–3.83 (m, 2 H, CH_2O), 3.49 (d, J = 11.3 Hz, 1 H, CH_2N), 3.13 (d, J = 11.5 Hz, 1 H, CH_2N), 2.49 (d, J = 11.5 Hz, 1 H, CH_2N), 2.36–2.28 (m, 1 H, CH_2 furan), 2.17 (d, J = 11.3 Hz, 1 H, CH_2N), 1.89–1.80 (m, 2 H, CH_2 furan), 1.71–1.61 (m, 1 H, CH_2 furan), 1.36 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3); ^{13}C NMR δ 173.0 (CO), 87.5 ($C_{6,13}$), 69.0 (CH_2O), 57.2 (CH_2N), 57.0 (CH_2N), 52.8 ($C_{3,10}$), 33.7 ($OCH_2CH_2CH_2$), 27.2 (CH_3), 25.3 ($OCH_2CH_2CH_2$), 25.0 (CH_3); IR (KBr) ν 1648 (CO), 1534 cm^{-1}. Anal. Calcd for $C_{20}H_{36}N_4O_4$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.62; H, 8.93; N, 13.98.

(3*S*,6*R*,10*S*,13*R*)-6,13-Dimethyl-6,13-dimethoxy-3,10-bis(1′-methylethyl)-1,4,8,11-tetraazacyclotetradecane-5,12-dione (7ab). Dioxocyclam **6ab** (28 mg, 0.07 mmol) was hydrogenated in CH_2Cl_2 at 45 psi of H_2 with 10% Pd/C (7 mg) for 37 h at room temperature. Filtration through Celite, washing with 5% aqueous $NaHCO_3$, drying over $MgSO_4$, and evaporation of the solvent gave 20 mg (70%) of product: mp 158–161 °C (CH_2Cl_2/hexane); $[\alpha]^{25}_D$ +65.7° (c = 1.02, CH_2Cl_2); ^1H NMR δ 6.60 (d, J = 10.3 Hz, 1 H, CONH), 3.97 (dddd, J_1 = 10.4 Hz, J_2 = 10.3 Hz, J_3 = 6.2 Hz, J_4 = 3.1 Hz, 1 H, CHN), 3.29 (s, 3 H, OCH_3), 3.10 (d, J = 11.7 Hz, 1 H, CH_2N), 2.76 (dd, J_1 = 13.0 Hz, J_2 = 10.4 Hz, 1 H, CH_2N), 2.62 (dd, J_1 = 13.0 Hz, J_2 = 3.1 Hz, 1 H, CH_2N), 2.48 (d, J = 11.7 Hz, 1 H, CH_2N), 2.16 (br s, 1 H, NH), 1.67 (oct, J = 6.7 Hz, 1 H, $CHMe_2$), 1.36 (s, 3 H, CH_3), 0.93 (d, J = 6.8 Hz, 3 H, CH_3), 0.90 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR δ 172.4 (CO), 80.5 ($C_{6,13}$), 55.8 (CH_2N), 52.7 (CH_2N), 51.7 (OCH_3 or CHN), 51.0 (CHN or OCH_3), 30.6 ($CHMe_2$), 19.7 (CH_3), 18.6 (CH_3), 18.5 (CH_3); IR (KBr) ν 1665 (CO), 1534 cm^{-1}. Anal. Calcd for $C_{20}H_{40}N_4O_4$: C, 59.97; H, 10.06; N, 13.99. Found: C, 59.97; H, 9.92; N, 13.99.

(3*S*,6*R*,10*S*,13*R*)-6,13-Dimethyl-6,13-bis(phenylmethoxy)-3,10-bis-(1′-methylethyl)-1,4,8,11-tetraazacyclotetradecane-5,12-dione (7bb). Dioxocyclam **6bb** (42 mg, 0.08 mmol) was hydrogenated in CH_2Cl_2 at 45 psi of H_2 with 10% Pd/C (12 mg) for 60 h at 70–80 °C. Filtration through Celite, washing with 5% aqueous $NaHCO_3$, drying over $MgSO_4$, and evaporation of the solvent gave 43 mg (96%) of product: mp 129–130 °C (CH_2Cl_2/hexane); $[\alpha]^{25}_D$ +28.9° (c = 1.39, CH_2Cl_2); ^1H NMR δ 7.36–7.26 (m, 5 H, ArH), 7.05 (d, J = 10.0 Hz, 1 H, CONH), 4.58 (d, J = 11.5 Hz, 1 H, $PhCH_2$), 4.48 (d, J = 11.5 Hz, 1 H, $PhCH_2$), 3.96 (dddd, J_1 = 10.0 Hz, J_2 = 9.4 Hz, J_3 = 6.6 Hz, J_4 = 3.2 Hz, 1 H, CHN), 3.10 (d, J = 12.0 Hz, 1 H, CH_2N), 2.77 (dd, J_1 = 12.7 Hz, J_2 = 9.4 Hz, 1 H, CH_2N), 2.66 (d, J = 12.0 Hz, 1 H, CH_2N), 2.61 (dd, J_1 = 12.7 Hz, J_2 = 3.2 Hz, 1 H, CH_2N), 2.15 (br s, 1 H, NH), 1.65 (oct, J = 6.6 Hz, 1 H, $CHMe_2$), 1.46 (s, 3 H, CH_3), 0.90 (d, J = 6.8 Hz, 3 H, CH_3), 0.85 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR δ 172.4 (CO), 138.5, 128.4, 127.5, 126.9 (Ar), 80.8 ($C_{6,13}$), 65.4 (CH_2Ph), 56.3 (C-H_2N), 52.3 (CH_2N), 52.2 (CHN), 30.5 ($CHMe_2$), 19.6 (CH_3), 19.5 (CH_3), 18.7 (CH_3); IR (KBr) ν 1661 (CO), 1526 cm^{-1}. Anal. Calcd for $C_{32}H_{48}N_4O_4$: C, 69.53; H, 8.75; N, 10.14. Found: C, 69.69; H, 8.60; N, 10.07.

(3*S*,6*R*,10*S*,13*R*)-3,10-Bis(1′-methylethyl)-6,13-bis(oxypropylene)-1,4,8,11-tetraazacyclotetradecane-5,12-dione (7cb). Dioxocyclam **6cb** (54 mg, 0.13 mmol) was hydrogenated in CH_2Cl_2 at 45 psi of H_2 with 10% Pd/C (17 mg) for 34 h at 70–80 °C. Filtration through Celite, washing with 5% aqueous $NaHCO_3$, drying over $MgSO_4$, and evaporation of the solvent gave 50 mg (92%) of product: mp 173–176 °C (CH_2Cl_2/hexane); $[\alpha]^{25}_D$ +40.2° (c = 1.22, CH_2Cl_2); ^1H NMR δ 6.52 (d, J = 10.5 Hz, 1 H, CONH), 3.99–3.81 (m, 3 H, 2 CH_2O and CHN), 3.47 (d, J = 11.2 Hz, 1 H, CH_2N), 2.78 (dd, J_1 = 13.0 Hz, J_2 = 11.1 Hz, 1 H, CH_2N), 2.7 (br s, 1 H, NH), 2.66 (dd, J_1 = 13.0 Hz, J_2 = 3.2 Hz, 1 H, CH_2N), 2.46 (ddd, J_1 = 12.4 Hz, J_2 = 6.1 Hz, J_3 = 5.5 Hz, 1 H, HC(3′)), 2.34 (d, J = 11.2 Hz, 1 H, CH_2N), 1.90–1.79 (m, 2 H, CH_2 furan), 1.73–1.59 (m, 2 H, 1CH_2 furan and $CHMe_2$), 0.91 (d, J = 6.8 Hz, 3 H, CH_3), 0.87 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR δ 173.1 (CO), 87.7 ($C_{6,13}$), 68.8 (CH_2O), 56.2 (CH_2N), 53.0 (CH_2N), 51.6 (CHN), 33.3 (OCH_2CH_2C-H_2), 30.5 ($CHMe_2$), 25.3 ($OCH_2CH_2CH_2$), 19.7 (CH_3), 18.3 (CH_3); IR (KBr) ν 1664 (CO), 1528 cm^{-1}. Anal. Calcd for $C_{22}H_{40}N_4O_4$: C, 62.24; H, 9.50; N, 13.20. Found: C, 62.32; H, 9.33; N, 13.44.

Acknowledgment. Support for this research by National Science Foundation Grant CHE-8921992 is gratefully acknowledged.

Registry No. 1a, 141345-35-9; **1b**, 141345-36-0; **2a**, 20540-69-6; **2b**, 117041-03-9; **2c**, 54040-15-2; **3aa**, 141345-37-1; **3ab**, 141345-38-2; **3ba**, 141345-39-3; **3bb**, 141345-40-6; **3ca**, 141345-41-7; **3cb**, 141345-42-8; **4aa**, 141345-43-9; **4ab**, 141345-44-0; **4ba**, 141345-45-1; **4bb**, 141345-46-2; **4ca**, 141345-47-3; **4cb**, 141345-48-4; **5aa**, 141345-49-5; **5ab**, 141345-50-8; **5ba**, 141345-51-9; **5bb**, 141345-52-0; **5ca**, 141345-53-1; **5cb**, 141345-54-2; **6aa**, 141345-55-3; **6ab**, 141345-56-4; **6ba**, 141345-57-5; **6bb**, 141345-58-6; **6ca**, 141345-59-7; **6cb**, 141345-60-0; **7aa**, 141345-61-1; **7ab**, 141345-62-2; **7ba**, 141345-63-3; **7bb**, 141345-64-4; **7ca**, 141345-65-5; **7cb**, 141345-66-6; chromium hexacarbonyl, 13007-92-6; 4-chlorobutyryl chloride, 4635-59-0; 2-methyl-1,2-propanediamine, 811-93-8; *tert*-butyl isocyanide, 7188-38-7; 4,4-dimethyl-Δ^2-imidazoline, 2305-59-1; (*S*)-valinol, 2026-48-4; (*S*)-*N*-(benzyloxycarbonyl)valinol, 6216-65-5; (*S*)-3-methyl-2-[(benzyloxycarbonyl)amino]butyl azide, 141345-67-7; (*S*)-3-methyl-1,2-butanediamine, 40630-14-6; (*S*)-4-(1′-methylethyl)-Δ^2-imidazoline, 141345-68-8.