Iminodithiocarbonates as Formaldehyde Imine Equivalents: Sequential Two Step Approach to 4-Unsubstituted β-Lactams through Chromium(0) Carbene Photocycloaddition–Nickel Boride Desulfurization

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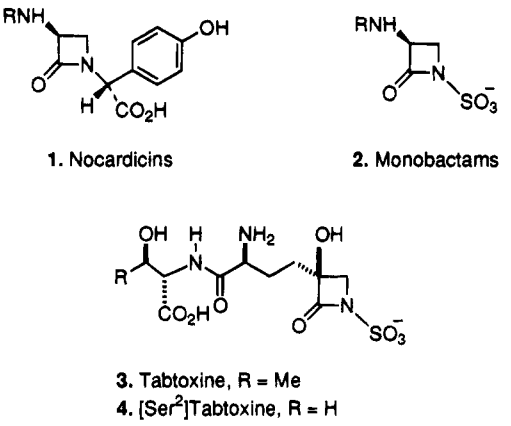
Introduction

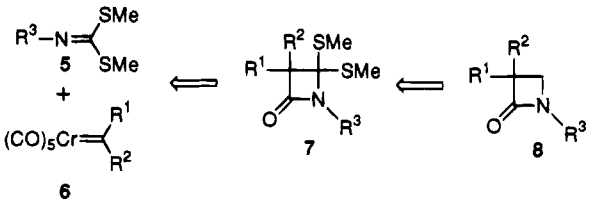
Two important groups of monocyclic β-lactam antibiotics described first in the mid-seventies are nocardicins **1**[2] and monobactams **2**.[3] Both types of antibiotics have a 4-unsubstituted β-lactam ring as characteristic feature. Additionally, other monocyclic β-lactams lacking substituents at C4 of the 2-azetidinone ring have been isolated from natural sources. Some examples are tabtoxin **3**,[4] and its lower homologue [Ser^2]-tabtoxin **4**, (Chart 1).[5]

A variety of syntheses of 4-unsubstituted 2-azetidinones have been reported,[6] including the classical Staüdinger reaction.[7] Most of the ketene based approaches to these systems are based on unstable formaldehyde imines (generated *in situ* from the trimers)[7c,d] or on the use of formaldehyde imine equivalents, namely substrates bearing a functionalized C=N double bond in order to place an appropriate substituent at the C4 position of the 2-azetidinone ring which is further eliminated.[7a,b,e] Our recent synthesis of 4-oxo-2-azetidinones (malonoimides)[8] uses β-lactams **7** having a thioketal functionality at C4 of the four membered ring as the key intermediates. Compounds **7** are easily available by photocycloaddition of chromium carbene complexes **6** and iminodithiocarbonates **5**. It is clear that 4-unsubstituted-2-azetidinones **8**, may be accessible from compounds **7** through a desulfurization reaction (Scheme 1).[9] The elimination of the thioketal moiety by NiB_2 and by other reagents is discussed.

Chart 1



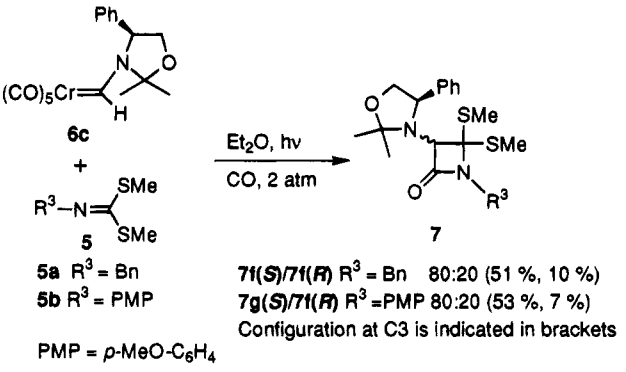
Scheme 1



Results and Discussion

4,4-*Bis*(methylthio)-β-lactams **7** were obtained in good yields following our previously reported method.[8] This approach is suitable for the preparation of chiral 2-azetidinones using chiral aminocarbene **6c** (Scheme 2).[10]

Scheme 2



We first tested Raney-Ni to remove the thioketal group in compounds **7** using 3-alkoxy-substituted 2-azetidinones **7a** and **7b** as substrates. The corresponding desulfurized β-lactams **8a** and **8b** were obtained in 50% and 20% isolated yield, respectively. However, extensive decomposition of the starting β-lactam to uncharacterized

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(2) (a) Aoki, H.; Sakai, H.; Kohsaka, M.; Konomi, T.; Hosoda, J.; Kubochi, Y.; Iguchi, E.; Imanaka, H. *J. Antibiot.* **1976**, *29*, 492, 890. (b) Hashimoto, M.; Komori, T.; Kamiya, T. *J. Am. Chem. Soc.* **1976**, *98*, 3023. (c) Hosoda, J.; Konomi, T.; Tani, N.; Aoki, H.; Imanaka, H. *Agric. Biol. Chem.* **1977**, *41*, 2013.

(3) (a) Imada, A.; Kitano, K.; Kintaka, K.; Muroi, M.; Asai, M. *Nature (London)*, **1981**, *289*, 590. (b) Sykes, R. B.; Cimarusti, C. M.; Bonner, D. P.; Bush, K.; Floyd, D. M.; Georgopapadakou, N. H.; Koster, W. H.; Liu, W. C.; Parker, W. L.; Principe, P. A.; Rathnum, M. L.; Slusarchyk, W. A.; Trejo, W. H.; Wells, J. S. *Nature (London)*, **1981**, *291*, 489. (c) Wells, J. S.; Hunter, J. C.; Astle, G. L.; Sherwood, J. C.; Ricca, C. M.; Trejo, W. H.; Bonner, D. P.; Sykes, R. B. *J. Antibiot.* **1982**, *35*, 814.

(4) Stuart, W. W. *Nature (London)*, **1971**, *229*, 174.

(5) Tayior, P. A.; Schnoes, H. K.; Durbin, R. D. *Biochim. Biophys. Acta* **1972**, *286*, 107.

(6) Salitura, G. M.; Townsend, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 760 and pertinent references therein.

(7) Acid chloride-base approach: (a) Kamiya, T.; Hashimoto, M.; Nakaguchi, O.; Oku, T. *Tetrahedron* **1979**, *35*, 323. (b) Curran, W. V.; Sassiver, M. L.; Ross, A. S.; Fields, T. L.; Boothe, J. H. *J. Antibiot.* **1985**, *35*, 329. (c) Nakaguchi, O.; Oku, T.; Takeno, H.; Hashimoto, M.; Kamiya, T. *Chem. Pharm. Bull.* **1987**, *35*, 3985. Chromium carbene complexes approach: (d) Hegedus, L. S.; D'Andrea, S. *J. Org. Chem.* **1988**, *53*, 3113. (e) Narukawa, Y.; Juneau, K.; Snustad, D.; Miller, D. B.; Hegedus, L. S. *Org. Chem.* **1992**, *57*, 5453.

(8) Alcaide, B.; Domínguez, G.; Plumet, J.; Sierra, M. A. *J. Org. Chem.* **1992**, *57*, 447.

(9) An entry to 2-azetidinones of type **8** starting from iminodithiocarbonates has been previously reported by Sharma. See: Sharma, S. D.; Mehra, U.; Khurana, J. P. S.; Pandhi, S. B. *Synthesis* **1987**, 990. However, this approach is restricted to compounds with a phenoxy substituent at the C3 position of the β-lactam ring, and, as discussed in the text, the Raney-Ni desulfurization used by Sharma is not compatible with nitrogen and other substituents.

(10) The use of chiral iminodithiocarbonates as substrates in the synthesis of chiral β-lactams **7** was not possible. Preparation of these substrates starting from optically pure α-amino esters resulted in total racemization, independently of the synthetic approach used.

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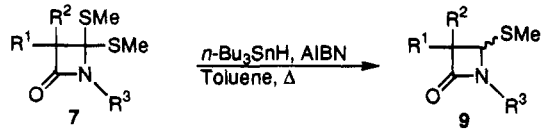
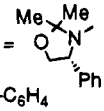
products derived from ring opening made the purification step very difficult. Furthermore, 2-azetidinone **7d** gave intractable reaction mixtures. The low yield of the Raney-Ni mediated desulfurization of β-lactams is well documented in the case of 4-mercapto-substituted 2-azetidinones, and is one of the failings of most of the syntheses of 4-unsubstituted-2-azetidinones starting from thioimidates.[7a] Desulfurization of β-lactams **7** by Bu^n_3-SnH (TBTH) was next tested.[11] Compounds **7a** and **7b** reacted smoothly with TBTH in the presence of AIBN in boiling benzene to yield a mixture of *cis,trans*-4-(methylthio)-2-azetidinones **9** in essentially quantitative yield. 3-Amino substituted-2-azetidinones **7d** and **7g(S)** formed the monosulfurated derivatives under analogous conditions. Compound **7g(S)** gave a single diastereomer (de > 95%) while **7d** formed a *cis-trans* mixture (Scheme 3). All attempts to eliminate the remaining mercapto group (syringe pump, slow addition of the tin reagent), increasing the reaction times and using different concentration of the reagents were unsuccessful. In all cases no reaction was observed. Methodology to remove the methylthio group in compounds analogous to **9** has been reported, but yields are low.[7a] Nevertheless, it was desirable for our synthetic goals to effect the transformation in a single step. Attempts to obtain the more easily removable diphenyl thioketal by reaction of β-lactams **7** with PhSH in the presence of $BF_3{\cdot}Et_2O$ resulted in clean opening of the lactam ring to form *N*-benzyl-2-methoxy-2-(methylthiocarbonyl)propanamide **10**.[12,13]

Scheme 3

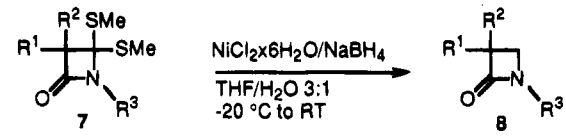


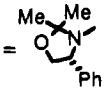
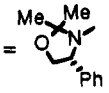
7a R^1 = Me, R^2 = MeO, R^3 = Bn — **9a** (91 %, *cis/trans* 60:40)
7d R^1 = H, R^2 = Bn_2N, R^3 = Bn — **9b** (90 %, *cis/trans* 70:30)
7g R^1 = H, R^2 =  R^3 = PMP — **9c** (40 %, *cis/trans* 100:0)

PMP = *p*-MeO-C_6H_4

The use of Ni-based desulfurization agents is well established.[14] We tested first NiCRA (Nickel complex reducing agents) to desulfurize 2-azetidinone **7a**. In our case, the optimum composition of NiCRA was NiCRA (5:2:1) generated from $Ni(OAc)_2$, NaH, and *t*-AmOH.[15] In fact, we obtained a 30% yield of pure **8a** together with variable amounts of different uncharacterized open chain compounds. It was necessary to use very large excess of the reducing agent and very large volume of solvent to obtain positive results. These reaction conditions make this approach infeasible. On the other hand, desulfurizations mediated by nickel borides using acceptable excesses of the reagent have been recently reported.[16]

Scheme 4



7a R^1 = Me R^2 = OMe R^3 = Bn **8a** (65 %)
7b R^1 = Me R^2 = OBn R^3 = Bn **8b** (70 %)
7c R^1 = Me R^2 = OBn R^3 = PMP **8c** (60 %)
7d R^1 = H R^2 = NBn_2 R^3 = Bn **8d** (40 %)
7e R^1 = H R^2 = NBn_2 R^3 = PMP **8e** (35 %)
7f R^1 = H R^2 =  R^3 = Bn **8f** (18 %)
7g R^1 = H R^2 =  R^3 = PMP **8g** (20 %)
7h R^1 = Ph R^2 = Ph R^3 = PMP **8h** (90 %)

PMP = *p*-$MeOC_6H_4$

Thus, compounds **7** reacted smoothly with Ni_2B generated from $NiCl_2 \times 6H_2O$ and $NaBH_4$ to produce the desired 4-unsubstituted-β-lactams in fair to good yields. Both 3-alkoxy- and 3-amino-substituted 2-azetidinones were desulfurized by Ni_2B without fragmentation of the 4-membered ring. Pure compounds **8** were obtained by flash chromatography of the crude mixtures (Scheme 4). β-Lactams **7** having alkoxy- and aryl substituents[17] yield the corresponding unsubstituted compounds **8** in good to excellent yields, while only moderate yields of desulfurized products were obtained with 3-amino substituted β-lactams. Nevertheless, the Ni_2B mediated desulfurization is overall at least as efficient as other approaches to obtain 4-unsubstituted-β-lactams having 3-amino substituents and considerably more efficient for 3-alkoxy or 3-aryl substituents. Finally chiral β-lactams **7f** and **7g** are desulfurized without racemization.

In conclusion, a sequential two step synthesis of 4-unsubstituted-β-lactams starting from readily available iminodithiocarbonates has been developed. Our approach is highly effective to prepare these compounds with alkoxy or aryl substituents at the 3-position of the four membered ring. 3-Amino-substituted β-lactams are also available through the reported methodology but in lower yields. Nevertheless, this approach may be competitive with other reported synthesis of these compounds.

Experimental Section

General Procedure. General experimental data and procedures have been previously reported.[8] Compounds **7a**, **7c**, **7d**, and **7e** have been previously described by us.[8] 4,4-Bis(methylthio) β-lactams **7b**, **7f**, and **7g**, were prepared following our reported method.[8] Compound **7h** was prepared following the Metzger's[18] method. See the supplementary material for full

(11) Caubère, P.; Coutrot, P. In *Comprehensive Organic Synthesis*, Trost, B. M., Ed.; Pergamon Press: Oxford, UK, 1991; Vol. 8, p 845.
(12) Protic or Lewis acid ring opening of β-lactams analogous to **7** have been previously reported. Sullivan, D. F.; Scopes, D. I. C.; Kluge, A. F.; Edwards, J. A. *J. Org. Chem.* **1976**, *41*, 1112. See also ref 9.
(13) 4,4-Diphenylthio substituted β-lactams have been recently synthesized by reaction of diphenyliminodithiocarbonates, prepared by interchange of dimethyliminodithio carbonates and PhSH, and activated ketenes: Bachi, M. D.; Bar-Ner, N. *Biomed. Chem. Lett.* **1993**, *3*, 2439. In our hands all attempts to reproduce Bachi's results were fruitless.
(14) Reviews: (a) Luh, T.-Y.; Ni, Z.-J. *Synthesis* **1990**, 89. (b) Ganem, B.; Osby, J. O. *Chem. Rev.* **1986**, *86*, 763. (c) Caubère, P. *Angew. Chem.; Int. Ed. Engl.* **1983**, *22*, 599. See also ref. 11.
(15) Becker, S.; Fort, Y.; Caubère, P. *J. Org. Chem.* **1990**, *55*, 6194.
(16) Back, T. G.; Baron, D.; Yang, K. *J. Org. Chem.* **1993**, *58*, 2407.
(17) Preliminary studies directed toward tabtoxine synthesis show that alkoxy-substituted-β-lactams **8b** and **8c** are easily transformed in 3-hydroxy-*NH*-β-lactams in multigram scale by standard manipulations. These results will be published in full elsewhere.
(18) Metzger, C.; Wegler, R. *Chem. Ber.* **1968**, *101*, 1120.

experimental procedure and spectroscopic data. The following chemicals were prepared according to literature procedures: pentacarbonyl[(benzyloxy)(methyl)carbene] chromium(0) **6a**,[19] pentacarbonyl[(*N,N*-dibenzylamino)methylene]chromium(0) **6b**,[20] pentacarbonyl[5(*S*)-2,2-dimethyl-5-isopropyl-1,3-azaoxacyclopentyl)methylene]chromium(0) **6c**,[20] diphenylketene,[21] *N*-aliphatic-iminodithiocarbonates were prepared by using a phase transfer catalysis modification of the previously reported method[12] which was used for *N*-aryliminodithiocarbonates.

General Procedure for Desulfurization of 4,4-Bis(methylthio)azetidin-2-ones 7 with *n*-Bu$_3$SnH/AIBN. *n*-Bu$_3$SnH (5 mmol) in benzene (7.5 mL) was added dropwise during a 0.5 h period to a boiling solution of β-lactam **7** (1 mmol) and AIBN (5% w/w) in anhydrous benzene (15 mL). The resulting mixture was heated for an additional 4 h, washed with water and extracted with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$), and the solvent removed in vacuo. Pure compounds **9** were obtained by silica gel flash chromatography.

1-Benzyl-3-methoxy-3-methyl-4-methylthioazetidin-2-one (9a). From 0.21 g (0.70 mmol) of **7a**, 0.01 g (0.07 mmol) of AIBN and 1.02 g (3.50 mmol) of *n*-Bu$_3$SnH was obtained 0.16 g (91%) of pure **9a** by silica-gel flash chromatography (hexane/EtOAc 20%) as 60:40 mixture of inseparable *cis-trans* isomers as colorless oil. ^{1}H NMR: δ 1.46 (s, 3H, maj.), 1.48 (s, 3H, min), 1.75 (s, 3H, maj.), 1.99 (s, 3H, min.), 3.39 (s, 3H, maj.), 3.57 (s, 3H, min.), 4.06 (d, 1H, J = 15.2 Hz, maj. + min.), 4.22 (s, 1H, min.), 4.48 (s, 1H, maj.), 4.77 (d, 1H, J = 15.2 Hz, min.), 4.84 (d, 1H, J = 15.2 Hz, maj.), 7.26 (m, 5H, maj. + min.); ^{13}C NMR δ 168.1 (min.), 168.0 (CO, maj), 135.1, 135.0, 129.0, 128.4, 128.3, 128.1, 128.0 (Arom, maj. + min.), 91.5 (maj.), 89.4 (min.), 70.9 (min.), 69.5 (maj.), 54.0 (min.), 53.1 (maj.), 43.3 (min.), 43.1 (maj.), 17.4 (min.), 16.5 (maj.), 15.5 (maj.), 13.1 (min.); IR (Cl_3CH) ν 1760 cm.$^{-1}$ Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.13; H, 6.82; N, 5.58; S, 12.73. Found: C, 61.84; H, 6.50; N, 5.87; S, 12.48.

1-Benzyl-3-(dibenzylamino)-4-(methylthio)azetidin-2-one (9b). From 0.10 g (0.22 mmol) of **7d**, 5 mg (0.04 mmol) of AIBN and 0.32 g (1.09 mmol) of *n*-Bu$_3$SnH was obtained 0.08 g (90%) of pure **9b** by silica-gel flash chromatography (hexane/EtOAc 20%) as 70:30 mixture of inseparable *cis-trans* isomers as colorless oil. ^{1}H NMR: δ 1.74 (s, 3H, *c*), 2.09 (s, 3H, *c*), 3.56 (d, 2H, J = 13.5 Hz, *t*), 3.85 (d, 2H, J = 13.5 Hz, *t*), 3.92 (d, 2H, J = 14.1 Hz, *c*), 4.01 (d, 2H, J = 14.1 Hz, *c*), 4.16 (d, 1H, J = 15.3 Hz, *c*), 4.16 (d, 1H, J = 14.7 Hz, *t*), 4.21 (d, 1H, J = 2.1 Hz, *t*), 4.39 (d, 1H, J = 4.8 Hz, *c*), 4.48 (d, 1H, J = 2.1 Hz, *t*), 4.51 (d, 1H, J = 4.8 Hz, *c*), 4.75 (d, 1H, J = 14.7 Hz, *t*), 4.76 (d, 1H, J = 15.3 Hz, *c*), 7.23−7.45 (m, 15H, *c* +*t*); ^{13}C NMR δ 167.5 (*c*), 167.0 (*t*), 138.3, 137.9, 135.4, 135.0, 128.9, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.3, 127.0, 73.5 (*t*), 71.9 (*c*), 67.9 (*c*), 59.2 (*t*), 55.3 (*c*), 54.8 (*t*), 43.8 (*c*), 43.3 (*t*), 17.5 (*t*), 13.6 (*c*); IR (Cl_3CH) ν 1750 cm.$^{-1}$ Anal. Calcd for $C_{25}H_{26}N_2OS$: C, 74.59; H, 6.52; N, 6.96; S, 7.95. Found: C, 74.84; H, 6.62; N, 7.14; S, 7.53.

1-*p*-Anisyl-3(*S*)-((5*S*)-2,2-dimethyl-5-isopropyl-1,3-azaoxacyclopentyl)-4-methylthioazetidin-2-one (9c). From 0.15 g (0.34 mmol) of **7g(*S*)**, 8 mg (0.06 mmol) of AIBN and 0.49 g (1.70 mmol) of *n*-Bu$_3$SnH was obtained 0.05 g (40%) of pure **9c** by silica-gel flash chromatography (hexane/EtOAc 20%) as a single *cis*-isomer as colorless oil. $[\alpha]_D^{25}$ = −15.6° (c = 1.02, $CHCl_3$): ^{1}H NMR: δ 1.54 (s, 3H), 1.59 (s, 3H), 2.07 (s, 3H), 3.76 (s, 3H), 3.83 (dd, 1H, J_1 = 6.0 Hz, J_2 = 8.7 Hz), 4.34 (t, 1H, J = 8.5 Hz), 4.60 (d, 1H, J = 4.4 Hz), 4.94 (m, 2H), 6.83 (d, 2H, J = 9.0 Hz), 7.18−7.37 (m, 5H), 7.51 (d, 2H, J = 9.0 Hz); ^{13}C NMR δ 162.6, 155.8, 142.5, 130.0, 128.2, 128.1, 127.2, 119.8, 114.3, 97.0, 71.4, 68.1, 65.9, 64.0, 55.5, 27.9, 23.7, 13.6; IR (Cl_3CH) ν 1745 cm^{-1}; Anal. Calcd for $C_{22}H_{26}N_2O_3S$: C, 66.31; H, 6.53; N, 7.03; S, 8.04. Found: C, 66.12; H, 6.50; N, 7.21; S, 7.92.

General Procedure for Desulfuration of 4,4-Bis(methylthio)azetidin-2-ones 7 with NiB_2. β-Lactam **7** (1 mmol) and $NiCl_2 \times 6H_2O$ (14 mmol) were dissolved in a 3:1 MeOH/THF mixture (30 mL). The solution was cooled to −20 °C, and $NaBH_4$ (42 mmol) was added in small portions (Caution: vigorous reaction with hydrogen evolution). The inmediate formation of a black precipitate was observed, and the mixture was stirred for an additional 15 min and was allowed to reach RT. The precipitate was then filtered through Celite and washed with MeOH/THF. The solvent was eliminated and the resulting crude mixture was extracted with methylene chloride. Pure compounds **8** were obtained by chromatography. Spectroscopic and analytical data for some representative forms of **8** follows. Full spectroscopic and analytical data of compounds **8** not included in this Experimental Section are included in the supplementary material.

1-Benzyl-3-(benzyloxy)-3-methylazetidin-2-one (8b). From 0.74 g (2.0 mmol) of **7b**, 6.66 g (28 mmol) of $NiCl_2 \times 6H_2O$ and 3.19 g (84.00 mmol) of $NaBH_4$ was obtained 0.39 g (70%) of pure **8b** by silica-gel flash chromatography (hexane/EtOAc 20%) as colorless oil. ^{1}H NMR: δ 1.60 (s, 3H), 3.05 (d, 1H, J = 5.9 Hz), 3.39 (d, 1H, J = 5.9 Hz), 4.43 (s, 2H), 4.62 (q, 2H, J = 10.8 Hz), 7.25−7.37 (m, 10H); ^{13}C NMR δ 169.5, 137.8, 135.2, 128.9, 128.6, 128.5, 128.4, 127.9, 127.7, 87.4, 67.8, 51.9, 45.6, 19.5; IR (Cl_3CH) ν 1740 cm^{-1}; Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.76; N, 4.98. Found: C, 77.04; H, 6.92; N, 4.79.

1-Benzyl-3-(*N,N*-dibenzylamino)azetidin-2-one (8d). From 0.14 g (2.0 mmol) of **7d**, 1.06 g (4.48 mmol) of $NiCl_2 \times 6H_2O$ and 0.51 g (13.42 mmol) of $NaBH_4$ was obtained 0.05 g (40%) of pure **8d** by silica-gel flash chromatography (hexane/EtOAc 20%) as colorless oil. ^{1}H NMR: δ 3.04 (m, 2H), 3.64 (d, 2H, J = 13.8 Hz), 3.79 (d, 2H, J = 13.8 Hz), 4.27 (dd, 1H, J_1 = 2.7 Hz, J_2 = 4.2 Hz), 4.30 (d, 1H, J = 15 Hz), 4.39 (d, 1H, J = 15 Hz), 7.19−7.32 (m, 15H); ^{13}C NMR δ 168.8 (CO), 138.1, 135.4, 128.8, 128.7, 128.2, 128.0, 127.6, 127.1, 68.7, 54.7, 45.6, 43.4; IR (Cl_3CH) ν 1750 cm^{-1}; Anal. Calcd for $C_{24}H_{24}N_2O$: C, 80.87; H, 6.74; N, 7.86. Found: C, 81.13; H, 6.86; N, 7.69.

1-Benzyl-3(*S*)-((5*S*)-2,2-dimethyl-5-isopropyl-1,3-azaoxacyclopentyl)azetidin-2-one (8f(*S*)). From 0.08 g (0.18 mmol) of **7f(*S*)**, 0.62g (2.62 mmol) of $NiCl_2 \times 6H_2O$ and 0.29 g (7.63 mmol) of $NaBH_4$ was obtained 0.01 g (18%) of pure **8f(*S*)** by silica-gel flash chromatography (hexane/EtOAc 20%) as colorless oil. $[\alpha]_D^{25}$ = +27° (c = 0.16, $CHCl_3$):^{1}H NMR: δ 1.46 (s, 3H), 1.48 (s, 3H), 2.45 (dd, 1H, J = 2.7, 5.7 Hz), 2.99 (t, 1H, J = 5.7 Hz), 3.72 (dd, 1H, J = 4.2, 6.6 Hz), 4.19 (s, 2H), 4.31 (m, 3H), 7.03 (m, 2H), 7.22−7.28 (m, 8H); ^{13}C NMR δ 168.6, 142.9, 135.4, 128.6, 128.4, 128.1, 127.5, 127.4, 96.2, 72.4, 64.8, 61.9, 45.9, 45.6, 27.7, 23.8; IR (Cl_3CH) ν 1740 cm^{-1}; Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 75.20; H, 6.85; N, 8.24.

1-*p*-Anisyl-3(*S*)-((5*S*)-2,2-dimethyl-5-isopropyl-1,3-azaoxacyclopentyl)azetidin-2-one (8g(*S*)). From 0.27 g (0.62 mmol) of **7g(*S*)**, 2,31 g (9.72 mmol) of $NiCl_2 \times 6H_2O$ and 1.10 g (29.10 mmol) of $NaBH_4$ was obtained 0.04 g (20%) of pure **8g(*S*)** by silica-gel flash chromatography (hexane/EtOAc 15%) as colorless oil. $[\alpha]_D^{25}$ = +125° (c = 0.68, $CHCl_3$): ^{1}H NMR: δ 1.49 (s, 3H), 1.50 (s, 3H), 2.69 (dd, 1H, J_1 = 2.7, 5.7 Hz), 3.37 (t, 1H, J = 5.7 Hz), 3.75 (s, 3H), 3.80 (dd, 1H, J = 5.7, 7.8 Hz), 4.30 (m, 2H), 4.39 (dd, 1H, J = 2.7, 5.7 Hz), 6.79 (d, 2H, J = 8.7 Hz), 7.06 (d, 2H, J = 8.7 Hz), 7.17−7.20 (m, 3H), 7.30−7.34 (m, 2H); ^{13}C NMR δ 165.4, 156.1, 142.4, 131.3, 128.5, 127.7, 127.5, 117.9, 114.2, 96.2, 72.2, 63.8, 61.8, 55.4, 45.2, 27.7, 23.9; IR (Cl_3CH) ν 1740 cm^{-1}; Anal. Calcd for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.82; N, 7.95. Found: C, 71.65; H, 6.92; N, 8.07.

1-(*p*-Anisyl)-3,3-diphenylazetidin-2-one (8h). From 2.30 g (5.40 mmol) of **7h**, 18.3 g (77.0 mmol) of $NiCl_2 \times 6H_2O$ and 8.6 g (0.23 mol) of $NaBH_4$ was obtained 1.59 g (90%) of pure **8h** by crystallization from hexane/EtOAc mixtures. Colorless solid. Mp. 135−138 °C (hexane/EtOAc). ^{1}H NMR δ 3.70 (s, 3H), 4.16 (s, 2H), 6.82 (d, 2H, J = 8.90 Hz), 7.23−7.44 (m, 12H); ^{13}C NMR δ 165.7, 156.1, 139.9, 131.6, 128.7, 128.5, 127.2, 126.9, 117.6, 114.2, 65.1, 55.3, 53.6; IR ($CHCl_3$) ν 1740 cm^{-1}; Anal. Calcd for $C_{22}H_{19}NO_2$: C, 80.24; H, 5.77; N, 4.25. Found: C, 80.40; H, 5.69; N, 4.50.

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Supplementary Material Available: Full spectral and analytical data for compounds **7b**, **7f**, **7g**, **7h**, **8a**, **8c**, **8e**, and **10** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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