Synthesis of an Optically Active 4-Acetoxyazetidinone Intermediate for Penems and Carbapenems

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The synthesis of the novel (3*R*,4*R*)-4-acetoxy-3-[(1*S*)-1-*t*-butyldimethylsilyloxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]azetidin-2-one (**1a**), a valuable key intermediate for penems and carbapenems bearing a 6-hydroxyacetamide side chain, and its diastereomer **1b**, from dimethyl *cis*-2,3-oxirane dicarboxylate, is described. The allocation of absolute configurations to the diastereomers **1a** and **1b** ensued *via* single-crystal X-ray analysis of the isomer **1b**.

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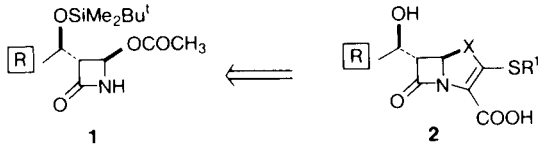
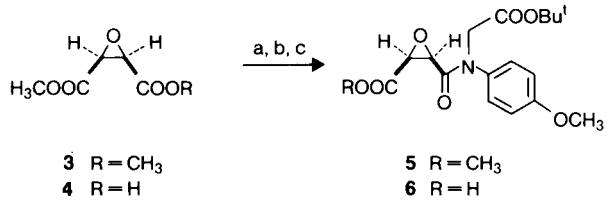
The penems **2** (X = S) [1] and carbapenems **2** (X = CH_2) [2] represent two classes of potent β-lactam antibiotics which have been intensively investigated over the last decade. During this period numerous synthetic derivatives have been prepared. However, in the great majority of these compounds, the original 1-hydroxyethyl side chain (R = CH_3) of the naturally occurring thienamycin [3] was not modified. A disadvantage of many molecules **2** in general, but particularly pronounced among the carbapenems, is their susceptibility to renal dehydropeptidase, an enzyme responsible for their metabolic inactivation *in vivo* [4]. In our attempt to achieve broad antibacterial activity and metabolic stability in a single compound we were interested in modifying R in the common side chain.



An optically active 4-acetoxyazetidinone **1** was envisaged as key intermediate for the synthesis of the antibiotics **2**. Compounds **1** with R = CH_3 have been used in numerous instances for the synthesis of penems [5] and carbapenems [6], but only a few examples exist concerning the preparation and use of azetidinones **1** with R ≠ CH_3 [7]. Recently we prepared a new type of carbapenem [8] *via* the racemic intermediate **1** with R = $COOCH_3$. Our aim now was to make available similar derivatives **2**, bearing a 6-hydroxyacetamide side chain, in optically active form.

In this report we describe the synthesis of (3*R*,4*R*)-4-acetoxy-3-[(1*S*)-1-*t*-butyldimethylsilyloxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]azetidin-2-one (**1a**), a key intermediate for the antibiotics **2** with R = CONHR'. Our synthetic plan for **1a** originated from the proven value of oxiranes [9] and oxirane dicarboxylates [8] in the stereoselective construction of other azetidinones. We considered the oxirane diamides **7** to be appropriate azetidinone precursors.

Scheme I. Preparation of the Racemic Acid **6** [a].



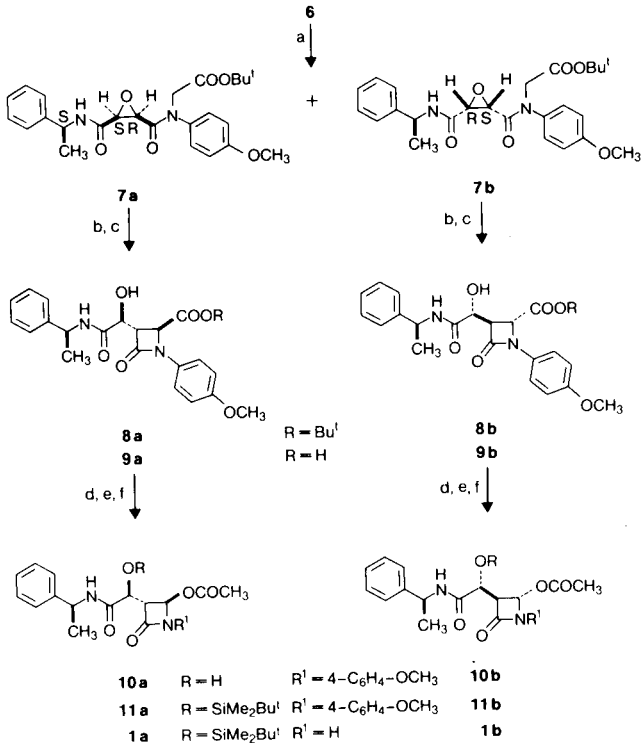
3 R = CH_3
4 R = H

5 R = CH_3
6 R = H

[a] Reagents: a Ficin (catalytic), 0.1 *M* phosphate buffer *p*H 7, room temperature, 20 hours, 47%. [b] DCC, CH_3O-C_6H_4-NH-CH_2-COOBu^t, THF, room temperature, 30 minutes, 90%. c MeOH, MeONa, H_2O (1 equivalent), room temperature, 15 hours, 98%.

Asymmetric synthesis employing the enzymatic [10] or non-enzymatic [11] differentiation between two identical groups in meso and prochiral compounds is now well established. Therefore, in an initial attempt, we investigated the direct preparation of the diasteromers **7** by subsequent condensation of the meso compound *cis*-2,3-oxiranedicarboxylic acid [12] with (*S*)-(-)-phenethylamine and *t*-butyl *N*-(4-methoxyphenyl)glycinate [9c] in a "one pot" reaction. However, this approach proved inefficient in terms of yield and product purity. Thus, in a more lengthy approach, dimethyl 2,3-oxiranedicarboxylate (**3**) [13] was selectively hydrolyzed in water at *p*H 7 in the presence of a catalytical amount of the enzyme ficin to afford the racemic mono acid **4** (Scheme I). Dicyclohexylcarbodiimide (DCC)/1-hydroxy-1*H*-benztriazole (HOBT)-mediated condensation of the acid **4** with *t*-butyl *N*-(4-methoxyphenyl)-glycinate [9c] gave the epoxyamide **5**, which was hydrolyzed at room temperature in methanol containing 1 equivalent of sodium hydroxide to furnish the acid **6** in good overall yield. Condensation of racemic **6** with the chiral auxiliary (*S*)-(-)-phenethylamine gave rise to a mixture of the two diasteromeric *cis*-2,3-oxiranediamides **7** which were separated by chromatography on silica gel to provide the less polar **7a** (22%) and the more polar **7b** (41%), both in pure form (Scheme II).

Scheme II. Elaboration of the Optically Active Acetoxyazetidinones **1a** and **1b** [a]



[a] Reagents: a (*S*)-(-)-phenethylamine, DCC, HOBT, THF, room temperature, 1 hour. b Bu_4NF, molecular sieves 4 Å, THF, 0°, 1.5 hours. c $CF_3COOH:CH_2Cl_2$ 1:1, room temperature, 3 hours. d $Pb(OAc)_2$, HOAc, DMF, 60°, 5 minutes. e Bu^tMe_2SiCl, DMAP, DMF, room temperature, 7-9 d, f $(NH_4)_2Ce(NO_3)_6$, CH_3CN, H_2O, 0°, 30 minutes.

Each of these two diastereomers was then introduced separately into the further reaction sequence. According to literature precedent [9] the relative configuration of the subsequent azetidinone step **8** should be predetermined by the *cis* geometry of the epoxyamides **7**. Indeed, treatment of **7a** and **7b** each with tetrabutylammoniumfluoride in THF at 0° [8,14] selectively produced the *trans*-azetidinones **8a** (36%) and **8b** (38%). Cleavage of the

Table 1

Positional Parameters and Their Estimated Standard Devitations

Atom	X	Y	Z	B(A2)
SI1	0.2386(8)	0.8612(5)	0.31515(9)	11.4(1)
O1C	−0.217(1)	0.8356(9)	0.4011(2)	7.2(2)
O2C	0.343(1)	1.201(1)	0.3752(2)	8.7(2)
O3C	0.404(1)	0.631(1)	0.4608(2)	9.6(3)
O1	0.1717(9)	0.8152(8)	0.3516(1)	5.1(1)
O2	0.265(1)	0.8669(9)	0.4541(2)	6.8(2)
N1H	−0.073(1)	0.620(1)	0.3765(2)	6.2(2)

Table 1 (continued)

Atom	X	Y	Z	B(A2)
N1BU	0.428(1)	0.972(1)	0.4091(2)	7.9(3)
C1BU	0.156(1)	0.973(1)	0.4018(2)	5.2(2)
C2BU	0.319(1)	1.075(1)	0.3930(3)	6.5(3)
C3BU	0.286(1)	0.860(1)	0.4198(2)	4.8(2)
C1CH	0.059(1)	0.898(1)	0.3723(2)	4.6(2)
C2CH	−0.204(2)	0.484(1)	0.3874(3)	6.6(3)
C1C	−0.092(1)	0.780(1)	0.3843(2)	5.3(2)
C3C	0.335(2)	0.750(1)	0.4734(3)	6.9(3)
C1M	−0.201(2)	0.359(1)	0.3583(3)	9.2(4)
C2M	0.330(2)	0.784(2)	0.5073(2)	8.6(4)
C1A	−0.149(1)	0.400(1)	0.4179(2)	5.3(2)
C2A	−0.268(2)	0.308(1)	0.4336(3)	7.9(3)
C3A	−0.230(2)	0.214(1)	0.4606(2)	8.8(4)
C4A	−0.058(2)	0.219(2)	0.4730(2)	8.0(4)
C5A	0.073(2)	0.308(1)	0.4581(2)	7.3(3)
C6A	0.023(2)	0.393(1)	0.4302(3)	6.6(3)
C1SI	0.281(3)	0.696(2)	0.2919(3)	22.6(8)
C2SI	0.525(2)	0.883(3)	0.3209(4)	16.3(7)
C3SI	0.159(3)	1.054(2)	0.3027(3)	19.6(8)
C1TB	0.359(3)	0.732(3)	0.2583(3)	19.9(8)
C2TB	0.363(4)	0.542(2)	0.3049(4)	22(1)
C3TB	0.004(2)	0.678(3)	0.2871(4)	16.9(7)
H1CH	−0.004(9)	0.987(9)	0.358(1)	3(2)*
H2CH	−0.32(1)	0.52(1)	0.374(2)	7(2)*
H1N	0.30(1)	0.783(9)	0.347(2)	4(2)*
H1BU	0.530(8)	0.950(7)	0.412(1)	2(1)*
H2BU	0.05(1)	1.03(1)	0.415(2)	5(2)*
H3BU	0.24(2)	0.74(2)	0.397(3)	23(6)*
H1P	−0.368(9)	0.275(8)	0.428(1)	2(1)*
H2P	−0.29(1)	0.16(1)	0.479(2)	12(3)*
H3P	−0.013(9)	0.143(9)	0.493(1)	4(2)*
H4P	0.21(3)	0.25(2)	0.467(4)	31(8)*
H5P	0.091(9)	0.452(8)	0.424(1)	2(2)*
H1M	−0.29(1)	0.409(9)	0.341(2)	5(2)*
H2M	0.252(9)	0.767(9)	0.516(1)	4(2)*
H4M	0.22(1)	1.084(9)	0.285(2)	5(2)*
H5M	0.161(1)	1.10(1)	0.299(2)	4(3)*
H6M	0.23(2)	0.71(1)	0.248(2)	12(3)*
H7M	0.40(1)	0.75(1)	0.246(2)	8(3)*
H9M	0.36(2)	0.55(1)	0.327(2)	12(4)*
H10M	−0.04(1)	0.66(1)	0.314(2)	9(3)*

Starred atoms were refined isotropically. Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: (4/3)*[a2*B(1,1)+b2*B(2,2)+c2*B(3,3)+ab(cos gamma)*B(1,2)+ac(cos beta)*B(1,3)+bc(cos alpha)*B(2,3)]

Table 2

Bond Distance in Angstroms

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
SI1	O1	1.616(7)	C3A	C4A	1.38(2)
SI1	C1SI	1.65(2)	C4A	C5A	1.35(2)
SI1	C2SI	2.16(2)	C5A	C6A	1.380(15)
SI1	C3SI	1.72(2)	C1SI	C1TB	1.52(2)
O1C	C1C	1.237(12)	C1SI	C1TB	1.47(3)
O2C	C2BU	1.243(13)	C1SI	C3TB	2.08(3)
O3C	O2	2.156(11)	H1CH	C1CH	1.02(7)
O3C	C3C	1.191(14)	H2CH	C2CH	1.06(8)
O1	C1CH	1.361(11)	H1N	O1	1.01(7)
O2	C3BU	1.413(11)	H1BU	N1BU	0.79(6)
O2	C3C	1.325(13)	H2BU	C1BU	1.04(8)
N1H	C2CH	1.519(13)	H3BU	C3BU	1.38(15)
N1H	C1C	1.315(13)	H1P	C2A	0.81(6)
N1BU	C1BU	2.050(13)	H2P	C3A	0.95(9)
N1BU	C2BU	1.327(14)	H3P	C1A	1.08(7)
N1BU	C3BU	1.551(13)	H4P	C5A	1.18(19)
C1BU	C2BU	1.503(15)	H5P	C6A	0.73(6)
C1BU	C3BU	1.512(14)	H1M	C1M	1.03(7)
C1BU	C1CH	1.531(13)	H2M	C2M	0.69(7)
C2BU	C3BU	2.042(14)	H4M	C3SI	0.88(7)
C1CH	C1C	1.540(14)	H5M	C3SI	0.40(10)
C2CH	C1M	1.553(15)	H6M	C1TB	1.04(11)
C2CH	C1A	1.474(14)	H7M	C1TB	0.64(9)
C3C	C2M	1.417(15)	H9M	C2TB	0.90(10)
C1A	C2M	1.32(2)	H10M	C3TB	1.15(8)
C1A	C6A	1.380(15)			
C2A	C3A	1.37(2)			

Numbers in parentheses are estimated standard deviations in the least significant digits.

t-butyl esters by trifluoroacetic acid in dichloromethane at room temperature gave the crystalline acids **9a** and **9b** in excellent yield. These were subjected to oxidative decarboxylation by lead tetraacetate [15] to afford the *trans*-acetoxyazetidinones **10a** (31%) and **10b** (33%). Protection of the hydroxy groups to give the *t*-butyldimethylsilyl ethers **11a** (76%) and **11b** (89%) and subsequent oxidative cleavage of the *p*-methoxyphenyl residue by ceric(IV) ammonium nitrate [16] concluded the synthesis of the azetidinones **1a** (73%) and **1b** (65%).

The *relative* stereochemistry of the two diastereomeric sequences **a** and **b** was established unambiguously from their nmr spectroscopic data; the allocation of *absolute* configurations ensued *via* single-crystal X-ray analysis, the diasteromer **1b** being chosen arbitrarily. According to this analysis the azetidinone **1b** has *trans* geometry and the absolute configuration 1′(*R*)3(*S*)4(*S*). The fourth asymmetric centre was pre-ordained by the incorporation of (*S*)-(-)-phenethylamine (Figure 1). The diasteromer **1a** thus has the required 1′(*S*)3(*R*)4(*R*) configuration.

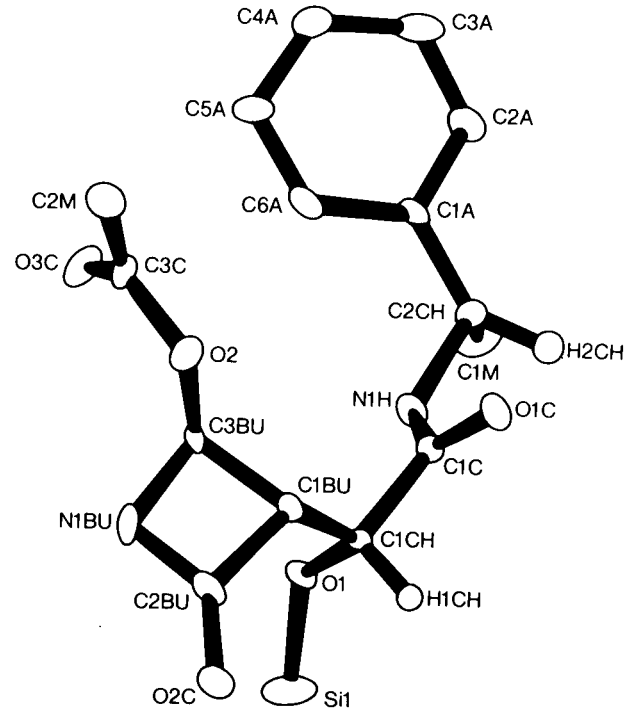


Figure 1. X-Ray crystal structure of azetidinone **1b**.

EXPERIMENTAL

Melting points were determined on a Büchi capillary melting point apparatus and are uncorrected. The ir spectra were determined on a Perkin-Elmer 281 infrared spectrophotometer. Optical rotations were determined using a Perkin-Elmer 241 MC polarimeter. The nmr spectra were recorded on Bruker WP 200, WM 250 and AM 300 spectrometers in either deuteriochloroform, acetone-d_6 or DMSO-d_6 solution. Chemical shifts are reported as δ values in ppm relative to tetramethylsilane (δ 0.0) as an internal standard. Data are reported as follows: chemical shift (multiplicity, coupling constants, integrated intensity, assignment). Mass spectra were obtained on the following mass spectrometers: Electron ionisation (ei) on a Kratos MS 80; Desorption chemical ionisation (dci) on a Finnigan MAT 311 A. All reactions were performed under a positive atmosphere of nitrogen with the aid of a Firestone valve. Reactions were monitored by analytical thin-layer chromatography using 5 × 10 cm, tlc plates: silica gel 60 F-254, layer thickness 0.25 mm, E. Merck. Silica gel columns for chromatography utilized E. Merck silica gel 60 (230-400 mesh ASTM) and a slightly positive pressure of air. "Anhydrous" solvents were distilled shortly before use from an appropriate drying agent.

Dimethyl *cis*-2,3-Oxiranedicarboxylate (**3**).

A solution of 247.0 g (1.87 moles) of *cis*-2,3-oxiranedicarboxylic acid [12] and 5 ml (94.0 mmoles, 0.05 equivalents) of 96% sulfuric acid in 1500 ml of methanol was refluxed through a Soxhlet extractor, filled with 100 g of dry molecular sieves (3 Å) for 22 hours. After cooling, the solution was poured into a mixture of cold sodium bicarbonate solution and

Table 3.

Bond Angles in Degrees

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
O1	SI1	C1SI	114.5(7)	N1BU	C3BU	C1BU	87.6(8)
O1	SI1	C2SI	102.9(6)	N1BU	C3BU	C2BU	40.4(6)
O1	SI1	C3SI	111.6(7)	C1BU	C3BU	C2BU	47.2(6)
C1SI	SI1	C2SI	86(1)	O1	C1CH	C1BU	112.8(8)
C1SI	SI1	C3SI	127.0(8)	O1	C1CH	C1C	111.1(8)
C2SI	SI1	C3SI	108(1)	C1BU	C1CH	C1C	109.3(7)
O2	O3C	O3C	32.9(6)	N1H	C2CH	C1M	102.6(8)
SI1	O1	C1CH	131.1(6)	N1H	C2CH	C1A	113.1(9)
O3C	O2	C3BU	92.3(6)	C1M	C2CH	C1A	110.8(9)
O3C	O2	C3C	29.3(5)	O1C	C1C	N1H	124.1(9)
C3BU	O2	C3C	121.5(8)	O1C	C1C	C1CH	120.6(9)
C2CH	N1H	C1C	122.6(8)	N1H	C1C	C1CH	115.2(8)
C1BU	N1BU	C2BU	47.1(6)	O3C	C3C	O2	118.(1)
C1BU	N1BU	C3BU	47.4(5)	O3C	C3C	C2M	126.(1)
C2BU	N1BU	C3BU	94.5(8)	O2	C3C	C2M	116.(1)
N1BU	C1BU	C2BU	40.3(6)	C2CH	C1A	C2A	119.(1)
N1BU	C1BU	C3BU	45.0(5)	C2CH	C1A	C6A	126.(1)
N1BU	C1BU	C1CH	125.5(7)	C2A	C1A	C6A	115.(1)
C2BU	C1BU	C3BU	85.3(7)	C1A	C2A	C3A	124.(1)
C2BU	C1BU	C1CH	113.8(8)	C2A	C3A	C4A	118.(1)
C3BU	C1BU	C1CH	117.1(8)	C3A	C4A	C5A	122.(1)
O2C	C2BU	N1BU	134(1)	C4A	C5A	C6A	115.(1)
O2C	C2BU	C1BU	133(1)	C1A	C6A	C5A	125.(1)
O2C	C2BU	C3BU	176.2(9)	SI1	C1SI	C1TB	117.(1)
N1BU	C2BU	C1BU	92.7(8)	SI1	C1SI	C2TB	122.(1)
N1BU	C2BU	C3BU	45.1(6)	SI1	C1SI	C3TB	85.(1)
C1BU	C2BU	C3BU	47.5(5)	C1TB	C1SI	C2TB	109.(2)
O2	C2BU	N1BU	111.0(8)	C1TB	C1SI	C3TB	108.(1)
O2	C3BU	C1BU	113.0(8)	C2TB	C1SI	C3TB	113.(2)
O2	C3BU	C2BU	121.0(7)				

Numbers in parentheses are estimated standard deviations in the least significant digits.

ether, extracted several times with ether, washed with sodium chloride solution, and dried over magnesium sulfate. Evaporation of the solvent *in vacuo* gave 200.6 g (67%) of the dimethyl ester **3** as an oil, bp 112°/1 mm; ^{1}H nmr (300 MHz, deuteriochloroform): δ 3.72 (s, 2H, CH), 3.81 (s, 6H, $COOCH_3$).

Anal. Calcd. for $C_6H_8O_5$: C, 45.01; H, 5.04. Found: C, 44.6; H, 5.3.

Methyl (2*RS*,3*SR*)-2,3-Oxiranedicarboxylate (**4**).

To a stirred solution of 4.0 g (25.0 mmoles) of the dimethyl dicarboxylate **3** in 25 ml of 0.1 *M* phosphate buffer (*p*H 7) was added 2.5 mg of the enzyme ficin (EC 3.4.22.3) and the mixture was stirred at room temperature for 20 hours, the *p*H being kept constant by addition of 1 *N* sodium hydroxide from an automatic titrator. After addition of 25 ml (25 mmoles) of sodium hydroxide, the mixture was cooled and the *p*H adjusted to 2 by addition of 5 *N* sulfuric acid. The solution was saturated with solid sodium chloride and exhaustively extracted with ethyl acetate. The combined organic extracts were dried over magnesium sulfate and then concentrated under reduced pressure to afford 1.71 g (47%) of the racemic [17] acid **4** as an oil: bp about 150°/1.5 mm (Kugelrohr); ms (dci, ammonia): m/z 147 (M + H), 164 (M + NH_4).

Anal. Calcd. for $C_5H_6O_5$: C, 41.11; H, 4.14. Found: C, 41.0; H, 4.3.

(2*RS*,3*SR*)-*N*-(*t*-Butoxycarbonylmethyl)-*N*-(4-methoxyphenyl-3-methoxycarbonyl-2,3-epoxypropionamide (**5**).

A solution of 188.0 g (0.88 mole) of dicyclohexylcarbodiimide (DCC) in 300 ml of THF was added dropwise, within 15 minutes, to a solution of 129.0 g (0.88 mmole) of the monoacid **4** and 196.0 g (0.8 moles) of *t*-butyl-*N*-(4-methoxyphenyl)glycinate [9c] in 1100 ml of THF. The mixture was

Table 4

General Temperature Factor Expressions - B's

Name	B(1,1)	B(2,2)	B(3,3)	B(1,2)	B(1,3)	B(2,3)	Beev
SI1	19.2(4)	7.5(2)	7.5(2)	3.6(3)	5.5(2)	1.6(2)	11.4(1)
O1C	5.1(4)	5.7(4)	10.7(4)	−0.5(4)	1.3(4)	−1.2(4)	7.2(2)
O2C	8.0(5)	7.1(4)	10.9(5)	−2.8(5)	0.2(5)	1.3(4)	8.7(2)
O3C	10.9(6)	7.5(4)	10.3(5)	3.7(5)	−2.9(5)	0.8(4)	9.6(3)
O1	5.2(3)	4.6(3)	5.7(3)	0.0(4)	2.5(3)	−1.0(3)	5.1(1)
O2	7.8(4)	6.5(4)	6.2(3)	2.4(4)	−0.3(4)	−0.8(3)	6.8(2)
N1H	5.8(5)	4.0(4)	8.7(5)	−0.4(4)	1.2(4)	−1.0(4)	6.2(2)
N1BU	3.9(4)	8.1(6)	11.8(6)	1.0(5)	−2.2(5)	−0.7(6)	7.9(3)
C1BU	4.0(5)	4.3(5)	7.2(5)	−0.1(5)	0.8(5)	−0.1(5)	5.2(2)
C2BU	6.0(6)	5.3(5)	8.2(6)	−2.1(6)	1.7(5)	−1.9(5)	6.5(3)
C3BU	2.4(4)	5.7(5)	6.1(5)	−0.4(5)	0.3(4)	0.2(5)	4.8(2)
C1CH	4.7(5)	4.2(4)	4.9(4)	−1.0(5)	−0.3(4)	1.0(4)	4.6(2)
C2CH	6.6(6)	5.2(5)	8.1(6)	−1.9(6)	−1.7(5)	1.4(5)	6.6(3)
C1C	4.6(5)	4.4(5)	6.8(5)	0.4(5)	1.0(5)	−0.2(5)	5.3(2)
C3C	5.5(6)	5.2(6)	10.0(6)	1.3(6)	−2.4(6)	0.8(5)	6.9(3)
C1M	13.7(9)	6.5(6)	7.3(6)	−3.8(7)	−4.8(7)	−0.0(5)	9.2(4)
C2M	8.9(8)	13(1)	3.9(5)	−1.3(9)	0.4(6)	−0.1(6)	8.6(4)
C1A	4.9(5)	3.9(4)	7.1(5)	−1.8(5)	1.6(5)	−0.9(5)	5.3(2)
C2A	7.5(7)	6.3(6)	9.9(7)	−3.5(6)	−0.4(7)	−0.8(6)	7.9(3)
C3A	15(1)	5.7(6)	6.1(5)	−0.6(9)	2.3(7)	−0.3(5)	8.8(4)
C4A	11.2(9)	7.4(7)	5.3(5)	0.0(9)	0.2(6)	0.7(6)	8.0(4)
C5A	11.5(9)	5.1(5)	5.5(5)	−0.2(7)	1.8(6)	0.7(5)	7.3(3)
C6A	6.4(6)	4.8(5)	8.6(6)	−2.4(5)	3.0(5)	−1.3(5)	6.6(3)
C1SI	42(2)	15(1)	11.4(8)	10(2)	16(1)	3(1)	22.6(8)
C2SI	7.7(8)	25(2)	16(1)	−9(1)	3.8(8)	0(1)	16.3(7)
C3SI	32(2)	17(1)	9.5(7)	7(2)	3(1)	7.6(8)	19.6(8)
C1TB	31(2)	20(2)	8.9(7)	0(2)	11.4(9)	−1(1)	19.9(8)
C2TB	46(3)	6.5(7)	13(1)	8(1)	4(2)	−0.8(8)	22(1)
C3TB	10(1)	31(2)	10.0(9)	−9(1)	−1.0(8)	−1(1)	16.9(7)

The form of the anisotropic thermal parameter is: $\exp[-0{,}25\{h^2a^2B(1,1)+k^2b^2B(2,2)+l^2c^2B(3,3)+2hkabB(1,2)+2hlacB(1,3)+2klbcB(2,3)\}]$ where a, b, and c are reciprocal lattice constants.

stirred for a further 30 minutes at room temperature, the resultant precipitate was removed by filtration, and the filtrate evaporated *in vacuo*. After purification of the product on 1800 g of silica gel (toluene:ethyl acetate 7:3), 263.2 g (90%) of the racemic amide **5** was obtained as crystals, mp 89°; Rf = 0.16 (toluene:ethyl acetate 4:1); ir (chloroform): 1737 (C=O, ester), 1681 (C=O, amide), 1509 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 1.44 (s, 9H, CH_3-C), 3.46 and 3.51 (AB, J = 4.5 Hz, 2H, oxirane-H), 3.82 (s, 6H, OCH_3, $COOCH_3$), 4.08 and 4.36 (AB, J = 16 Hz, CH_2COO), 6.91 and 7.31 (AB, J = 9 Hz, 4H, *p*-H_3CO-C_6H_4); ms (dci, ammonia): m/z 366 (M + H).

(2*RS*,3*SR*)-*N*-(*t*-Butoxycarbonylmethyl)-*N*-(4-methoxyphenyl)-3-carboxy-2,3-epoxypropionamide (**6**).

A solution of 230 mg (10.0 mg-atoms) of sodium in 10 ml of anhydrous methanol was added at room temperature to a solution of the methyl ester **5**. Exactly 180 μl (10 mmoles, 1 equivalent) of water was added to this solution, and the mixture was stirred for a further 15 hours. The reaction mixture was subsequently evaporated *in vacuo*, dissolved in 15 ml of water, washed with ether, covered with 10 ml of ethyl acetate and adjusted to *p*H 2.5 using 2.5 *N* sulfuric acid with cooling. The mixture was extracted 4 times with ethyl acetate, the organic phase was dried over magnesium sulfate, and the solvent was evaporated **in vacuo** to afford 3.44 g (98%) of the racemic acid **6** as a colorless solid: Rf = 0.36 (*n*-butyl acetate:1-butanol:acetic acid:phosphate buffer *p*H 7 50:9:25:15); ^1H nmr (200 MHz, DMSO-d_6): δ 1.39 (s, 9H, $C(CH_3)_3$), 3.52 and 3.59 (AB, J = 5 Hz, 2H, H-2, H-3), 3.78 (s, 3H, OCH_3), 4.22 (bs, 2H, NCH_2COO), 7.02 and 7.35 (AB, J = 9.5 Hz, 4H, *p*-H_3CO-C_6H_4), 12.87 (bs, 1H, COOH). The solid was used for subsequent conversions without further purification.

(2*R*,3*S*)-1-(*t*-Butoxycarbonylmethyl)-1-(4-methoxyphenyl)-4-[(1*S*)-1-phenylethyl]-2,3-oxiranedicarboxamide (**7a**) and (2*S*,3*R*)-1-(*t*-Butoxycarbonylmethyl)-1-(4-methoxyphenyl)-4-[(1*S*)-1-phenylethyl]-2,3-oxiranedicarboxamide (**7b**).

To a stirred solution of 9.53 g (27.12 mmoles) of the acid **6** in 40 ml of

anhydrous THF was successively added 3.50 ml (27.12 mmoles) of (*S*)-(-)-phenethylamine, 5.60 g (27.12 mmoles) of dicyclohexylcarbodiimide (DCC) in 8.6 ml of THF, and 3.70 g (27.12 mmoles) of 1-hydroxy-1*H*-benztriazole (HOBT). The initially clear solution was stirred for 1 hour at room temperature. The resultant precipitate was removed by filtration and the filtrate solution was evaporated *in vacuo*. Chromatography of the residue on 1700 g of silica gel (toluene:ethyl acetate 4:1) afforded 2.75 g (22%) of the less polar epoxide **7a** as a foam; Rf = 0.38 (toluene:ethyl acetate 7:3); $[\alpha]_D^{20}$ 164.4° (c 0.897, chloroform); ir (potassium bromide): 3384, 1746 (C=O, ester), 1682 (C=O, amide), 1606, 1444, 1370 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 1.48 (s, $C(CH_3)_3$), 1.48 (d, J = 7.5 Hz, $CHCH_3$), together 13H, 3.41 and 3.46 (AB, J = 5.5 Hz, 2H, oxirane-H), 3.83 (s, 3H, OCH_3), 4.23 and 4.35 (AB, J = 16 Hz, 2H, CH_2COO), 5.12 (q, J = 7.5 Hz, 1H, $CHCH_3$), 6.96 (d, J = 9 Hz, 2H, *p*-H_3CO-C_6H_4), 7.3-7.4 (m, 7H, Ph, *p*-H_3CO-C_6H_4).

Anal. Calcd. for $C_{25}H_{30}N_2O_6$: C, 66.07; H, 6.65; N, 6.16. Found: C, 66.3; H, 6.9; N, 6.2.

In addition, 5.06 g (41%) of the more polar epoxide **7b** as a colorless foam; Rf = 0.26 (toluene:ethyl acetate 7:3); $[\alpha]_D^{20}$ −189.4° (c, 0.405, chloroform); ^1H nmr (200 MHz, acetone-d_6): δ 1.44 (s, 9H, $C(CH_3)_3$), 1.49 (d, J = 7 Hz, 3H, $CHCH_3$), 3.38 and 3.54 (AB, J = 6 Hz, 2H, oxirane-H), 3.83 (s, 3H, OCH_3), 3.92 and 4.36 (AB, J = 17 Hz, 2H, CH_2COO), 5.08 (m, 1H, $CHCH_3$), 6.95 and 7.23 (d, J = 9 Hz, 4H, *p*-H_3CO-C_6H_4), 7.38 (m, 5H, Ph).

Anal. Calcd. for $C_{25}H_{30}N_2O_6$: C, 66.07; H, 6.65; N, 6.16. Found: C, 66.1; H, 6.8; N, 6.3.

(3*S*,4*S*)-4-*t*-Butoxycarbonyl-3-[(1*S*)-1-hydroxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]-1-(4-methoxyphenyl)azetidin-2-one (**8a**).

A solution of 5.52 g (12.14 mmoles) of the epoxide **7a** in 20 ml of anhydrous THF was added dropwise to a mixture, cooled to 0°, of 18 ml (18.2 mmoles) of 1 *N* tetrabutylammonium fluoride in THF and 6 g of molecular sieves (4 Å) in 10 ml of THF. After 1.5 hours the mixture was filtered, toluene was added to the filtrate solution, and the THF was removed under reduced pressure. The remaining toluene solution was washed several times with water and dried over magnesium sulfate. After evaporation of the solvent *in vacuo* and chromatography of the residue on 500 g of silica gel (toluene:ethyl acetate 7:3), 1.97 g (36%) of the azetidinone **8a** was obtained as colorless crystals: mp 184°; Rf = 0.19 (toluene:ethyl acetate 7:3); $[\alpha]_D^{20}$ −47.3° (c 0.8085, chloroform); ir potassium bromide): 3348 (OH), 1769 (C=O, β-lactam), 1748 (C=O, ester), 1658 (C=O, amide), 1515 cm^{-1}; ^1H nmr (250 MHz, chloroform): δ 1.45 (2, 9H, $(C(CH_3)_3)$, 1.54 (d, J = 7 Hz, 3H, $CHCH_3$), 3.60 (dd, J = 7.5 Hz, 2 Hz, 1H, H-3), 3.79 (s, 3H, OCH_3), 4.01 (d, J = 4.5 Hz, 1H, OH), 4.42 (dd, J = 7.5 Hz, 4.5 Hz, 1H, HO-C*H*-CON), 4.48 (d, J = 2 Hz, 1H, H-4), 5.14 (dq, J = 8 Hz, 7 Hz, 1H, $CHCH_3$), 6.88 (d, J = 9 Hz, 2H, *p*-H_3CO-C_6H_4), 7.2-7.4 (m, 7H, Ph, *p*-H_3CO-C_6H_4), 7.83 (d, J = 8 Hz, 1H, CONH).

Anal. Calcd. for $C_{25}H_{30}N_2O_6$: C, 66.06; H, 6.65; N, 6.16. Found: C, 66.3; H, 6.6; N, 6.0.

(3*R*,4*R*)-4-*t*-Butoxycarbonyl-3-[(1*R*)-1-hydroxymethyl)-1-((1*S*)-1-phenylethylaminocarbonyl)]-1-(4-methoxyphenylazetidin-2-one (**8b**).

As described for the preparation of **8a**, 16.55 g (36.41 mmoles) of the epoxide **7b** afforded, after chromatography of the crude product on 1400 g of silica gel (toluene:ethyl acetate 3:2), 6.24 g (38%) of the azetidinone **8b** as colorless crystals: mp 131°; Rf = 0.29 (toluene:ethyl acetate 1:1); ir (chloroform): 3340, 1750 (C=O, β-lactam, ester), 1665 (C=O, amide), 1510 cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 1.45 (s, 9H, $C(CH_3)_3$), 1.59 (d, J = 7 Hz, 3H, $CHCH_3$), 3.73 (dd, J = 7.5 Hz, 0.5 Hz, 1H, H-3), 3.80 (s, 3H, OCH_3), 4.49 (m, 2H, HO-C*H*-CON, H-4), 5.16 (dq, J = 8.5 Hz, 7 Hz, 1H, $CHCH_3$), 6.86 and 7.28 (AB, J = 9.5 Hz, *p*-H_3CO-C_6H_4), 7.38 (m, Ph) together 9H, 7.80 (d, J = 8.5 Hz, 1H, CONH).

Anal. Calcd. for $C_{25}H_{30}N_2O_6$: C, 66.06; H, 6.65; N, 6.16. Found: C, 66.1; H, 6.8; N, 6.2

(3*S*,4*S*)-4-Carboxy-3-[(1*S*)-1-hydroxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]-1-(4-methoxyphenyl)azetidin-2-one (**9a**).

To a stirred solution of 1.97 g (4.33 mmoles) of the *t*-butyl ester **8a** in 18 ml of dichloromethane at room temperature was added 18 ml of trifluoroacetic acid. After 3 hours, the solution was evaporated *in vacuo*, toluene was added, and the mixture was re-evaporated. This procedure was repeated twice, and the crystalline residue was then triturated with ether, filtered and dried *in vacuo* over phosphorus pentoxide to give 1.56 g (90%) of the acid **9a** as colorless crystals: mp 186°; Rf = 0.68 (*n*-butyl acetate:1-butanol:acetic acid:phosphate buffer *p*H 7 50:9:25:15); $[\alpha]_D^{20}$ −74.5° (c, 0.306, acetone); ir (potassium bromide): 3320, 1750 (C=O, β-lactam), 1658 (C=O, amide), 1630, 1515, 1248 cm^{-1}; ^1H nmr (200 MHz, DMSO-d_6): δ 1.44 (d, J = 7 Hz, 3H, $CHCH_3$), 3.66 (dd, J = 2 Hz, 1.5 Hz, 1H, H-3), 3.74 (s, 3H, OCH_3), 4.34 (m, 1H, HO-C*H*-CON), 4.60 (d, J = 2 Hz, 1H, H-4), 5.00 (dq, J = 9 Hz, 7 Hz, 1H, $CHCH_3$), 6.36 (d, J = 6 Hz, 1H, OH), 6.97 and 7.25 (AB, J = 9 Hz, 4H, *p*-H_3CO-C_6H_4), 7.38 (m, 5H, Ph), 8.36 (d, J = 9 Hz, 1H, CONH), 12.80 (bs, 1H, COOH); ms (dci, ammonia) m/z 399 (M + H).

Anal. Calcd. for $C_{21}H_{22}N_2O_6$: C, 63.31; H, 5.57. Found: C, 63.2; H, 5.7.

(3*R*,4*R*)-4-Carboxy-3-[(1*R*)-1-hydroxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]-1-(4-methoxyphenyl)azetidin-2-one (**9b**).

As described for the preparation of the acid **9a**, 6.24 g (13.73 mmoles) of the *t*-butyl ester **8b** afforded 5.15 g (94%) of the acid **9b** as light colored crystals: mp 175°; Rf = 0.61 (*n*-butyl acetate:1-butanol:acetic acid: phosphate buffer *p*H 7, 50:9:25:15); $[\alpha]_D^{20}$ 92.1° (c, 0.438, acetone); ir (potassium bromide): 1746 (C=O, β-lactam), 1654 (C=O, amide), 1512, 1249 cm^{-1}; ^1H nmr (200 MHz, acetone-d_6): δ 1.56 (d, J = 7 Hz, 3H, $CHCH_3$), 3.81 (s, 3H, OCH_3), 3.90 (dd, J = 2 Hz, 2 Hz, 1H, H-3), 4.66 (m, 2H, HO-C*H*-CON, H-4), 5.18 (dq, J = 8 Hz, 7 Hz, 1H, $CHCH_3$), 6.98 (d, J = 9.5 Hz, 2H, *p*-H_3CO-C_6H_4), 7.3-7.5 (m, 7H, Ph, *p*-H_3CO-C_6H_4), 8.00 (d, J = 8 Hz, 1H, CONH); ms (dci, ammonia): m/z 399 (M + H).

(3*R*,4*R*)-4-Acetoxy-3-[(1*S*)-1-hydroxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]-1-(4-methoxyphenyl)azetidin-2-one (**10a**).

To a stirred solution of 1.69 g (4.23 mmoles) of the acid **9a** in 18 ml of DMF and 5 ml of glacial acetic acid was added 1.89 g (4.23 mmoles) of lead tetraacetate and the mixture was heated for exactly 5 minutes at 60° in a preheated oil bath. The mixture was then cooled and poured into a mixture of water, sodium chloride solution and ethyl acetate. It was extracted with ethyl acetate (4 ×) and the organic extracts were washed with water (3 ×) and sodium bicarbonate solution until neutral, and dried over magnesium sulfate. Evaporation of the solvent *in vacuo*, chromatography of the residue on 60 g of silica gel (toluene:ethyl acetate 3:2) and recrystallization from toluene, afforded 0.54 g (31%) of the acetate **10a** as colorless fiber-like crystals, mp 202°; Rf = 0.30 (toluene:ethyl acetate 1:1); $[\alpha]_D^{20}$ −28.6° (c 0.312, acetone); ir (potassium bromide) 3290, 1746 (C=O, β-lactam, ester), 1650 (C=O, amide), 1627, 1515, 1250 cm^{-1}; ^1H nmr (200 MHz, acetone-d_6): δ 1.51 (d, J = 6.5 Hz, 3H, $CHCH_3$), 3.73 (dd, J = 2 Hz, 1 Hz, 1H, H-3), 3.78 (s, 3H, OCH_3), 4.48 (d, J = 2 Hz, 1H, HO-C*H*-CON), 5.10 (dq, J = 9 Hz, 6.5 Hz, 1H, $CHCH_3$), 6.63 (d, J = 1 Hz, 1H, H-4), 6.95 (d, J = 10 Hz, 2H, *p*-H_3CO-C_6H_4), 7.2-7.4 (m, 7H, Ph, *p*-H_3CO-C_6H_4), 7.79 (d, J = 9 Hz, 1H, CONH); ms (dci, ammonia): m/z 437 (M + H).

Anal. Calcd. for $C_{24}H_{24}N_2O_6$: C, 66.05; H, 5.54. Found: C, 66.2; H, 5.5.

(3*S*,4*S*)-4-Acetoxy-3-[(1*R*)-1-hydroxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]-1-(4-methoxyphenyl)azetidin-2-one (**10b**).

As described for the preparation of the acetate **10a**, 8.51 g (21.36 mmoles) of the acid **9b** and 9.50 g (21.36 mmoles) of lead tetraacetate in 90 ml of DMF and 25 ml of glacial acetic acid afforded, after 5 minutes at 60° and chromatography of the crude product on 240 g of silica gel (toluene:ethyl acetate 1:1), 2.89 g (33%) of the acetate **10b** as colorless crystals, mp 197°; Rf = 0.18 (toluene:ethyl acetate 3:2); ir (potassium bromide): 3300 (OH), 1753 (C=O, β-lactam, ester), 1652 (C=O, amide), 1515 cm^{-1}; ^1H nmr (200 MHz, acetone-d_6): δ 1.49 (d, J = 7.5 Hz, 3H, $CHCH_3$), 2.03 (s, with acetone, $OCOCH_3$), 3.76 (s, OCH_3), 3.76 (m, OH, H-3) together 5H, 4.50 (d, J = 2 Hz, 1H, HO-C*H*-CON), 5.05 (dq, J = 9 Hz, 7.5 Hz, 1H, $CHCH_3$), 6.61 (d, J = 1 Hz, 1H, H-4), 6.91 (d, J = 9.5 Hz, 2H, *p*-H_3OC-C_6H_4), 7.2-7.4 (m, 7H, Ph, *p*H_3CO-C_6H_4), 7.79 (d, J = 9 Hz,

1H, CONH).

Anal. Calcd. for $C_{24}H_{24}N_2O_6$: C, 66.05; H, 5.54; N, 6.42. Found: C, 66.3; H, 5.6; N, 6.3.

(3*R*,4*R*)-4-Acetoxy-3-[(1*S*)-1-*t*-butyldimethylsilyloxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]-1-(4-methoxyphenyl)azetidin-2-one (**11a**).

To a stirred solution of 424 mg (1.03 mmoles) of **10a** and 232 mg (1.54 mmoles) of *t*-butyldimethylsilyl chloride in 7 ml of anhydrous DMF was added 197 mg (1.61 mmoles) of dimethylaminopyridine. The mixture was stirred for 9 days at room temperature and was then poured into a mixture of cold 1 *N* hydrochloric acid and ethyl acetate, extracted with ethyl acetate (2 ×), washed with water and sodium bicarbonate solution, and dried over magnesium sulfate. Evaporation of the solvent *in vacuo* and chromatography of the crude product on 25 g of silica gel (toluene:ethyl acetate 4:1), afforded 409 mg (76%) of the silyl ether **11a** as colorless crystals, mp 115°; Rf = 0.60 (toluene:ethyl acetate 3:2); ir (chloroform): 3390, 1750 (C=O, β-lactam ester), 1663 (C=O, amide), 1510, 840 cm^{-1}; ^1H nmr (200 MHz, acetone-d_6): δ 0.03 (s, 6H, CH_3-Si), 0.78 (s, 9H, CH_3-C-Si), 1.50 (d, J = 8 Hz, 3H, CHC*H*$_3$), 3.70 (dd, J = 2 Hz, 0.5 Hz, 1H, H-3), 3.79 (s, 3H, OCH_3), 4.53 (d, J = 2 Hz, 1H, C*H*-OSi), 5.05 (dq, J = 9 Hz, 8 Hz, 1H, C*H*CH$_3$), 6.67 (d, J = 0.5 Hz, 1H, H-4), 6.95 and 7.40 (AB, J = 10 Hz, 4H, *p*-H_3CO-C_6H_4); 7.40 (m, 5H, Ph); ms (dci, ammonia): m/z 527 (M + H).

(3*S*,4*S*)-4-Acetoxy-3-[(1*R*)-1-*t*-butyldimethylsilyloxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]-1-(4-methoxyphenyl)azetidin-2-one (**11b**).

As described for the preparation of the silyl ether **11a**, 2.21 g (5.36 mmoles) of the alcohol **10b**, 1.21 (8.04 mmoles) of *t*-butyldimethylsilyl chloride and 1.03 g (8.41 mmoles) of dimethylaminopyridine in 37 ml of DMF afforded, after 7 days at room temperature and filtration of the crude product on 50 g of silica gel (toluene:ethyl acetate 4:1), 2.50 g (89%) of the silyl ether **11b** as a light colored solid, mp 120°; Rf = 0.27 (toluene:ethyl acetate 4:1); ir (potassium bromide): 3426, 1767 (C=O, β-lactam), 1748 (C=O, ester), 1681 (C=O, amide), 1511, 1399, 1264 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 0.03 (s, 3H, CH_3Si), 0.15 (s, 3H, CH_3Si), 0.83 (s, 9H, CH_3-C-Si), 1.53 (d, J = 8 Hz, 3H, C*H*$_3$CH), 1.98 (s, 3H, $OCOCH_3$), 3.78 (s, 3H, OCH_3), 3.81 (dd, J = 2 Hz, 0.5 Hz, 1H, H-3), 4.59 (d, J = 2 Hz, 1H, C*H*-OSi), 5.08 (dq, J = 8 Hz, 8 Hz, 1H, CH_3C*H*), 6.51 (d, J = 0.5 Hz, 1H, H-4), 6.84 (d, J = 10 Hz, 2H, *p*-H_3CO-C_6H_4), 6.93 (d, J = 8 Hz, 1H, CONH), 7.3-7.4 (m, 7H, Ph, *p*-H_3CO-C_6H_4); ms (dci, ammonia): m/z 527 (M + H).

(3*R*,4*R*)-4-Acetoxy-3-[(1*S*)-1-*t*-butyldimethylsilyloxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]azetidin-2-one (**1a**).

To a stirred solution of 590 mg (1.12 mmoles) of the *N*-protected azetidinone **11a** in 4 ml of acetonitrile at 0° was added a solution of 1.84 g (3.36 mmoles) of ceric(IV) ammonium nitrate in 6 ml of water at a rate such that the internal temperature did not exceed +5°. The mixture was stirred at 0° for 30 minutes and poured into a mixture of sodium chloride and sodium bicarbonate solution and ethyl acetate. The mixture was extracted with ethyl acetate, washed with sodium bicarbonate and sodium chloride solution and dried over magnesium sulfate. Evaporation of the solvent *in vacuo* and chromatography of the residue on 60 g of silica gel (toluene:ethyl acetate 3:2), gave 342 mg (73%) of the azetidinone **1a**, as a stiff colorless foam: Rf = 0.24 (toluene:ethyl acetate 3:2); ir (chloroform): 3390, 1782 (C=O, β-lactam), 1739 (C=O, ester), 1662 (C=O, amide), 1500 cm^{-1}; ^1H nmr (250 MHz, acetone-d_6): δ 0.01 and 0.07 (s, 6H, CH_3Si), 0.85 (s, 9H, CH_3-C-Si), 1.45 (d, J = 7.5 Hz, 3H, C*H*$_3$CH), 2.04 (s, 3H, $OCOCH_3$), 3.52 (dd, J = 2 Hz, 1 Hz, 1H, H-3), 4.41 (d, J = 2 Hz, 1H, CH-O-Si), 5.07 (dq, J = 8 Hz, 7.5 Hz, 1H, CH_3C*H*), 6.03 (d, J = 1 Hz, 1H, H-4), 7.2-7.4 (m, 6H, Ph, NH), 8.12 (bs, 1H, NH); ms (ei): m/z 405 (M-CH_3), 363 (M-C_4H_9), 321 (363-CH_2CO), 303 (363-$HOCOCH_3$), 212, 199 ($C_7H_{11}N_2O_3Si$), 105 (Ph-CH=NH), 75 (C_2H_7OSi), 73 (C_3H_9Si), 45, 43 ($COCH_3$); (dci, ammonia): m/z 421 (M + H), 361 (M-$OCOCH_3$).

Anal. Calcd. for $C_{21}H_{32}N_2O_5Si$: C, 59.97; H, 7.67; N, 6.66. Found: C, 60.0; H, 7.7; N, 6.7.

(3*S*,4*S*)-4-Acetoxy-3-[(1*R*)-1-*t*-butyldimethylsilyloxymethyl-1-((1*S*)-1-phenylethylaminocarbonyl)]azetidin-2-one (**1b**).

As described for the preparation of the azetidinone **1a**, 3.06 g (5.81 mmoles) of the *N*-protected azetidinone **11b** and 9.60 g (17.43 mmoles) of ceric(IV) ammonium nitrate in 20 ml of acetonitrile and 30 ml of water afforded, after chromatography of the crude product on 350 g of silica gel (toluene:ethyl acetate 7:3) and recrystallization from *n*-heptane, 1.59 g (65%) of the azetidinone **1b** as colorless needles, mp 126°; Rf = 0.35 (toluene:ethyl acetate 3:2); $[\alpha]_D^{25}$ −9.3° (c, 0.925, chloroform); ir (potassium bromide): ir 3420, 1786 (C=O, β-lactam), 1750 (C=O, ester), 1680 (C=O, amide), 1526, 1228 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 0.14 and 0.16 (s, 6H, CH_3-Si), 0.95 (s, 9H, CH_3-C-Si), 1.51 (d, J = 8 Hz, 3H, C*H*$_3$CH), 1.96 (s, 3H, $OCOCH_3$), 3.75 (dd, J = 2 Hz, 1 Hz, 1H, H-3), 4.51 (d, J = 2 Hz, 1H, CH-OSi), 5.12 (dq, J = 9.5 Hz, 8 Hz, 1H, CH_3C*H*), 5.63 (d, J = 1 Hz, 1H, H-4), 5.43 (bs, 1H, azetidinone NH), 6.91 (d, J = 9.5 Hz, 1H, CONH), 7.2-7.3 (m, 5H, Ph); ms (ci, ammonia): m/z 421 (M + H).

Anal. Calcd. for $C_{21}H_{32}N_2O_5Si$: C, 59.97; H, 7.67; N, 6.66. Found: C, 59.8; H, 7.5; N, 6.6.

Single-Crystal X-Ray Structure Determination of Azetidinone **1b**.

Crystals suitable for X-ray diffraction analysis were grown from the melt. A 0.075 × 0.30 × 0.50 mm crystal was selected for data collection. Lattice constants and intensity data were measured at 297 K on an Enraf-Nonius CAD 4 automated diffractometer using graphite-monochromatized CuKα radiation. Unit cell dimensions were obtained by least-squares methods from the adjusted angular settings of 25 large-angle reflections. The crystal data are: $C_{21}H_{32}N_2O_5Si$, orthorhombic space group $P2_12_12_1$, a = 7.4475(7) Å, b = 7.9168(6) Å, c = 40.955(4) Å, N = 2414.7, Z = 4, φ_c = 1.156 g/cm^3, μ(CuKα) = 11.0 cm^{-1}. Data collection was attempted to $\theta < 65°$ in the ω-2θ scanning mode. A total of 2412 reflections was collected (−h,k,−l) yielding 2412 unique intensities and 1290 reflections with $I > 3.0\,\sigma(I)$. This set of reflections was used in the structure solution. Data reduction included corrections for background, Lorentz and polarization effects, extinction and absorption by a semi-empirical method [18]. By direct methods (MULTAN-RANTAN) [19] 24 out of 29 non-hydrogen atoms were located, the missing 5 non-hydrogen by difference Fourier methods. The non-methyl H positions were calculated geometrically. The methyl H atoms were located from Fourier difference maps as far as possible (8 out of 21). Full-matrix least-squares refinement was carried out with anisotropic temperature factors for non-H atoms, isotropic factors for H atoms, using all reflections with $I > 3.0\sigma(I)$ and $\sin\theta/\lambda < 0.5$ Å^{-1}. The final R_1 (1102 reflections, 339 variables) was 0.064.

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† BAYER AG, ZF-DZA Strukturforschung; responsible for performing the single-crystal X-ray of azetidinone **1b**.

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