ESTER-IMINE CONDENSATIONS: PREPARATION OF RACEMIC INTERMEDIATES FOR THE SYNTHESIS OF THE CARBAPENEM ANTIBIOTICS PS-5 AND PS-6

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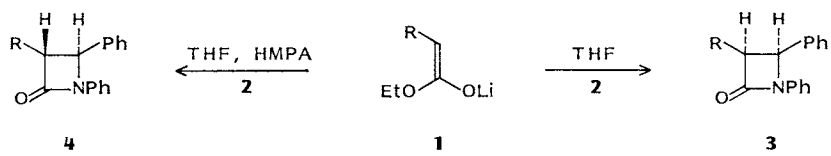
The lithium enolates of ethyl butyrate (**7**) and ethyl isovalerate (**19**) react with *N-p*-methoxyphenylcinnamaldimine (**8**) in tetrahydrofuran (THF) - hexamethylphosphoric triamide (HMPA) to afford predominantly *trans* β-lactams **9** (67%) and **20** (78%), respectively. β-Lactam **9** was converted to PS-5 (**5**) intermediate **18** in 21% overall yield (8 steps). β-Lactam **20** was converted to PS-6 (**6**) analog **28** in 22% overall yield using an eight step sequence.

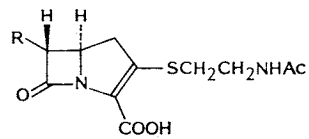
We recently reported that lithium enolates of α-monoalkylated acetates react with *N*-trimethylsilyl[1,2] and *N*-aryl aldimines[2] to afford β-lactams. One interesting aspect of the *N*-aryl aldimine condensation was the manner in which reaction conditions could be varied to control the stereochemical course of reactions. For example, treatment of tetrahydrofuran solutions of ester enolates (**1**) with *N*-benzylidenaniline (**2**) gave predominantly *cis* β-lactams (**3**) whereas addition of hexamethylphosphoric triamide (HMPA) to the reaction mixture, before or after enolate generation, gave mainly *trans* β-lactams (**4**). Evidence was presented which suggested that HMPA promoted *cis-trans* isomerization was responsible for the formation of *trans* β-lactams under the later conditions. Since our initial report, further evidence has been gathered which suggests that the isomerization occurs at C(3) rather than C(4).[3] We have now used this method of *trans*-3,4-dialkylated β-lactam synthesis to prepare racemic intermediates in previous syntheses of the carbapenem antibiotic PS-5 (**5**) and carbapenems related to PS-6 (**6**).[4~10]

Results and Discussion

A formal total synthesis of racemic PS-5 (**5**) is outlined in Scheme 1. Treatment of ethyl butyrate with lithium diisopropylamide followed by cinnamaldimine **8** in tetrahydrofuran - HMPA



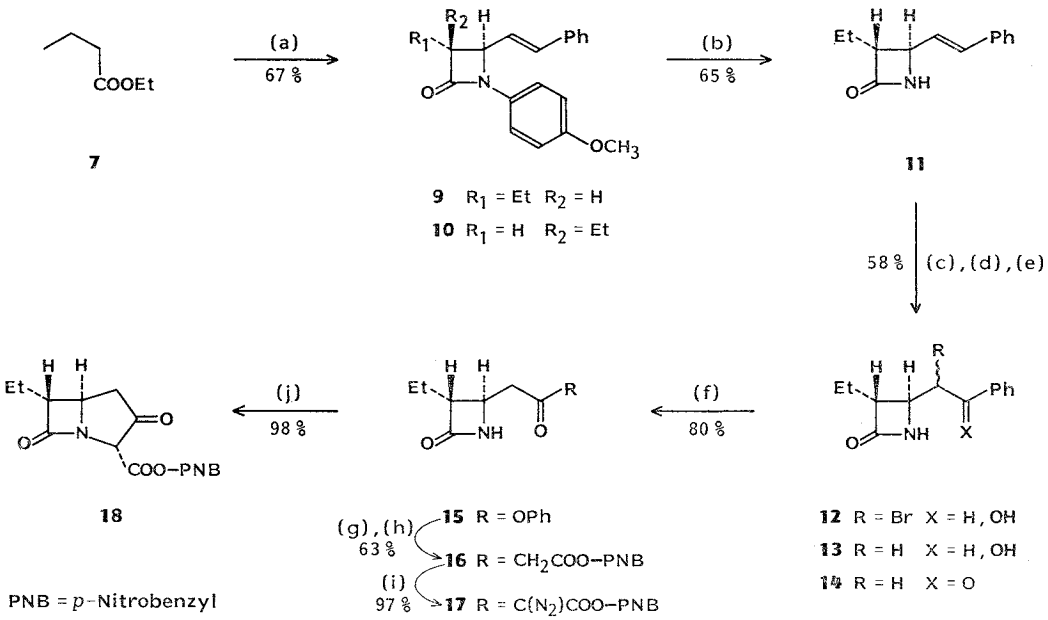
4 **1** **3**



PhCH=NPh
2

5 R = Et
6 R = *iso*-Pr

Scheme 1.



(a) Lithium diisopropylamide (LDA), THF; PhCH=CHCH=NPh*p*OCH$_3$ (**8**), HMPA, THF. (b) Ceric ammonium nitrate, CH_3CN, H_2O. (c) *N*-Bromosuccinimide (NBS), DMSO, H_2O. (d) *n*Bu$_3$SnH, 2,2′-azobisisobutyronitrile (AIBN), PhH, 80°C. (e) JONES' reagent. (f) CF_3CO_3H, Na_2HPO_4, CH_2Cl_2. (g) NaOH, EtOH then HCl, EtOH. (h) Carbonyldiimidazole, THF then Mg[OC(O)CH_2COO-PNB]$_2$. (i) TsN_3, Et_3N, CH_3CN. (j) $Rh_2(OAc)_4$, PhH.

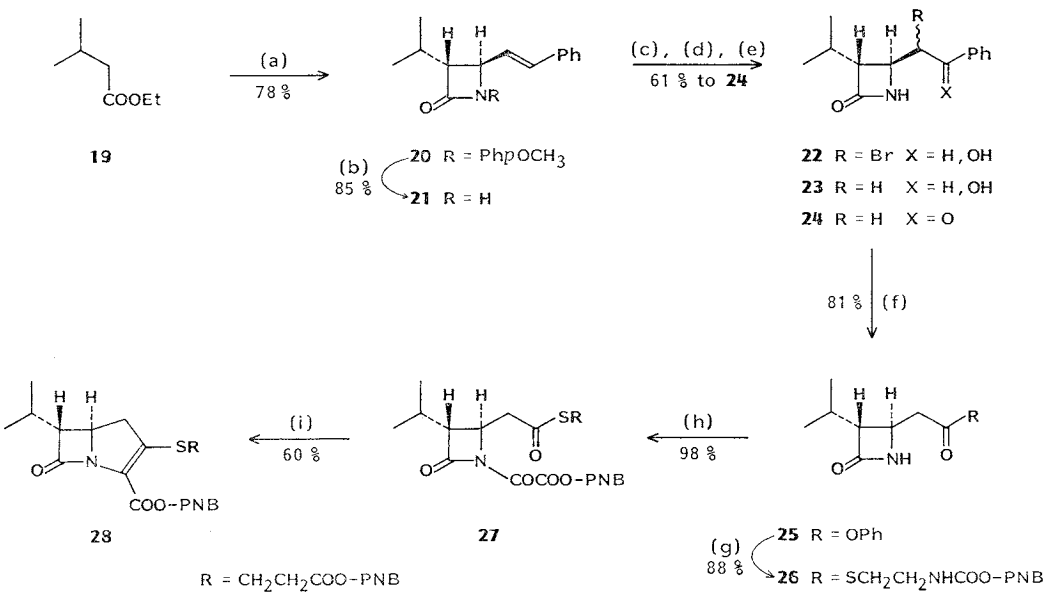
gave a 67% yield of an inseparable 4 : 1 mixture of β-lactams **9** and **10**, respectively. The stereoisomer ratio was determined by integration of signals due to H(4) at δ 4.28 (dd, J=8.3 and 2.3 Hz) and 4.71 (dd, J=8.0 and 5.8 Hz) for **9** and **10**, respectively. Epimerization experiments were not performed to see if this ratio represented an equilibrium mixture of stereoisomers. The mixture of **9** and **10** was oxidized using ceric ammonium nitrate to give a 65% yield of *trans* β-lactam **11** after chromatographic separation from the corresponding *cis* stereoisomer.[11]

We next turned to converting the 4-β-styryl substituent into an acetic acid residue, a group which has proved to be quite versatile in carbapenem synthesis.[12] Several methods for converting **11** into ketone **14** were initially investigated. We eventually settled on a three-step procedure which involved the preparation of bromohydrin **12** (81%),[13] reduction to a mixture of diastereomeric alcohols **13** (85%)[14] and oxidation[15] to afford **14** (83%). This reaction sequence could be conducted without purification of intermediates in 67% overall yield. The desired C(4) side-chain transformation was completed by Baeyer-Villiger oxidation of **14** to give azetidinone **15** (80%).[16]

A formal total synthesis of PS-5 (**5**) was completed by converting phenyl ester **15** to bicyclic β-lactam **18**. Thus, treatment of **15** with ethanolic sodium hydroxide followed by neutralization and sequential treatment of the resulting crude acid with carbonyldiimidazole and magnesium mono-*p*-nitrobenzylmalonate[17,18] gave the known β-ketoester **16** (63%),[7~9] which was converted to diazoketone **17** (97%) and carbapenem **18** (98%) using established procedures.[7,8,19] Since **18** had previously been converted to **5**, this completed a formal synthesis of racemic PS-5.[7~9]

As expected, substituting ethyl isovalerate (**19**) for ethyl butyrate in the aforementioned sequence

Scheme 2.



(a) LDA, THF; **8**, HMPA, THF. (b) Ceric ammonium nitrate, H_2O, CH_3CN. (c) NBS, H_2O, DMSO. (d) n-Bu_3SnH, AIBN, PhH, 80°C. (e) JONES' reagent. (f) CF_3CO_3H, Na_2HPO_4, CH_2Cl_2. (g) $HSCH_2CH_2NHCOO$-PNB, DBU, CH_2Cl_2. (h) ClCOCOO-PNB, Et_3N, CH_2Cl_2. (i) $(EtO)_3P$, toluene, 100°C.

gave racemic structures related to the carbapenem PS-6 (**6**). Thus, **25** was prepared in 33% overall yield from **19** as shown in Scheme 2. In this sequence, the ratio of **20** and the corresponding *cis* β-lactam was 10:1 by NMR and separation of the stereoisomers was accomplished after *N*-dearylation. As in the PS-5 series, the conversion of **21** to **24** could be accomplished without purification of intermediates (61%).

Phenyl esters such as **15** and **25** should be useful intermediates in the synthesis of cysteaminyl side-chain analogs of **5** and **6**. This was illustrated by the preparation of **28** using a well-documented intramolecular Wittig procedure for construction of the carbapenem nucleus.[20~22] Thus, treatment of **25** with *N*-(*p*-nitrobenzyloxycarbonyl)cysteamine and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave **26** (88%) which was acylated to afford oxalamide **27** (98%). Treatment of **27** with triethylphosphite gave **28** (60%).

In summary, ester-imine condensations provide straightforward access to carbapenems related to PS-5 and PS-6 and a new protocol for converting an azetidinone C(4)-styryl group into an acetic acid residue has been developed.

Experimental

All melting points are uncorrected. ^1H NMR spectra were recorded on Varian EM-390, Bruker WP-200 or Bruker AM-500 instruments and are reported in ppm from internal tetramethylsilane on the δ scale. Data are reported as follows: Chemical shift [multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), coupling constants, integration, interpretation]. ^{13}C NMR spectra were recorded on a Bruker WP-80 instrument and are recorded in ppm from internal tetramethylsilane: Chemical shift (multiplicity). IR spectra were recorded using a Perkin-Elmer 457 spectrometer. Mass spectra were recorded using a Kratos MS-30. The parent ions of some compounds were not ob-

served. In these cases, fragmentation patterns were in accord with the assigned structures. Combustion analyses were performed by Micro-Analysis, Inc., Wilmington, DE.

Solvents and reagents were purified prior to use. All reactions were carried out under a blanket of nitrogen or argon in flame-dried flasks unless stated otherwise. Column chromatography was performed over EM Laboratories silica gel (70~230 mesh) or LoBar columns (medium pressure).

*rel**-(3*R*,4*R*)-*N*-(*p*-Methoxyphenyl)-3-ethyl-4-(*E*-2-phenylethenyl)-2-azetidinone (**9**) and *rel*-(3*S*,4*R*)-*N*-(*p*-Methoxyphenyl)-3-ethyl-4-(*E*-2-phenylethenyl)-2-azetidinone (**10**)

To a solution of 8.70 ml (62.1 mmol) of diisopropylamine in 100 ml of THF cooled in a dry ice-acetone bath was added 38.0 ml (57.0 mmol) of 1.50 M *n*-BuLi in hexane over a 5-minute period at −70°C. The mixture was stirred for 30 minutes and 7.20 ml (54.3 mmol) of ethyl butyrate in 100 ml of THF was added over a 5-minute period. The mixture was stirred for 30 minutes and 15 ml of HMPA in 15 ml of THF was added over a 2-minute period. The cold solution was stirred for 10 minutes followed by addition of 12.9 g (54.3 mmol) of imine **8** in 100 ml of THF over a 5-minute period. The resulting solution was stirred at −70°C for 1 hour, warmed to room temperature, stirred for 2 hours and diluted with 1 liter of ether. The solution was washed with two 500-ml portions of 1 N aqueous HCl. The aqueous layers were extracted with 500 ml of ether. The combined organic layers were washed with 500 ml of brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 16.8 g of a dark brown oil. The oil was flash chromatographed twice over 200-g portions of silica gel (EtOAc, 1 : 9) to give 11.2 g (67%) of a 4 : 1 mixture of **9** and **10**, respectively. A small portion of this mixture was separated by chromatography at medium pressure to give pure samples of **9** and **10**. Lactam **9**: MP 82.5~83.5°C; IR ($CHCl_3$) 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.07 (3H, t, J=7.2 Hz, CH_3CH_2), 1.89 (2H, m, CH_2), 3.05 (1H, ddd, J=8.4, 6.2 and 2.3 Hz, CHCO), 3.75 (3H, s, CH_3O), 4.28 (1H, dd, J=8.3 and 2.3 Hz, CHN), 6.29 (1H, dd, J=16.8 and 8.3 Hz, C*H*=CHPh), 6.77 (1H, d, J=16.8 Hz, CH=C*H*Ph), 6.83 (2H, d, J=9.0 Hz, ArH), 7.23~7.40 (7H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 11.39 (q), 21.66 (t), 55.51 (q), 59.06 (d), 59.93 (d), 114.44 (d), 118.22 (d), 126.63 (d), 127.67 (d), 128.28 (d), 128.71 (d), 131.99 (s), 133.63 (d), 135.87 (s), 156.05 (s), 166.82 (s); exact mass calcd for $C_{20}H_{21}NO_2$ m/z 307.1572, found m/z 307.1553. Lactam **10**: Oil; IR ($CHCl_3$) 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.07 (3H, t, J=7.2 Hz, CH_3CH_2), 1.89 (2H, m, CH_2), 3.38 (1H, ddd, J=13.2, 7.5 and 5.8 Hz, CHCO), 3.75 (1H, s, OCH_3), 4.71 (1H, dd, J=8.0 and 5.8 Hz, CHN), 6.26 (1H, dd, J=15.6 and 8.0 Hz, C*H*=CHPh), 6.78 (1H, d, J=15.6 Hz, CH=C*H*Ph), 6.82 (2H, d, J=9.0 Hz, ArH), 7.22~7.45 (7H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 12.26 (q), 18.99 (t), 55.51 (q), 56.12 (d), 57.25 (d), 114.44 (d), 118.27 (d), 124.83 (d), 126.63 (d), 128.33 (d), 128.77 (d), 132.00 (s), 135.27 (d), 136.09 (s), 155.99 (s), 167.36 (s); exact mass calcd for $C_{20}H_{21}NO_2$ m/z 307.1572, found m/z 307.1553.

rel-(3*R*,4*R*)-3-Ethyl-4-(*E*-2-phenylethenyl)-2-azetidinone (**11**) and *rel*-(3*S*,4*R*)-3-Ethyl-4-(*E*-2-phenylethenyl)-2-azetidinone

To a solution of 8.18 g (26.6 mmol) of **9** and **10** (4 : 1, respectively) in 250 ml of acetonitrile cooled in an ice bath was added 43.7 g (79.7 mmol) of ceric ammonium nitrate in 350 ml of water over a 5-minute period. The mixture was stirred for 30 minutes at 0°C, diluted with 1 liter of water, and extracted with three 400-ml portions of EtOAc. The combined organic layers were washed with 500 ml of 5% aqueous sodium bicarbonate solution, three 500-ml portions of 10% aqueous sodium sulfite solution and 500 ml of 5% aqueous sodium bicarbonate solution. Each aqueous layer was extracted with two 150-ml portions of EtOAc. The combined organic layers were washed with 500 ml of brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in 200 ml of dichloromethane, swirled over charcoal (Norit A) for a day and filtered through celite. The filtrate was concentrated *in vacuo* and flash chromatographed twice over 200-g portions of silica gel (EtOAc, 1 : 4) to give 3.48 g (65%) of **11** and 0.70 g (13%) of its *rel*-(3*S*,4*R*)-diastereomer, both as colorless oils. Lactam **11**: IR ($CHCl_3$) 3410, 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.06 (t, J=7.0 Hz, CH_3), 1.82 (2H, m, CH_2), 2.95 (1H, m, CHCO), 3.96 (1H, dd, J=7.5 and 2.0 Hz, CHN), 6.00 (1H, br s, NH), 6.26 (1H, dd, J=16.0 and 7.5 Hz, C*H*=CHPh), 6.61 (1H, d, J=16.0 Hz, CH=C*H*Ph), 7.33 (5H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 11.31 (q), 21.34 (t), 55.97 (d), 60.50 (d), 126.49 (d), 128.02 (d), 128.66 (d, overlapping

* *rel*: Relative configuration.

carbons), 131.86 (d), 136.01 (s), 170.76 (s); exact mass calcd for $C_{13}H_{15}NO$ *m/z* 201.1154, found *m/z* 201.1137. *rel*-(3*S*,4*R*)-Diastereomer of **11**: IR ($CHCl_3$) 3410, 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.01 (3H, t, J=7.2 Hz, CH_3), 1.74 (2H, m, CH_2), 3.30 (1H, m, CHCO), 4.39 (1H, t, J=7.2 Hz, CHN), 6.11 (1H, br s, NH), 6.24 (1H, dd, J=16.0 and 7.2 Hz, C*H*=CHPh), 6.68 (1H, d, J=16.0 Hz, CH=C*H*Ph), 7.40 (5H, br s, ArH); ^{13}C NMR ($CDCl_3$) δ 12.02 (q), 18.85 (t), 53.41 (d), 57.37 (d), 125.98 (d), 126.49 (d), 128.02 (d), 128.66 (d), 133.52 (d), 136.20 (s), 171.53 (s); exact mass calcd for $C_{13}H_{15}NO$ *m/z* 201.1154, found *m/z* 201.1150.

rel-(3*R*,4*S*)-3-Ethyl-4-(1-bromo-2-hydroxy-2-phenyl)ethyl-2-azetidinone (**12**)

To a solution of 774 mg (3.85 mmol) of **11** in 20 ml of DMSO and 0.2 ml of water was added 754 mg (4.23 mmol) of *N*-bromosuccinimide in one portion. The mixture was stirred for a day at room temperature, diluted with 100 ml of dichloromethane and washed with two 100-ml portions of water. Each aqueous wash was extracted with 50 ml of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was flash chromatographed twice over 40-g portions of silica gel (EtOAc, 1:1) to give 935 mg (81%) of a diastereomeric mixture of bromohydrins **12** as a white solid: MP 87~104°C; IR ($CHCl_3$) 3410, 1755 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, major stereoisomer) δ 0.87 (3H, t, J=7.2 Hz, CH_3), 1.63 (2H, m, CH_2), 2.62 (1H, br s, OH), 2.77 (1H, tt, J=6.9 and 2.0 Hz, CHCO), 3.50 (1H, dd, J=6.0 and 2.0 Hz, CHN), 4.41 (1H, dd, J=6.0 and 4.6 Hz, CHBr), 5.11 (1H, d, J=4.6 Hz, CHPh), 5.89 (1H, br s, NH), 7.40 (5H, s, ArH). Weak signals at δ 1.05 (t), 3.01 (tt), 3.69 (dd), 4.16 (dd), and 5.03 (d) in the ^1H NMR of this material were attributed to the minor diastereomer of the bromohydrin; MS *m/z* (relative intensity) 107 [100, $(PhCH{=}OH)^+$].

rel-(3*R*,4*R*)-3-Ethyl-4-(2-hydroxy-2-phenyl)ethyl-2-azetidinone (**13**)

A mixture of 607 mg (2.04 mmol) of **12**, 0.55 ml (3.11 mmol) of tri-*n*-butyltin hydride and 3 mg of 2,2′-azobisisobutyronitrile (AIBN) in 20 ml of benzene was heated at reflux for 6 hours. The solution was concentrated *in vacuo* and flash chromatographed over 20 g of silica gel (EtOAc, 2:1) to give 380 mg (85%) of a diastereomeric mixture of alcohol **13** as a white solid: MP 98~125°C; IR ($CHCl_3$) 3410, 1745 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.00 (3H, m, CH_3), 1.57 (1H, br s, OH), 1.73 (2H, m, C*H*$_2$CH$_3$), 1.90~2.27 (2H, m, C*H*$_2$COH), 2.73 (1H, m, CHCO), 3.47 (1H, m, CHN), 4.82 (1H, m, CHOH), 5.59 and 5.85 (1H, two br s, NH), 7.33 (5H, br s, ArH); MS *m/z* (relative intensity) 107 [100, $(PhCH{=}OH)^+$].

rel-(3*R*,4*R*)-3-Ethyl-4-(2-phenyl-2-oxo)ethyl-2-azetidinone (**14**)

To a solution of 280 mg (1.28 mmol) of lactam **13** in 12 ml of acetone cooled in an ice bath was added JONES' reagent dropwise with stirring until the red color persisted. The mixture was stirred for 10 minutes at 0°C and several drops of 2-PrOH were added until the mixture became blue-green in color. The mixture was filtered and the residual blue-green solid was washed with 15 ml of acetone. The combined acetone solutions were diluted with 100 ml of water and extracted with two 50-ml portions of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residual solid was flash chromatographed over 20 g of silica gel (EtOAc, 1:2) to give 231 mg (83%) of lactam **14** as a white solid: MP 94~95°C; IR ($CHCl_3$) 3420, 1750, 1680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.05 (3H, t, J=7.2 Hz, CH_3), 1.81 (2H, m, CH_3CH_2), 2.83 (1H, td, J=7.0 and 2.3 Hz, CHCO), 3.20 (1H, dd, J=17.7 and 9.0 Hz, C*H*$_2$CO), 3.43 (1H, dd, J=17.7 and 4.2 Hz, C*H*$_2$CO), 3.81 (1H, ddd, J=9.0, 4.2 and 2.3 Hz, CHN), 6.10 (1H, br s, NH), 7.40~7.60 (3H, m, ArH), 7.9 (2H, d, J=8 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 11.37 (q), 21.43 (t), 43.85 (t), 50.03 (d), 58.39 (d), 128.04 (d), 128.86 (d), 133.73 (d), 136.41 (s), 170.36 (s), 198.08 (s); exact mass calcd for $C_{13}H_{15}NO_2$ *m/z* 217.1103, found *m/z* 217.1093.

rel-(3*R*,4*R*)-3-Ethyl-4-(phenyloxycarbonyl)methyl-2-azetidinone (**15**)

To a solution of 0.18 ml (6.66 mmol) of 90% hydrogen peroxide in 15 ml of dichloromethane cooled in an ice bath was added 1.00 ml (7.08 mmol) of trifluoroacetic anhydride over a 1-minute period. The mixture was stirred for 10 minutes at 0°C and 2.95 g (20.8 mmol) of disodium hydrogen phosphate was added in one portion. The resulting mixture was stirred for 10 minutes at 0°C and 501 mg (2.31

mmol) of **14** in 15 ml of dichloromethane was added over a 2-minute period. The mixture was stirred for 30 minutes at 0°C, warmed to room temperature, stirred for 12 hours, diluted with 100 ml of dichloromethane and washed twice with two 100-ml portions of water. The combined aqueous layers were extracted with 50 ml of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was flash chromatographed over 20 g of silica gel (EtOAc, 1 : 2) to give 430 mg (80%) of lactam **15** as a colorless oil: IR ($CHCl_3$) 3420, 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.05 (3H, t, J=7.2 Hz, CH_3), 1.79 (2H, m, CH_2CH_3), 2.85 (1H, dd, J=16.8 and 8.5 Hz, CH_2CO), 2.86 (1H, m, CHCO), 2.99 (1H, dd, J=16.8 and 5.1 Hz, CH_2CO), 3.75 (1H, ddd, J= 8.5, 5.1 and 2.3 Hz, CHN), 6.10 (1H, br s, NH), 7.04~7.43 (5H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 11.32 (q), 21.38 (t), 39.86 (t), 50.03 (d), 58.55 (d), 121.48 (d), 126.24 (d), 129.63 (d), 150.35 (s), 169.65 (s), 170.03 (s); MS *m/z* (relative intensity) 190 (3), 140 (9), 112 (7), 98 (38), 96 (100), 94 (51).

rel-(3*R*,4*R*)-Ethyl-4-[2-oxo-3-(*p*-nitrobenzyloxycarbonyl)propyl]-2-azetidinone (**16**)

To a solution of 276 mg (1.18 mmol) of **15** in 20 ml of EtOH was added 2.0 ml of 2.0 N aqueous sodium hydroxide. The mixture was stirred for 20 minutes at room temperature and 2.0 ml of 2.0 N aqueous HCl was added over a 1-minute period. The mixture was concentrated *in vacuo*, dissolved in 5 ml of MeOH and filtered. The filtrate was concentrated *in vacuo* and the residual solid was washed with 5 ml of cold ether. The residual solid was dissolved in 15 ml of THF and 190 mg (1.79 mmol) of carbonyldiimidazole was added. The mixture was stirred for 8 hours at room temperature, 900 mg (1.80 mmol) of anhydrous magnesium mono-*p*-nitrobenzylmalonate was added and the mixture was stirred for 18 hours at room temperature. The resulting solution was diluted with 150 ml of dichloromethane and washed with two 150-ml portions of 0.5 N aqueous HCl. Each aqueous wash was extracted with two 100-ml portions of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was flash chromatographed twice over 20-g portions of silica gel (EtOAc, 2 : 1) to give 248 mg (63%) of lactam **16** as a white solid: MP 86.5~87.5°C; IR ($CHCl_3$) 3420, 1755, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.00 (3H, t, J=7.2 Hz, CH_3), 1.75 (2H, m, CH_2CH_3), 2.72 (1H, td, J=6.9 and 2.2 Hz, CHCO), 2.78 (1H, dd, J=18.2 and 8.7 Hz, CH_2CO), 3.01 (1H, dd, J=18.2 and 4.4 Hz, CH_2CO), 3.56 (2H, s, CH_2COO), 3.64 (ddd, J=8.7, 4.4 and 2.2 Hz, CHN), 5.26 (2H, s, CH_2Ar), 6.12 (1H, br s, NH), 7.52 (2H, d, J=8.7 Hz, ArH), 8.21 (2H, d, J=8.7 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 11.25 (q), 21.34 (t), 48.11 (t), 49.07 (d and t), 58.39 (d), 65.74 (t), 123.94 (d), 128.41 (s), 128.60 (d), 142.27 (s), 166.35 (s), 170.12 (s), 200.53 (s); MS *m/z* (relative intensity) 291 (2), 153 (24), 136 (31), 112 (52), 96 (100).

rel-(3*R*,4*R*)-3-Ethyl-4-[3-diazo-2-oxo-3-(*p*-nitrobenzyloxycarbonyl)propyl]-2-azetidinone (**17**)

To a solution of 130 mg (0.39 mmol) of **16** in 4 ml of acetonitrile cooled in an ice bath was added 55 μl (0.39 mmol) of triethylamine and 92 mg (0.47 mmol) of tosyl azide. The mixture was stirred for 1 hour at 0°C and concentrated *in vacuo*. The residue was flash chromatographed over 15 g of silica gel (EtOAc, 3 : 2) to give 136 mg (97%) of **17** as a white solid: MP 111~113°C; IR ($CHCl_3$) 3420, 2140, 1755, 1720, 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.00 (3H, t, J=7.2 Hz, CH_3), 1.76 (2H, m, CH_2CH_3), 2.81 (1H, td, J=6.9 and 2.3 Hz, CHCO), 3.03 (1H, dd, J=17.9 and 9.0 Hz, CH_2CO), 3.36 (1H, dd, J=17.9 and 4.1 Hz, CH_2CO), 3.68 (1H, ddd, J=9.0, 4.1 and 2.3 Hz, CHN), 5.32 (2H, s, CH_2Ar), 6.03 (1H, br s, NH), 7.53 (2H, d, J=8.7 Hz, ArH), 8.24 (2H, d, J=8.7 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 11.31 (q), 21.34 (t), 45.49 (t), 49.77 (d), 58.20 (d), 65.12 (t), 75.95 (s), 124.06 (d), 128.79 (d), 142.01 (s), 160.73 (s), 170.25 (s), 189.99 (s), ketone C=O not recorded.

p-Nitrobenzyl *rel*-(2*R*,5*R*,6*R*)-6-Ethyl-3,7-dioxo-1-azabicyclo[3.2.0]heptane-2-carboxylate (**18**)

A mixture of 124 mg (0.34 mmol) of **17** and 0.5 mg of dirhodium tetraacetate in 7 ml of dry benzene was heated at reflux for 30 minutes. The mixture was filtered through Celite and the Celite was washed with 5 ml of dichloromethane. The filtrate was concentrated *in vacuo* to give 112 mg of **18** as a colorless oil: IR ($CHCl_3$) 1760 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.10 (3H, t, J=7.4 Hz, CH_3), 1.93 (2H, m, CH_2CH_3), 2.39 (1H, dd, J=18.6 and 7.7 Hz, CH_2CO), 2.89 (1H, dd, J=18.6 and 6.8 Hz, CH_2CO), 3.13 (1H, td, J=6.0 and 1.5 Hz, CHCO), 3.88 (1H, ddd, J=7.7, 6.8 and 1.5 Hz, CHN), 4.76 (1H, s, CHCOO), 5.29 (2H, m, CH_2Ar), 7.54 (2H, d, J=8.7 Hz, ArH), 8.23 (2H, d, J=8.7 Hz, ArH); ^{13}C

NMR ($CDCl_3$) δ 11.44 (q), 22.17 (t), 41.53 (t), 53.92 (d), 62.74 (d), 63.95 (d), 66.19 (t), 123.94 (d), 128.41 (d), 129.12 (s), 141.95 (s), 165.01 (s), 174.91 (s), 206.98 (s); exact mass calcd for $C_{16}H_{16}N_2O_6$ *m/z* 332.1009, found *m/z* 332.0971.

rel-(3*R*,4*R*)-*N*-(*p*-Methoxyphenyl)-3-isopropyl-4-(*E*-2-phenylethenyl)-2-azetidinone (**20**)

To a solution of 1.60 ml (11.4 mmol) of diisopropylamine in 15 ml of THF cooled in a dry ice-acetone bath was added 7.50 ml (10.1 mmol) of 1.35 M *n*-BuLi in hexane over a 5-minute period at −70°C. The mixture was stirred for 30 minutes and 1.50 ml (10.0 mmol) of ethyl isovalerate in 10 ml of THF was added over a 5-minute period. The mixture was stirred for 30 minutes and 4.0 ml of HMPA in 4.0 ml of THF was added over a 2-minute period. The cold solution was stirred for 10 minutes followed by addition of 2.42 g (10.2 mmol) of imine **8** in 30 ml of THF over a 5-minute period. The resulting solution was stirred at −70°C for 1 hour, warmed to room temperature, stirred for 2 hours, and diluted with 200 ml of dichloromethane. The solution was washed with two 150-ml portions of saturated aqueous ammonium chloride solution. The aqueous washes were extracted with 100 ml of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give 6.60 g of a dark-brown oil. The oil was chromatographed twice over to 50-g portions of silica gel (EtOAc, 1:7) to give 2.52 g (78%) of β-lactam **20**. ^1H NMR analysis showed the β-lactam contained about 10% of the *cis*-diastereomer which could not be separated by chromatography. A pure sample of β-lactam **20** was obtained by recrystallization from dichloromethane-hexane (1:5): MP 95~96°C; IR ($CHCl_3$) 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.05 (3H, d, J=7.0 Hz, $CHCH_3$), 1.15 (3H, d, J=7.0 Hz, $CHCH_3$), 2.10 (1H, sextet, J=7.0 Hz, $CHCH_3$), 2.91 (1H, dd, J=8.3 and 2.4 Hz, CHCO), 3.76 (3H, s, OCH_3), 4.34 (1H, dd, J=8.5 and 2.4 Hz, CHN), 6.28 (1H, dd, J=15.9 and 8.5 Hz, PhCH=C*H*), 6.77 (1H, d, J=15.9 Hz, PhC*H*=CH), 6.83 (2H, d, J=9.0 Hz, ArH), 7.20~7.45 (5H, m, ArH), 7.52 (2H, d, J=9.0 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 20.13 (q), 20.30 (q), 28.44 (d), 55.51 (d), 58.24 (q), 64.36 (d), 114.44 (d), 118.16 (d), 126.63 (d), 127.89 (d), 128.27 (d), 128.71 (d), 131.99 (s), 133.47 (d), 135.93 (s), 155.99 (s), 166.38 (s); exact mass calcd for $C_{21}H_{23}NO_2$, *m/z* 321.1728, found *m/z* 321.1760.

Anal Calcd for $C_{21}H_{23}NO_2$: C 78.47, H 7.21.
Found: C 78.76, H 7.30.

rel-(3*R*,4*R*)-3-Isopropyl-4-(*E*-2-phenylethenyl)-2-azetidinone (**21**) and *rel*-(3*S*,4*R*)-3-Isopropyl-4-(*E*-2-phenylethenyl)-2-azetidinone

To a solution of 976 mg (3.04 mmol) of β-lactam **20** in 30 ml of acetonitrile cooled in an ice bath was added 4.82 g (8.79 mmol) of ceric ammonium nitrate in 45 ml of water over a 5-minute period. The mixture was stirred for 30 minutes at 0°C, diluted with 200 ml of water, and extracted with three 50-ml portions of EtOAc. The combined organic layers were washed with 100 ml of 5% aqueous sodium bicarbonate solution. The aqueous layer was extracted with 50 ml of EtOAc. The combined organic layers were washed with three 100-ml portions of 10% aqueous sodium sulfite solution. The combined aqueous layers were extracted with 50 ml of EtOAc. The combined organic layers were washed with 50 ml of 5% aqueous sodium bicarbonate solution and 50 ml of brine. The resulting solution was swirled over charcoal (Norit A) for 30 minutes, magnesium sulfate was added, and the mixture was filtered through Celite. The filtrate was concentrated *in vacuo* and flash chromatographed over 10 g of silica gel to give 753 mg of slightly yellow solid in which was chromatographed (Chromatotron, 4 mm; EtOAc, 1:3) to give 554 mg (85%) of **3** and 66 mg (10%) of its *rel*-(3*S*,4*R*)-diastereomer. Lactam **21**: MP 99~100°C; IR ($CHCl_3$) 3400, 1755 cm^{-1}; ^1H NMR (200 MHz, $CHCl_3$) δ 1.04 (3H, d, J=6.7 Hz, $CHCH_3$), 1.11 (3H, d, J=6.7 Hz, $CHCH_3$), 2.10 (1H, sextet, J=6.7 Hz, $CHCH_3$), 2.81 (1H, dd, J=8.2 and 2.3 Hz, CHCO), 4.04 (1H, dd, J=7.5 and 2.3 Hz, CHN), 5.95 (1H, br s, NH), 6.25 (1H, dd, J=15.8 and 7.5 Hz, PhCH=C*H*), 6.61 (1H, d, J=15.8 Hz, PhC*H*=CH), 7.26~7.40 (5H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 19.97 (q), 20.35 (q), 28.12 (d), 54.36 (d), 65.95 (d), 126.52 (d), 128.11 (d), 128.71 (d), 128.98 (d), 131.82 (d), 136.15 (s), 170.21 (s); exact mass calcd for $C_{14}H_{17}NO$ *m/z* 215.1310, found *m/z* 215.1283.

Anal Calcd for $C_{14}H_{17}NO$: C 78.10, H 7.96.
Found: C 78.59, H 7.83.

rel-(3*S*,4*R*)-Diastereomer of **3**: MP 151~152°C; IR ($CHCl_3$) 3400, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (3H, d, J=6.5 Hz, $CHCH_3$), 1.17 (3H, d, J=6.5 Hz, $CHCH_3$), 2.05 (1H, m, $CHCH_3$), 3.05 (1H, ddd, J=11.2, 5.4 and 1.5 Hz, CHCO), 4.37 (1H, dd, J=7.7 and 5.4 Hz, CHN), 6.01 (1H, br s, NH), 6.26 (1H, dd, J=15.9 and 7.7 Hz, $PhCH=CH$), 6.66 (1H, d, J=15.9 Hz, $PhCH=CH$), 7.26~7.42 (5H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 20.46 (q), 21.50 (q), 25.93 (d), 53.65 (d), 63.21 (d), 126.47 (d), 126.58 (d), 128.16 (d), 128.77 (d), 133.80 (d), 136.31 (s), 170.65 (s); exact mass calcd for $C_{14}H_{17}NO$ m/z 215.1310, found m/z 215.1312.

rel-(3*R*,4*S*)-3-Isopropyl-4-(1-bromo-2-hydroxy-2-phenyl)ethyl-2-azetidinone (**22**)

To a solution of 601 mg (2.80 mmol) of **21** in 15 ml of DMSO and 0.1 ml of water was added 510 mg (2.87 mmol) of *N*-bromosuccinimide in one portion. The mixture was stirred at room temperature for 10 hours, diluted with 100 ml of dichloromethane and washed with two 100-ml portions of water. The combined aqueous layers were extracted with 50 ml of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was flash chromatographed twice over 30-g portions of silica gel (EtOAc, 1 : 1) to give 748 mg (86%) of a diastereomeric mixture of **22** as a white solid. An analytical sample of one diastereomer was obtained by recrystallization from dichloromethane - hexane: MP 177~179°C; IR ($CHCl_3$) 3400, 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.82 (3H, d, J=6.7 Hz, CH_3), 0.96 (3H, d, J=6.7 Hz, CH_3), 1.87 (1H, sextet, J=6.7 Hz, CH_3CH), 2.59 (1H, d, J=3.6 Hz, OH), 2.77 (dt, J=7.2 and 1.9 Hz, CHCO), 3.45 (1H, dd, J=4.0 and 1.9 Hz, CHN), 4.44 (1H, t, J=4.0 Hz, CHBr), 5.17 (1H, dd, J=4.0 and 3.6 Hz,CHPh), 5.87 (1H, br s, NH), 7.39 (5H, m, ArH); MS m/z (relative intensity) 107 (100).

Anal Calcd for $C_{14}H_{18}BrNO_2$: C 53.86, H 5.81.
Found: C 54.16, H 5.88.

rel-(3*R*,4*R*)-3-Isopropyl-4-(2-hydroxy-2-phenyl)ethyl-2-azetidinone (**23**)

A mixture of 740 mg (2.37 mmol) of **22**, 0.62 ml (3.51 mmol) of tri-*n*-butyltin hydride and 3 mg of AIBN in 20 ml of benzene was heated at reflux for 3 hours. The solution was concentrated *in vacuo* and chromatographed over 20 g of silica gel (EtOAc, 1 : 1) to give 480 mg (87%) of a diastereomeric mixture of alcohol **23** as a white solid: MP 64~82°C; IR ($CHCl_3$) 3400, 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.00 (6H, m, $2CH_3$), 1.84~2.25 (4H, m, CH_2, OH and $CHCH_3$), 2.58 (1H, dt, J=7.9 and 1.8 Hz, CHCO), 3.52 (1H, m, CHN), 4.81 (1H, m, CHPh), 5.68 and 5.94 (1H, br s, NH), 7.36 (5H, m, ArH); MS m/z (relative intensity) 107 (100).

rel-(3*R*,4*R*)-3-Isopropyl-4-(2-phenyl-2-oxoethyl)-2-azetidinone (**24**)

To a solution of 450 mg (1.93 mmol) of lactam **23** in 15 ml of acetone cooled in an ice bath was added JONES' reagent dropwise with stirring until a red color persisted. The mixture was stirred for 10 minutes at 0°C and several drops of 2-PrOH were added until the mixture became blue-green in color. The mixture was filtered and the residual solid was washed with 10 ml of acetone. The combined acetone solutions were diluted with 100 ml of water and extracted with two 40-ml portions of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residual solid was chromatographed over 20 g of silica gel (EtOAc, 1 : 2) to give 358 mg (80%) of lactam **24** as a white solid. An analytically pure sample of lactam **24** was obtained by recrystallization from CH_2Cl_2 - petroleum ether (1 : 10): MP 85.5~86°C; IR ($CHCl_3$) 3400, 1750, 1680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.02 (3H, d, J=6.7 Hz, CH_3), 1.20 (3H, d, J=6.7 Hz, CH_3), 2.17 (1H, sextet, J=6.7 Hz, $CHCH_3$), 2.70 (1H, dd, J=8.0 and 2.2 Hz, CHCO), 3.17 (1H, dd, J=17.7 and 8.8 Hz, CH_2CO), 3.44 (1H, dd, J=17.7 and 3.4 Hz, CH_2CO), 3.85 (1H, ddd, J=8.8, 3.4 and 2.2 Hz, CHN), 6.10 (1H, br s, NH), 7.44~7.97 (5H, m, ArH); ^{13}C NMR ($CDCl_3$) 19.86 (q), 20.35 (q), 27.79 (d), 43.97 (t), 48.23 (d), 63.60 (d), 128.00 (d), 128.77 (d), 133.66 (d), 136.42 (s), 169.66 (s), 198.09 (s); exact mass calcd for $C_{14}H_{17}NO_2$ m/z 231.1259, found m/z 231.1224.

Anal Calcd for $C_{14}H_{17}NO_2$: C 72.70, H 7.41.
Found: C 72.47, H 7.44.

rel-(3*R*,4*R*)-3-Isopropyl-4-(phenyloxycarbonylmethyl)-2-azetidinone (**25**)

To a solution of 0.50 ml (18.5 mmol) of 90% H_2O_2 solution in 40 ml of dichloromethane cooled

in an ice bath was added 2.85 ml (20.0 mmol) of trifluoroacetic anhydride over a 1-minute period. The mixture was stirred for 10 minutes at 0°C and 6.09 g (42.2 mmol) of disodium hydrogen phosphate was added in one portion. The resulting mixture was stirred for 10 minutes at 0°C and 1.50 g (6.49 mmol) of **6** in 30 ml of dichloromethane was added over a 2-minute period. The mixture was stirred for 30 minutes at 0°C, warmed to room temperature, stirred for 10 hours, diluted with 200-ml of dichloromethane and washed with two 200-ml portions of water. The combined aqueous layers were extracted with 100 ml of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give 1.45 g of white solid. The residue was chromatographed over 50 g of silica gel (EtOAc, 1:4) to give 1.29 g (81%) of β-lactam **25** as a white solid: MP 97~98°C; IR ($CHCl_3$) 3400, 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.03 (3H, d, J=6.7 Hz, $CHCH_3$), 1.11 (3H, d, J=6.7 Hz, $CHCH_3$), 2.08 (1H, m, $CHCH_3$), 2.73 (1H, dd, J=8.0 and 2.2 Hz, CHCO), 2.87 (1H, dd, J=16.8 and 9.2 Hz, CH_2COO), 2.99 (1H, dd, J=16.8 and 4.3 Hz, CH_2COO), 3.80 (1H, ddd, J=9.2, 4.3 and 2.2 Hz, CHN), 6.08 (1H, br s, NH), 7.06~7.44 (5H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 19.97 (q), 20.41 (q), 27.84 (d), 44.03 (t), 48.29 (d), 63.65 (d), 128.06 (d), 128.88 (d), 133.69 (d), 136.47 (s), 169.66 (s), 198.15 (s).

Anal Calcd for $C_{14}H_{17}NO_3$: C 68.00, H 6.93.
Found: C 67.89, H 6.75.

rel-(3*R*,4*R*)-3-Isopropyl-4-{[2-(*p*-nitrobenzyloxycarbonylamino)ethylthio]carbonylmethyl}-2-azetidinone (**26**)

A mixture of 530 mg (2.14 mmol) of β-lactam **25**, 1.10 g (4.30 mmol) of 2-(*p*-nitrobenzyloxycarbonylamino)ethanethiol and 50 μl of DBU in 20 ml of dichloromethane was stirred at room temperature for 5 hours. The solution was concentrated to approximately 5 ml total volume and chromatographed over 20 g of silica gel (EtOAc, 1:1) to give 770 mg (88%) of β-lactam **26** as a white solid: MP 108~109°C; IR ($CHCl_3$) 3470, 3440, 1765, 1740, 1695 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.99 (3H, d, J=6.7 Hz, $CHCH_3$), 1.08 (3H, d, J=6.7 Hz, $CHCH_3$), 2.02 (1H, m, $CHCH_3$), 2.65 (1H, dd, J=8.2 and 2.0 Hz, CHCO), 2.79 (1H, dd, J=15.2 and 9.2 Hz, CH_2COO), 2.96 (1H, dd, J=15.2 and 4.0 Hz, CH_2COO), 2.99~3.19 (2H, m, SCH_2), 3.37~3.48 (2H, m, CH_2N), 3.71 (1H, ddd, J=9.2, 4.0 and 2.0 Hz, CHN), 5.21 (3H, s, $COOCH_2$ and NHCOO), 6.30 (1H, br s, NH), 7.53 (2H, d, J=9.0 Hz, ArH), 8.24 (2H, d, J=9.0 Hz, ArH); ^{13}C NMR ($CDCl_3$) 19.9 (q), 20.3 (q), 27.7 (d), 29.40 (t), 40.7 (t), 48.9 (d), 49.2 (t), 64.0 (d), 65.5 (t), 123.8 (d), 128.3 (d), 143.9 (s), 156.0 (s), 169.3 (s), 196.8 (s), one aryl carbon (s) not detected; MS *m/z* (relative intensity) 256 (10), 209 (12), 153 (20), 136 (100).

Anal Calcd for $C_{18}H_{23}N_3O_6S$: C 52.80, H 5.66.
Found: C 52.91, H 5.84.

rel-(3*R*,4*R*)-*N*-(*p*-Nitrobenzoxalyl)-3-isopropyl-4-{[2-(*p*-nitrobenzyloxycarbonylamino)ethylthio]carbonylmethyl}-2-azetidinone (**27**)

To a solution of 1.60 ml (18.3 mmol) of oxalyl chloride in 20 ml of dichloromethane cooled in an ice bath was added 580 mg (3.78 mmol) of *p*-nitrobenzyl alcohol. The mixture was stirred for 20 minutes at 0°C, the cold bath was removed and the mixture was stirred for 1 hour at room temperature. The solution was concentrated *in vacuo* and the residual white solid was dissolved in 15 ml of dichloromethane. The solution was cooled in an ice bath and 0.53 ml (3.80 mmol) of triethylamine was added. The mixture was stirred briefly and 770 mg (1.88 mmol) of β-lactam **26** in 15 ml of dichloromethane was added dropwise over a 2-minute period. The mixture was stirred for 1 hour at 0°C, diluted with 100 ml of dichloromethane, and washed with 100 ml of water. The aqueous layer was extracted with 50 ml of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residual yellowish oil was flash chromatographed over 20 g of silica gel (EtOAc, 1:1) to afford 1.14 g (98%) of β-lactam **27** as a yellowish syrup: IR ($CHCl_3$) 3440, 1800, 1750, 1720, 1700 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.01 (3H, d, J=6.7 Hz, CH_3), 1.08 (3H, d, J=6.7 Hz, CH_3), 2.10 (1H, m, $CHCH_3$), 2.98~3.20 (4H, m, CHCO, CH_2COS and SCH_2), 3.25~3.45 (3H, m, CH, CH_2COS and CH_2N), 4.25 (1H, m, NCH), 5.21 (2H, s, CH_2Ar), 5.30 (1H, br s, NH), 5.43 (2H, s, CH_2Ar), 7.5 and 7.6 (4H, two d's, J=9 Hz, ArH), 8.1 and 8.2 (4H, two d's, J=9 Hz, ArH), MS *m/z* (relative intensity) 153 (22), 136 (100), 106 (33), 100 (30).

p-Nitrobenzyl *rel*-(5*R*,6*R*)-3-{2-(*p*-Nitrobenzyloxycarbonylamino)ethylthio}-6-isopropyl-7-oxo-1-azabicyclo[3.2.0]hept-2-en-2-carboxylate (**28**)

A solution of 1.14 g (1.85 mmol) of β-lactam **9** and 1.60 ml (9.33 mmol) of triethylphosphite in 30 ml of toluene was heated at 70~80°C for 6 hours. To the solution was added 10 mg of hydroquinone and the mixture was heated at 100°C for 30 hours. The mixture was concentrated *in vacuo* and chromatographed twice over 60-g portions of silica gel (EtOAc, 1:2) to give 637 mg (59%) of carbapenem **28** as a slightly yellow solid: MP 167~168°C; IR ($CHCl_3$) 3440, 1770, 1720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.03 (3H, d, J=6.7 Hz, CH_3), 1.10 (3H, d, J=6.7 Hz, CH_3), 2.10 (1H, m, $CHCH_3$), 2.96 (2H, m, CH_2S), 3.03 (1H, m, C(6)H), 3.06 (dd, J=18.0 and 8.2 Hz, C(4)H), 3.32 (dd, J=18.0 and 10.0 Hz, C(4)H), 3.43 (2H, m, NCH_2), 4.00 (1H, dt, J=9.0 and 3.0 Hz, C(5)H), 5.19~5.54 (5H, m, CH_2Ar and NH), 7.47~8.23 (8H, m, ArH); exact mass calcd for $C_{27}H_{28}N_4O_9S$ m/z 584.1578, found m/z 584.1663.

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References

1) Hart, D. J.; K. Kanai, D. G. Thomas & T. K. Yang: Preparation of primary amines and 2-azetidinones *via* *N*-trimethylsilyl imines. J. Org. Chem. 48: 289~294, 1983
2) Hart, D. J.; D. C. Ha & T. K. Yang: *N*-Trimethylsilyl imines: Applications to the synthesis of β-lactams. J. Am. Chem. Soc. 106: 4816~4825, 1984
3) Burnett, D. A.; J. C. Gallucci & D. J. Hart: Synthesis of 3-(1'-hydroxyethyl)-2-azetidinones *via* ester-imine condensations. J. Org. Chem. 50: 5120~5123, 1985
4) Yamamoto, K.; T. Yoshioka, Y. Kato, N. Shibamoto, K. Okamura, Y. Shimauchi & T. Ishikura: Structure and stereochemistry of antibiotic PS-5. J. Antibiotics 33: 796~803, 1980
5) Corbett, D. F. & A. J. Eglington: Conversion of the olivanic acids into antibiotics of the PS-5 type: Use of a new carboxy protecting group. J. Chem. Soc. Chem. Commun. 1980: 1083~1084, 1980
6) Bateson, J. H.; R. I. Hickling, P. M. Roberts, T. C. Smale & R. Southgate: Olivanic acids and related compounds: Total synthesis of (±)-PS-5 and (±)-*epi*-PS-5. J. Chem. Soc. Chem. Commun. 1980: 1084~1085, 1980
7) Kametani, T.; T. Honda, A. Nakayama, Y. Sasaki, T. Mochizuki & K. Fukumoto: A short and stereoselective synthesis of the carbapenem antibiotic PS-5. J. Chem. Soc. Perkin Trans. I 1981: 2228~2232, 1981
8) Favara, D.; A. Omodei-Salè, P. Consonni & A. Depaoli: A facile synthesis of trans (+)-4-carboxymethyl-3-ethylazetidin-2-one and its conversion into natural PS-5. Tetrahedron Lett. 23: 3105~3108, 1982
9) Wasserman, H. H. & W. T. Han: A synthesis of antibiotic (±)-PS-5. Tetrahedron Lett. 25: 3747~3750, 1984
10) Evans, D. A. & E. B. Sjogren: The asymmetric synthesis of β-lactam antibiotics-III. Enantioselective synthesis of (+) PS-5. Tetrahedron Lett. 27: 3119~3122, 1986
11) Kronenthal, D. R.; C. Y. Han & M. K. Taylor: Oxidative *N*-dearylation of 2-azetidinones. *p*-Anisidine as a source of azetidinone nitrogen. J. Org. Chem. 47: 2765~2768, 1982
12) Ratcliffe, R. W. & G. Albers-Schönberg: The chemistry of thienamycin and other carbapenem antibiotics. *In* Chemistry and Biology of β-Lactam Antibiotics. Vol. 2. Nontraditional β-Lactam Antibiotics. *Eds.*, R. B. Morin & M. Gorman, pp. 227~313, Academic Press, New York, 1982
13) Dalton, D. R.; J. B. Hendrickson & D. Jones: An improved procedure for the preparation of bromohydrins. J. Chem. Soc. Chem. Commun. 1966: 591~592, 1966
14) Kuivila, H. G.: Reduction of organic compounds by organotin hydrides. Synthesis 1970: 499~509, 1970
15) Bowden, K.; I. M. Heibron, E. R. H. Jones & B. C. L. Weedon: Researches on acetylenic compounds. Part. I. The preparation of acetylenic ketones by oxidation of acetylenic carbinols and glycols. J. Chem. Soc. 1946: 39~45, 1946

16) EMMONS, W. D. & G. B. LUCAS: Peroxytrifluoroacetic acid. V. The oxidation of ketones to esters. J. Am. Chem. Soc. 77: 2287~2288, 1955
17) SALZMANN, T. N.; R. W. RATCLIFFE, B. G. CHRISTENSEN & F. A. BOUFFARD: A stereocontrolled synthesis of (+)-thienamycin. J. Am. Chem. Soc. 102: 6161~6163, 1980
18) BROOKS, D. W.; L. D.-L. LU & S. MASAMUNE: C-Acylation under virtually neutral conditions. Angew. Chem. Int. Ed. Engl. 18: 72~74, 1979
19) RATCLIFFE, R. W.; T. N. SALZMANN & B. G. CHRISTENSEN: A novel synthesis of the carbapen-2-em ring system. Tetrahedron Lett. 21: 31~34, 1980
20) AFONSO, A.; F. HON, J. WEINSTEIN, A. K. GAHGULY & A. T. MCPHAIL: New synthesis of penems, the oxalimide cyclization reaction. J. Am. Chem. Soc. 104: 6138~6139, 1982
21) YOSHIDA, A.; Y. TAJIMA, N. TAKEDA & S. OIDA: A efficient carbapenem synthesis *via* an intramolecular wittig reaction of new trialkoxyphosphorane-thiolesters. Tetrahedron Lett. 25: 2793~2796, 1984
22) BATTISTINI, C.; C. SCARAFILE, M. FOGLIO & G. FRANCESCHI: A new route to penems and carbapenems. Tetrahedron Lett. 25: 2395~2398, 1984