Synthetic Studies on Optically Active β-Lactams. II.[1] Asymmetric Synthesis of β-Lactams by [2+2]Cyclocondensation Using Heterocyclic Compounds Derived from L-(+)-Tartaric Acid, (*S*)- or (*R*)-Glutamic Acid, and (*S*)-Serine as Chiral Auxiliaries[2,3]

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Asymmetric synthesis of β-lactams by the [2+2]cyclocondensation of an imine (7) to chiral ketene species (2b, 4b, and 6c) bearing heterocycles derived from L-(+)-tartaric acid, (*S*)-glutamic acid, and (*S*)-serine was carried out. The reaction of 2b with 7 gave the *trans*-β-lactams with 74% diastereomeric excess, and *cis*-β-lactams were predominantly formed with high diastereomeric purity (up to 96%) when 4b and 6c were employed. Asymmetric synthesis of (3*S*,4*S*)- and (3*R*,4*R*)-1-benzyl-3-[(benzyloxycarbonyl)amino]-4-hydroxymethyl-2-azetidinones (26 and 30g) using (*R*)-4b as a ketene species and the chiral imine (21) prepared from L-(+)-tartaric acid was also achieved.

Keywords asymmetric cyclocondensation; L-(+)-tartaric acid; (*S*)-pyroglutamic acid; (*S*)-serine; optically active β-lactam; chiral ketene species; chiral imine

A convenient procedure for the synthesis of the β-lactam skeleton is the cyclocondensation of ketene species to imines. Chiral synthesis of the β-lactam ring system[4,5] has been extensively studied in connection with the synthesis of β-lactam antibiotics from a variety of optically active starting materials, and by asymmetric induction. Several asymmetric syntheses of β-lactams by [2+2]cycloaddition[6] including chiral ketene-imine cyclocondensation reaction[7] have been reported. We have already reported highly diastereoselective β-lactam formation[2,3] by asymmetric cyclocondensation employing chiral heterocycles (**2b**, **4b**, and **6c**) derived from L-(+)-tartaric acid, (*S*)-glutamic acid, and (*S*)-serine as ketene species, and a chiral imine (**21**) prepared from L-(+)-tartaric acid. The details of this work are presented here.

Synthesis of Chiral Auxiliaries (2b, 4b, and 6c) as Ketene Species Chiral heterocyclic compounds (**2b**, **4b**, and **6c**) were prepared as shown in Chart 1. The tartarimide derivative (**2b**) was synthesized from diethyl di-*O*-methyl-L-tartrate (**1a**).[8] Conversion of **1a** to the corresponding half ester with 1 eq of aqueous base followed by condensation of glycine benzyl ester *p*-toluenesulfonate using diethyl phosphorocyanidate[9] afforded the amido-ester (**1b**). Brief heating of **1b** in toluene with sodium powder brought about cyclization to yield the tartarimide derivative (**2a**), which was hydrogenated to remove the benzyl group, providing **2b** in 40% yield from **1a**. The chiral 2-pyrrolidinone derivative (**4b**) was obtained from (*S*)-5-[(methoxymethoxy)methyl]-2-pyrrolidinone (**3**).[10a] Alkylation of **3** with benzyl bromoacetate (NaH, tetrahydrofuran (THF)–dimethylformamide (DMF)) followed by removal of the benzyl group of **4a** provided **4b** in 45% yield from **3**. The (*S*)-4-[(methoxymethoxy)methyl]-2-oxazolidinone derivative (**6c**) was prepared from *N*-benzyloxycarbonyl (Z)-(*S*)-serine methyl ester (**5a**). After protection of the hydroxy group of **5a** as the methoxymethyl (MOM) ether, reduction of the ester in **5b** with sodium borohydride ($NaBH_4$) in EtOH followed by removal of the Z group by hydrogenation gave the corresponding amino alcohol **5c**, which was cyclized with diethyl carbonate in the presence of potassium carbonate to afford the 2-oxazolidinone **6a**. Alkylation of **6a** with benzyl bromoacetate followed by removal of the benzyl group in the same manner as used for the preparation of **4b** provided **6c** in 21% yield from **5b**.

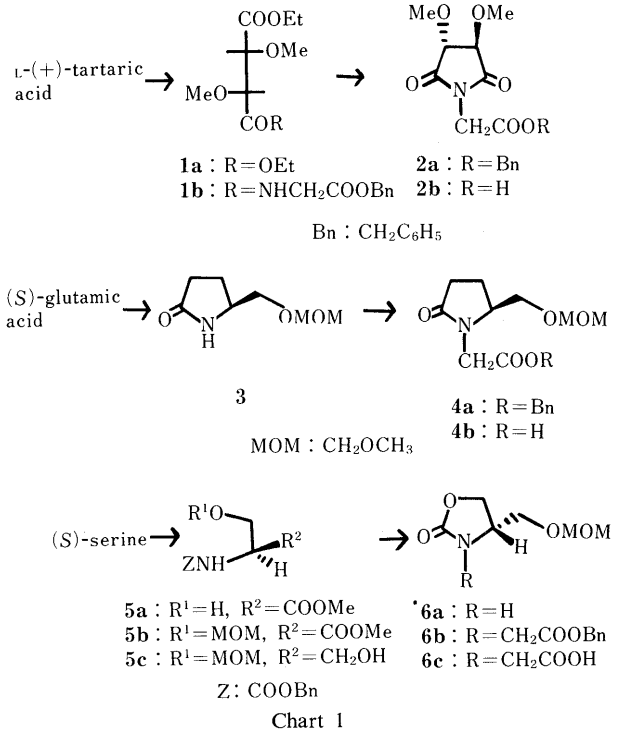


Chart 1

Asymmetric Synthesis of β-Lactams by [2+2]Cyclocondensation of 2b, 4b, and 6c with the Imine (7) Asymmetric β-lactam synthesis by [2+2]cyclocondensation of **2b**, **4b**, and **6c** with benzalaniline (**7**) was examined as illustrated in Chart 2. Transformation of the carboxylic acids (**2b**, **4b**, and **6c**) to the mixed anhydrides was achieved with trifluoroacetic anhydride in the presence of triethylamine (TEA) in methylene chloride[11] at 0 °C. The reaction of the unpurified mixed anhydride with benzalaniline was carried out in the presence of TEA in methylene chloride at −20 or 0 °C to give the β-lactams as a mixture of diastereomers. Each isomer was separated by column chromatography on silica gel, and characterized. The *cis* or *trans* relationship between the C-3 and C-4 substituents was determined based on the coupling constants (2 Hz for *trans*, 5—6 Hz for *cis*) in the ^1H nuclear magnetic resonance (^1H-NMR) spectrum. The ratio of the isomers was determined by high-performance liquid chromatographic analysis of the crude products. The results are summarized in Table I. The

cyclocondensation reactions proceeded in moderate yields and exhibited a high degree of stereochemical control. Using the tartarimide derivative (**2b**), the *trans*-β-lactams (**8**) were obtained with 68—74% diastereomeric excess (d.e.). On the other hand, *cis*-β-lactams (**12** and **17**) were predominantly formed with high diastereomeric purity up to 96% using **4b** and **6c**.

The stereochemistry of the newly formed asymmetric centers in the β-lactams was evaluated in the following manner. The isolated major *trans*-diastereomer (**8a**) was treated with sodium methoxide (1 eq) in methanol to afford the amido-ester (**9**), which was reacted with PCl_5 in the presence of pyridine in CH_2Cl_2, followed by addition of methanol and water to cleave the amide bond of **9** *via* the methyl imino ether to provide *trans*-3-amino-1,4-diphenyl-2-azetidinone (**10**) in 40% yield. The cleavage of the N–C_4 bond of **10** by hydrogenolysis using 10% palladium carbon[12] (Pd–C) in EtOH afforded (*R*)-phenylalanine anilide (**11**) (mp 62 °C, $[\alpha]_D^{20}$ +135° ($CHCl_3$); an authentic sample prepared from (*R*)-phenylalanine has mp 63 °C and $[\alpha]_D^{20}$ +137° ($CHCl_3$)), which established the absolute configurations of **8a** as (3*R*,4*R*).

Table I. Asymmetric Induction in β-Lactam Formation

Reagent	Reaction temp. (°C)	Yield (%)	*cis*/*trans*[a]	Ratio of diastereomers[a]	Asymmetric induction (%)
2b	0	47	0/100	84/16[b]	68
2b	−20	40	0/100	87/13[b]	74
4b	0	71	86/14[c]	97/3[d]	94
4b	−20	62	84/16[c]	98/2[d]	96
6c	0	70	97/3[c]	96/4[d]	92
6c	−20	61	99/1[c]	97/3[d]	94

a) The ratio of the isomers was determined by HPLC (Waters, Radial pak cartridge silica (10 μ), $CHCl_3$/Hex/AcOEt=30/12/1 for **8**, $CHCl_3$/AcOEt=1/3 for **12**, and $CHCl_3$/AcOEt=6/1 for **17** as eluants. *b*) Ratio of the *trans*-diastereomers (**8a**/**8b**). *c*) The minor diastereomer of the *trans*-β-lactam was not detected. *d*) Ratio of the *cis*-diastereomers (**12a**/**12b** or **17a**/**17b**).

Removal of the MOM group of the isolated major *cis*-diastereomer (**12a**) followed by Jones oxidation of **13a** gave the carboxylic acid **13b**, which was treated with lead tetraacetate in DMF in the presence of potassium acetate and subsequently with 50% aqueous acetic acid at 50 °C to provide the hydroxyl lactam (**14b**). The imide derivative (**15**), prepared from **14b** by Jones oxidation, was converted to *cis*-3-amino-1,4-diphenyl-2-azetidinone (**16b**) in 42% overall yield from **12a** by imide ring opening followed by cleavage of the amide bond in **16a** *via* the methyl imino ether as described for the preparation of **10**. Since optically pure (*R*)-phenylalanine anilide (**11**) was obtained in 61%

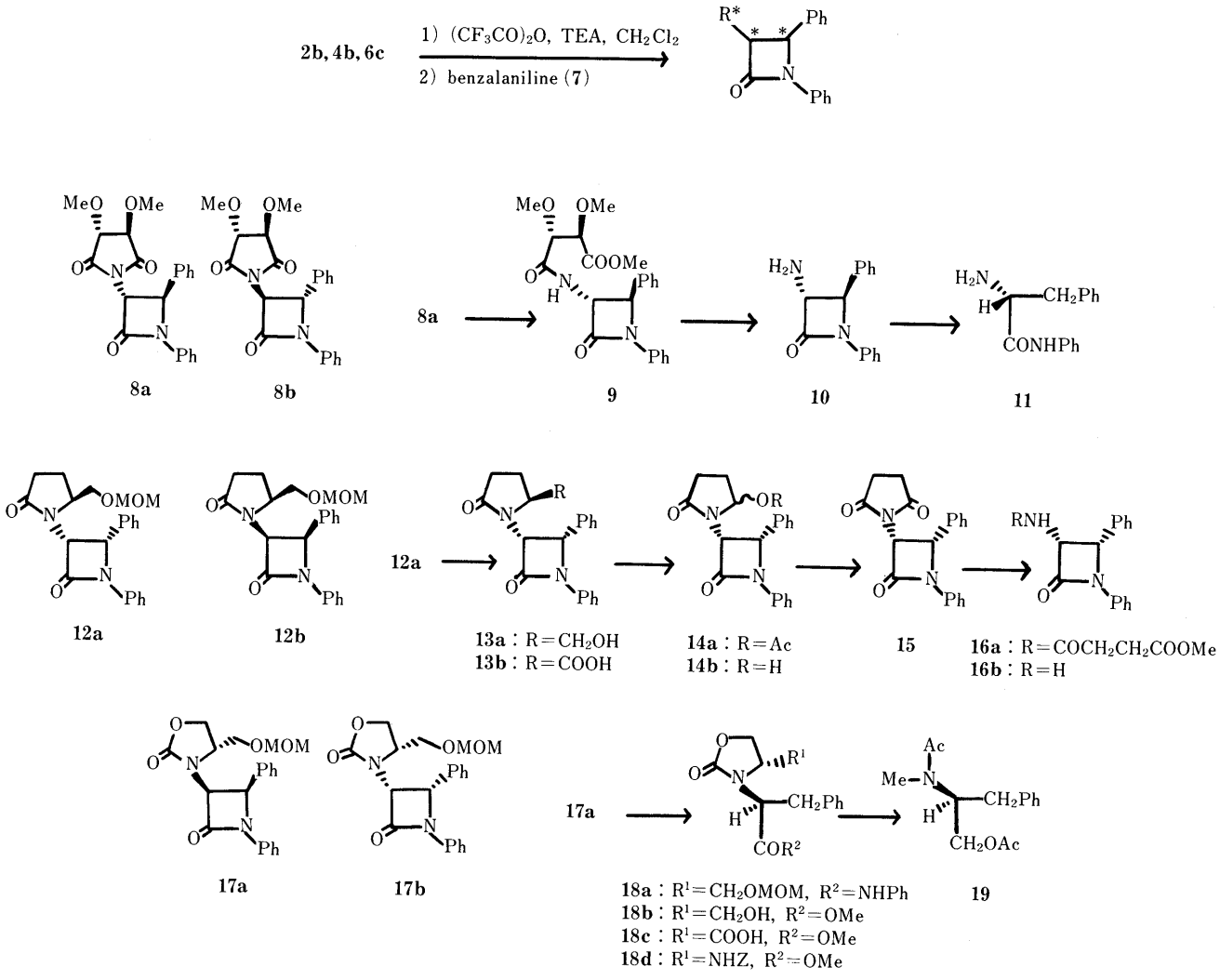


Chart 2

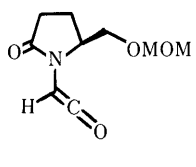
yield by N–C_4 bond cleavage of **16b**, the absolute configurations of **12a** were determined as (3*R*,4*S*).

The N–C_4 bond cleavage of the isolated major *cis*-diastereomer (**17a**) gave the phenylalanine derivative (**18a**) in 40% yield; this product was hydrolyzed to remove the MOM and the amido groups followed by esterification with diazomethane to provide the hydroxy methyl ester (**18b**). Jones oxidation of **18b** and subsequent Curtius reaction of the resulting carboxylic acid (**18c**) with diphenyl phosphorazidate[13] in the presence of benzyl alcohol in benzene gave **18d** in 67% yield. Reduction of **18d** with lithium aluminum hydride ($LiAlH_4$) followed by acidic hydrolysis and subsequent acetylation with acetic anhydride afforded the diacetyl derivative of *N*-methyl-(*S*)-phenylalaninol (**19**) ($[\alpha]_D^{20}$ −45.4° ($CHCl_3$); an authentic sample prepared from Z-(*S*)-phenylalanine methyl ester by $LiAlH_4$ reduction followed by acetylation has $[\alpha]_D^{20}$ −48.5° ($CHCl_3$)). Therefore, the stereochemistry of the original β-lactam **17a** is (3*S*,4*R*).[14]

Asymmetric Synthesis of (3*S*,4*S*)- and (3*R*,4*R*)-1-Benzyl-3-[(benzyloxycarbonyl)amino]-4-hydroxymethyl-2-azetidinone (26 and 30g) Since the chiral auxiliary **4b** having a 5-substituted-2-pyrrolidinone structure was found to be effective for the preparation of chiral *cis*-3-amino-4-substituted-2-azetidinone, **4b** was applied to the asymmetric synthesis of *cis*-3-amino-4-hydroxymethyl-2-azetidinone, whose (3*S*,4*S*)-derivative (**26**)[15,16] is a useful intermediate for the synthesis of various mono- and bicyclic β-lactam antibiotics. On the other hand, the chiral imine (**21**) having a similar stereochemical relationship to the ketene species (**20**) derived from **4b** can be expected to exhibit the high diastereoselectivity in [2+2]cyclocondensation to ketene species; it was therefore prepared from L-(+)-tartaric acid and used for the asymmetric β-lactam synthesis.

As the β-lactam **12a** having (3*R*,4*S*)-configurations was predominantly formed from (*S*)-**4b**, the corresponding (*R*)-derivative was condensed at 0 °C with the imine derived from benzylamine and *trans*-cinnamaldehyde *via* the mixed anhydride using trifluoroacetic anhydride to afford a diastereomeric mixture of *cis*-β-lactams (**22a** and **22b**), which were readily isolated by column chromatography on silica gel (**22a**:**22b**=91:9, 82% d.e.) in 73% yield (Chart 3). The major diastereomer **22a** was converted into an amine (**25b**) in 16% yield by a parallel series of reactions to those used for the preparation of **16b**. After protection of the amino group in **25b** with the Z group, **25c** was treated with $NaIO_4$ in the presence of a catalytic amount of osmium tetroxide in aqueous dioxane[17] followed by reduction with $NaBH_4$ to provide **26** in 48% yield. The absolute configurations of **26** were confirmed as (3*S*,4*S*) from the optical rotation of **26** ($[\alpha]_D^{20}$ −33° ($CHCl_3$)), whose enantiomer **30g** ($[\alpha]_D^{20}$ +32.2° ($CHCl_3$)) was chemically correlated to the known (4*R*)-1-benzyl-4-hydroxymethyl-2-azetidinone (**31b**) as shown in Chart 4.

The imine (**21**), prepared from benzylamine and the aldehyde (**27c**) derived from 2,3-*O*-isopropylidene-L-threitol



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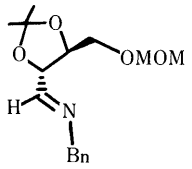

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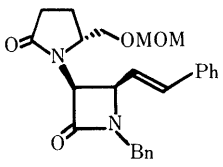
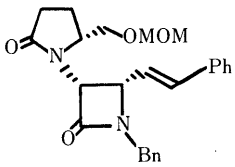
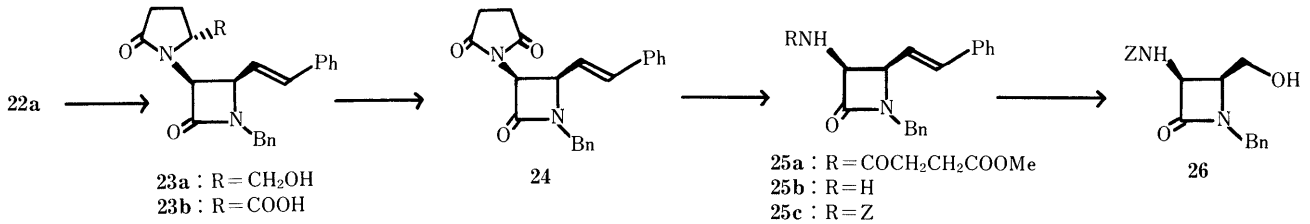


22a



22b



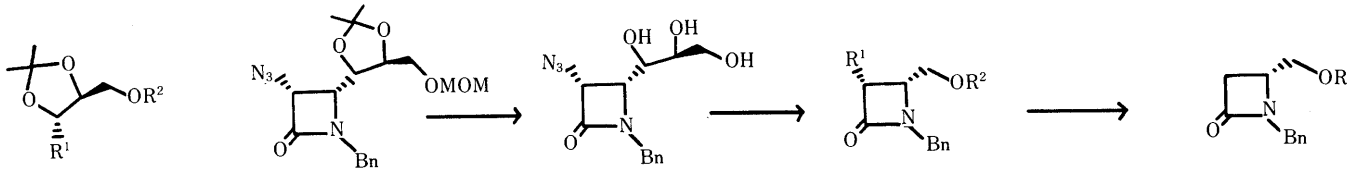
23a : R=CH_2OH
23b : R=COOH

24

25a : R=$COCH_2CH_2COOMe$
25b : R=H
25c : R=Z

26

Chart 3



27a : R^1=CH_2OH, R^2=H
27b : R^1=CH_2OH, R^2=MOM
27c : R^1=CHO, R^2=MOM

28

29

30a : R^1=N_3, R^2=H
30b : R^1=N_3, R^2=MOM
30c : R^1=NH_2, R^2=MOM
30d : R^1=HCONH, R^2=MOM
30e : R^1=CN, R^2=MOM
30f : R^1=ZNH, R^2=MOM
30g : R^1=ZNH, R^2=H

31a : R=MOM
31b : R=H

Chart 4

(**27a**)[18,19] by monomethoxymethylation followed by Swern oxidation, was condensed with azidoacetic acid *via* the mixed anhydride using trifluoroacetic anhydride in the presence of TEA in methylene chloride at 0 °C. After usual work-up and careful purification of the crude reaction mixture by column chromatography, the single *cis*-β-lactam (**28**) ($J_{3,4}=6$ Hz) was obtained in 51% yield and other diastereomers were not detected.[15,16] A triol (**29**), obtained by acidic hydrolysis of **28**, was treated with $NaIO_4$ in aqueous *tert*-butanol followed by reduction with $NaBH_4$ to provide *cis*-3-azido-4-hydroxymethyl-2-azetidinone (**30a**) in 52% yield. After protection of the hydroxy group in **30a** as the MOM ether, the azido group in **30b** was hydrogenated with Pd–C to provide an amine **30c** in 74% yield, which was formylated with 90% formic acid in acetic acid to afford **30d** in 80% yield. The amine **30c** was also converted to *cis*-1-benzyl-3-[(benzyloxycarbonyl)amino]-4-hydroxymethyl-2-azetidinone (**30g**) in 45% yield by benzyloxycarbonylation followed by removal of the MOM group in **30f** by acidic treatment. Dehydration of **30d** with $POCl_3$ in the presence of 2,6-lutidine in methylene chloride gave the 3-isonitrile derivative (**30e**), which was treated with tributyltin hydride[20] in benzene to give **31a** in 76% yield. Since (*R*)-1-benzyl-4-hydroxymethyl-2-azetidinone (**31b**) (mp 105—106 °C, $[\alpha]_D^{20}$ −84.4° (EtOH), lit.[1] for (*S*)-isomer, mp 110 °C, $[\alpha]_D^{20}$ +80.5° (EtOH) was obtained by acidic hydrolysis of **31a**, (3*R*,4*R*)-configurations were established for **30**.

Thus, the use of chiral auxiliaries **2b**, **4b**, **6c**, and **21** in the asymmetric ketene-imine cyclocondensation reaction provided a highly diastereoselective route to the preparation of optically active β-lactams. Further studies of asymmetric reactions employing chiral 2-pyrrolidinone and 2-oxazolidinone derivatives are in progress.

Experimental[21]

Benzyl *N*-[(2*R*,3*R*)-2,3-Dimethoxy-3-(ethoxycarbonyl)propanoyl]-glycinate (1b) A mixture of 1 N aqueous NaOH (8.8 ml) and diethyl 2,3-*O*-dimethyl-L-tartrate[8] (**1a**, 2.06 g, 8.8 mmol) in EtOH (8 ml) was stirred at room temperature for 1 h. After removal of the EtOH *in vacuo*, the aqueous layer was washed with ether, acidified with 10% aqueous HCl, and then extracted with AcOEt. The organic extracts were washed with saturated aqueous NaCl. Drying followed by evaporation gave a crude half ester of **1a** (1.25 g, yield 69%. IR ν_{max}^{film} cm^{-1}: 2500, 1740. ^{1}H-NMR ($CDCl_3$): 1.30 (3H, t, $J=7$ Hz, CH_3), 3.45 (6H, s, $2\times OCH_3$), 4.26 (2H, s, $2\times CH$), 4.28 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 9.70 (1H, s, COOH)) as an oil, which, without further purification, was condensed with glycine benzyl-ester *p*-toluenesulfonate (2.52 g, 7.5 mmol) using diethyl phosphorocyanidate (895 mg, 5.5 mmol) in the presence of TEA (1.26 g, 12.5 mmol) in DMF (15 ml) at room temperature overnight. After usual work-up, the crude product was purified by column chromatography (silica gel, $CHCl_3$: ether = 5 : 1) to give **1b** (1.6 g, yield 91%) as an oil, $[\alpha]_D^{20}$ +59.7° ($c=0.8$, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1740, 1670. ^{1}H-NMR ($CDCl_3$): 1.30 (3H, t, $J=7$ Hz, CH_3), 3.40 (6H, s, $2\times OCH_3$), 3.90—4.50 (6H, m, OCH_2, $2\times CH$, CH_2COO), 5.18 (2H, s, $C\underline{H}_2Ph$), 7.10 (1H, br s, CONH), 7.30 (5H, s, C_6H_5). MS *m/z*: 353 (M^+).

(3*R*,4*R*)-1-[(Benzyloxycarbonyl)methyl]-3,4-(dimethoxy)pyrrolidine-2,5-dione (2a) A mixture of sodium powder (170 mg, 7.3 mmol) and **1b** (1.47 g, 4.2 mmol) in toluene (15 ml) was stirred at 110 °C for 5 min. After cooling to room temperature, the insoluble materials were filtered off and the filtrate was concentrated *in vacuo* to give a residue, which was purified by column chromatography (silica gel, $CHCl_3$: ether = 7 : 1) to provide **2a** (910 mg, yield 71%) as crystals, mp 55 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +104.6° ($c=1$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1790, 1750, 1720. ^{1}H-NMR ($CDCl_3$): 3.65 (6H, s, $2\times OCH_3$), 4.20 and 4.25 (2×2H, $2\times$ s, $2\times CH$, CH_2COO), 5.15 (2H, s, $C\underline{H}_2Ph$), 7.30 (5H, s, C_6H_5). *Anal.* Calcd for $C_{15}H_{17}NO_6$: C, 58.62; H, 5.58; N, 4.56. Found: C, 58.58; H, 5.50; N, 4.35.

(3*R*,4*R*)-1-Carboxymethyl-3,4-(dimethoxy)pyrrolidine-2,5-dione (2b) **2a** (755 mg, 2.5 mmol) was hydrogenated with 5% Pd–C (80 mg) in EtOH (10 ml) under hydrogen at atmospheric pressure at room temperature for 6 h and then the mixture was filtered. The filtrate was concentrated *in vacuo* to give a residue, which was purified by column chromatography (silica gel, $CHCl_3$: MeOH : H_2O = 8 : 3 : 1) to afford **2b** (480 mg, yield 90%) as an oil, $[\alpha]_D^{20}$ +170° ($c=0.84$, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 2600, 1790, 1720. ^{1}H-NMR ($CDCl_3$): 3.70 (6H, s, $2\times OCH_3$), 4.25 (4H, $2\times CH$, CH_2COO), 9.30 (1H, br s, COOH). MS *m/z*: 217 (M^+).

Asymmetric Synthesis of β-Lactams (8) Using 2b TEA (0.16 ml, 1.1 mmol) was added to a solution of **2b** (230 mg, 1.1 mmol) in methylene chloride (3 ml) at 0 °C, then trifluoroacetic anhydride (0.15 ml, 1.1 mmol) was added. The mixture was stirred at 0 °C for 30 min and a solution of benzalaniline (0.15 g, 0.84 mmol) and TEA (0.16 ml, 1.1 mmol) in CH_2Cl_2 (3 ml) was added at 0 °C over a period of 15 min. After being stirred at 0 °C for 20 h, the mixture was diluted with AcOEt and washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and water. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$: hexane = 1 : 20 : 2) gave **8a** (250 mg, yield 38.5%) and **8b** (55 mg, yield 8.5%) as crystals. **8a**: mp 233 °C ($CHCl_3$–ether–hexane), $[\alpha]_D^{20}$ +188° ($c=0.5$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1780, 1740. ^{1}H-NMR ($CDCl_3$): 3.64 (6H, s, $2\times OCH_3$), 4.20 (2H, s, $2\times CH$), 5.04 (1H, d, $J=2$ Hz, C_4-H), 5.24 (1H, d, $J=2$ Hz, C_3-H), 7.0—7.4 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{21}H_{20}N_2O_5$: C, 66.30; H, 5.30; N, 7.36. Found: C, 66.28; H, 5.52; N, 7.28. **8b**: mp 198—200 °C, $[\alpha]_D^{20}$ +77.3° ($c=0.3$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 3.68 (6H, s, $2\times OCH_3$), 4.21 (2H, s, $2\times CH$), 5.04 (1H, d, $J=2$ Hz, C_4-H), 5.19 (1H, d, $J=2$ Hz, C_3-H), 7.0—7.4 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{21}H_{20}N_2O_5$: C, 66.30; H, 5.30; N, 7.36. Found: C, 66.20; H, 5.12; N, 7.18.

(3*R*,4*R*)-1,4-Diphenyl-3-[(2*R*,3*R*)-2,3-dimethoxy-3-(methoxycarbonyl)-propionamido]-2-azetidinone (9) A mixture of **8a** (166 mg, 0.44 mmol) and sodium methoxide (24 mg, 0.44 mmol) in MeOH (10 ml) was stirred at room temperature for 10 min. After dilution with AcOEt, the mixture was washed with 10% aqueous HCl and water. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 1) afforded **9** (160 mg, yield 88%) as an oil, $[\alpha]_D^{20}$ +19.2° ($c=2.3$, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1770, 1680. ^{1}H-NMR ($CDCl_3$): 3.40 (3H, s, OCH_3), 3.46 (3H, s, OCH_3), 3.75 (3H, s, $COOCH_3$), 4.14 (1H, d, $J=2$ Hz, C_4-H), 4.26 (1H, d, $J=2$ Hz, C_3-H), 4.90 (2H, s, $2\times CH$), 7.0—7.5 (10H, m, $2\times C_6H_5$). MS *m/z*: 412 (M^+).

(3*R*,4*R*)-3-Amino-1,4-diphenyl-2-azetidinone (10) A solution of PCl_5 (114 mg, 0.55 mmol) in CH_2Cl_2 (3 ml) was added at −20 °C to a solution of **9** (130 mg, 0.32 mmol) and pyridine (76 mg, 0.63 mmol) in CH_2Cl_2 (3 ml). The mixture was stirred at −20 °C for 1 h and at room temperature for 3 h, then 2 ml of MeOH was added and the whole was stirred at room temperature for 2 h. After addition of water (5 ml), the mixture was stirred at room temperature for 30 min and the organic solvents were removed *in vacuo*. The aqueous layer was washed with ether, basified with 10% aqueous NaOH, and then extracted with AcOEt. The organic extracts were washed with saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 1) gave **10** (34 mg, yield 45%) as crystals, mp 58—60 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −74° ($c=0.2$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1745. ^{1}H-NMR ($CDCl_3$): 1.85 (2H, br s, NH_2), 3.96 (1H, d, $J=2$ Hz, C_4-H), 4.57 (1H, d, $J=2$ Hz, C_3-H), 6.8—7.5 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{15}H_{14}N_2O\cdot H_2O$: C, 70.29; H, 6.29; N, 10.93. Found: C, 69.73; H, 6.09; N, 10.75.

(*R*)-Phenylalanine Anilide (11) **10** (25 mg, 0.11 mmol) was hydrogenated with 10% Pd–C (25 mg) in EtOH (3 ml) under hydrogen at atmospheric pressure at 70 °C for 9 h. After removal of the Pd–C, the filtrate was evaporated *in vacuo* to give a residue, which was purified by column chromatography (silica gel, AcOEt : $CHCl_3$ = 5 : 1) to give **11** (11 mg, yield 40%) as crystals, mp 62 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +135° ($c=0.2$, $CHCl_3$). The physical data and NMR spectrum were identical with those of an authentic sample (mp 63 °C, $[\alpha]_D^{20}$ +137° ($c=0.3$, $CHCl_3$) prepared from (*R*)-Z-phenylalanine.

(5*S*)-1-[(Benzyloxycarbonyl)methyl]-5-[(methoxymethoxy)methyl]-2-pyrrolidinone (4a) A solution of **3**[10a] (4.5 g, 28.3 mmol) in THF (15 ml) was added at 0 °C to a suspension of NaH (60% oil suspension, hexane-washed, 1.13 g, 28.3 mmol) in THF–DMF (1 : 1, 30 ml) and the mixture was stirred at room temperature for 1 h. After addition of benzyl bromoacetate (7.13 g, 31.1 mmol), the whole was stirred at room temperature for 20 h, and diluted with AcOEt–benzene (2 : 1, 150 ml). Then, the mixture was washed with water, 10% aqueous HCl, and saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 10 : 1) gave **4a** (7.04 g, yield 81%) as an oil, $[\alpha]_D^{20}$ +2.7°

($c=3$, EtOH). IR ν_{max}^{film} cm^{-1}: 1750, 1690. ^{1}H-NMR ($CDCl_3$): 1.32—2.60 (4H, m, $2\times CH_2$), 3.20 (3H, s, OCH_3), 3.40—3.62 (2H, m, $C\underline{H}_2OMOM$), 3.92 (1H, m, CH), 3.95 and 4.40 (2H, AB, $J=17$ Hz, CH_2COO), 4.40 (2H, s, OCH_2O), 5.12 (2H, s, $C\underline{H}_2Ph$), 7.30 (5H, s, C_6H_5). MS m/z: 307 (M^+).

(5*S*)-1-Carboxymethyl-5-[(methoxymethoxy)methyl]-2-pyrrolidinone (4b) This sample was prepared in 79% yield as an oil in the same manner as described above for the preparation of **2b**, $[\alpha]_D^{20}$ +6.2° ($c=1.9$, EtOH). IR ν_{max}^{film} cm^{-1}: 2500, 1740, 1660. ^{1}H-NMR ($CDCl_3$): 1.50—2.70 (4H, m, $2\times CH_2$), 3.32 (3H, s, OCH_3), 3.50—3.80 (2H, m, $C\underline{H}_2OMOM$), 4.05 (1H, m, CH), 3.88 and 4.30 (2H, AB, $J=17$ Hz, CH_2COO), 4.55 (2H, s, OCH_2O), 9.60 (1H, br s, COOH). MS m/z: 218 ($(M+1)^+$), 217 (M^+).

Asymmetric Synthesis of the β-Lactams (12) Using 4b Asymmetric synthesis of the β-lactam (**12**) using **4b** was performed in the same manner as described above for the preparation of **8**. The crude product was purified by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 5) to give **12a** (yield 63%), **12b** (yield 2%), and the *trans*-isomer (yield 6%) as crystals. **12a**: mp 183 °C, $[\alpha]_D^{20}$ +40° ($c=1$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760, 1690. ^{1}H-NMR ($CDCl_3$): 2.50−3.42 (4H, m, $2\times CH_2$), 2.98—3.50 (2H, m, $C\underline{H}_2OMOM$), 3.35 (3H, s, OCH_3), 3.55 (1H, m, CH), 4.52 (2H, s, OCH_2), 5.20 (1H, d, $J=6$ Hz, C_4-H), 5.36 (1H, d, $J=6$ Hz, C_3-H), 7.0—7.5 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{22}H_{24}N_2O_4$: C, 69.45; H, 6.36; N, 7.36. Found: C, 69.27; H, 6.44; N, 7.22. **12b**: mp 120—123 °C (ether–hexane), $[\alpha]_D^{20}$ −23° ($c=0.2$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760, 1690. ^{1}H-NMR ($CDCl_3$): 1.52—2.60 (4H, m, $2\times CH_2$), 3.28 (3H, s, OCH_3), 3.38—3.90 (3H, m, $C\underline{H}C\underline{H}_2OMOM$), 4.60 (2H, s, OCH_2O), 5.36 (1H, d, $J=6$ Hz, C_4-H), 5.62 (1H, d, $J=6$ Hz, C_3-H), 7.0—7.6 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{22}H_{24}N_2O_4$: C, 69.45; H, 6.36; N, 7.36. Found: C, 69.32; H, 6.53; N, 7.11. *trans*-Isomer: mp 108 °C (ether–hexane), $[\alpha]_D^{20}$ −32° ($c=0.4$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760, 1690. ^{1}H-NMR ($CDCl_3$): 1.62—2.70 (4H, m, $2\times CH_2$), 3.32 (3H, s, OCH_3), 3.50—3.70 (2H, m, $C\underline{H}_2OMOM$), 4.08 (1H, m, CH), 4.55 (2H, s, OCH_2O), 4.92 (1H, d, $J=2$ Hz, C_4-H), 5.18 (1H, d, $J=2$ Hz, C_3-H), 7.0—7.4 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{22}H_{24}N_2O_4$: C, 69.45; H, 6.36; N, 7.36. Found: C, 69.19; H, 6.53; N, 7.09.

(3*R*,4*S*)-1,4-Diphenyl-3-[(5*S*)-5-(hydroxymethyl)pyrrolidin-2-on-1-yl]-2-azetidinone (13a) A mixture of **12a** (1.15 g, 3.0 mmol), 10% aqueous HCl (6 ml), and MeOH (6 ml) was stirred at 55 °C for 2 h. After dilution with AcOEt, the mixture was washed with saturated aqueous $NaHCO_3$, and water. Drying followed by evaporation *in vacuo* gave a residue, which was recrystallized from AcOEt–hexane to afford **13a** (860 mg, yield 85%) as crystals, mp 224 °C (AcOEt), $[\alpha]_D^{20}$ +14.0° ($c=1$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760, 1690. ^{1}H-NMR ($CDCl_3$): 1.30—2.35 (5H, m, $2\times CH_2$, OH), 3.20—3.48 (2H, m, $C\underline{H}_2OH$), 3.72 (1H, m, CH), 5.30 (1H, d, $J=6$ Hz, C_4-H), 5.38 (1H, d, $J=6$ Hz, C_3-H), 7.30 (10H, s, $2\times C_6H_5$). *Anal.* Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.33; H, 5.82; N, 8.13.

(3*R*,4*S*)-1,4-Diphenyl-3-[(5*S*)-5-(carboxyl)pyrrolidin-2-on-1-yl]-2-azetidinone (13b) A mixture of Jones reagent (1.2 ml) and **13a** (792 mg, 2.36 mmol) in 12 ml of acetone was stirred at room temperature for 2 h. After addition of isopropyl alcohol (0.6 ml), the mixture was diluted with AcOEt and washed with half-saturated aqueous NaCl. Drying followed by evaporation *in vacuo* gave **13b** (760 mg, yield 89%) as crystals, mp 260—262 °C (MeOH–$CHCl_3$–ether), $[\alpha]_D^{20}$ +39.4° ($c=0.7$, MeOH). IR ν_{max}^{Nujol} cm^{-1}: 2600, 1780, 1720. ^{1}H-NMR ($CDCl_3$): 1.52—2.50 (4H, m, $2\times CH_2$), 4.00 (1H, m, CH), 5.05 (1H, d, $J=6$ Hz, C_4-H), 5.45 (1H, d, $J=6$ Hz, C_3-H), 7.30 (10H, s, $2\times C_6H_5$). *Anal.* Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.62; H, 5.23; N, 7.93.

(3*R*,4*S*)-3-(Pyrrolidine-2,5-dion-1-yl)-1,4-diphenyl-2-azetidinone (15) Lead tetraacetate (0.91 g, 2.05 mmol) was added to a solution of **13b** (720 mg, 2.05 mmol) and potassium acetate (300 mg, 3.1 mmol) in DMF (10 ml). After being stirred at 50 °C for 2.5 h, the mixture was diluted with AcOEt–benzene (2 : 1, 150 ml) and washed with water, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. Drying followed by evaporation *in vacuo* gave crude **14a** (0.8 g), which was dissolved in a mixture of acetic acid–water (1 : 2, 12 ml) and AcOEt (4 ml). After being stirred at 50 °C for 3 h, the mixture was diluted with AcOEt, and washed with water and saturated aqueous $NaHCO_3$. Drying followed by evaporation *in vacuo* gave crude **14b** (590 mg), which was treated with Jones reagent (0.5 ml) in acetone (10 ml) at room temperature for 1.5 h. After dilution with AcOEt, the mixture was washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 1) gave **15** (545 mg, yield 83%) as crystals, mp 238—240 °C (AcOEt–$CHCl_3$–hexane), $[\alpha]_D^{20}$ −3.03° ($c=0.6$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1780, 1730. ^{1}H-NMR ($CDCl_3$): 2.30 (4H, s, $2\times CH_2$), 5.35 (2H, s, $2\times CH$), 7.0—7.5 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.75. Found: C, 71.16; H, 5.07; N, 8.74.

(3*R*,4*S*)-1,4-Diphenyl-3-[3-(methoxycarbonyl)propionamido]-2-azetidinone (16a) Compound **16a** was obtained in 84% yield from **15** in the same manner as described above for the preparation of **9**, mp 126 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −14.9° ($c=0.8$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1750, 1680. ^{1}H-NMR ($CDCl_3$): 2.02—2.60 (4H, m, $2\times CH_2$), 3.55 (3H, s, OCH_3), 5.30 (1H, d, $J=6$ Hz, C_4-H), 5.58 (1H, dd, $J=6$, 8 Hz, C_3-H), 6.45 (1H, d, $J=8$ Hz, NH), 7.0—7.6 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.18; H, 5.75; N, 7.92.

(3*R*,4*S*)-3-Amino-1,4-diphenyl-2-azetidinone (16b) A solution of PCl_5 (269 mg, 1.29 mmol) in CH_2Cl_2 (2 ml) was added at −20 °C to a solution of **16a** (260 mg, 0.74 mmol) and pyridine (116 mg, 1.45 mmol) in 10 ml of CH_2Cl_2 over a period of 5 min. After being stirred at −10—−20 °C for 2 h, 4 ml of methanol was added and the mixture was stirred at −10 °C for 40 min and at room temperature for 30 min. Then, the mixture was poured into water (10 ml) and stirred at room temperature for 30 min. After removal of the organic solvents *in vacuo*, the aqueous layer was washed with ether, basified with aqueous NaOH, and extracted with AcOEt. The organic extracts were washed with saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 3 : 1) gave **16b** (127 mg, yield 80%) as crystals, mp 209 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +193° ($c=0.84$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760. ^{1}H-NMR ($CDCl_3$): 1.32 (2H, br s, NH_2), 4.55 (1H, d, $J=6$ Hz, C_4-H), 5.20 (1H, d, $J=6$ Hz, C_3-H), 6.9—7.5 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92; N, 11.76. Found: C, 75.49; H, 5.96; N, 11.77.

(*R*)-Phenylalanine Anilide (11) This sample was prepared in 61% yield from **16b** in the same manner as described above for the preparation of **11** from **10**, mp 63 °C, $[\alpha]_D^{20}$ +136° ($c=0.3$, $CHCl_3$).

***N*-Benzyloxycarbonyl-*O*-methoxymethyl-(*R*)-serinol (5c)** A mixture of $NaBH_4$ (744 mg, 19.9 mmol) and *N*-Z-*O*-methoxymethyl-(*S*)-serine methyl ester (**5b**) (5.6 g, 18.8 mmol, prepared from *N*-Z-(*S*)-serine methyl ester (**5a**) by methoxymethylation with chloromethyl methyl ether and *N*,*N*-diethylaniline in CH_2Cl_2, $[\alpha]_D^{20}$ +4.75° ($c=2$, $CHCl_3$)) in EtOH (35 ml) was stirred at room temperature for 3 h. After neutralization with 10% aqueous HCl, the mixture was diluted with AcOEt and washed with saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 2) afforded **5c** (4.2 g, yield 83%) as an oil, $[\alpha]_D^{20}$ −1.88° ($c=1$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 3.00 (1H, br s, OH), 3.30 (3H, s, OCH_3), 3.50—4.02 (3H, m, $C\underline{H}C\underline{H}_2OMOM$) 4.55 (2H, s, OCH_2O), 5.05 (2H, s, $C\underline{H}_2Ph$), 5.45 (1H, br s, NH), 7.30 (5H, s, C_6H_5).

(4*S*)-4-[(Methoxymethoxy)methyl]-2-oxazolidinone (6a) After removal of the Z group in **5c** (3.9 g, 13 mmol) by hydrogenation with 5% Pd–C (500 mg) in EtOH (35 ml), the crude amino alcohol (1.95 g) and diethyl carbonate (4 ml) were heated at 130—140 °C for 30 min in the presence of potassium carbonate (260 mg). After addition of CH_2Cl_2, the insoluble materials were filtered off and the filtrate was concentrated *in vacuo* to give a residue, which was purified by column chromatography (silica gel, AcOEt : hexane = 4 : 1) to give **6a** (1.50 g, yield 65%) as an oil, $[\alpha]_D^{20}$ −37.5° ($c=1$, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1750. ^{1}H-NMR ($CDCl_3$): 3.38 (3H, s, OCH_3), 3.50—3.78 (3H, m, $C\underline{H}_2OMOM$, CH), 4.02—4.50 (2H, m, OCH_2C), 4.65 (2H, s, OCH_2O), 6.30 (1H, br s, NH). MS m/z: 161 (M^+).

(4*S*)-3-[(Benzyloxycarbonyl)methyl]-4-[(methoxymethoxy)methyl]-2-oxazolidinone (6b) This sample was obtained as an oil in 96% yield from **6a** in the same manner as described above for the preparation of **4a**, $[\alpha]_D^{20}$ +22° ($c=3$, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1750. ^{1}H-NMR ($CDCl_3$): 3.22 (3H, s, OCH_3), 3.50—3.70 (2H, m, $C\underline{H}_2OMOM$), 3.90 and 4.20 (2H, AB, $J=18$ Hz, CH_2COO), 3.85—4.70 (3H, m, $OC\underline{H}_2CH$, CH), 4.42 (2H, s, OCH_2O), 5.10 (2H, s, $C\underline{H}_2Ph$), 7.22 (5H, s, C_6H_5). MS m/z: 309 (M^+).

(4*S*)-3-Carboxymethyl-4-[(methoxymethoxy)methyl]-2-oxazolidinone (6c) This sample was obtained as an oil in 86% yield from **6b** in the same manner as described above for the preparation of **4b**, $[\alpha]_D^{20}$ +25.4° ($c=1.4$, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1750, 1715. ^{1}H-NMR ($CDCl_3$): 3.30 (3H, s, OCH_3), 3.50—3.82 (2H, m, $C\underline{H}_2OMOM$), 3.9—4.6 (3H, m, OCH_2C, CH), 3.92 and 4.20 (2H, AB, $J=18$ Hz, $C\underline{H}_2COOH$), 4.52 (2H, s, OCH_2O), 8.62 (1H, s, COOH). MS m/z: 219 (M^+).

Asymmetric Synthesis of the β-Lactams (17) Using 6c Asymmetric synthesis of the β-lactams (**17**) using **6c** was performed in the same manner as described above for the preparation of **12**. The crude product was purified by column chromatography (silica gel, AcOEt : $CHCl_3$: hexane = 1 : 18 : 2) to give **17a** (yield 67%), **17b** (yield 1.8%), and the *trans*-isomer (yield 0.7%). **17a**: mp 129—131 °C, $[\alpha]_D^{20}$ −44° ($c=1$, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760. ^{1}H-NMR ($CDCl_3$): 2.75—3.00 (1H, m, $C\underline{H}_2OMOM$), 3.25 (3H, s, OCH_3), 3.20—3.45 (1H, m, $C\underline{H}_2OMOM$), 3.70—4.15 (3H, m, CH, OCH_2C), 4.40 (2H, s, OCH_2O), 5.15 (1H, d, $J=6$ Hz, C_4-H), 5.35

(1H, d, J=6 Hz, C_3-H), 7.0—7.5 (10H, m, 2×C_6H_5). *Anal.* Calcd for $C_{21}H_{22}N_2O_5$: C, 65.93; H, 5.79; N, 7.36. Found: C, 66.06; H, 5.75; N, 7.26. **17b**: oil, $[\alpha]_D^{20}$ +30° (c=0.3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1755. ^{1}H-NMR ($CDCl_3$): 3.32 (3H, s, OCH_3), 3.20—3.40 (2H, m, CH_2OMOM), 3.60—3.80 (2H, m, OCH_2C), 3.92—4.00 (1H, m, CH), 4.60 (2H, s, OCH_2O), 5.35 (1H, d, J=6 Hz, C_4-H), 5.52 (1H, d, J=6 Hz, C_3-H), 7.1—7.6 (10H, m, 2×C_6H_5). MS m/z: 382 (M^+). *trans*-Isomer: oil, $[\alpha]_D^{20}$ +6.5° (c=1.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1755. ^{1}H-NMR ($CDCl_3$): 3.26 (3H, s, OCH_3), 3.60—3.75 (2H, m, CH_2OMOM), 4.12—4.60 (3H, m, CH, OCH_2C), 4.45 (2H, s, OCH_2O), 4.84 (1H, d, J=2 Hz, C_4-H), 5.15 (1H, d, J=2 Hz, C_3-H), 7.0—7.4 (10H, m, 2×C_6H_5). MS m/z: 382 (M^+).

(2*S*)-2-[(4*S*)-4-[(Methoxymethoxy)methyl]oxazolidin-2-on-3-yl]-3-phenylpropionanilide (18a) A solution of **17a** (300 mg, 0.79 mmol) in EtOH (30 ml) was submitted to hydrogenolysis over 10% Pd–C (300 mg) at 80 °C for 48 h. After removal of the catalyst and the ethanol, the residue was purified by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 1) to provide **18a** (140 mg, yield 46.5%) as an oil, $[\alpha]_D^{20}$ −42.7° (c=0.8, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1750, 1690. ^{1}H-NMR ($CDCl_3$): 3.00—3.65 (5H, m, $CHCONHPh$, CH_2Ph, CH_2OMOM), 3.25 (3H, s, OCH_3), 3.90—4.18 (3H, m, $CHCH_2OMOM$, OCH_2C), 4.55 (2H, s, OCH_2O), 7.0—7.6 (10H, m, 2×C_6H_5), 9.25 (1H, br s, NHPh). MS m/z: 384 (M^+).

Methyl (2*S*)-2-[(4*S*)-4-(Hydroxymethyl)oxazolidin-2-on-3-yl]-3-phenylpropionate (18b) A mixture of **18a** (414 mg, 1 mmol), 10% aqueous HCl (7 ml), and EtOH (3 ml) was heated at 100 °C for 8 h. After removal of the EtOH, the mixture was extracted with AcOEt. The organic extracts were washed with saturated aqueous NaCl. Drying followed by evaporation *in vacuo* gave a residue, which was treated with ethereal diazomethane to afford the methyl ester **18b** (0.28 g, 92.5%) as an oil after purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 3 : 1), $[\alpha]_D^{20}$ −83.3° (c=0.8, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1750. ^{1}H-NMR ($CDCl_3$): 2.75—3.70 (5H, m, CH_2OH, CH_2Ph, CHCOOMe), 3.83 (3H, s, OCH_3), 3.80—4.30 (3H, CH, OCH_2C), 4.72 (1H, br s, OH), 7.2—7.4 (5H, m, C_6H_5). MS m/z: 279 (M^+).

Methyl (2*S*)-2-[(4*R*)-4-[(Benzyloxycarbonyl)amino]oxazolidin-2-on-3-yl]-3-phenylpropionate (18d) A mixture of Jones reagent (1 ml) and **18b** (0.26 g, 0.93 mmol) in acetone (4 ml) was stirred at 0 °C for 3 h. After addition of isopropyl alcohol (0.3 ml), the mixture was diluted with ether (30 ml) and washed with half-saturated aqueous NaCl. Then, the mixture was extracted with saturated aqueous $NaHCO_3$. The aqueous extracts were acidified with aqueous HCl and extracted with AcOEt. The organic extracts were washed with saturated aqueous NaCl. Drying followed by evaporation *in vacuo* gave a crude methyl (2*S*)-2-[(4*R*)-4-(carboxy)oxazolidin-2-on-3-yl]-3-phenylpropionate (**18c**, 271 mg, $[\alpha]_D^{20}$ −0.83° (c=1, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 3.15—3.45 (2H, m, CH_2Ph), 3.70 (3H, s, OCH_3), 3.72 (1H, m, CH), 4.10—4.45 (3H, m, OCH_2C, CH), 7.02 (1H, br s, COOH), 7.30 (5H, s, C_6H_5)) as an oil. A mixture of crude **18c** (0.16 g, 0.55 mmol), diphenyl phosphoroazidate (165 mg, 0.6 mmol), and TEA (61 mg, 0.6 mmol) in 5 ml of benzene was refluxed for 1 h, then benzyl alcohol (71 mg, 0.66 mmol) was added and the mixture was refluxed for a further 5 h. After dilution with AcOEt, the whole was washed successively with 5% aqueous HCl, water, saturated aqueous $NaHCO_3$, and water. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 5 : 1) gave **18d** (156 mg, yield 72%) as crystals, mp 123—124 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −43.2° (c=0.7, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1780, 1760, 1690. ^{1}H-NMR ($CDCl_3$): 3.15—3.40 (2H, m, CH_2Ph), 3.70 (3H, s, OCH_3), 3.80—4.80 (4H, m $CHCOOMe$, OCH_2C, NH), 5.05 (2H, s, CH_2Ph), 5.45 (1H, m, CH), 7.0—7.4 (10H, m, 2×C_6H_5). *Anal.* Calcd for $C_{21}H_{22}N_2O_6$: C, 63.31; H, 5.57; N, 7.03. Found: C, 63.28; H, 5.56; N, 7.07.

(2*S*)-1-Acetoxy-2-(*N*-methylacetamido)-3-phenylpropane (19) $LiAlH_4$ (40 mg) was added at 0 °C to a solution of **18d** (100 mg, 0.25 mmol) in THF (3 ml). The mixture was stirred at room temperature for 30 min, and then refluxed for 30 min. After addition of 10% aqueous HCl (3 ml) and MeOH (3 ml), the mixture was refluxed for 3 h. After removal of the organic solvents *in vacuo*, the aqueous layer was basified with 10% aqueous NaOH and extracted with AcOEt. The organic extracts were washed with saturated aqueous NaCl. Drying followed by concentration *in vacuo* gave a residue, which was acetylated with acetic anhydride (0.2 ml) in pyridine (1 ml) at room temperature. After dilution with AcOEt and usual work-up, a residual oil was purified by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 3) to give **19** (23 mg, yield 37%) as an oil, $[\alpha]_D^{20}$ −45.4° (c=0.3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1740, 1660. ^{1}H-NMR ($CDCl_3$): 1.75 and 1.95 (3H, 2×s, CH_3CO), 2.00 (3H, s, CH_3CO), 2.75—2.95 (5H, m, N-CH_3, CH_2Ph), 4.05—5.20 (3H, m, CH, CH_2OAc), 7.30 (5H, s, C_6H_5). The physical data and NMR spectrum were identical with those of an authentic sample ($[\alpha]_D^{20}$ −48.5° (c=0.3, $CHCl_3$)), prepared from *N*-Z-(*S*)-phenylalanine methyl ester by reaction with $LiAlH_4$ followed by acetylation with acetic anhydride.

(3*S*,4*R*)- and (3*R*,4*S*)-1-Benzyl-3-[(5*R*)-5-((methoxymethoxy)methyl)-pyrrolidin-2-on-1-yl]-4-styryl-2-azetidinone (22a and 22b) A mixture of *trans*-cinnamaldehyde (640 mg, 4.84 mmol), benzylamine (518 mg, 4.84 mmol), and molecular sieves 4A (4 g) in 20 ml of benzene was stirred at room temperature for 2 h. After removal of the molecular sieves 4A by filtration, the filtrate was evaporated *in vacuo* to give a crude imine (1.07 g, yield quant.), which was dissolved in a solution of TEA (610 mg, 6.1 mmol) in CH_2Cl_2 (10 ml). This solution was added at 0 °C over a period of 15 min to the mixed anhydride, prepared from (*R*)-**4b** (1.3 g, 6.1 mmol), trifluoroacetic anhydride (0.86 ml, 6.1 mmol), and TEA (610 mg, 6.1 mmol) in CH_2Cl_2 (14 ml) at 0 °C for 30 min. After being stirred at 0 °C for 15 h, the mixture was diluted with AcOEt and washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and water. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 3) afforded the *cis*-β-lactams **22a** (1.35 g, yield 66.4%) and **22b** (133 mg, yield 6.5%) as crystals. **22a**: mp 92 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −62.7° (c=0.7, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1770, 1700. ^{1}H-NMR ($CDCl_3$): 1.70—2.60 (4H, m, 2×CH_2), 3.35 (3H, s, OCH_3), 3.45—4.00 (3H, m, $CHCH_2OMOM$), 4.25 and 4.55 (2H, AB, J=15 Hz, CH_2Ph), 4.32 (1H, dd, J=5, 8 Hz, C_4-H), 4.87 (1H, d, J=5 Hz, C_3-H), 6.10 (1H, dd, J=8, 16 Hz, CH=CHPh), 6.52 (1H, d, J=16 Hz, CH=CHPh), 7.20 and 7.30 (10H, 2×s, 2×C_6H_5). *Anal.* Calcd for $C_{25}H_{28}N_2O_4$: C, 71.40; H, 6.71; N, 6.66. Found: C, 71.40; H, 6.74; N, 6.59. **22b**: mp 114 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +75.4° (c=0.6, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1770, 1700. ^{1}H-NMR ($CDCl_3$): 1.64—2.54 (4H, m, 2×CH_2), 3.30 (3H, s, OCH_3), 3.40—3.80 (3H, m, $CHCH_2OMOM$), 4.20 and 4.68 (2H, AB, J=15 Hz, CH_2Ph), 4.28 (1H, dd, J=8, 16 Hz, C_4-H), 4.50 (2H, OCH_2O), 4.84 (1H, d, J=5 Hz, C_3-H), 6.24 (1H, dd, J=8, 16 Hz, CH=CHPh), 6.44 (1H, d, J=16 Hz, CH=CHPh), 7.2—7.4 (10H, m, 2×C_6H_5). *Anal.* Calcd for $C_{25}H_{28}N_2O_4$: C, 71.41; H, 6.71; N, 6.66. Found: C, 71.35; H, 6.64; H, 6.56.

(3*S*,4*R*)-1-Benzyl-3-[(5*R*)-5-(hydroxymethyl)pyrrolidin-2-on-1-yl]-4-styryl-2-azetidinone (23a) This sample was obtained in 78% yield from **22a** in the same manner as described above for the preparation of **13a**, mp 156 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −121.2° (c=0.66, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760, 1695. ^{1}H-NMR ($CDCl_3$): 1.35—2.70 (5H, m, 2×CH_2, OH), 3.30—3.90 (3H, m, CH_2OMOM, C_4-H), 4.20 and 4.60 (2H, AB, J=15 Hz, CH_2Ph), 4.75 (1H, d, J=6 Hz, C_3-H), 5.92—6.75 (2H, m, CH=CHPh), 7.30 (10H, s, 2×C_6H_5). *Anal.* Calcd for $C_{23}H_{24}N_2O_3$: C, 73.38; H, 6.43; N, 7.42. Found: C, 72.93; H, 6.43; N, 7.38.

(3*S*,4*R*)-1-Benzyl-3-[(5*R*)-5-(carboxyl)pyrrolidin-2-on-1-yl]-4-styryl-2-azetidinone (23b) This sample was obtained in 80% yield from **23a** in the same manner as described above for the preparation of **13b**, mp 188 °C (dec., MeOH–AcOEt–hexane), $[\alpha]_D^{20}$ −74° (c=0.5, MeOH). ^{1}H-NMR ($CDCl_3$ + CD_3OD): 2.00—2.60 (4H, m, 2×CH_2), 4.00—4.90 (4H, m, C_4-H, CH_2Ph, CH), 4.75 (1H, d, J=6 Hz, C_3-H), 6.40 (1H, br s, COOH), 7.30 (10H, s, 2×C_6H_5). *Anal.* Calcd for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.18. Found: C, 70.51; H, 5.71; N, 7.10.

(3*S*,4*R*)-1-Benzyl-3-(pyrrolidine-2,5-dion-1-yl)-4-styryl-2-azetidinone (24) A mixture of **23b** (932 mg, 2.39 mmol), lead tetraacetate (1.06 g, 2.4 mmol), and potassium acetate (410 mg, 2.78 mmol) in DMF (20 ml) was stirred at room temperature for 3 h. After dilution with AcOEt–benzene (3 : 1, 160 ml), the mixture was washed with water, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. Drying followed by evaporation *in vacuo* gave a residue (745 mg), which was dissolved in a mixture of AcOEt (5 ml) and 50% aqueous AcOH (10 ml). After being stirred at 50 °C for 1.5 h, the mixture was diluted with AcOEt and washed with water, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. Drying followed by evaporation *in vacuo* gave a residue (615 mg), which was oxidized with Jones reagent (0.8 ml) in acetone (10 ml). After dilution with AcOEt, the mixture was washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (AcOEt : $CHCl_3$ = 3 : 1) gave **24** (410 mg, yield 46%) as an oil, $[\alpha]_D^{20}$ −28.6° (c=0.4, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1770, 1720. ^{1}H-NMR ($CDCl_3$): 2.60 (4H, s, 2×CH_2), 4.20 and 4.65 (2H, AB, J=15 Hz, CH_2Ph), 4.35 (1H, dd, J=6, 8 Hz, C_4-H), 5.25 (1H, d, J=6 Hz, C_3-H), 5.92 (1H, dd, J=8, 15 Hz, CH=CHPh), 6.45 (1H, d, J=15 Hz, CH=CHPh), 7.20 and 7.25 (10H, 2×s, 2×C_6H_5). MS m/z: 360 (M^+).

(3*S*,4*R*)-1-Benzyl-3-[(3-methoxycarbonyl)propionamido]-4-styryl-2-azetidinone (25a) This sample was obtained in 61% yield from **24** in the same manner as described above for the preparation of **16a**, mp 100 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +6.7° (c=0.6, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1770, 1750, 1665. ^{1}H-NMR ($CDCl_3$): 2.50 (4H, s, 2×CH_2), 3.48 (1H, s, OCH_3), 4.10

and 4.60 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.30 (1H, dd, J=6, 8 Hz, C_4-H), 5.30 (1H, dd, J=6, 8 Hz, C_3-H), 6.02 (1H, dd, J=8, 15 Hz, C$\underline{H}$=CHPh), 6.50 (1H, d, J=15 Hz, CH=C$\underline{H}$Ph), 7.25 (10H, s, 2×C_6H_5), 7.40 (1H, d, J=8 Hz, NH). *Anal.* Calcd for $C_{23}H_{24}N_2O_4$: C, 70.39; H, 6.16; N, 7.14. Found: C, 70.47; H, 6.08; N, 7.00.

(3*S*,4*R*)-3-Amino-1-benzyl-4-styryl-2-azetidinone (25b) This sample was obtained as an oil in 86% yield from **25a** in the same manner as described for the preparation of **16b**, $[\alpha]_D^{20}$ −194.3° (c=0.35, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1750, 1600. ^{1}H-NMR ($CDCl_3$): 1.80 (2H, br s, NH_2), 4.05 and 4.62 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.05—4.32 (2H, m, 2×CH), 6.00 (1H, dd, J=6, 16 Hz, C$\underline{H}$=CHPh), 6.48 (1H, d, J=16 Hz, CH=C$\underline{H}$Ph), 7.30 (10H, m, 2×C_6H_5). MS m/z: 278 (M^+).

(3*S*,4*R*)-1-Benzyl-3-[(benzyloxycarbonyl)amino]-4-styryl-2-azetidinone (25c) A mixture of **25b** (103 mg, 0.37 mmol), TEA (57 mg, 0.57 mmol), and benzyloxycarbonyl chloride (100 mg, 0.59 mmol) in CH_2Cl_2 (4 ml) was stirred at room temperature for 3 h. After dilution with AcOEt, the mixture was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (AcOEt : $CHCl_3$ = 1 : 5) gave **25c** (120 mg, yield 80%) as crystals, mp 133 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −37° (c=0.2, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760, 1720. ^{1}H-NMR ($CDCl_3$): 4.07 and 4.60 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.30 (1H, dd, J=6, 8 Hz, C_4-H), 5.00 (2H, s, OCH_2O), 5.10 (1H, m, C_3-H), 5.70 (1H, m, NH), 6.00 (1H, dd, J=8, 15 Hz, C$\underline{H}$=CHPh), 6.55 (1H, d, J=15 Hz, CH=C$\underline{H}$Ph), 7.30 (10H, s, 2×C_6H_5). *Anal.* Calcd for $C_{26}H_{24}N_2O_3$: C, 75.71; H, 5.87; N, 6.79. Found: C, 75.43; H, 5.89; N, 6.74.

(3*S*,4*S*)-1-Benzyl-3-[(benzyloxycarbonyl)amino]-4-hydroxymethyl-2-azetidinone (26) A mixture of OsO_4 (5 mg) and **25c** (60 mg, 0.15 mmol) in dioxane–H_2O (3 : 1, 2 ml) was stirred at room temperature for 5 min, then $NaIO_4$ (65 mg, 0.3 mmol) was added. After being stirred at room temperature for 2 h, the mixture was diluted with ether and washed with water. Drying followed by evaporation *in vacuo* gave a residue, which was reduced with $NaBH_4$ (30 mg) in THF (3 ml) at room temperature for 30 min. After dilution with AcOEt, the mixture was washed with saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 1) gave **26** (30 mg, yield 60%) as crystals, mp 143 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −33.0° (c=0.3, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 2.60 (1H, br s, OH), 3.50—3.80 (3H, m, C$\underline{H}_2$OMOM, C_4-H), 4.25 and 4.45 (2H, AB, J=15 Hz, NC$\underline{H}_2$Ph), 5.02 (2H, s, OC$\underline{H}_2$Ph), 5.10 (1H, dd, J=6, 8 Hz, C_3-H), 6.10 (1H, d, J=8 Hz, NH), 7.20 (10H, s, 2×C_6H_5). *Anal.* Calcd for $C_{19}H_{20}N_2O_4$: C, 67.04; H, 5.92; N, 8.23. Found: C, 66.71; H, 5.94 N, 8.09.

2,3-*O*-Isopropylidene-1-*O*-methoxymethyl-L-threitol (27b) A mixture of 2,3-*O*-isopropylidene-L-threitol[18] (**27a**) (3.16 g, 19.5 mmol), chloromethyl methyl ether (1.57 g, 23.4 mmol), and *N*,*N*-diethylaniline (3.47 g, 23.4 mmol) in CH_2Cl_2 (25 ml) was stirred at −10 °C for 30 h. After dilution with AcOEt, the mixture was washed with 10% aqueous HCl and saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 3) afforded **27b** (3.12 g, yield 48%) as an oil, $[\alpha]_D^{20}$ −7.1° (c=2.7, EtOH). IR ν_{max}^{film} cm^{-1}: 3450. ^{1}H-NMR ($CDCl_3$): 1.40 (6H, s, 2×CH_3), 3.00 (1H, br s, OH), 3.35 (3H, s, OCH_3), 3.70—4.20 (6H, m, 2×CH_2, 2×CH), 4.60 (2H, s, OCH_2O).

(3*R*,4*R*)-3-Azido-1-benzyl-4-[(1*S*,2*S*)-1,2-[(isopropylidene)dioxy]-3-(methoxymethoxy)propanyl]-2-azetidinone (28) The aldehyde **27c** (bp 83—85 °C (0.3 mmHg), $[\alpha]_D^{20}$ +11° (c=0.8, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1740. ^{1}H-NMR ($CDCl_3$): 1.40 and 1.45 (6H, 2×s, 2×CH_3), 3.30 (3H, s, CH_3), 3.55—3.75 (2H, m, C$\underline{H}_2$OMOM), 4.05—4.30 (2H, m, 2×CH), 4.60 (2H, s, OCH_2O), 9.70 (1H, s, CHO)) was analogously prepared in 58% yield from **27b** according to the reported procedure.[19] A mixture of **27c** (1.71 g, 8.4 mmol) and benzylamine (900 mg, 8.4 mmol) in benzene (25 ml) was stirred at room temperature for 2 h in the presence of molecular sieves 4A (5 g). After removal of the molecular sieves by filtration, the filtrate was evaporated *in vacuo* to give a crude imine (**21**, 2.52 g, yield quant.). IR ν_{max}^{film} cm^{-1}: 1670, 1600. ^{1}H-NMR ($CDCl_3$): 1.55 (6H, s, 2×CH_3), 3.30 (3H, s, OCH_3), 3.60—3.80 (2H, m, C$\underline{H}_2$OMOM), 4.00—4.40 (2H, m, 2×CH), 4.60 (2H, s, OCH_2O), 7.20 (5H, s, C_6H_5), 7.65—7.80 (1H, m, CH=N). A solution of the crude imine (2.52 g) and TEA (1.78 ml, 12.6 mmol) in CH_2Cl_2 (20 ml) was added at 0 °C over a period of 15 min to the mixed anhydride, prepared from azidoacetic acid (1.27 g, 12.6 mmol), trifluoroacetic anhydride (1.78 ml, 12.6 mmol), and TEA (1.75 ml, 12.6 mmol) in CH_2Cl_2 (20 ml) at 0 °C for 30 min. After being stirred at 0 °C for 12 h, the mixture was diluted with AcOEt and washed with 10% aqueous HCl, water, saturated aqueous $NaHCO_3$, and water. Drying followed by evaporation and purification by column chromatography (silica gel, $CHCl_3$: AcOEt : hexane = 5 : 1 : 2) gave **28** (1.61 g, yield 51%) as an oil, $[\alpha]_D^{20}$ +12.5° (c=0.8, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 2100, 1770. ^{1}H-NMR ($CDCl_3$): 1.30 and 1.40 (6H, 2×s, 2×CH_3), 3.30 (3H, s, OCH_3), 3.50—4.30 (5H, m, 2×CH, C_4-H, C$\underline{H}_2$OMOM), 4.18 and 4.80 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.58 (2H, s, OCH_2O), 4.65 (1H, d, J=6 Hz, C_3-H), 7.30 (5H, s, C_6H_5). MS m/z: 376 (M^+).

(3*R*,4*R*)-3-Azido-1-benzyl-4-[(1*S*,2*S*)-1,2,3-(trihydroxy)propanyl]-2-azetidinone (29) A mixture of **28** (1.55 g, 4.12 mmol), and *p*-toluenesulfonic acid monohydrate (20 mg) in MeOH (10 ml) was stirred at 70 °C for 3 h. After dilution with AcOEt, the mixture was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt) gave **29** (795 mg, yield 66%) as an oil, $[\alpha]_D^{20}$ +51.7° (c=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400, 2150, 1750. ^{1}H-NMR ($CDCl_3$): 3.00 (3H, br s, 3×OH), 3.65—3.92 (5H, m, 2×CH, C_4-H, C$\underline{H}_2$OH), 4.32 and 4.75 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.65 (1H, d, J=5 Hz, C_3-H), 7.30 (5H, s, C_6H_5). MS m/z: 292 (M^+).

(3*R*,4*R*)-3-Azido-1-benzyl-4-hydroxymethyl-2-azetidinone (30a) A solution of **29** (717 mg, 2.46 mmol) in 50% aqueous 2-butanol (8 ml) was added to a solution of $NaIO_4$ (1.5 mg, 7.37 mmol) in 50% aqueous 2-butanol (10 ml) at 0 °C. The mixture was stirred at room temperature for 2 h and extracted with ether. The organic extracts were washed with water. Drying followed by evaporation *in vacuo* gave a residue, which was reduced with $NaBH_4$ (360 mg, 9.5 mmol) in THF (10 ml) at 0 °C for 1 h. After dilution with AcOEt, the mixture was washed with saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 2) gave **30a** (450 mg, yield 79%) as an oil, $[\alpha]_D^{20}$ +108.7° (c=0.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400, 2100, 1750. ^{1}H-NMR ($CDCl_3$): 2.10 (1H, br s, OH), 3.50—3.85 (3H, m, C$\underline{H}_2$OH, C_4-H), 4.20 and 4.55 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.70 (1H, d, J=5 Hz, C_3-H), 7.25 (5H, s, C_6H_5). MS m/z: 232 (M^+).

(3*R*,4*R*)-3-Azido-1-benzyl-4-[(methoxymethoxy)methyl]-2-azetidinone (30b) A mixture of **30a** (406 mg, 1.5 mmol), chloromethyl methyl ether (350 mg, 4.35 mmol), and *N*,*N*-diethylaniline (648 mg, 4.35 mmol) in CH_2Cl_2 (7 ml) was stirred at room temperature for 24 h. After dilution with AcOEt, the mixture was washed with 10% aqueous HCl, water, and saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 5) gave **30b** (380 mg, yield 92%) as an oil, $[\alpha]_D^{20}$ +73.7° (c=1.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 2100, 1760. ^{1}H-NMR ($CDCl_3$): 3.30 (3H, s, OCH_3), 3.50—4.00 (3H, m, C$\underline{H}_2$OMOM, C_4-H), 4.20 and 4.58 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.68 (1H, d, J=6 Hz, C_3-H), 7.25 (5H, s, C_6H_5). MS m/z: 276 (M^+).

(3*R*,4*R*)-3-Amino-1-benzyl-4-[(methoxymethoxy)methyl]-2-azetidinone (30c) **30b** (364 mg, 1.3 mmol) was hydrogenated using 5% Pd–C (90 mg) in AcOEt (5 ml) under hydrogen at atmospheric pressure at room temperature for 4 h. After removal of the catalyst by filtration, the filtrate was evaporated *in vacuo* to give a residue, which was purified by column chromatography (silica gel, AcOEt : $CHCl_3$: MeOH = 9 : 1 : 5) to give **30c** (260 mg, yield 80%) as an oil, $[\alpha]_D^{20}$ +1.3° (c=1.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1740. ^{1}H-NMR ($CDCl_3$): 1.70 (2H, br s, NH_2), 3.30 (3H, s, OCH_3), 3.60—3.80 (3H, m, C$\underline{H}_2$OMOM, C_4-H), 3.16 and 3.55 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.35 (1H, m, C_3-H), 4.50 (2H, s, OCH_2O), 7.30 (5H, s, C_6H_5). MS m/z: 250 (M^+).

(3*R*,4*R*)-1-Benzyl-3-formamido-4-[(methoxymethoxy)methyl]-2-azetidinone (30d) Acetic anhydride (0.4 ml) was added at 0 °C to a solution of **30c** (200 mg, 0.8 mmol) in 90% formic acid (3 ml), and the mixture was stirred at room temperature for 8 h. After neutralization with aqueous NaOH, the mixture was extracted with AcOEt. The organic extracts were washed with water. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt) gave **30d** (195 mg, yield 88%) as crystals, mp 83—84 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −31° (c=1.3, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1760, 1680. ^{1}H-NMR ($CDCl_3$): 3.25 (3H, s, OCH_3), 3.50—3.90 (3H, m, C$\underline{H}_2$OMOM, C_4-H), 4.25 and 4.55 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.45 (2H, OCH_2O), 5.38 (1H, dd, J=6, 9 Hz, C_3-H), 7.0—7.5 (6H, m, CONH, C_6H_5), 8.17 (1H, s, CHO). *Anal.* Calcd for $C_{14}H_{18}N_2O_4$: C, 60.42; H, 10.07; N, 6.52. Found: C, 60.59; H, 9.82; N, 6.31.

(3*R*,4*R*)-1-Benzyl-3-isocyano-4-[(methoxymethoxy)methyl]-2-azetidinone (30e) A mixture of **30d** (180 mg, 0.65 mmol), $POCl_3$ (153 mg, 1 mmol), and 2,6-lutidine (208 mg, 1.95 mmol) in CH_2Cl_2 (5 ml) was stirred at room temperature for 4 h, then 50 mg (0.33 mmol) of $POCl_3$ was added. After being stirred at room temperature for a further 8 h, the mixture was diluted with AcOEt and washed with 5% aqueous HCl, water, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 4) gave **30e** (135 mg, yield 80%) as an oil, $[\alpha]_D^{20}$ +55.0° (c=0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 2140, 1770. ^{1}H-NMR ($CDCl_3$): 3.30 (3H, s, OCH_3),

3.65—4.00 (3H, m, C$\underline{H}_2$OMOM, C_4-H), 4.25 and 4.55 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.50 (2H, s, OCH_2O), 4.70 (1H, d, J=6 Hz, C_3-H), 7.25 (5H, s, C_6H_5). MS m/z: 260 (M^+).

(3*R*,4*R*)-1-Benzyl-3-[(benzyloxycarbonyl)amino]-4-[(methoxymethoxy)-methyl]-2-azetidinone (30f) This sample was obtained as an oil in 73% yield from **30c** in the same manner as described above for the preparation of **25c**, $[\alpha]_D^{20}$ −8° (c=0.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1760, 1720. ^{1}H-NMR ($CDCl_3$): 3.30 (3H, s, OCH_3), 3.60—3.92 (3H, m, C$\underline{H}_2$OMOM, C_4-H), 4.22 and 4.55 (2H, AB, J=15 Hz, C$\underline{H}_2$Ph), 4.30 and 4.45 (2H, AB, J=15 Hz, OCH_2O), 5.10 (2H, s, $OC\underline{H}_2$Ph), 5.25 (1H, dd, J=6, 9 Hz, C_3-H), 5.80 (1H, dd, J=6, 9 Hz, NH), 7.15—7.40 (10H, m, 2×C_6H_5).

(3*R*,4*R*)-1-Benzyl-3-[(benzyloxycarbonyl)amino]-4-hydroxymethyl-2-azetidinone (30g) A mixture of **30f** (35 mg, 0.09 mmol) and 10% aqueous HCl (2 ml) in MeOH (2 ml) was stirred at 70 °C for 2 h. After dilution with AcOEt, the mixture was washed with water. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 1) gave **30g** (19 mg, yield 62%) as crystals, mp 143 °C, $[\alpha]_D^{20}$ +32.2° (c=0.3, $CHCl_3$). The NMR spectrum was identical with that of **26**.

(4*R*)-1-Benzyl-4-[(methoxymethoxy)methyl]-2-azetidinone (31a) A mixture of **30e** (120 mg, 0.46 mmol), tributyltin hydride (339 mg, 1.17 mmol), and a catalytic amount of α,α′-azobis-isobutyronitrile in benzene (10 ml) was stirred at 80 °C for 30 min. After cooling to room temperature, the solvent was evaporated *in vacuo* to give a residue, which was purified by column chromatography (silica gel, AcOEt : $CHCl_3$ = 4 : 1) to give **31a** (103 mg, yield 95%) as an oil, $[\alpha]_D^{20}$ −28.7° (c=0.4, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1760. ^{1}H-NMR ($CDCl_3$): 2.80—3.00 (2H, m, C_3-H), 3.28 (3H, s, OCH_3), 3.52—3.70 (3H, C_4-H, C$\underline{H}_2$OMOM), 4.22 and 4.60 (2H, AB, J=16 Hz, C$\underline{H}_2$Ph), 4.48 (2H, s, OCH_2O), 7.30 (5H, s, C_6H_5). MS m/z: 235 (M^+).

(4*R*)-1-Benzyl-4-hydroxymethyl-2-azetidinone (31b) A mixture of **31a** (90 mg, 0.38 mmol) and 10% aqueous HCl (2 ml) in MeOH (4 ml) was stirred at 70 °C for 3 h. After dilution with AcOEt, the mixture was washed with saturated aqueous $NaHCO_3$ and water. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt) gave **31b** (63 mg, yield 86%), mp 105—106 °C, $[\alpha]_D^{20}$ −84.4° (c=1, EtOH).

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