Chemistry of *O*-Silylated Ketene Acetals: A Stereoselective Synthesis of Optically Active Carbapenem Antibiotics, (+)-Thienamycin and (+)-PS-5

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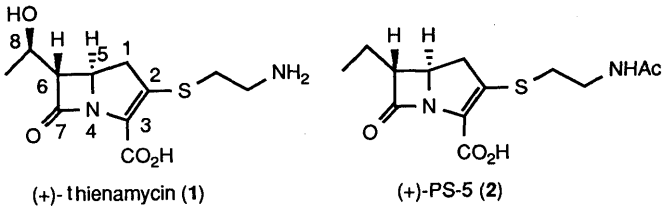
A stereoselective synthesis of the chiral thienamycin intermediate (16) involving a diastereoselective Michael addition and a silicon-induced Pummerer-type reaction is described. In a similar way, the key intermediate for (+)-PS-5 was also prepared from 4-(phenylsulfinylmethyl)butanamide (21).

Keywords *O*-silylated ketene acetal; silicon-induced Pummerer-type reaction; diastereoselective Michael addition; synthesis; carbapenem antibiotics; (+)-thienamycin; (+)-PS-5

Since the discovery of the carbapenem antibiotics, represented by thienamycin (**1**), the development of synthetic route to these compounds has been the subject of much research[1] because of their prominent antibacterial activities and broad activity spectra. Most of the routes, however, are based on an aldol-type reaction of 4-acetoxyazetidinones with properly designed metal enolates.[1] Recently, we have reported a conceptually new approach to (+)-**1** involving a diastereoselective Michael addition and a silicon-induced Pummerer-type reaction.[2-4] We present here a full account of this work and an application of the method to a stereoselective synthesis of (+)-PS-5 (**2**). The main difficulties in the synthesis of (+)-**1** are the control of the relative and absolute stereochemistry of the three contiguous chiral centers and the choice of a suitable chiral starting material. Our novel synthetic strategy relies on the recognition that the chiral propenoate (**3**) can be utilized as a key intermediate for the optically active β-amido sulfoxide (**4**). The asymmetric center in **3** directs the introduction of the correct absolute stereochemistry at the neighboring carbon center (the C-3 position of the β-lactam ring) in the asymmetric Michael addition reaction. The optically active **4** is used in the next silicon-induced Pummerer-type reaction[2-4] to give the chiral β-lactam (**5**) bearing the correct absolute stereochemistry at the C-6 and C-8 positions (carbapenem numbering).

Diastereoselective Michael Addition Reaction of Thiophenol to Chiral Propenoates The starting chiral α,β-unsaturated esters (**3**) were obtained from readily available (*R*)-(−)-ethyl 3-hydroxybutanoate (**6**, $[\alpha]_D^{25}$ −40.9° (*c*= 0.81, $CHCl_3$), lit.[5] $[\alpha]_D^{25}$ −43.6° (*c*=1.2, $CHCl_3$)). Reaction of **6** with 2 eq of lithium diisopropylamide (LDA) in tetrahydrofuran (THF) followed by treatment with formaldehyde gave the hydroxymethylated compound (**7**). Selective tosylation of the primary alcohol of **7** with *p*-toluenesulfonyl chloride (*p*-TsCl) followed by base-induced elimination of the tosyloxy group yielded the ethyl 2-(1-hydroxyethyl)propenoate (**3a**), which was silylated to give the silyl ethers (**3b—d**). Since Perlmutter and Tabone recently presented[6,7] a diastereoselective nucleophilic conjugate addition of benzylamine to 2-(1-hydroxyalkyl)-propenoates, we examined the nucleophilic addition of thiophenol to the propenoates (**3a—d**) bearing a chiral substituent at the C-2 position and found that the bulky silyl ethers (**3b—d**) gave Michael addition products (**9b—d**) with high diastereoselectivity (Table I). The assignment of the stereochemistry of **9a—d** was made by 500 MHz proton nuclear magnetic resonance (^{1}H-NMR) spectrometric measurement (Fig. 1) based on a method similar to that reported by Kurihara *et al.*[8] Thus, the highly diastereopure



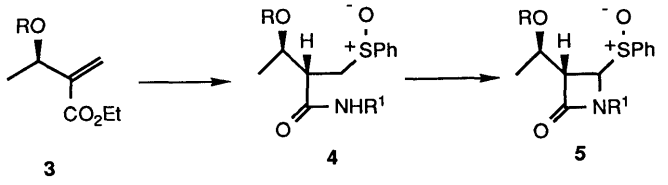


Chart 1

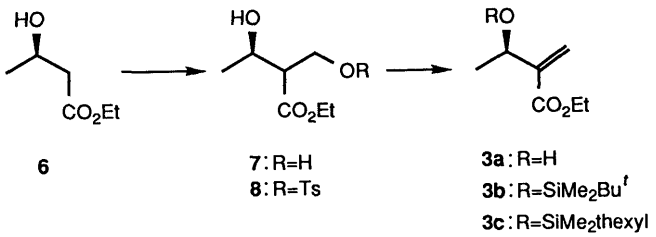
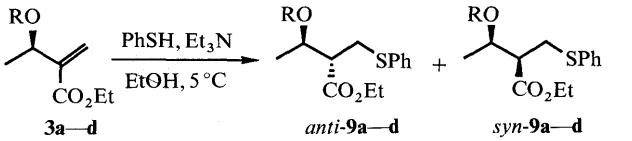


Chart 2

TABLE I. Michael Addition of Thiophenol to Chiral Propenoates (**3a—d**)



3	R	Product (9)	Yield (%)	*anti*:*syn*[a]
3a	H	**9a**	100	50:50
3b	$SiMe_2Bu^t$	**9b**	99	79:21
3c	$SiMe_2$thexyl	**9c**	98	79:21
3d	$SiPh_2Bu^t$	**9d**	96	89:11

a) Determined by 500 MHz ^{1}H-NMR.

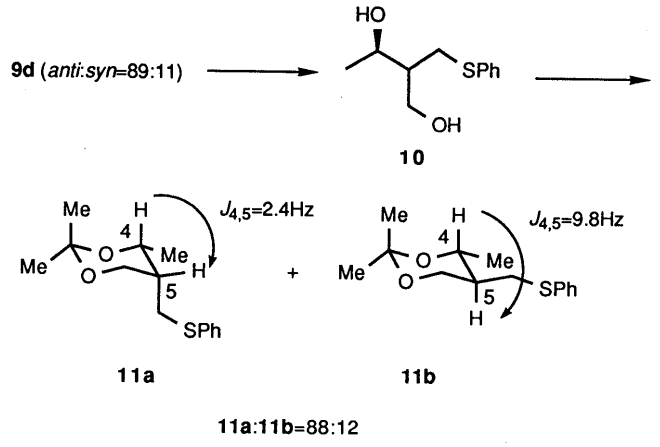


Fig. 1

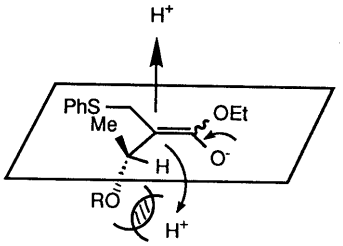


Fig. 2

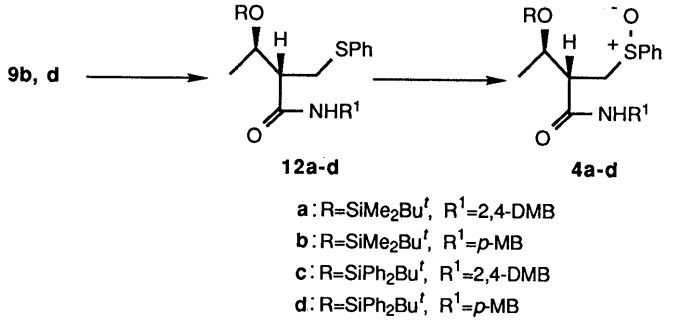


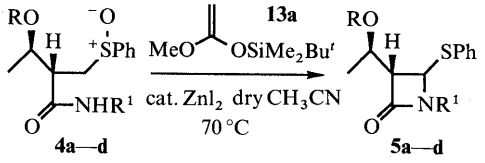
Chart 3

mixture (**9d**) was reduced by lithium aluminum hydride ($LiAlH_4$) to give the corresponding alcohol (**10**), which was treated with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid (*p*-TsOH) to give the 1,3-dioxane derivatives (**11a, b**). Since the major product (**11a**) has a smaller vicinal coupling constant ($J_{4,5}=2.4$ Hz) than that ($J_{4,5}=9.8$ Hz) of the minor product (**11b**), the major product (**11a**) is *anti*-**9d** and the minor one (**11b**) is *syn*-**9d**. The structures of other adducts were similarly confirmed.

While mechanistic details of the diastereoselective addition of thiophenol to **3b—d** remain unknown, a plausible transition state is illustrated in Fig. 2. The *anti*-selectivity can be explained by preferential protonation to the face of the olefinic bond opposite to that of the pre-existing bulky siloxy group.[9]

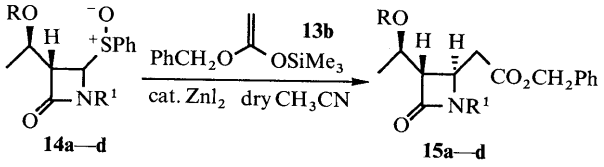
Synthesis of (+)-Thienamycin (1) Next, we examined a synthesis of the optically active intermediate for (+)-**1** from the chiral ester (**9**), in which the *O*-silylated ketene acetal is used twice for the key steps, the silicon-induced Pummerer-type reaction of β-amido sulfoxide and the C-4

Table II. Silicon-Induced Pummerer-Type Reaction of **4a—d**



4	R	R^1	Product (5)	Yield (%)	*trans*:*cis*
4a	$SiMe_2Bu^t$	2,4-DMB	**5a**	65	4.1:1
4b	$SiMe_2Bu^t$	*p*-MB	**5b**	56	4.0:1
4c	$SiPh_2Bu^t$	2,4-DMB	**5c**	64	4.4:1
4d	$SiPh_2Bu^t$	*p*-MB	**5d**	74	4.4:1

Table III. Carbon–Carbon Bond Formation of 4-Sulfinylazetidin-2-ones (**14a—d**)



14a	R	R^1	Product (15)	Yield (%)
14a (*trans*:*cis*=4:1)	$SiMe_2Bu^t$	2,4-DMB	**15a**	75
14a (*trans*)	$SiMe_2Bu^t$	2,4-DMB	**15a**	81
14b (*trans*)	$SiMe_2Bu^t$	*p*-MB	**15b**	64
14c (*trans*)	$SiPh_2Bu^t$	2,4-DMB	**15c**	71
14d (*trans*)	$SiPh_2Bu^t$	*p*-MB	**15d**	63

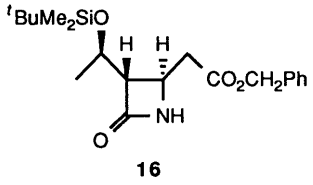


Fig. 3

substitution reaction of the 4-arylsulfinylazetidin-2-one.

Amidation of the mixture of diastereomers (*anti*-**9b, d** and *syn*-**9b, d**) with 2,4-dimethoxybenzylamine (2,4-$DMBNH_2$) or *p*-methoxybenzylamine (*p*-$MBNH_2$) in the presence of trimethylaluminum ($AlMe_3$) in boiling benzene[10] gave the corresponding mixture of diastereomers (*anti*-**12a—d** and *syn*-**12a—d**). These diastereomers could be separated from each other by column chromatography on silica gel. Oxidation of *anti*-**12a—d** with sodium periodate ($NaIO_4$) in MeOH yielded the β-amido sulfoxides (**4a—d**). Cyclization of **4a—d** was achieved by our silicon-induced Pummerer-type reaction[2-4] using *O*-methyl-*O*-*tert*-butyldimethylsilyl ketene acetal (**13a**) to give the 4-phenylthioazetidinones (**5a—d**). The results are summarized in Table II. Oxidation of **5** with *m*-chloroperbenzoic acid (*m*-CPBA) in CH_2Cl_2 gave the sulfoxide (**14**), which was treated with **13b** in the presence of a catalytic amount of zinc iodide (ZnI_2) in CH_3CN to give the *trans*-azetidinone ester (**15**), selectively (Table III). The *trans*-**15** was produced selectively even if a *trans*/*cis* mixture of **14** was used as the starting material. Therefore, it is presumed that the carbon–carbon bond formation in the reaction of **14** with **13b** proceeds *via* a nucleophilic attack of the ester enolate anion on the iminium

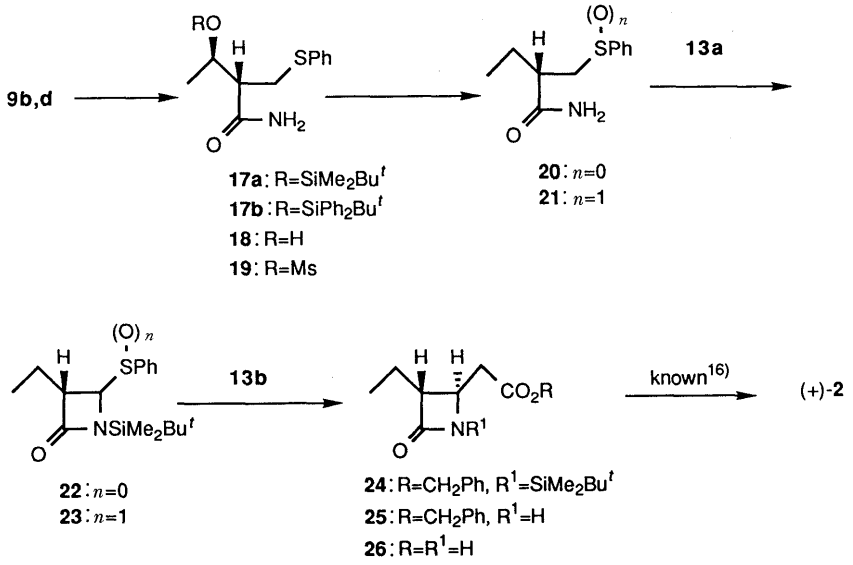


Chart 4

intermediates to give the *trans*-azetidinone ester (**15**). Deprotection of **15a** by the known method[11] yielded the *N*-unsubstituted *trans*-azetidinone ester (**16**), which had previously been transformed into (+)-**1**.[12]

Synthesis of (+)-PS-5 (2) Finally, our attention was focused on the synthesis of (+)-**2**. Our strategy relies on the recognition that ethyl (2*S*,3*R*)-3-silyloxy-2-(phenylthiomethyl)butanoate (**9**) can be utilized as a synthon which is the same as the intermediate for (+)-**1**. The asymmetric center (the C-3 position) of **9** necessary for the diastereoselective Michael addition of thiophenol is removed by the following deoxygenation step. Introduction of the correct stereochemistry at the C-4 position of the azetidin-2-one ring system follows the previously reported methodology *via* a *trans* substitution reaction.[2,4]

Amidation of **9b, d** with ammonium chloride (NH_4Cl) in the presence of $AlMe_3$ in benzene gave the amides (**17a, b**), which were desilylated with $BF_3 \cdot OEt_2$ in CH_3CN or tetrabutylammonium fluoride (Bu_4NF) in THF to give the hydroxy compound (**18**). The hydroxy group on the side chain of **18** was removed in high yield by mesylation with methanesulfonyl chloride (MsCl) followed by reduction by Fujimoto's method.[13] Thus, treatment of **18** with MsCl and Et_3N in CH_2Cl_2 gave the mesylate (**19**), which was reduced with NaI–Zn in refluxing 1,2-dimethoxyethane (DME) to give the deoxygenated compound (**20**). A similar deoxygenation method was used in the synthesis of (+)-**2** by Chiba and Nakai[14] and Georg and Kant.[15] Oxidation of **20** with $NaIO_4$ in MeOH gave the β-amido sulfoxide (**21**), which was treated with *O*-methyl-*O*-*tert*-butyldimethylsilyl ketene acetal (**13a**) and a catalytic amount of ZnI_2 in CH_3CN to produce a mixture of *cis*- and *trans*-azetidinones (**22**). Oxidation of the mixture (**22**) with *m*-CPBA in CH_2Cl_2 followed by reaction with **13b** in the presence of a catalytic amount of ZnI_2 in CH_3CN afforded the *trans*-azetidinone ester (**24**). Desilylation of **24** with Bu_4NF and AcOH in THF followed by reductive debenzylation on 10% Pd–C in EtOH gave the *trans*-4-carboxy-3-ethylazetidinone (**26**), which is a key intermediate of (+)-**2**.[16]

In our method, three (or two) contiguous asymmetric centers were constructed in a novel, highly stereocontrolled way and all steps were performed in moderate to good yield.

Experimental

All melting and boiling points are uncorrected. ^{1}H-NMR spectra were recorded on a Hitachi R-22 (90 MHz) or a JEOL JNM-GX 500 (500 MHz) spectrometer (with tetramethylsilane as an internal standard unless otherwise noted). Infrared (IR) absorption spectra were recorded on a JASCO HPIR-102 spectrophotometer. Low- and high-resolution mass spectra (MS) were obtained with a JEOL JMSD-300 instrument, with a direct inlet system at 70 eV. For column chromatography, E. Merck silica gel (70—230 mesh ASTM) was used. For preparative thin layer chromatography (preparative TLC), E. Merck TLC plates pre-coated with Silica gel $60F_{254}$ (0.5 mm) were used.

Ethyl (3*R*)-3-Hydroxy-2-(hydroxymethyl)butanoate (7) A solution of LDA [prepared from diisopropylamine (5.7 ml, 40.9 mmol) and a 1.5 M solution of *n*-butyllithium in hexane (26.1 ml, 39.2 mmol)] in THF (100 ml) was cooled to −78 °C and treated dropwise with a solution of ethyl 3(*R*)-hydroxy butanoate (2.35 g, 17.8 mmol) in THF (10 ml) under a nitrogen atmosphere. The mixture was stirred for 30 min at −78 °C, then allowed to warm to −23 °C, and stirred for an additional 30 min. Formaldehyde monomer [from pyrolysis of paraformaldehyde (5.0 g, 167 mmol)] was added to the mixture at −23 °C over a period of 45 min. The reaction mixture was quenched with saturated aqueous NH_4Cl, then 1 N hydrochloric acid (40 ml) was added. The mixture was extracted with ethyl acetate (200 ml × 3) and the extract was washed with saturated aqueous $NaHCO_3$ (40 ml) and brine (40 ml), then dried over Na_2SO_4. The solvent was removed under reduced pressure to give a crude oil, which was purified by column chromatography on silica gel with 80% AcOEt in hexane to give **7** (1.94 g, 67%) as a pale yellow oil. $[\alpha]_D^{26}$ −40.9° (c=0.81, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3450, 1710. ^{1}H-NMR ($CDCl_3$) δ: 1.25 (3H, d, J=7 Hz, CH_3CH<), 1.28 (3H, t, J=7 Hz, CH_3CH_2), 2.43—2.71 (1H, m, >$CHCO_2Et$), 3.18 (2H, br s, OH × 2), 3.96 (3H, m, >$CHCH_3$, CH_2OH), 4.21 (2H, q, J=7 Hz, CH_2CH_3). MS *m/z*: 163 (M^++1).

Ethyl (3*R*)-3-Hydroxy-2-(*p*-toluenesulfonylmethyl)butanoate (8) A mixture of **7** (1.78 g, 11.0 mmol), pyridine (16 ml), and *p*-TsCl (2.31 g, 12.1 mmol) in dry CH_2Cl_2 (10 ml) was stirred at 5 °C for 5 d under nitrogen. The reaction mixture was concentrated *in vacuo* and the residue was poured into water (50 ml). The mixture was extracted with CH_2Cl_2 (100 ml × 3). The extract was washed with 10% hydrochloric acid (50 ml × 2), saturated aqueous $NaHCO_3$ (50 ml) and brine (100 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure to give crude **8** (2.86 g, 82%), which was utilized directly in the next step. A pure sample was obtained by column chromatography on silica gel (eluant: 50% AcOEt in hexane) as a pale yellow oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 3540, 1720, 1365, 1175. ^{1}H-NMR ($CDCl_3$) δ: 1.21 (3H, d, J=7 Hz, CH_3CH<), 1.24 (3H, t, J=7 Hz, CH_3CH_2), 2.16 (1H, br m, OH), 2.44 (3H, s, CH_3Ar), 2.70 (1H, m,

>CHCO$_2$Et), 4.16 (2H, q, J=7 Hz, CH$_2$CH$_3$), 4.19 (3H, m, CH$_2$OTs, >CHCH$_3$), 7.29 (2H, d, J=8 Hz, ArH), 7.15 (2H, d, J=8 Hz, ArH). MS m/z: 317 (M^++1). Exact Mass Calcd for $C_{14}H_{20}O_6S$: 316.0981. Found: 316.0981.

Ethyl 2-[(*R*)-1-Hydroxyethyl]propenoate (3a) Crude **8** (2.60 g, from **7** 9.99 mmol) was dissolved in toluene (8 ml). A solution of 1,8-diazabicyclo[5.4.0]undecene-7 (DBU, 2.50 g, 16.5 mmol) in toluene (13 ml) was added to the above solution, and the mixture was stirred at room temperature for 5 min. The reaction mixture was poured into water (100 ml), and extracted with CH_2Cl_2 (100 ml × 3). The combined organic layer was washed with brine (50 ml), dried over $MgSO_4$, and evaporated *in vacuo*. The residual oil was distilled under reduced pressure to give **3a** (1.09 g, 76% from **7**) as a colorless oil, bp 58—62 °C (0.8 mmHg). $[\alpha]_D^{20.5}$ +18.36° (c=1.38, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3500, 3000, 1700, 1630. ^{1}H-NMR ($CDCl_3$) δ: 1.33 (3H, t, J=7 Hz, CH$_3$CH$_2$), 1.40 (3H, d, J=6.5 Hz, CH$_3$CH<), 2.92 (1H, br s, OH), 4.26 (2H, q, J=7 Hz, CH$_2$CH$_3$), 4.64 (1H, q, J=6.5 Hz, >CHCH$_3$), 5.84, 6.23 (2H, each s, CH$_2$=C<). *Anal.* Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.50; H, 8.68.

Ethyl 2-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]propenoate (3b) A mixture of **3a** (4.03 g, 28.0 mmol), imidazole (7.62 g, 112 mmol), and *tert*-butyldimethylsilyl chloride (8.43 g, 56.0 mmol) in *N*,*N*-dimethylformamide (DMF, 15 ml) was stirred at room temperature for 2 d. The reaction mixture was poured into water (50 ml), and extracted with hexane (300 ml × 3). The combined organic layer was washed with brine (100 ml), dried over Na_2SO_4 and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with 2% AcOEt in hexane to give **3b** (7.22 g, quant.) as a colorless oil, bp 130—140 °C (20 mmHg). $[\alpha]_D^{20}$ +28.7° (c=0.50, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1710, 1630. ^{1}H-NMR ($CDCl_3$) δ: 0.40, 0.06 (each 3H, each s, Me$_2$Si), 0.90 (9H, s, *tert*-BuSi), 1.27 (3H, d, J=6.5 Hz, CH$_3$CH<), 1.31 (3H, t, J=7 Hz, CH$_3$CH$_2$), 4.22 (2H, q, J=7 Hz, CH$_2$CH$_3$), 4.69 (1H, m, >CHCH$_3$), 5.90, 6.14 (total 2H, each s, CH$_2$=C<). MS m/z: 201 (M^+−*tert*-Bu). *Anal.* Calcd for $C_{13}H_{26}O_3Si$: C, 60.42; H, 10.14. Found: C, 60.61; H, 10.09.

Ethyl 2-[(*R*)-1-{(Dimethylthexylsilyl)oxy}ethyl]propenoate (3c) In a similar fashion, **3a** (273 mg, 1.90 mmol) was treated with imidazole (284 mg 4.18 mmol) and dimethylthexylsilyl chloride (0.411 ml, 2.09 mmol) in DMF (3 ml) to give **6c** (482 mg, 89%) as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 2950, 1710, 1630. ^{1}H-NMR ($CDCl_3$) δ: 0.60, 0.12 (total 6H, each s, Me$_2$Si), 0.88 (6H, s, Me$_2$C<), 0.94 (6H, d, J=6.5 Hz, Me$_2$CH), 1.30 (3H, d, J=6.5 Hz, CH$_3$CH<), 1.33 (3H, t, J=7 Hz, CH$_3$CH$_2$), 1.67 (1H, m, CHMe$_2$), 4.23 (2H, q, J=7 Hz, CH$_2$CH$_3$), 4.71 (1H, q, J=6.5 Hz, >CHCH$_3$), 5.95, 6.19 (total 2H, each s, CH$_2$=C<). Exact Mass Calcd for $C_{15}H_{30}O_3Si-C_6H_{13}$: 201.0944. Found: 201.0914.

Ethyl 2[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]propenoate (3d) In a similar fashion, **3a** (2.84 g, 19.7 mmol) was treated with imidazole (2.98 g, 43.4 mmol) and *tert*-butyldiphenylsilyl chloride (5.65 ml, 21.7 mmol) in DMF (15 ml) to give **3d** (7.56 g, quant.) as a colorless oil, bp 140—150 °C (0.1 mmHg) (bulb-to-bulb). $[\alpha]_D^{20.5}$ +36.03° (c=0.82, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 2950, 1710, 1630. ^{1}H-NMR ($CDCl_3$) δ: 1.05 (9H, s, *tert*-BuSi), 1.17 (3H, d, J=6.5 Hz, CH$_3$CH<), 1.19 (3H, t, J=7 Hz, CH$_3$CH$_2$), 4.09 (2H, q, J=7 Hz, CH$_2$CH$_3$), 4.72 (1H, q, J=6.5 Hz, >CHCH$_3$), 6.04, 6.18 (total 2H, each m, CH$_2$=C<), 7.24—7.74 (10H, m, Ph × 2). MS m/z: 325 (M^+−*tert*-Bu). *Anal.* Calcd for $C_{23}H_{30}O_3Si$: C, 72.21; H, 7.90. Found: C, 72.34; H, 7.95.

General Procedure for Diastereoselective Michael Addition Reaction of Thiophenol to Propenoates (3a—d) Thiophenol (2 mmol) and triethylamine were added to a stirred solution of propenoate (**3**, 1 mmol) in EtOH (4 ml) at 5 °C. After 1—2 d under the same conditions, the mixture was concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel with 2% AcOEt in hexane to give **9** as a mixture of diastereomers (*anti*-**9** and *syn*-**9**). The ratio of the mixture was determined by 500 MHz ^{1}H-NMR.

Ethyl (3*R*)-3-Hydroxy-2-(phenylthiomethyl)butanoate (9a) A mixture of diastereomers (**9a**, 371 mg, 100%, *anti*: *syn*=50 : 50) was obtained from **3a** (210.6 mg, 1.463 mmol), thiophenol (322 mg, 2.93 mmol), and triethylamine (0.6 ml) in EtOH (4 ml) as a pale yellow oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 3500, 3000, 1730. ^{1}H-NMR ($CDCl_3$) δ: 1.22, 1.23 (total 3H, each d, J=6.7 Hz, CH$_3$CH<), 1.27, 1.28 (total 3H, each t, J=7.3 Hz, CH$_3$CH$_2$), 2.29 (1/2 × 1H, d, J=4.9 Hz, OH), 2.53 (1/2 × 1H, d, J=7.9 Hz, OH), 2.62—2.69 (1H, m, >CHCO$_2$Et), 3.21 (1/2 × 1H, dd, J=5.5, 13.4 Hz, CHHSPh), 3.24 (1/2 × 2H, d, J=7.3 Hz, CH$_2$SPh), 3.27 (1/2 × 1H, dd, J=8.6, 13.4 Hz, CHHSPh), 4.07 (1H, m, >CHCH$_3$), 4.17 (2H, q, J=7.3 Hz, CH$_2$CH$_3$), 7.19—7.39 (5H, m, Ph). Exact Mass Calcd for $C_{13}H_{18}O_3S$: 254.0974. Found: 254.0972.

Ethyl (3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-2-(phenylthiomethyl)butanoate (9b) A mixture of diastereomers (**9b**, 670 mg, 99%, *anti*: *syn*=79 : 21) was obtained from **3b** (474 mg, 1.84 mmol), thiophenol (404 mg, 3.67 mmol), and triethylamine (0.7 ml) in EtOH (4 ml) as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 1725. ^{1}H-NMR ($CDCl_3$) δ: 0.02, 0.04 (total 21/100 × 6H, each s, Me$_2$Si), 0.05 (79/100 × 6H, s, Me$_2$Si), 0.86 (21/100 × 9H, s, *tert*-Bu), 0.88 (79/100 × 9H, s, *tert*-Bu), 1.16 (3H, d, J=6.7 Hz, CH$_3$CH<), 1.25 (3H, t, J=7.3 Hz, CH$_3$CH$_2$), 2.62 (79/100 × 1H, ddd, J=3.7, 6.7, 10.4 Hz, >CHCO$_2$Et), 2.70 (21/100 × 1H, ddd, J=5.5, 6.7, 7.8 Hz, >CHCO$_2$Et), 3.12 (79/100 × 1H, dd, J=10.4, 13.5 Hz, CHHSPh), 3.13 (21/100 × 2H, d, J=8.0 Hz, CH$_2$SPh), 3.29 (79/100 × 1H, dd, J=3.7, 13.5 Hz, CHHSPh), 4.01 (79/100 × 1H, quint, J=6.7 Hz, >CHCH$_3$), 4.11 (79/100 × 2H, q, J=7.3 Hz, CH$_2$CH$_3$), 4.15 (21/100 × 3H, m, >CHCH$_3$, CH$_2$CH$_3$), 7.16—7.36 (5H, m, Ph). Exact Mass Calcd for $C_{19}H_{32}O_3SSi-tert$-Bu: 311.1137. Found: 311.1137. *Anal.* Calcd for $C_{19}H_{32}O_3SSi$: C, 61.91; H, 8.75. Found: C, 61.90; H, 9.11.

Ethyl (3*R*)-3-[(Dimethylthexylsilyl)oxy]-2-(phenylthiomethyl)butanoate (9c) A mixture of diastereomers (**9c**, 280 mg, 97%, *anti*: *syn*=79 : 21) was obtained from **3c** (209 mg, 0.731 mmol), thiophenol (161 mg, 1.46 mmol), and triethylamine (0.3 ml) in EtOH (2 ml) as a pale yellow oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 2975, 1725. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (21/100 × 6H, s, Me$_2$Si), 0.08, 0.09 (total 79/100 × 6H, each s, Me$_2$Si), 0.80, 0.81 (total 21/100 × 6H, each s, Me$_2$C<), 0.82, 0.83 (total 79/100 × 6H, each s, Me$_2$C<), 0.85, 0.86 (total 21/100 × 6H, each d, J=5.5 Hz, Me$_2$CH), 0.870, 0.874 (total 79/100 × 6H, each d, J=6.7 Hz, Me$_2$CH), 1.12 (21/100 × 3H, d, J=6.1 Hz, CH$_3$CH<), 1.16 (79/100 × 3H, d, J=6.1 Hz, CH$_3$CH<), 1.25 (79/100 × 3H, t, J=7.3 Hz, CH$_3$CH$_2$), 1.26 (21/100 × 3H, t, J=7.3 Hz, CH$_3$CH$_2$), 2.62 (79/100 × 1H, ddd, J=3.7, 6.7, 10.4 Hz, >CHCO$_2$Et), 2.69 (21/100 × 1H, dt, J=9.8, 4.9 Hz, >CHCO$_2$Et), 3.12 (79/100 × 1H, dd, J=10.4, 13.4 Hz, CHHSPh), 3.14 (21/100 × 2H, d, J=13.4 Hz, CH$_2$SPh), 3.289 (79/100 × 1H, dd, J=3.7, 13.45 Hz, CHHSPh), 3.98 (21/100 × 1H, quint, J=6.1 Hz, >CHCH$_3$), 4.01 (79/100 × 1H, quint, J=6.1 Hz, >CHCH$_3$), 4.119, 4.112 (total 79/100 × 2H, each q, J=7.3 Hz, CH$_2$CH$_3$), 4.132, 4.144 (total 21/100 × 2H, each q, J=7.3 Hz, CH$_2$CH$_3$), 7.16—7.37 (5H, m, Ph). Exact Mass Calcd for $C_{21}H_{36}O_3SSi-C_6H_{13}$: 311.1137. Found: 311.1157.

Ethyl (3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-2-(phenylthiomethyl)butanoate (9d) A mixture of diastereomers (**9d**, 407 mg, 96%, *anti*: *syn*=89 : 11) was obtained from **3d** (330 mg, 0.865 mmol), thiophenol (190 mg, 1.73 mmol), and triethylamine (0.3 ml) in EtOH (4 ml) as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 2950, 1725. ^{1}H-NMR ($CDCl_3$) δ: 1.03 (12H, s, *tert*-Bu, CH$_3$CH<), 1.21 (89/100 × 3H, t, J=7.3 Hz, CH$_3$CH$_2$), 1.22 (11/100 × 3H, t, J=7.3 Hz, CH$_3$CH$_2$), 2.75 (1H, ddd, J=4.3, 6.1, 10.4 Hz, >CHCO$_2$Et), 3.12 (89/100 × 1H, dd, J=10.4, 13.4 Hz, CHHSPh), 3.20 (11/100 × 2H, m, CH$_2$SPh), 3.24 (89/100 × 1H, dd, J=4.3, 13.4 Hz, CHHSPh), 4.10 (3H, m, >CHCH$_3$, CH$_2$CH$_3$), 7.24—7.66 (15H, m, Ph × 3). Exact Mass Calcd for $C_{29}H_{36}O_3SSi-tert$-Bu: 435.1449. Found: 435.1464.

(3*R*)-3-Hydroxy-2-(hydroxymethyl)-1-(phenylthio)butane (10) A solution of **9d** (119 mg, 0.243 mmol) in dry THF (3 ml) was added to a stirred suspension of $LiAlH_4$ (46.2 mg, 1.22 mmol) in dry THF (2 ml) at 0 °C under nitrogen. After 10 min, AcOEt (10 ml) and water (1 ml) were added, and the precipitate was removed through a Celite pad. Concentration and purification by column chromatography on silica gel (50% AcOEt in hexane) gave **10** (39.2 mg, 76%) as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 3625, 3575—3200. ^{1}H-NMR ($CDCl_3$) δ: 1.249 (89/100 × 3H, d, J=6.8 Hz, CH$_3$CH<), 1.303 (11/100 × 3H, d, J=6.8 Hz, CH$_3$CH<), 1.695 (11/100 × 1H, m, >CHCH$_2$SPh), 1.825 (89/100 × 1H, m, >CHCH$_2$SPh), 2.097 (1H, dd, J=4.5, 5.2 Hz, HOCH$_2$), 2.336 (11/100 × 1H, d, J=5.0 Hz, HOCH<), 2.444 (89/100 × 1H, d, J=3.4 Hz, HOCH<), 3.027 (89/100 × 1H, dd, J=9.1, 13.3 Hz, CHHSPh), 3.083 (11/100 × 1H, dd, J=5.5, 13.3 Hz, CHHSPh), 3.140 (89/100 × 1H, dd, J=4.4, 13.3 Hz, CHHSPh), 3.180 (11/100 × 1H, dd, J=6.0, 13.3 Hz, CHHSPh), 3.830 (89/100 × 1H, dt, J=10.4, 4.2 Hz, CHHOH), 3.873 (11/100 × 1H, m, CHHOH), 4.025 (89/100 × 1H, dt, J=10.4, 5.2 Hz, CHHOH), 4.063 (11/100 × 1H, m, CHHOH), 4.122 (11/100 × 1H, m, >CHOH), 4.178 (89/100 × 1H, tq, J=3.4, 6.8 Hz, >CHOH), 7.15—7.41 (5H, m, Ph). Exact Mass Calcd for $C_{11}H_{16}O_2S$: 212.0869. Found: 212.0844.

(4*R*)-5-(Phenylthiomethyl)-1,1,4-trimethyl-1,3-dioxane (11) A mixture of **10** (89 : 11, 32.2 mg, 1.52 mmol) and *p*-TsOH (3 mg) in 2,2-dimethoxypropane (2 ml) was stirred at room temperature for 5 min. The reactant was directly purified by preparative TLC with 10% AcOEt in hexane to give **11** (34.5 mg, 90%) as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 3020, 1150, 1080. ^{1}H-NMR ($CDCl_3$) δ: 1.195 (88/100 × 3H, d, J=6.1 Hz, CH$_3$CH<), 1.213 (12/100 × 3H, d, J=6.1 Hz, CH$_3$CH<), 1.388, 1.447 (total 12/100 × 6H, each s, Me$_2$C<), 1.402, 1.454 (88/100 × 6H, each s, Me$_2$C<), 1.426 (88/100 × 1H, m, >CHCH$_2$SPh), 1.807 (12/100 × 1H, m,

>CHCH$_2$SPh), 2.637 (12/100 × 1H, dd, J=9.2, 12.8 Hz, CHHSPh), 3.024 (12/100 × 1H, dd, J=3.7, 12.8 Hz, CHHSPh), 3.200 (88/100 × 2H, d, J=7.3 Hz, CH$_2$SPh), 3.683 (12/100 × 1H, dd, J=10.5, 11.6 Hz, CHHO), 3.808 (12/100 × 1H, dq, J=9.8, 6.9 Hz, >CHCH$_3$), 3.964 (88/100 × 1H, dd, J=2.4, 11.9 Hz, CHHO), 3.990 (12/100 × 1H, dd, J=5.0, 11.6 Hz, CHHO), 4.117 (88/100 × 1H, dd, J=1.2, 11.9 Hz, CHHO), 4.227 (88/100 × 1H, dq, J=2.4, 6.1 Hz, >CHCH$_3$), 7.13—7.37 (5H, m, Ph). (The signals indicated this product to be a mixture of diastereomers (**11a** : **11b** = 88 : 12).) Exact Mass Calcd for $C_{14}H_{20}O_2S$: 252.1184. Found: 252.1184.

General Procedure for the Preparation of Amides (12a—d) A 1.0 M solution of $AlMe_3$ in hexane (20 mmol) was added to a stirred suspension (or solution) of methoxybenzylamine (20 mmol) in dry benzene (20 ml) at 0 °C under nitrogen. The mixture was stirred at 0 °C for 20 min and at room temperature for 40 min. The ester (**9b** or **d**) (5 mmol) in dry benzene (30 ml) was added to the mixture, which was refluxed for 3 d and cooled to 0 °C. Then 10% hydrochloric acid was added to decompose excess $AlMe_3$, and the mixture was extracted with AcOEt : Et_2O = 1 : 1 (300 ml × 3). The combined organic layer was washed with water, saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was subjected to Lobar column chromatography on silica gel with CH_2Cl_2 or 15% AcOEt in hexane to give the corresponding amides (*anti*-**12** and *syn*-**12**).

(3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (12a) This (1.82 g, 77%, *anti* : *syn* = 79 : 21) was obtained from **9b** (1.79 g, 4.86 mmol, *anti* : *syn* = 79 : 21), 2,4-DMBNH$_2$·HCl (3.97 g, 19.4 mmol), and $AlMe_3$ (1.0 M solution in hexane, 19.4 ml, 19.4 mmol) as a pale yellow oil. *Anal.* Calcd for $C_{26}H_{39}NO_4SSi$: C, 63.76; H, 8.03; N, 2.86; S, 6.55. Found: C, 63.71; H, 8.13; N, 2.84; S, 6.46. Both isomers were isolated in a pure state by column chromatography.

(2*S*,3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (*anti*-**12a**): $[\alpha]_D^{22}$ −21.11° (c=2.24, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3350, 1665. ^{1}H-NMR ($CDCl_3$) δ: 0.024, 0.031 (total 6H, each s, Me_2Si), 0.823 (9H, s, *tert*-Bu), 1.045 (3H, d, J=6.1 Hz, CH_3CH<), 2.407 (1H, dt, J=6.1, 7.4 Hz, >CHCO), 3.040 (1H, dd, J=6.1, 14.0 Hz, CHHSPh), 3.356 (1H, dd, J=7.9, 14.0 Hz, CHHSPh), 3.772, 3.785 (total 6H, each s, OMe × 2), 4.105 (1H, quint, J=6.1 Hz, >CHCH$_3$), 4.273, 4.420 (total 2H, each dd, J=6.1, 14.0 Hz, NHCH$_2$Ar), 6.48 (1H, br m, NH), 6.40—7.35 (8H, m, ArH). Exact Mass Calcd for $C_{26}H_{39}NO_4SSi$: 489.2366. Found: 489.2366.

(2*R*,3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (*syn*-**12a**): $[\alpha]_D^{22}$ +0.748° (c=1.07, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3400, 1660. ^{1}H-NMR ($CDCl_3$) δ: 0.0537, 0.0720 (total 6H, each s, Me_2Si), 0.779 (9H, s, *tert*-Bu), 1.184 (3H, d, J=6.5 Hz, CH_3CH<), 2.367 (1H, ddd, J=3.7, 5.9, 8.9 Hz, >CHCO), 3.034 (1H, dd, J=8.9, 13.5 Hz, CHHSPh), 3.251 (1H, dd, J=5.9, 13.5 Hz, CHHSPh), 3.779, 3.794 (total 6H, each s, OMe × 2), 4.21—4.27 (1H, m, >CHCH$_3$), 4.243, 4.439 (total 2H, each dd, J=5.5, 14.0 Hz, NHCH$_2$Ar), 6.863 (1H, br s, NH), 6.40—7.40 (8H, m, ArH). Exact Mass Calcd for $C_{26}H_{39}NO_4SSi$: 489.2366. Found: 489.2359.

(3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (12b) This (202 mg, 78%, *anti* : *syn* = 80 : 20) was obtained from **9b** (207 mg, 0.564 mmol, *anti* : *syn* = 79 : 21), *p*-MBNH$_2$ (386 g, 2.82 mmol), and $AlMe_3$ (1.0 M solution in hexane, 2.8 ml, 2.8 mmol) as a yellow oil. Both isomers were isolated in a pure state by column chromatography.

(2*S*,3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (*anti*-**12b**): $[\alpha]_D^{22}$ −19.80° (c=0.970, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3010, 1660. ^{1}H-NMR ($CDCl_3$) δ: 0.0195, 0.0342 (total 6H, each s, Me_2Si), 0.8005 (9H, s, *tert*-Bu), 1.094 (3H, d, J=6.1 Hz, CH_3CH<), 2.461 (1H, dt, J=6.3, 7.9 Hz, >CHCO), 3.034 (1H, dd, J=6.3, 14.0 Hz, CHHSPh), 3.395 (1H, dd, J=7.9, 14.0 Hz, CHHSPh), 3.790 (3H, s, OMe), 4.149 (1H, quint, J=6.3 Hz, >CHCH$_3$), 4.298, 4.417 (total 2H, each dd, J=5.5, 14.6 Hz, NHCH$_2$Ar), 6.436 (1H, br m, NH), 6.81—7.40 (9H, m, ArH). Exact Mass Calcd for $C_{25}H_{37}NO_3SSi$: 459.2263. Found: 459.2281.

(2*R*,3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (*syn*-**12b**): $[\alpha]_D^{22}$ +14.44° (c=2.106, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3010, 1660. ^{1}H-NMR ($CDCl_3$) δ: 0.057, 0.079 (total 6H, each s, Me_2Si), 0.760 (9H, s, *tert*-Bu), 1.209 (3H, d, J=6.1 Hz, CH_3CH<), 2.404 (1H, ddd, J=3.7, 6.1, 9.2 Hz, >CHCO), 3.046 (1H, dd, J=9.2, 13.4 Hz, CHHSPh), 3.277 (1H, dd, J=6.1, 13.4 Hz, CHHSPh), 3.790 (3H, s, OMe), 4.215 (1H, dd, J=4.9, 14.7 Hz, NHCHHAr), 4.254 (1H, dq, J=3.7, 6.1 Hz, >CHCH$_3$), 4.478 (1H, dd, J=6.1, 14.7 Hz, NHCHHAr), 6.903 (1H, br s, NH), 6.83—7.36 (9H, m, ArH). Exact Mass Calcd for $C_{25}H_{37}NO_3SSi$: 459.2260. Found: 459.2253.

(3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (12c) This (1.04 g, 63%, *anti* : *syn* = 88 : 12) was obtained from **9d** (1.32 g, 2.67 mmol, *anti* : *syn* = 89 : 11), 2,4-DMBNH$_2$·HCl (1.64 g, 8.02 mmol), and $AlMe_3$ (1.0 M solution in hexane, 8.0 ml, 8.0 mmol) as a pale yellow oil. Both isomers were isolated in a pure state by column chromatography.

(2*S*,3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (*anti*-**12c**): $[\alpha]_D^{25}$ −10.20° (c=1.57, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3375. ^{1}H-NMR ($CDCl_3$) δ: 0.928 (3H, d, J=6.1 Hz, CH_3CH<), 0.975 (9H, s, *tert*-Bu), 2.584 (1H, dt, J=4.9, 7.3 Hz, >CHCO), 2.900 (1H, dd, J=7.3, 14.0 Hz, CHHSPh), 3.318 (1H, dd, J=7.3, 14.0 Hz, CHHSPh), 3.705, 3.790 (total 6H, each s, OMe × 2), 4.178 (1H, dq, J=4.9, 6.1 Hz, >CHCH$_3$), 4.317, 4.454 (total 2H, each dd, J=6.1, 14.0 Hz, NHCH$_2$Ar), 6.564 (1H, br t, J=6.1 Hz, NH), 6.3—7.7 (18H, m, ArH). Exact Mass Calcd for $C_{36}H_{43}NO_4SSi$: 613.2679. Found: 613.2677.

(2*R*,3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (*syn*-**12c**): $[\alpha]_D^{26}$ +5.585° (c=0.716, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3378. ^{1}H-NMR ($CDCl_3$) δ: 0.986 (9H, s, *tert*-Bu), 1.079 (3H, d, J=6.7 Hz, CH_3CH<), 2.260 (1H, ddd, J=3.7, 6.7, 7.7 Hz, >CHCO), 3.174 (1H, dd, J=6.7, 13.4 Hz, CHHSPh), 3.243 (1H, dd, J=7.7, 13.4 Hz, CHHSPh), 3.717, 3.809 (total 6H, each s, OMe × 2), 4.095 (1H, dq, J=3.7, 6.7 Hz, >CHCH$_3$), 4.269, 4.404 (total 2H, each dd, J=5.5, 14.0 Hz, NHCH$_2$Ar), 6.204 (1H, br t, J=7.1 Hz, NH), 6.4—7.7 (18H, m, ArH). Exact Mass Calcd for $C_{36}H_{43}NO_4SSi$: 613.2681. Found: 613.2681.

(3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (12d) This (3.35 g, 87%, *anti* : *syn* = 88 : 12) was obtained from **9d** (3.25 g, 6.61 mmol, *anti* : *syn* = 89 : 11), *p*-MBNH$_2$ (4.53 g, 33.1 mmol), and $AlMe_3$ (1.0 M solution in hexane, 33.1 ml, 33.1 mmol) as a pale yellow oil. Both isomers were isolated in a pure state by column chromatography.

(2*S*,3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (*anti*-**12d**): $[\alpha]_D^{23}$ −13.32° (c=2.82, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3358, 1666. ^{1}H-NMR ($CDCl_3$) δ: 0.953 (9H, s, *tert*-Bu), 0.972 (3H, d, J=5.8 Hz, CH_3CH<), 2.618 (1H, dt, J=5.8, 7.0 Hz, >CHCO), 2.898 (1H, dd, J=7.0, 14.0 Hz, CHHSPh), 3.346 (1H, dd, J=7.0, 14.0 Hz, CHHSPh), 3.789 (3H, s, OMe), 4.214 (1H, quint, J=5.8 Hz, >CHCH$_3$), 4.310, 4.447 (total 2H, each dd, J=5.5, 14.5 Hz, NHCH$_2$Ar), 6.491 (1H, br s, NH), 6.836 (2H, d, J=8.4 Hz, ArH), 7.16—7.59 (17H, m, ArH). Exact Mass Calcd for $C_{35}H_{41}NO_3SSi$: 583.2577. Found: 583.2577.

(2*R*,3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (*syn*-**12d**): $[\alpha]_D^{28}$ +8.891° (c=1.500, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3350, 1650. ^{1}H-NMR ($CDCl_3$) δ: 0.976 (9H, s, *tert*-Bu), 1.113 (3H, d, J=6.1 Hz, CH_3CH<), 2.269 (1H, m, >CHCO), 3.184 (1H, dd, J=6.7, 13.4 Hz, CHHSPh), 3.261 (1H, dd, J=8.6, 13.4 Hz, CHHSPh), 3.803 (3H, s, OMe × 2), 4.101 (1H, dq, J=3.5, 6.1 Hz, >CHCH$_3$), 4.153 (1H, dd, J=4.9, 14.7 Hz, NHCHHAr), 4.449 (1H, dd, J=5.8, 14.7 Hz, NHCHHAr), 6.054 (1H, br m, NH), 6.58—7.62 (19H, m, ArH). Exact Mass Calcd for $C_{35}H_{41}NO_3SSi$: 583.2574. Found: 583.2567.

General Procedure for the Preparation of β-Amido Sulfoxides (4a—d) $NaIO_4$ (1.5 mmol) was added to a stirred solution of the sulfide (*anti*-**12a—d**, 1 mmol) in MeOH (10 ml). The mixture was stirred at room temperature overnight, then diluted with CH_2Cl_2. Insoluble material was filtered off, and the solvent was removed *in vacuo*. The residue was subjected to column chromatography on silica gel with 30—50% AcOEt in hexane to give the corresponding sulfoxide.

(2*S*,3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-(2,4-dimethoxybenzyl)-2-(phenylsulfinylmethyl)butanamide (4a) This (1.15 g, 89%) was obtained from *anti*-**12a** (1.25 g, 2.55 mmol), and $NaIO_4$ (819 mg, 3.83 mmol) in MeOH as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 3460, 3400, 1660, 1620, 1595, 1040. ^{1}H-NMR ($CDCl_3$) δ: 0.0098, 0.0207, 0.0413, 0.0476 (total 6H, each s, Me_2Si), 0.792, 0.815 (total 9H, each s, *tert*-Bu), 1.026, 1.088 (total 3H, each d, J=6.1 Hz, CH_3CH<), 2.756 (1/2 × 1H, dd, J=3.0, 12.5 Hz, CHHS(O)Ph), 2.688 (1/2 × 1H, q, J=6.1 Hz, >CHCO), 2.847 (1/2 × 1H, dd, J=6.1, 13.5 Hz, CHHS(O)Ph), 3.013 (1/2 × 1H, ddd, J=3.0, 5.0, 10.5 Hz, >CHCO), 3.262 (1/2 × 1H, dd, J=10.5, 12.5 Hz, CHHS(O)Ph), 3.372 (1/2 × 1H, dd, J=6.1, 13.5 Hz, CHHS(O)Ph), 3.783, 3.785, 3.788, 3.807 (total 6H, each s, OMe × 2), 3.964 (1/2 × 1H, quint, J=6.1 Hz, >CHCH$_3$), 4.109 (1/2 × 1H, dq, J=5.0, 6.1 Hz, >CHCH$_3$), 4.153, 4.339 (total 1/2 × 2H, each dd, J=5.5, 14.0 Hz, NHCH$_2$Ar), 4.312, 4.498 (total 1/2 × 2H, each dd, J=5.5, 15.0 Hz, NHCH$_2$Ar), 6.696, 6.909 (total 1H, each br t, J=5.5 Hz, NH), 6.39—7.69 (8H, m, ArH). (The signals indicated this product to be a 1 : 1 mixture of geometrical isomers.) Exact Mass

Calcd for $C_{26}H_{39}NO_5SSi$: 505.2315. Found: 505.2314.

(2*S*,3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-(*p*-methoxybenzyl)-2-(phenylsulfinylmethyl)butanamide (4b) This (125 mg, 78%) was obtained from *anti*-**12b** (155 mg, 0.339 mmol), and $NaIO_4$ (119 mg, 0.554 mmol) in MeOH as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 3355, 1655, 1027. ^{1}H-NMR ($CDCl_3$) δ: 0.0146, 0.0293, 0.0476 (total 6H, each s, Me_2Si), 0.775, 0.792 (total 9H, each s, *tert*-Bu), 1.047, 1.135 (total 3H, each d, J=6.1 Hz, CH_3CH<), 2.640 (1/2 × 1H, dd, J=3.0, 12.8 Hz, CHHS(O)Ph), 2.768 (1/2 × 1H, dt, J=5.9, 6.1 Hz, >CHCO), 2.853 (1/2 × 1H, dd, J=6.1, 13.4 Hz, CHHS(O)Ph), 3.058 (1/2 × 1H, ddd, J=3.0, 4.9, 10.5 Hz, >CHCO), 3.295 (1/2 × 1H, dd, J=10.5, 12.8 Hz, CHHS(O)Ph), 3.389 (1/2 × 1H, dd, J=5.9, 13.4 Hz, CHHS(O)Ph), 3.790, 3.796 (total 3H, each s, OMe), 3.990 (1/2 × 1H, dq, J=4.9, 6.1 Hz, >CHCH$_3$), 4.158, 4.228, 4.338, 4.513 (total 2H, each dd, J=5.8, 14.3 Hz, NHCH$_2$Ar), 4.162 (1/2 × 1H, m, >CHCH$_3$), 6.742, 6.950 (total 1H, each br s, NH), 6.82—7.70 (9H, m, ArH). (The signals indicated this product to be a 1 : 1 mixture of geometrical isomers.) Exact Mass Calcd for $C_{25}H_{37}NO_4SSi$: 475.2213. Found: 475.2225.

(2*S*,3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-*N*-(2,4-dimethoxybenzyl)-2-(phenylsulfinylmethyl)butanamide (4c) This (404 mg, 66%) was obtained from *anti*-**12c** (597 mg, 0.975 mmol), and $NaIO_4$ (417 mg, 1.95 mmol) in MeOH as a colorless gum. IR ν_{max} ($CHCl_3$) cm^{-1}: 3450, 3390, 1660, 1039. ^{1}H-NMR ($CDCl_3$) δ: 0.913, 0.953 (total 3H, each d, J=6.0 Hz, CH_3CH<), 0.976, 0.980 (total 9H, each s, *tert*-Bu), 2.553 (1/2 × 1H, dd, J=1.2, 11.3 Hz, CHHS(O)Ph), 2.689 (1/2 × 1H, dd, J=6.1, 13.5 Hz, CHHS(O)Ph), 2.855 (1/2 × 1H, dt, J=6.1, 4.5 Hz, >CHCO), 3.129 (1/2 × 2H, m, >CHCO, CHHS(O)Ph), 3.350 (1/2 × 1H, dd, J=6.1, 13.5 Hz, CHHS(O)Ph), 3.720, 3.749, 3.780 (total 6H, each s, OMe × 2), 3.930, 4.093 (total 1H, each dq, J=4.5, 6.0 Hz, >CHCH$_3$), 4.225, 4.392 (total 1/2 × 2H, dd, J=5.1, 13.9 Hz, NHCH$_2$Ar), 4.358, 4.538 (total 1/2 × 2H, each dd, J=6.0, 13.9 Hz, NHCH$_2$Ar), 6.682, 6.872 (total 1H, each br m, NH), 6.39—7.62 (18H, m, ArH). (The signals indicated this product to be a 1 : 1 mixture of geometrical isomers). MS m/z: 504 (M^+ − SOPh), 503 (M^+ − HOSPh). Exact Mass Calcd for $C_{36}H_{43}NO_5SSi$ − HOSPh: 503.2488. Found: 503.2486.

(2*S*,3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-*N*-(*p*-methoxybenzyl)-2-(phenylsulfinylmethyl)butanamide (4d) This (2.07 g, 83%) was obtained from *anti*-**12d** (2.43 g, 4.16 mmol), and $NaIO_4$ (1.34 g, 6.25 mmol) in MeOH as a colorless powder, mp 41—43 °C (hexane/CH_2Cl_2). IR ν_{max} ($CHCl_3$) cm^{-1}: 3380, 1655, 1040. ^{1}H-NMR ($CDCl_3$) δ: 0.941, 0.999 (total 3H, each d, J=6.1 Hz, CH_3CH<), 0.957, 0.959 (total 9H, each s, *tert*-Bu), 2.550 (1/2 × 1H, d, J=9.8 Hz, CHHS(O)Ph), 2.724 (1/2 × 1H, dd, J=6.1, 14.0 Hz, CHHS(O)Ph), 2.919 (1/2 × 1H, dt, J=4.5, 6.1 Hz, >CHCO), 3.160 (1/2 × 2H, m, >CHCO, CHHS(O)Ph), 3.366 (1/2 × 1H, dd, J=6.1, 14.0 Hz, CHHS(O)Ph), 3.788 (3H, s, OMe), 3.972, 4.148 (total 1H, each m, >CHCH$_3$), 4.178, 4.552 (total 1/2 × 2H, dd, J=6.1, 14.6 Hz, NHCH$_2$Ar), 4.355 (1/2 × 2H, m, NHCH$_2$Ar), 6.695, 6.928 (total 1H, each br m, NH), 6.82—7.62 (19H, m, ArH). (The signals indicated this product to be a 1 : 1 mixture of geometrical isomers.) MS m/z: 542 (M^+ − *tert*-Bu), 473 (M^+ − HOSPh). Exact Mass Calcd for $C_{35}H_{41}NO_4SSi$ − HOSPh: 473.2385. Found: 473.2380.

General Procedure for the Reaction of β-Amido Sulfoxides (4a—d) with the Ketene Silyl Acetal (13a) The ketene silyl acetal (**13a**, 3—5 mmol) was added to a stirred solution of β-amido sulfoxide (**4**, 1 mmol) and ZnI_2 (0.05—0.1 mmol) in dry CH_3CN (10 ml) at room temperature under nitrogen. The mixture was stirred at 70 °C for 8 h, then partitioned between CH_2Cl_2 (100 ml) and saturated aqueous $NaHCO_3$ (50 ml). The aqueous layer was extracted with CH_2Cl_2 (100 ml × 2). The combined extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel with 10% hexane–AcOEt to give the cyclized product.

(3*S*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (5a) This (*trans*-**5a**, 481 mg, 52%, *cis*-**5a**, 116 mg, 13%) was obtained from **4a** (952 mg, 1.89 mmol), **13a** (1.77 g, 9.43 mmol), and ZnI_2 (60.3 mg, 0.189 mmol) in CH_3CN as a pale yellow oil.

(3*S*,4*R*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (*trans*-**5a**): $[\alpha]_D^{22}$ −36.09° (c=1.05, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1750, 1620, 1595. ^{1}H-NMR ($CDCl_3$) δ: −0.074, 0.015 (total 6H, each s, Me_2Si), 0.774 (9H, s, *tert*-Bu), 1.177 (3H, d, J=6.7 Hz, CH_3CH<), 2.918 (1H, dd, J=2.4, 3.7 Hz, >CHCO), 3.743, 3.795 (total 6H, each s, OMe × 2), 4.137 (1H, dq, J=3.7, 6.7 Hz, >CHCH$_3$), 4.285, 4.499 (2H, AB-q, J=15.3 Hz, >NCH$_2$Ar), 4.907 (1H, d, J=2.4 Hz, >CHSPh), 6.35—7.40 (8H, m, ArH). Exact Mass Calcd for $C_{26}H_{37}NO_4SSi$ − *tert*-Bu: 430.1505. Found: 430.1504.

(3*S*,4*S*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (*cis*-**5a**): $[\alpha]_D^{23}$ −35.08° (c=1.23, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1745, 1615, 1590. ^{1}H-NMR ($CDCl_3$) δ: 0.012 (6H, s, Me_2Si), 0.93 (9H, s, *tert*-Bu), 1.45 (3H, d, J=6.7 Hz, CH_3CH<), 3.44 (1H, t, J=5.0 Hz, >CHCO), 3.59, 3.75 (total 6H, each s, OMe × 2), 4.11, 4.56 (2H, AB-q, J=15.0 Hz, >NCH$_2$Ar), 4.43 (1H, m, >CHCH$_3$), 4.95 (1H, d, J=5.0 Hz, >CHSPh), 6.15—7.31 (8H, m, ArH). Exact Mass Calcd for $C_{26}H_{37}NO_4SSi$: 487.2210. Found: 487.2198.

(3*S*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (5b) This (*trans*-**5b**, 29.3 mg, 45.0%, *cis*-**5b**, 7.30 mg, 11.2%) was obtained from **4b** (67.8 mg, 0.143 mmol), **13a** (134 mg, 0.715 mmol), and ZnI_2 (4.60 mg, 0.0143 mmol) in CH_3CN as a pale yellow oil.

(3*S*,4*R*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (*trans*-**5b**): $[\alpha]_D^{22}$ −23.13° (c=1.58, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1745, 1520. ^{1}H-NMR ($CDCl_3$) δ: −0.0098, 0.0342 (total 6H, each s, Me_2Si), 0.798 (9H, s, *tert*-Bu), 1.173 (3H, d, J=6.1 Hz, CH_3CH<), 2.976 (1H, br s, >CHCO), 3.792 (3H, s, OMe), 4.098, 4.628 (2H, AB-q, J=15.0 Hz, >NCH$_2$Ar), 4.184 (1H, dq, J=3.5, 6.1 Hz, >CHCH$_3$), 4.897 (1H, d, J=1.8 Hz, >CHSPh), 6.803, 7.101 (total 4H, each d, J=8.6 Hz, Ar-H), 7.14—7.35 (5H, m, SPh). Exact Mass Calcd for $C_{25}H_{35}NO_3SSi$ − *tert*-Bu: 400.1400. Found: 400.1400.

(3*S*,4*S*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (*cis*-**5b**): $[\alpha]_D^{22}$ −33.83° (c=0.541, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1745. ^{1}H-NMR ($CDCl_3$) δ: 0.105, 0.121 (total 6H, each s, Me_2Si), 0.923 (9H, s, *tert*-Bu), 1.439 (3H, d, J=6.1 Hz, CH_3CH<), 3.456 (1H, t, J=4.8 Hz, >CHCO), 3.755 (3H, s, OMe), 3.939, 4.650 (2H, AB-q, J=15.0 Hz, >NCH$_2$Ar), 4.425 (1H, dq, J=4.8, 6.1 Hz, >CHCH$_3$), 4.960 (1H, d, J=4.8 Hz, >CHSPh), 6.704, 6.803 (total 4H, each d, J=8.5 Hz, ArH), 6.83—7.33 (5H, m, SPh). Exact Mass Calcd for $C_{25}H_{35}NO_3SSi$ − *tert*-Bu: 400.1403. Found: 400.1411.

(3*S*)-3-[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (5c) This (*trans*-**5c**, 189 mg, 52%, *cis*-**5c**, 42.9 mg, 12%) was obtained from **4c** (371 mg, 0.590 mmol), **13a** (555 mg, 2.95 mmol), and ZnI_2 (18.8 mg, 0.0590 mmol) in CH_3CN as a pale yellow oil.

(3*S*,4*R*)-3-[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (*trans*-**5c**): $[\alpha]_D^{27}$ −22.88° (c=0.961, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1740, 1620, 1590. ^{1}H-NMR ($CDCl_3$) δ: 0.929 (9H, s, *tert*-Bu), 1.001 (3H, d, J=6.1 Hz, CH_3CH<), 2.949 (1H, dd, J=2.4, 5.3 Hz, >CHCO), 3.682, 3.781 (total 6H, each s, OMe × 2), 4.262 (1H, dq, J=5.3, 6.1 Hz, >CHCH$_3$), 4.266, 4.535 (2H, AB-q, J=15.2 Hz, >NCH$_2$Ar), 4.850 (1H, d, J=2.4 Hz, >CHSPh), 6.3—7.7 (18H, m, ArH). Exact Mass Calcd for $C_{36}H_{41}NO_4SSi$: 611.2525. Found: 611.2526.

(3*S*,4*S*)-3-[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (*cis*-**5c**): $[\alpha]_D^{26}$ −26.01° (c=0.961, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1750, 1615, 1590. ^{1}H-NMR ($CDCl_3$) δ: 1.068 (9H, s, *tert*-Bu), 1.304 (3H, d, J=6.7 Hz, CH_3CH<), 3.476 (1H, dd, J=4.2, 5.1 Hz, >CHCO), 3.595, 3.756 (total 6H, each s, OMe × 2), 4.147, 4.603 (2H, AB-q, J=15.1 Hz, >NCH$_2$Ar), 4.376 (1H, dq, J=4.2, 6.7 Hz, >CHCH$_3$), 4.968 (1H, d, J=5.1 Hz, >CHSPh), 6.2—7.9 (18H, m, ArH). Exact Mass Calcd for $C_{36}H_{41}NO_4SSi$: 611.2526. Found: 611.2534.

(3*S*)-3-[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (5d) This (*trans*-**5d**, 36.3 mg, 60%, inseparable 8 : 5 mixture of *cis*-**5d** and *anti*-**12d**, 13.5 mg) was obtained from **4d** (61.5 mg, 0.103 mmol), **13a** (96.5 mg, 0.513 mmol), and ZnI_2 (3.30 mg, 0.0103 mmol) in CH_3CN as a pale yellow oil.

(3*S*,4*R*)-3-[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (*trans*-**5d**): $[\alpha]_D^{25}$ −20.29° (c=0.237, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.96 (9H, s, *tert*-Bu), 0.99 (3H, d, J=6.7 Hz, CH_3CH<), 2.99 (1H, dd, J=1.8, 4.9 Hz, >CHCO), 3.78 (3H, s, OMe), 4.10, 4.63 (2H, AB-q, J=14.6 Hz, >NCH$_2$Ar), 4.22 (1H, dq, J=4.9, 6.7 Hz, >CHCH$_3$), 4.84 (1H, d, J=1.8 Hz, >CHSPh), 6.7—7.6 (19H, m, ArH). Exact Mass Calcd for $C_{35}H_{39}NO_3SSi$: 581.2417. Found: 581.2417. *Anal.* Calcd for $C_{35}H_{39}NO_3SSi$: C, 72.25; H, 6.76; N, 2.41; S, 5.51. Found: C, 72.31; H, 6.71; N, 2.37; S. 5.42.

(3*S*,4*S*)-3-[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (*cis*-**5d**): ^{1}H-NMR ($CDCl_3$) δ: 1.07 (9H, s, *tert*-Bu), 1.30 (3H, d, J=6.7 Hz, CH_3CH<), 3.50 (1H, dd, J=4.3, 5.5 Hz, >CHCO), 3.76 (3H, s, OMe), 3.96, 4.70 (2H, AB-q, J=15.3 Hz, >NCH$_2$Ar), 4.37 (1H, dq, J=4.3, 6.7 Hz, >CHCH$_3$), 4.98 (1H, d, J=5.5 Hz, >CHSPh), 6.7—7.8 (19H, m, ArH). MS m/z: 524 (M^+ − *tert*-Bu).

General Procedure for the Preparation of 4-Phenylsulfinylazetidin-2-ones (14a—d) *m*-CPBA (80%, 1 mmol) was added to a stirred solution of 4-phenylthioazetidin-2-one (**5a—d**, 1 mmol) in CH_2Cl_2 (10 ml) at 0 °C for 20 min. The reaction mixture was diluted with CH_2Cl_2 (100 ml) and washed

with saturated aqueous $NaHCO_3$ (50 ml). The aqueous layer was extracted with CH_2Cl_2 (100 ml × 2). The combined organic extract was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel with 30% AcOEt in hexane to give the corresponding sulfoxide.

(3*S*,4*R*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylsulfinyl)azetidin-2-one (*trans*-14a) This (*trans*-**14a**, 330 mg, 89%) was obtained from *trans*-**5a** (358 mg, 0.734 mmol), and *m*-CPBA (80%, 166 mg, 0.771 mmol) in CH_2Cl_2 as a pale yellow oil. IR ν_{max} ($CHCl_3$) cm^{-1}:1765, 1615, 1590, 1050. ^{1}H-NMR ($CDCl_3$) δ: −0.108, −0.100, −0.096, −0.008 (total 6H, each s, Me_2Si), 0.001 (55/100 × 3H, d, J=6.5 Hz, CH_3CH<), 0.702, 0.879 (total 9H, each s, *tert*-Bu), 0.972 (45/100 × 3H, d, J=6.5 Hz, CH_3CH<), 3.014 (45/100 × 1H, dd, J=1.8, 3.5 Hz, >CHCO), 3.502 (55/100 × 1H, br s, >CHCO), 3.782, 3.789, 3.808, 3.896 (total 6H, each s, OMe × 2), 4.03—4.11 (1H, m, >C<u>H</u>CH$_3$), 4.142, 4.445 (45/100 × 2H, AB-q, J=14.7 Hz, >NC<u>H</u>$_2$Ar), 4.399 (55/100 × 1H, d, J=1.8 Hz, >C<u>H</u>S(O)Ph), 4.512 (55/100 × 2H, d, J=1.8 Hz, >NC<u>H</u>$_2$Ar), 4.598 (45/100 × 1H, d, J=1.8 Hz, >C<u>H</u>S(O)Ph), 6.38—7.52 (8H, m, ArH). (The signals indicated this product to be a 55:45 mixture of geometrical isomers.) Exact Mass Calcd for $C_{26}H_{37}NO_5SSi$ − *tert*-Bu: 446.1457. Found: 446.1458.

(3*S*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylsulfinyl)azetidin-2-one (14a, *trans*/*cis* mixture) This (**14a**, *trans*/*cis* mixture, 29.0 mg, 82%) was obtained from **5a** (*trans*:*cis*=4.1:1, 34.3 mg, 0.0704 mmol), and *m*-CPBA (80%, 15.2 mg, 0.0704 mmol) in CH_2Cl_2 as a yellow oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 1770, 1040. MS *m*/*z*: 378 (M^+ − S(O)Ph), 377 (M^+ − HOSPh). ^{1}H-NMR ($CDCl_3$) (signals of *cis*-**14a**) δ: 0.1431, 0.1639, 0.1675, 0.1846 (total 20/100 × 6H, each s, Me_2Si), 0.8936, 0.9778 (total 20/100 × 9H, each s, *tert*-Bu), 1.3866, 1.5300 (total 20/100 × 3H, d, J=6.1 Hz, CH_2CH<), 2.7748, 4.2030 (10/100 × 2H, AB-q, J=15.0 Hz, >NC<u>H</u>$_2$Ar), 3.420 (10/100 × 1H, dd, J=5.0, 9.5 Hz, >CHCO), 3.516, 4.631 (10/100 × 2H, AB-q, J=15.0 Hz, >NC<u>H</u>$_2$Ar), 3.548 (10/100 × 1H, dd, J=3.5, 5.0 Hz, >CHCO), 3.6198, 3.6686, 3.7272, 3.7504 (total 20/100 × 6H, each s, OMe × 2), 4.258, 4.338 (total 20/100 × 1H, each d, J=5.0 Hz, >C<u>H</u>S(O)Ph), 4.6 (10/100 × 1H, m, >C<u>H</u>CH$_3$), 4.756 (10/100 × 1H, dq, J=9.5, 6.1 Hz, >C<u>H</u>CH$_3$), 6.08—7.70 (20/100 × 8H, m, ArH). (The signals indicated this product to be a 4:4:1:1 mixture of geometrical isomers.)

(3*S*,4*R*)-3-[(*R*)-1-{(*tert*-Butyldimethylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)-4-(phenylsulfinyl)azetidin-2-one (*trans*-14b) This (*trans*-**14b**, 90.5 mg, 80%) was obtained from *trans*-**5b** (110 mg, 0.241 mmol), and *m*-CPBA (80%, 57.2 mg, 0.265 mmol) in CH_2Cl_2 as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 1760, 1610, 1590, 1060. ^{1}H-NMR ($CDCl_3$) δ: −0.049, −0.040, −0.008, 0.002 (total 6H, each s, Me_2Si), 0.156 (55/100 × 3H, d, J=6.7 Hz, CH_3CH<), 0.7859 (9H + 45/100 × 3H, s, *tert*-Bu, CH_3CH<), 3.220 (45/100 × 1H, m, >CHCO), 3.535 (55/100 × 1H, br s, >CHCO), 3.784, 3.828 (total 3H, each s, OMe), 4.040, 4.558 (45/100 × 2H, AB-q, J=15.0 Hz, >NC<u>H</u>$_2$Ar), 4.135 (1H, m, >C<u>H</u>CH$_3$), 4.338 (55/100 × 1H, d, J=2.0 Hz, >C<u>H</u>S(O)Ph), 4.447, 4.614 (55/100 × 2H, AB-q, J=15.0 Hz, >NC<u>H</u>$_2$Ar), 4.533 (45/100 × 1H, d, J=2.0 Hz, >C<u>H</u>S(O)Ph), 6.7—7.6 (9H, m, ArH). (The signals indicated this product to be a 55:45 mixture of geometrical isomers.) Exact Mass Calcd for $C_{25}H_{35}NO_4SSi$ − *tert*-Bu: 416.1350. Found: 416.1347.

(3*S*,4*R*)-3-[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylsulfinyl)azetidin-2-one (*trans*-14c) This (*trans*-**14c**, 149 mg, 85%) was obtained from *trans*-**5c** (171 mg, 0.279 mmol), and *m*-CPBA (80%, 66.2 mg, 0.307 mmol) in CH_2Cl_2 as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 1770, 1050. ^{1}H-NMR ($CDCl_3$) δ: −0.106 (45/100 × 3H, d, J=6.1 Hz, CH_3CH<), 0.875, 0.964 (total 9H, each s, *tert*-Bu), 0.902 (55/100 × 3H, d, J=6.1 Hz, CH_3CH<), 3.147 (45/100 × 1H, dd, J=1.8, 6.1 Hz, >CHCO), 3.543 (55/100 × 1H, br s, >CHCO), 3.661, 3.792, 3.794, 3.897 (total 6H, each s, OMe × 2), 3.993, 4.498 (45/100 × 2H, AB-q, J=14.6 Hz, >NC<u>H</u>$_2$Ar), 4.045 (45/100 × 1H, quint, J=6.1 Hz, >C<u>H</u>CH$_3$), 4.178 (55/100 × 1H, dq, J=2.0, 6.1 Hz, >C<u>H</u>CH$_3$), 4.520 (45/100 × 1H, d, J=1.8 Hz, >C<u>H</u>S(O)Ph), 4.556 (55/100 × 1H, d, J=1.8 Hz, >C<u>H</u>S(O)Ph), 4.596 (55/100 × 2H, d, J=4.9 Hz, >NC<u>H</u>$_2$Ar), 6.28—7.66 (18H, m, ArH). (The signals indicated this product to be a 55:45 mixture of geometrical isomers.) Exact Mass Calcd for $C_{36}H_{41}NO_5SSi$ − *tert*-Bu: 570.1767. Found: 570.1757.

(3*S*,4*R*)-3-[(*R*)-1-{(*tert*-Butyldiphenylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)-4-(phenylsulfinyl)azetidin-2-one (*trans*-14d) This (*trans*-**14d**, 66.4 mg, 83%) was obtained from *trans*-**5d** (78.1 mg, 0.134 mmol), and *m*-CPBA (80%, 28.3 mg, 0.148 mmol) in CH_2Cl_2 as a colorless oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 1765, 1050. ^{1}H-NMR ($CDCl_3$) δ: −0.0586, 0.705 (total 3H, each d, J=6.1 Hz, CH_3CH<), 0.9604, 0.9665 (total 9H, each s, *tert*-Bu), 3.304 (41/100 × 1H, dd, J=1.8, 5.5 Hz, >CHCO), 3.556 (59/100 × 1H, br s, >CHCO), 3.774, 3.807 (total 3H, each s, OMe), 3.939, 4.554 (41/100 × 2H, AB-q, J=15.3 Hz, >NC<u>H</u>$_2$Ar), 4.100 (41/100 × 1H, quint, J=6.1 Hz, >C<u>H</u>CH$_3$), 4.230 (59/100 × 1H, dq, J=1.8, 6.1 Hz, >C<u>H</u>CH$_3$), 4.478 (1H, br s, >C<u>H</u>S(O)Ph), 4.544, 4.651 (59/100 × 2H, AB-q, J=15.3 Hz, >NC<u>H</u>$_2$Ar), 6.71—7.63 (19H, m, ArH). (The signals indicated this product to be a 59:41 mixture of geometrical isomers.) Exact Mass Calcd for $C_{35}H_{39}NO_4SSi$ − *tert*-Bu: 540:1663. Found: 540.1663.

General Procedure for the Reaction of Sulfoxides (14a—d) with the Ketene Silyl Acetal (13b) The ketene silyl acetal (**13b**, 0.2 mmol) was added to a stirred solution of 4-phenylsulfinylazetidinone (**14a—d**, 0.1 mmol) and ZnI_2 (0.01 mmol) in dry CH_3CN (1 ml) at room temperature under nitrogen. The mixture was stirred at the same temperature for 3 h, then partitioned between CH_2Cl_2 (30 ml) and saturated aqueous $NaHCO_3$ (10 ml). The aqueous layer was extracted with CH_2Cl_2 (30 ml × 3). The combined extract was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel with 30% hexane–AcOEt to give the ester.

(3*S*,4*R*)-4-(Benzyloxycarbonylmethyl)-3-[(*R*)-1′-{(*tert*-butyldimethylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)azetidine-2-one (15a) 1) This (18.4 mg, 81%) was obtained from *trans*-**14a** (21.7 mg, 0.0431 mmol), **13b** (19.2 mg, 0.0862 mmol), and ZnI_2 (1.40 mg, 0.0862 mmol) in CH_3CN as a colorless oil. $[\alpha]_D^{22}$ −3.675° (*c*=0.816, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1740, 1615, 1590. ^{1}H-NMR ($CDCl_3$) δ: −0.0244, 0.0232 (total 6H, each s, Me_2Si), 0.792 (9H, s, *tert*-Bu), 1.104 (3H, d, J=6.1 Hz, CH_3CH<), 2.494 (1H, dd, J=7.0, 14.6 Hz, C<u>H</u>HCO$_2$), 2.713 (1H, dd, J=5.5, 14.6 Hz, CH<u>H</u>CO$_2$), 2.879 (1H, dd, J=1.8, 4.0 Hz, >CHCO), 3.767 (6H, s, OMe × 2), 3.958 (1H, m, >C<u>H</u>CH$_2$CO$_2$), 4.138 (1H, dq, J=4.0, 6.1 Hz, >C<u>H</u>CH$_3$), 4.197, 4.332 (2H, AB-q, J=15.0 Hz, >NC<u>H</u>$_2$Ar), 5.031 (2H, s, CO_2CH_2Ph), 6.40—7.36 (8H, m, ArH). Exact Mass Calcd for $C_{29}H_{41}NO_6SSi$: 527.2700. Found: 527.2695. 2) This (35.6 mg, 75%) was obtained from *trans*/*cis*-**14a** (*trans*:*cis*=4.1:1, 45.5 mg, 0.0903 mmol), **13b** (30.1 mg, 0.135 mmol), and ZnI_2 (2.90 mg, 0.00903 mmol) in CH_3CN as a colorless oil.

(3*S*,4*R*)-4-(Benzyloxycarbonylmethyl)-3-[(*R*)-1-{(*tert*-butyldimethylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)azetidin-2-one (15b) This (22.0 mg, 64%) was obtained from *trans*-**14b** (32.6 mg, 0.0691 mmol), **13b** (30.7 mg, 0.138 mmol), and ZnI_2 (2.00 mg, 0.00691 mmol) in CH_3CN as a colorless oil. $[\alpha]_D^{26}$ −3.506° (*c*=1.11, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1740, 1615. ^{1}H-NMR ($CDCl_3$) δ: 0.0223, 0.0516 (total 6H, each s, Me_2Si), 0.8412 (9H, s, *tert*-Bu), 1.147 (3H, d, J=6.1 Hz, CH_3CH<), 2.536 (2H, dd, J=3.8, 6.7 Hz, CH_2CO_2), 2.884 (1H, dd, J=2.1, 4.5 Hz, >CHCO), 3.762 (3H, s, OMe), 3.999 (1H, dt, J=2.1, 6.7 Hz, >C<u>H</u>CH$_2$CO$_2$), 4.160 (1H, dq, J=4.5, 6.1 Hz, >C<u>H</u>CH$_3$), 4.248, 4.304 (2H, AB-q, J=15.0 Hz, >NC<u>H</u>$_2$Ar), 5.008 (2H, d, J=2.6 Hz, CO_2CH_2Ph), 6.810, 7.156 (total 4H, each d, J=8.5 Hz, ArH), 7.2—7.4 (5H, m, C<u>H</u>$_2$Ph). Exact Mass Calcd for $C_{28}H_{39}NO_5SSi$ − *tert*-Bu: 440.1890. Found: 440.1887.

(3*S*,4*R*)-4-(Benzyloxycarbonylmethyl)-3-[(*R*)-1-{(*tert*-butyldiphenylsilyl)oxy}ethyl]-1-(2,4-dimethoxybenzyl)azetidine-2-one (15c) This (47.8 mg, 63%) was obtained from *trans*-**14c** (72.7 mg, 0.116 mmol), **13b** (51.5 mg, 0.232 mmol), and ZnI_2 (3.70 mg, 0.0116 mmol) in CH_3CN as a colorless oil. $[\alpha]_D^{30}$ −3.79° (*c*=1.82, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1740, 1620, 1590. ^{1}H-NMR ($CDCl_3$) δ: 0.9445 (9H, s, *tert*-Bu), 0.9482 (3H, d, J=6.1 Hz, CH_3CH<), 2.527, 2.716 (total 2H, each dd, J=6.1, 15.3 Hz, C<u>H</u>$_2$CO$_2$), 2.922 (1H, dd, J=2.0, 4.8 Hz, >CHCO), 3.729, 3.763 (total 6H, each s, OMe × 2), 3.984 (1H, dt, J=2.0, 6.1 Hz, >C<u>H</u>CH$_2$CO$_2$), 4.187 (1H, m, >C<u>H</u>CH$_3$), 4.215, 4.371 (2H, AB-q, J=15.3 Hz, >NC<u>H</u>$_2$Ar), 5.012 (2H, s, CO_2CH_2Ph), 6.3—7.3 (18H, m, ArH). MS *m*/*z*: 651 (M^+), 594 (M^+ − *tert*-Bu). Exact Mass Calcd for $C_{39}H_{45}NO_6SSi$ − *tert*-Bu: 594.2312. Found: 594.2319.

(3*S*,4*R*)-4-(Benzyloxycarbonylmethyl)-3-[(*R*)-1-{(*tert*-butyldiphenylsilyl)oxy}ethyl]-1-(*p*-methoxybenzyl)azetidin-2-one (15d) This (28.0 mg, 54%) was obtained from *trans*-**14d** (50.2 mg, 0.0841 mmol), **13b** (28.0 mg, 0.126 mmol), and ZnI_2 (2.30 mg, 0.00841 mmol) in CH_3CN as a pale yellow oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 1740. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (9H, s, *tert*-Bu), 0.99 (3H, d, J=6.5 Hz, CH_3CH<), 2.54 (2H, d, J=6.0 Hz, CH_2CO_2), 2.91 (1H, dd, J=2.4, 5.5 Hz, >CHCO), 3.75 (3H, s, OMe), 3.99 (1H, dt, J=2.4, 6.0 Hz, >C<u>H</u>CH$_2$CO$_2$), 4.15 (1H, m, >C<u>H</u>CH$_3$), 4.26 (2H, s, >NC<u>H</u>$_2$Ar), 4.97 (2H, s, CO_2CH_2Ph), 6.74, 7.09 (total 4H, each d, J=9.0 Hz, ArH), 7.21—7.73 (15H, m, Ar). Exact Mass Calcd for $C_{36}H_{43}NO_5SSi$ − *tert*-Bu: 564.2206. Found: 564.2211.

(3*S*,4*R*)-4-(Benzyloxycarbonylmethyl)-3-[(*R*)-1-{(*tert*-butyldimethylsilyl)oxy}ethyl]azetidin-2-one (16) A mixture of **15a** (15.3 mg, 0.0290 mmol), $K_2S_2O_8$ (78.3 mg, 0.290 mmol), and K_2HPO_4 (25.2 mg, 0.145 mmol) in CH_3CN/H_2O (1/1, 2 ml) was stirred at 65—75 °C for 1.5 h under nitrogen. The mixture was diluted with AcOEt (50 ml), and washed with saturated

aqueous $NaHCO_3$ (20 ml). The aqueous layer was extracted with AcOEt (50 ml × 2). The combined organic layer was washed with brine (30 ml), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by preparative TLC with 40% AcOEt in hexane to give **16** (6.10 mg, 56%) as colorless crystals. $[\alpha]_D^{24}$ +14.46° (c=0.558, $CHCl_3$). mp 91—92 °C (hexane). {lit.[11] $[\alpha]_D^{24}$ +17.4° (c=1.75, $CHCl_3$). mp 92—93 °C (hexane)}. IR ν_{max} ($CHCl_3$) cm^{-1}: 3450, 1760, 1730. ^{1}H-NMR ($CDCl_3$) δ: 0.0659, 0.0696 (total 6H, each s, Me_2Si), 0.869 (9H, s, *tert*-Bu), 1.193 (3H, d, J=6.1 Hz, CH_3CH<), 2.612 (1H, dd, J=9.8, 16.4 Hz, C<u>H</u>HCO$_2$), 2.786 (1H, dd, J=3.6, 16.4 Hz, CH<u>H</u>CO$_2$), 2.808 (1H, dd, J=2.0, 5.0 Hz, >CHCO), 3.990 (1H, ddd, J=2.0, 3.6, 9.8 Hz, C<u>H</u>CH$_2$CO$_2$), 4.184 (1H, dq, J=5.0, 6.1 Hz, >C<u>H</u>CH$_3$), 5.147 (2H, s, CO_2CH_2Ph), 6.005 (1H, s, NH), 7.26—7.39 (5H, m, CH_2<u>Ph</u>). These assignments are in good accord with those in the literature.[11]

(2*S*,3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-2-(phenylthiomethyl)butanamide (*anti*-17a) and (2*R*,3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-2-(phenylthiomethyl)butanamide (*syn*-17a) A 0.1 M solution of $AlMe_3$ in hexane (7.0 ml, 7.0 mmol) was added to a stirred suspension of NH_4Cl (376 mg, 7.02 mmol) in dry benzene (15 ml) at 0 °C under nitrogen. The mixture was stirred at 0 °C for 20 min and at room temperature for 40 min. The ester **9b** (646 mg, 1.75 mmol) in dry benzene (5 ml) was added, and the whole was heated at 60 °C for 1 d, then cooled to 0 °C. A 10% hydrochloric acid solution was added to decompose excess $AlMe_3$, and the whole was extracted with CH_2Cl_2 (100 ml × 3). The combined organic layer was washed with water (50 ml), saturated aqueous $NaHCO_3$ (50 ml) and brine (50 ml), dried over Na_2SO_4, and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with CH_2Cl_2 to give **17a** (*anti*:*syn*=80:20, 526 mg, 89%). Both isomers were isolated in a pure state by recrystallization or column chromatography. *anti*-**17a**: Colorless crystals, mp 67—68 °C (hexane). $[\alpha]_D^{20}$ +10.4° (c=0.82, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3500, 3350, 1680. ^{1}H-NMR ($CDCl_3$) δ: 0.06, 0.09 (total 6H, each s, Me_2Si), 0.88 (9H, s, *tert*-Bu), 1.16 (3H, d, J=6.0 Hz, CH_3CH<), 2.56 (1H, dt, J=6.0, 7.3 Hz, >CHCO), 2.96 (1H, dd, J=7.3, 13.9 Hz, C<u>H</u>HSPh), 3.39 (1H, dd, J=7.3, 13.9 Hz, CH<u>H</u>SPh), 4.19 (1H, quint, J=6.0 Hz, >C<u>H</u>CH$_3$), 5.38, 6.31 (total 2H, each br s, NH_2), 7.16—7.38 (5H, m, SPh). Exact Mass Calcd for $C_{17}H_{29}NO_2SSi$: 339.1685. Found: 339.1680. *Anal.* Calcd for $C_{17}H_{29}NO_2SSi$: C, 60.13; H, 8.61; N, 4.12; S, 9.44. Found: C, 60.27; H, 8.75; N, 4.13; S, 9.32. *syn*-**17a**: A colorless oil. $[\alpha]_D^{20}$ −4.4° (c=0.39, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3500, 3350, 1680. ^{1}H-NMR ($CDCl_3$) δ: 0.14 (6H, s, Me_2Si), 0.91 (9H, s, *tert*-Bu), 1.26 (3H, d, J=6.1 Hz, CH_3CH<), 2.40 (1H, ddd, J=3.8, 6.3, 8.3 Hz, >CHCO), 3.08 (1H, dd, J=8.3, 13.3 Hz, C<u>H</u>HSPh), 3.26 (1H, dd, J=6.3, 13.3 Hz, CH<u>H</u>SPh), 4.28 (1H, dq, J=3.8, 6.1 Hz, >C<u>H</u>CH$_3$), 5.38, 6.31 (total 2H, each br s, NH_2), 7.16—7.38 (5H, m, SPh). MS *m*/*z*: 339 (M^+), 282 (M^+ − *tert*-Bu). Exact Mass Calcd for $C_{17}H_{29}NO_2SSi$ − *tert*-Bu: 282.0992. Found: 282.0975.

(2*S*,3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-2-(phenylthiomethyl)butanamide (*anti*-17b) and (2*R*,3*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-2-(phenylthiomethyl)butanamide (*syn*-17b) In a similar fashion, **9d** (1.30 g, 2.64 mmol) was treated with NH_4Cl (705 mg, 13.2 mmol) and a 1.0 M solution of $AlMe_3$ in hexane (13.2 ml, 13.2 mmol) in dry benzene to give **17b** (*anti*:*syn*=88:12, 920 mg, 75%) as colorless crystals. Both isomers were isolated in a pure state by column chromatography. *anti*-**17b**: mp 94—97 °C (hexane). $[\alpha]_D^{22}$ +27.11° (c=1.51, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3500, 3400, 3350, 1680. ^{1}H-NMR ($CDCl_3$) δ: 1.03 (3H, d, J=6.1 Hz, CH_3CH<), 1.06 (9H, s, *tert*-Bu), 2.72 (1H, dt, J=4.3, 7.3 Hz, >CHCO), 2.83 (1H, dd, J=7.3, 14.0 Hz, C<u>H</u>HSPh), 3.31 (1H, dd, J=7.3, 14.0 Hz, CH<u>H</u>SPh), 4.25 (1H, dq, J=4.3, 6.1 Hz, >C<u>H</u>CH$_3$), 5.46, 6.33 (total 2H, each br s, NH_2), 7.15—7.34 (15H, m, ArH). Exact Mass Calcd for $C_{27}H_{33}NO_2SSi$ − *tert*-Bu: 406.1295. Found: 406.1288. *syn*-**17b**: mp 142—144 °C (CH_2Cl_2/hexane). $[\alpha]_D^{22}$ +29.74° (c=1.049, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3500, 3400, 3350, 1680. ^{1}H-NMR ($CDCl_3$) δ: 1.06 (9H, s, *tert*-Bu), 1.14 (3H, d, J=6.7 Hz, CH_3CH<), 2.33 (1H, dt, J=3.1, 7.3 Hz, >CHCO), 3.22 (1H, d, J=7.3 Hz, C<u>H</u>HSPh), 3.23 (1H, d, J=7.3 Hz, CH<u>H</u>SPh), 4.15 (1H, dq, J=3.1, 6.7 Hz, >C<u>H</u>CH$_3$), 5.33, 5.83 (total 2H, each br s, NH_2), 7.15—7.22 (15H, m, ArH). *Anal.* Calcd for $C_{27}H_{33}NO_2SSi$: C, 69.93; H, 7.17; N, 3.02; S, 6.90. Found: C, 70.15; H, 7.16; N, 3.09; S, 6.90.

(2*S*,3*R*)-3-Hydroxy-2-(phenylthiomethyl)butanamide (18) i) BF_3·OEt (0.78 ml, BF_3=47%) was added to a stirred solution of *anti*-**17a** (934 mg, 2.76 mmol) in dry CH_3CN (18 ml) at 0 °C under nitrogen. The mixture was stirred for 15 min under the same conditions, then partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (80 ml × 4). The combined organic layer was washed with brine (100 ml). Concentration and crystallization gave **18** (614 mg, 99%) as colorless crystals, mp 117.5—119 °C (hexane/CH_2Cl_2). $[\alpha]_D^{19}$ −109.4° (c=0.38, MeOH). IR ν_{max} ($CHCl_3$) cm^{-1}: 3200—3550, 1675. ^{1}H-NMR ($CDCl_3$ with CD_3OD (5—10%)) δ: 1.17 (3H, d, J=6.5 Hz, CH_3CH<), 2.47 (1H, m, >CHCO), 2.72 (1H, br s, OH), 3.19 (2H, d, J=7 Hz, CH_2SPh), 4.02 (1H, m, >C<u>H</u>CH$_3$), 5.96, 6.47 (total 2H, each br m, NH_2), 7.09—7.40 (5H, m, SPh). Exact Mass Calcd for $C_{11}H_{15}NO_2S$: 225.0823. Found: 225.0833. *Anal.* Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22; S, 14.23. Found: C, 58.45; H, 6.84; N, 6.25; S, 13.99.

ii) A solution of $Bu_4NF \cdot xH_2O$ (709.7 mg) in dry THF (10 ml) was added to a stirred solution of *anti*-**17b** (521.6 mg, 1.127 mmol) in dry THF (10 ml) at room temperature. After 5 min, the mixture was partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2 (80 ml × 3). The combined organic layer was washed with brine (30 ml). Concentration and crystallization gave **18** (208.4 mg, 82.8%) as colorless crystals.

(2*S*,3*R*)-3-[(Methanesulfonyl)oxy]-2-(phenylthiomethyl)butanamide (19) MsCl (0.03 ml, 0.388 mmol) was added to a stirred mixture of **18** (40.0 mg, 0.178 mmol) and triethylamine (0.05 ml, 0.359 mmol) in dry CH_2Cl_2 (3 ml) at 0 °C under nitrogen. The mixture was stirred for 10 min under the same conditions, then partitioned between CH_2Cl_2 (50 ml) and water (30 ml). The aqueous layer was extracted with CH_2Cl_2 (50 ml × 2). The combined organic layer was washed with brine (50 ml), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel with 5% MeOH in CH_2Cl_2 to give **19** (46.2 mg, 85%) as a colorless oil. $[\alpha]_D^{19}$ +2.8° (c=0.69, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3520, 3400, 1690, 1355, 1330, 1175. ^{1}H-NMR ($CDCl_3$) δ: 1.42 (3H, d, J=7 Hz, CH_3CH<), 2.71—2.87 (1H, m, >CHCO), 3.02 (3H, s, $MeSO_2$), 3.13—3.24 (2H, m, CH_2SPh), 5.29 (1H, quint, J=7 Hz, >C<u>H</u>CH$_3$), 5.89 (2H, br s, NH_2), 7.16—7.36 (5H, m, SPh). Exact Mass Calcd for $C_{12}H_{17}NO_4S_2$: 303.0596. Found: 303.0586.

(2*S*)-2-(Phenylthiomethyl)butanamide (20) A mixture of **19** (746 mg, 2.20 mmol), NaI (1.65 g, 11.0 mmol), and zinc powder (1.43 g, 21.9 mmol) in DME (25 ml) was refluxed for 3.5 h under nitrogen. Zinc was removed through a Celite pad, and the filtrate was concentrated to half of the initial volume, then partitioned between CH_2Cl_2 (200 ml) and water (30 ml). The aqueous layer was extracted with CH_2Cl_2 (100 ml × 2). The combined organic layer was washed with brine (75 ml), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel with 2% MeOH in CH_2Cl_2 to give **20** (443 mg, 96%) as colorless crystals, mp 78—79 °C (CH_2Cl_2/hexane). $[\alpha]_D^{23}$ −61.8° (c=0.21, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3530, 3490, 3400, 1680. ^{1}H-NMR ($CDCl_3$) δ: 0.936 (3H, t, J=7.2 Hz, CH_3CH_2), 1.63 (2H, m, CH_2CH_3), 2.29 (1H, m, >CHCO), 3.00 (1H, dd, J=5.6, 13.0 Hz, C<u>H</u>HSPh), 3.21 (1H, dd, J=8.6, 13.0 Hz, CH<u>H</u>SPh), 5.69, 6.07 (total 2H, each br s, NH_2), 7.31 (5H, br s, SPh). *Anal.* Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69; S, 15.32. Found: C, 62.97; H, 7.11; N, 6.66; S, 15.15.

(2*S*)-2-(Phenylsulfinylmethyl)butanamide (21) Compound **20** (398 mg, 1.903 mmol) was converted to **21** (390 mg, 92%) by a similar reaction to that used in the case of **12**, with $NaIO_4$ (611 mg, 2.86 mmol). Colorless crystals, mp 161—170 °C (CH_2Cl_2/hexane). IR ν_{max} ($CHCl_3$) cm^{-1}: 3475, 3420, 1680, 1035. ^{1}H-NMR ($CDCl_3$) δ: 0.904 (17/100 × 3H, t, J=7.3 Hz, CH_3CH_2), 1.018 (83/100 × 3H, t, J=7.3 Hz, CH_3CH_2), 1.849 (83/100 × 2H, quint, J=7.3 Hz, CH_2CH_3), 1.860 (17/100 × 2H, quint, J=7.3 Hz, CH_2CH_3), 2.736 (17/100 × 1H, dd, J=2.9, 13.0 Hz, C<u>H</u>HS(O)Ph), 2.791 (1H, m, >CHCO), 2.857 (83/100 × 1H, dd, J=7.5, 13.4 Hz, C<u>H</u>HS(O)Ph), 3.158 (83/100 × 1H, dd, J=4.9, 13.4 Hz, C<u>H</u>HS(O)Ph), 3.176 (17/100 × 1H, dd, J=2.5, 13.0 Hz, C<u>H</u>HS(O)Ph), 5.420, 6.044 (total 83/100 × 2H, each br s, NH_2), 5.67, 6.43 (total 17/100 × 2H, each br s, NH_2), 7.49—7.68 (5H, m, SPh). *Anal.* Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22; S, 14.23. Found: C, 58.25; H, 6.69; N, 6.16; S, 14.05.

(3*S*)-1-(*tert*-Butyldimethylsilyl)-3-ethyl-4-(phenylthio)azetidin-2-one (22) Compound **21** (47.5 mg, 0.211 mmol) was converted to **22** (36.6 mg, 54.0%) by a similar reaction to that used in the case of **5**, with **13a** (139 mg, 0.739 mmol) and ZnI_2 (6.70 mg, 0.0211 mmol). A pale yellow oil. ^{1}H-NMR showed *cis*:*trans*=63:37. IR ν_{max} ($CHCl_3$) cm^{-1}: 1745. ^{1}H-NMR ($CDCl_3$) δ: 0.165, 0.194, 0.225, 0.231 (total 6H, each s, Me_2Si), 0.809 (37/100 × 3H, t, J=7.3 Hz, CH_3CH_2), 0.910, 0.921 (total 9H, each s, *tert*-Bu), 1.010 (63/100 × 3H, t, J=7.3 Hz, CH_3CH_2), 1.52—1.90 (2H, m, CH_2CH_3), 3.065 (37/100 × 1H, ddd, J=2.0, 6.5, 8.8 Hz, >CHCO), 3.415 (63/100 × 1H, ddd, J=4.9, 7.3, 8.5 Hz, >CHCO), 4.509 (37/100 × 1H, d, J=2.0 Hz >C<u>H</u>SPh), 4.996 (63/100 × 1H, d, J=4.9 Hz, >C<u>H</u>SPh), 7.16—7.40 (5H, m, SPh). Exact Mass Calcd for $C_{17}H_{27}NOSSi$: 321.1583. Found: 321.1583. *cis*-**22**: $[\alpha]_D^{30}$ +126.4° (c=2.247, $CHCl_3$). *trans*-**22**: $[\alpha]_D^{27}$ −96.03° (c=0.924, $CHCl_3$).

(3*S*)-1-(*tert*-Butyldimethylsilyl)-3-ethyl-4-(phenylsulfinyl)azetidin-2-one (23) Compound **22** (32.1 mg, 0.10 mmol) was converted to **23** (31.6 mg, 93.8%) by a similar reaction to that used in the case of **14**, with *m*-CPBA

(23.7 mg, 0.11 mmol). A pale yellow oil. IR ν_{max} ($CHCl_3$) cm^{-1}: 1750, 1035, 1030. ^{1}H-NMR ($CDCl_3$) δ: 0.221, 0.260, 0.299, 0.310, 0.370, 0.381, 0.410, 0.418 (total 6H, each s, Me_2Si), 0.437, 0.582, 0.839 (total 80/100 × 3H, each t, J=7.5 Hz, CH_3CH_2), 1.033 (9H + 20/100 × 3H, m, *tert*-Bu, CH_3CH_2), 1.21—1.41, 1.492, 1.904, 2.339 (total 2H, each m, CH_2CH_3), 2.911 (20/100 × 1H, dt, J=2.5, 6.7 Hz, >CHCO), 3.353, 3.493 (60/100 × 1H, dt, J=11.0, 5.5 Hz, >CHCO), 3.675 (20/100 × 1H, m, >CHCO), 3.978 (20/100 × 1H, d, J=2.0 Hz, >CHS(O)Ph), 4.131 (20/100 × 1H, d, J=2.5 Hz, >CHS(O)Ph), 4.412, 4.624 (total 60/100 × 1H, each d, J=5.5 Hz, >CHS(O)Ph), 7.50—7.71 (5H, m, S(O)Ph). (The signals indicated this product to be a 40 : 20 : 20 : 20 mixture of geometrical isomers.) Exact Mass Calcd for $C_{17}H_{27}NO_2SSi$ − *tert*-Bu: 280.0827. Found: 280.0828.

(3*R*,4*R*)-4-(Benzyloxycarbonylmethyl)-1-(*tert*-butyldimethylsilyl)-3-ethylazetidin-2-one (24) Compound **23** (31.6 mg, 0.0938 mmol) was converted to **24** (14.6 mg, 43%) by a similar reaction to that used in the case of **15**, with **13b** (25.0 mg, 0.1126 mmol) and ZnI_2 (3.0 mg, 0.00938 mmol). A pale yellow oil. $[\alpha]_D^{25}$ −36.4° (c=0.481, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1725. ^{1}H-NMR ($CDCl_3$) δ: 0.19, 0.23 (total 6H, each s, Me_2Si), 0.95 (9H, s, *tert*-Bu), 0.96 (3H, t, J=7.3 Hz, CH_3CH_2), 1.68 (2H, m, CH_2CH_3), 2.53 (1H, dd, J=9.8, 15.3 Hz, >CHCHHCO$_2$), 2.87 (1H, dt, J=2.5, 7.3 Hz, >CHCO), 2.88 (1H, dd, J=4.0, 15.3 Hz, >CHCHHCO$_2$), 3.59 (1H, ddd, J=2.5, 4.0, 9.8 Hz, >CHCH$_2$CO$_2$), 5.12 (2H, s, CH_2Ph), 7.3—7.6 (5H, m, SPh). Exact Mass Calcd for $C_{20}H_{31}NO_3Si$ − *tert*-Bu: 304.1366. Found: 304.1358.

(3*R*,4*R*)-4-(Benzyloxycarbonylmethyl)-3-ethylazetidin-2-one (25) A solution of $Bu_4NF \cdot 3H_2O$ (100 mg, 0.371 mmol) and AcOH (31.8 mg, 0.530 mmol) in dry THF (2 ml) was added dropwise to a stirred solution of **24** (95.5 mg, 0.265 mmol) in THF (1 ml) at 0 °C. The mixture was stirred at 0 °C for 10 min, diluted with CH_2Cl_2 (80 ml), washed with saturated aqueous $NaHCO_3$ (30 ml) and brine (20 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel with 50% AcOEt in hexane to give **25** (65.5 mg, 100%) as a colorless oil. $[\alpha]_D^{25}$ +33.7° (c=1.11, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3425, 1755, 1730. ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, t, J=7.1 Hz, $-CH_2CH_3$), 1.72 (2H, m, $-CH_2CH_3$), 2.6—2.9 (total 3H, m, $-CH_2CO_2$, >CHCO), 3.64 (1H, ddd, J=2.1, 6.0, 8.6 Hz, $-CHCH_2CO_2$), 5.13 (2H, s, $-CH_2$Ph), 6.24 (1H, br, NH), 7.35 (5H, s, Ph). Exact MS Calcd for $C_{14}H_{17}NO_3$ − NHCO: 204.1151. Found: 204.1152.

(3*R*,4*R*)-4-Carboxymethyl-3-ethylazetidin-2-one (26) A 10% Pd–C catalyst (25 mg) was added to a stirred solution of **25** (25.0 mg, 0.101 mmol) in EtOH (2 ml) at room temperature. The apparatus was filled with hydrogen and the mixture was stirred at room temperature for 1 d. Pd–C was collected by filtration and the solvent was removed *in vacuo* to give the acid, which was purified by recrystallization to give **26** (10.9 mg, 68.7%) as colorless crystals, mp 105—107 °C (CH_2Cl_2–C_6H_6), $[\alpha]_D^{24}$ +13.65° (c=0.300, EtOH). (lit.[16] 113—115 °C, $[\alpha]_D^{24}$ +16° (c=1, EtOH)). IR ν_{max} ($CHCl_3$) cm^{-1}: 3400, 3100—3350, 1750, 1725. ^{1}H-NMR ($CDCl_3$) δ: 1.025 (3H, t, J=7.3 Hz, CH_2CH_3), 1.710, 1.817 (each 1H, each d, quint, J=7.3, 14.6 Hz, $-CH_2CH_3$), 2.550 (1H, dd, J=9.8, 16.5 Hz, $-CHHCO_2H$), 2.778 (1H, dd, J=4.0, 16.5 Hz, $-CHHCO_2H$), 2.75—2.81 (1H, m, >CHCO), 3.638 (1H, m, >CHCH$_2$CO$_2$H), 7.080 (1H, br s, NH). Exact MS Calcd for $C_7H_{11}NO_3$: 157.0739. Found: 157.0747.

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