

# 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<sup>1)</sup> because of their prominent antibacterial activities and broad activity spectra. Most of the routes, however, are based on an aldol-type reaction of 4-acetoxazetidinones with properly designed metal enolates.<sup>1)</sup> Recently, we have reported a conceptually new approach to (+)-1 involving a diastereoselective Michael addition and a silicon-induced Pummerer-type reaction.<sup>2–4)</sup> 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  $\beta$ -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  $\beta$ -lactam ring) in the asymmetric Michael addition reaction. The optically active 4 is used in the next silicon-induced Pummerer-type reaction<sup>2–4)</sup> to give the chiral  $\beta$ -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  $\alpha,\beta$ -unsaturated esters (3) were obtained from readily available

(*R*)-(–)-ethyl 3-hydroxybutanoate (6,  $[\alpha]_D^{25} -40.9^\circ$  ( $c=0.81$ ,  $\text{CHCl}_3$ ), lit.<sup>5)</sup>  $[\alpha]_D^{25} -43.6^\circ$  ( $c=1.2$ ,  $\text{CHCl}_3$ )). 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<sup>6,7)</sup> 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 (<sup>1</sup>H-NMR) spectrometric measurement (Fig. 1) based on a method similar to that reported by Kurihara *et al.*<sup>8)</sup> Thus, the highly diastereopure

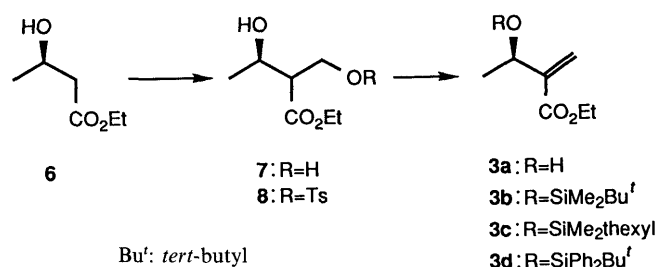


Chart 2

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

3	R	Product (9)	Yield (%)	<i>anti</i> : <i>syn</i> <sup>a)</sup>
3a	H	9a	100	50:50
3b	SiMe <sub>2</sub> Bu <sup>t</sup>	9b	99	79:21
3c	SiMe <sub>2</sub> hexyl	9c	98	79:21
3d	SiPh <sub>2</sub> Bu <sup>t</sup>	9d	96	89:11

a) Determined by 500 MHz <sup>1</sup>H-NMR.

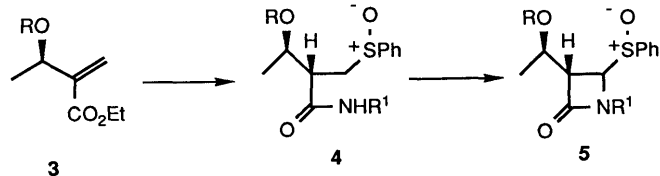
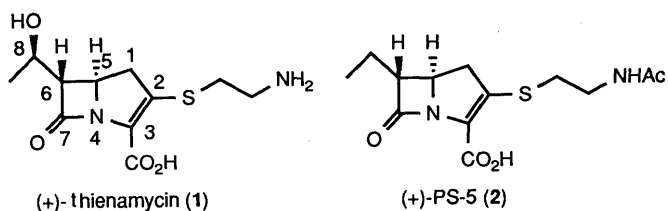


Chart 1

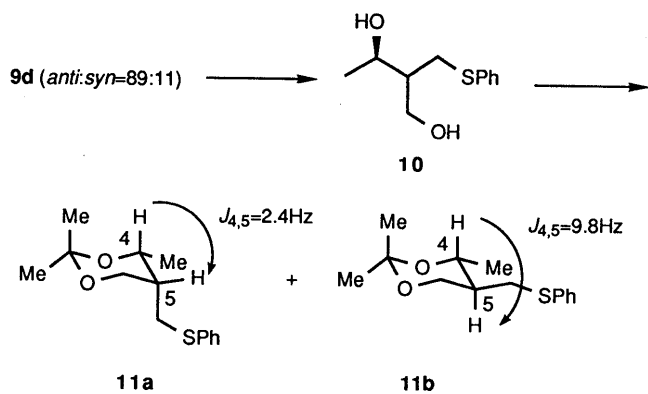


Fig. 1

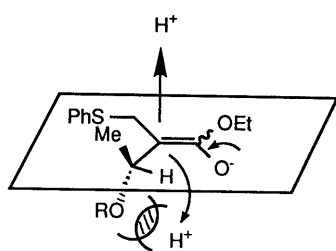
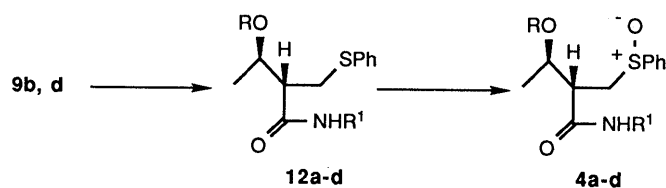


Fig. 2



- a:** R=SiMe<sub>2</sub>Bu<sup>t</sup>, R<sup>1</sup>=2,4-DMB  
**b:** R=SiMe<sub>2</sub>Bu<sup>t</sup>, R<sup>1</sup>=p-MB  
**c:** R=SiPh<sub>2</sub>Bu<sup>t</sup>, R<sup>1</sup>=2,4-DMB  
**d:** R=SiPh<sub>2</sub>Bu<sup>t</sup>, R<sup>1</sup>=p-MB

Chart 3

mixture (**9d**) was reduced by lithium aluminum hydride (LiAlH<sub>4</sub>) 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 silyloxy group.<sup>9)</sup>

**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  $\beta$ -amido sulfoxide and the C-4

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

4	R	R <sup>1</sup>	Product (5)	Yield (%)	<i>trans</i> : <i>cis</i>
<b>4a</b>	SiMe <sub>2</sub> Bu <sup>t</sup>	2,4-DMB	<b>5a</b>	65	4.1:1
<b>4b</b>	SiMe <sub>2</sub> Bu <sup>t</sup>	<i>p</i> -MB	<b>5b</b>	56	4.0:1
<b>4c</b>	SiPh <sub>2</sub> Bu <sup>t</sup>	2,4-DMB	<b>5c</b>	64	4.4:1
<b>4d</b>	SiPh <sub>2</sub> Bu <sup>t</sup>	<i>p</i> -MB	<b>5d</b>	74	4.4:1

TABLE III. Carbon-Carbon Bond Formation of 4-Sulfinylazetididin-2-ones (**14a-d**)

14a	R	R <sup>1</sup>	Product (15)	Yield (%)
<b>14a</b> ( <i>trans</i> : <i>cis</i> =4:1)	SiMe <sub>2</sub> Bu <sup>t</sup>	2,4-DMB	<b>15a</b>	75
<b>14a</b> ( <i>trans</i> )	SiMe <sub>2</sub> Bu <sup>t</sup>	2,4-DMB	<b>15a</b>	81
<b>14b</b> ( <i>trans</i> )	SiMe <sub>2</sub> Bu <sup>t</sup>	<i>p</i> -MB	<b>15b</b>	64
<b>14c</b> ( <i>trans</i> )	SiPh <sub>2</sub> Bu <sup>t</sup>	2,4-DMB	<b>15c</b>	71
<b>14d</b> ( <i>trans</i> )	SiPh <sub>2</sub> Bu <sup>t</sup>	<i>p</i> -MB	<b>15d</b>	63

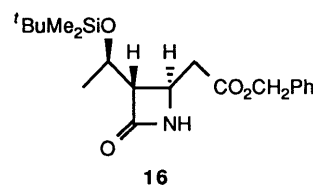


Fig. 3

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

Amidation of the mixture of diastereomers (*anti*-**9b, d** and *syn*-**9b, d**) with 2,4-dimethoxybenzylamine (2,4-DMBNH<sub>2</sub>) or *p*-methoxybenzylamine (*p*-MBNH<sub>2</sub>) in the presence of trimethylaluminum (AlMe<sub>3</sub>) in boiling benzene<sup>10)</sup> 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<sub>4</sub>) in MeOH yielded the  $\beta$ -amido sulfoxides (**4a-d**). Cyclization of **4a-d** was achieved by our silicon-induced Pummerer-type reaction<sup>2-4)</sup> using *O*-methyl-*O*-*tert*-butyldimethylsilyl ketene acetal (**13a**) to give the 4-phenylthioazetididinones (**5a-d**). The results are summarized in Table II. Oxidation of **5** with *m*-chloroperbenzoic acid (*m*-CPBA) in CH<sub>2</sub>Cl<sub>2</sub> gave the sulfoxide (**14**), which was treated with **13b** in the presence of a catalytic amount of zinc iodide (ZnI<sub>2</sub>) in CH<sub>3</sub>CN to give the *trans*-azetididinone 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

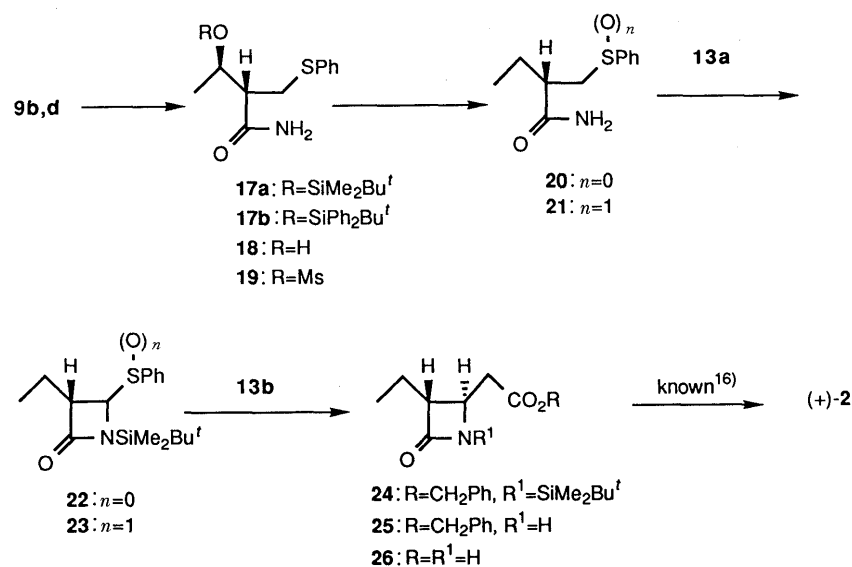


Chart 4

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

**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-(phenylthio)methyl)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.<sup>2,4)</sup>

Amidation of **9b, d** with ammonium chloride (NH<sub>4</sub>Cl) in the presence of AlMe<sub>3</sub> in benzene gave the amides (**17a, b**), which were desilylated with BF<sub>3</sub>·OEt<sub>2</sub> in CH<sub>3</sub>CN or tetrabutylammonium fluoride (Bu<sub>4</sub>NF) 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.<sup>13)</sup> Thus, treatment of **18** with MsCl and Et<sub>3</sub>N in CH<sub>2</sub>Cl<sub>2</sub> 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<sup>14)</sup> and Georg and Kant.<sup>15)</sup> Oxidation of **20** with NaIO<sub>4</sub> 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<sub>2</sub> in CH<sub>3</sub>CN to produce a mixture of *cis*- and *trans*-azetidinones (**22**). Oxidation of the mixture (**22**) with *m*-CPBA in CH<sub>2</sub>Cl<sub>2</sub> followed by reaction with **13b** in the presence of a catalytic amount of ZnI<sub>2</sub> in CH<sub>3</sub>CN afforded the *trans*-azetidinone ester (**24**). Desilylation of **24** with Bu<sub>4</sub>NF and AcOH in THF followed by reductive debenzoylation on 10% Pd-C in EtOH gave the *trans*-4-carboxy-3-ethylazetidinone (**26**), which is a key intermediate of (+)-**2**.<sup>16)</sup>

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. <sup>1</sup>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<sub>254</sub> (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<sub>4</sub>Cl, 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<sub>3</sub> (40 ml) and brine (40 ml), then dried over Na<sub>2</sub>SO<sub>4</sub>. 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. [α]<sub>D</sub><sup>26</sup> -40.9° (*c*=0.81, CHCl<sub>3</sub>). IR ν<sub>max</sub> (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3450, 1710. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.25 (3H, d, *J*=7 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.28 (3H, t, *J*=7 Hz, CH<sub>3</sub>CH<sub>2</sub>), 2.43–2.71 (1H, m, >CHCO<sub>2</sub>Et), 3.18 (2H, brs, OH × 2), 3.96 (3H, m, >CHCH<sub>3</sub>, CH<sub>2</sub>OH), 4.21 (2H, q, *J*=7 Hz, CH<sub>2</sub>CH<sub>3</sub>). MS *m/z*: 163 (*M*<sup>+</sup> + 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<sub>2</sub>Cl<sub>2</sub> (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<sub>2</sub>Cl<sub>2</sub> (100 ml × 3). The extract was washed with 10% hydrochloric acid (50 ml × 2), saturated aqueous NaHCO<sub>3</sub> (50 ml) and brine (100 ml), and dried over MgSO<sub>4</sub>. 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<sub>max</sub> (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3540, 1720, 1365, 1175. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.21 (3H, d, *J*=7 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.24 (3H, t, *J*=7 Hz, CH<sub>3</sub>CH<sub>2</sub>), 2.16 (1H, brm, OH), 2.44 (3H, s, CH<sub>3</sub>Ar), 2.70 (1H, m,

>CHCO<sub>2</sub>Et), 4.16 (2H, q, *J* = 7 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.19 (3H, m, CH<sub>2</sub>OTs, >CHCH<sub>3</sub>), 7.29 (2H, d, *J* = 8 Hz, ArH), 7.15 (2H, d, *J* = 8 Hz, ArH). MS *m/z*: 317 (M<sup>+</sup> + 1). Exact Mass Calcd for C<sub>14</sub>H<sub>20</sub>O<sub>6</sub>S: 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<sub>2</sub>Cl<sub>2</sub> (100 ml × 3). The combined organic layer was washed with brine (50 ml), dried over MgSO<sub>4</sub>, 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). [ $\alpha$ ]<sub>D</sub><sup>20.5</sup> + 18.36° (*c* = 1.38, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3500, 3000, 1700, 1630. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.33 (3H, t, *J* = 7 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.40 (3H, d, *J* = 6.5 Hz, CH<sub>3</sub>CH<), 2.92 (1H, br s, OH), 4.26 (2H, q, *J* = 7 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.64 (1H, q, *J* = 6.5 Hz, >CHCH<sub>3</sub>), 5.84, 6.23 (2H, each s, CH<sub>2</sub>=C<). Anal. Calcd for C<sub>7</sub>H<sub>12</sub>O<sub>3</sub>: C, 58.31; H, 8.39. Found: C, 58.50; H, 8.68.

**Ethyl 2-[(*R*)-1-[(*tert*-Butyldimethylsilyloxy)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<sub>2</sub>SO<sub>4</sub> 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). [ $\alpha$ ]<sub>D</sub><sup>20</sup> + 28.7° (*c* = 0.50, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1710, 1630. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.40, 0.06 (each 3H, each s, Me<sub>2</sub>Si), 0.90 (9H, s, *tert*-BuSi), 1.27 (3H, d, *J* = 6.5 Hz, CH<sub>3</sub>CH<), 1.31 (3H, t, *J* = 7 Hz, CH<sub>3</sub>CH<sub>2</sub>), 4.22 (2H, q, *J* = 7 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.69 (1H, m, >CHCH<sub>3</sub>), 5.90, 6.14 (total 2H, each s, CH<sub>2</sub>=C<). MS *m/z*: 201 (M<sup>+</sup> - *tert*-Bu). Anal. Calcd for C<sub>13</sub>H<sub>26</sub>O<sub>3</sub>Si: C, 60.42; H, 10.14. Found: C, 60.61; H, 10.09.

**Ethyl 2-[(*R*)-1-[(Dimethylhexylsilyloxy)ethyl]propenoate (3c)** In a similar fashion, **3a** (273 mg, 1.90 mmol) was treated with imidazole (284 mg 4.18 mmol) and dimethylhexylsilyl chloride (0.411 ml, 2.09 mmol) in DMF (3 ml) to give **6c** (482 mg, 89%) as a colorless oil. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 2950, 1710, 1630. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.60, 0.12 (total 6H, each s, Me<sub>2</sub>Si), 0.88 (6H, s, Me<sub>2</sub>C<), 0.94 (6H, d, *J* = 6.5 Hz, Me<sub>2</sub>CH), 1.30 (3H, d, *J* = 6.5 Hz, CH<sub>3</sub>CH<), 1.33 (3H, t, *J* = 7 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.67 (1H, m, CHMe<sub>2</sub>), 4.23 (2H, q, *J* = 7 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.71 (1H, q, *J* = 6.5 Hz, >CHCH<sub>3</sub>), 5.95, 6.19 (total 2H, each s, CH<sub>2</sub>=C<). Exact Mass Calcd for C<sub>15</sub>H<sub>30</sub>O<sub>3</sub>Si - C<sub>6</sub>H<sub>13</sub>: 201.0944. Found: 201.0914.

**Ethyl 2-[(*R*)-1-[(*tert*-Butyldiphenylsilyloxy)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). [ $\alpha$ ]<sub>D</sub><sup>20.5</sup> + 36.03° (*c* = 0.82, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 2950, 1710, 1630. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.05 (9H, s, *tert*-BuSi), 1.17 (3H, d, *J* = 6.5 Hz, CH<sub>3</sub>CH<), 1.19 (3H, t, *J* = 7 Hz, CH<sub>3</sub>CH<sub>2</sub>), 4.09 (2H, q, *J* = 7 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.72 (1H, q, *J* = 6.5 Hz, >CHCH<sub>3</sub>), 6.04, 6.18 (total 2H, each m, CH<sub>2</sub>=C<), 7.24–7.74 (10H, m, Ph × 2). MS *m/z*: 325 (M<sup>+</sup> - *tert*-Bu). Anal. Calcd for C<sub>23</sub>H<sub>30</sub>O<sub>3</sub>Si: 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 <sup>1</sup>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  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3500, 3000, 1730. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.22, 1.23 (total 3H, each d, *J* = 6.7 Hz, CH<sub>3</sub>CH<), 1.27, 1.28 (total 3H, each t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 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<sub>2</sub>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<sub>2</sub>SPh), 3.27 (1/2 × 1H, dd, *J* = 8.6, 13.4 Hz, CHHSPh), 4.07 (1H, m, >CHCH<sub>3</sub>), 4.17 (2H, q, *J* = 7.3 Hz, CH<sub>2</sub>CH<sub>3</sub>), 7.19–7.39 (5H, m, Ph). Exact Mass Calcd for C<sub>13</sub>H<sub>18</sub>O<sub>3</sub>S: 254.0974. Found: 254.0972.

**Ethyl (3*R*)-3-[(*tert*-Butyldimethylsilyloxy)-2-(phenylthiomethyl)butano-**

**ate (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  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1725. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.02, 0.04 (total 21/100 × 6H, each s, Me<sub>2</sub>Si), 0.05 (79/100 × 6H, s, Me<sub>2</sub>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<sub>3</sub>CH<), 1.25 (3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 2.62 (79/100 × 1H, ddd, *J* = 3.7, 6.7, 10.4 Hz, >CHCO<sub>2</sub>Et), 2.70 (21/100 × 1H, ddd, *J* = 5.5, 6.7, 7.8 Hz, >CHCO<sub>2</sub>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<sub>2</sub>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<sub>3</sub>), 4.11 (79/100 × 2H, q, *J* = 7.3 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.15 (21/100 × 3H, m, >CHCH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>), 7.16–7.36 (5H, m, Ph). Exact Mass Calcd for C<sub>19</sub>H<sub>32</sub>O<sub>3</sub>SSi - *tert*-Bu: 311.1137. Found: 311.1137. Anal. Calcd for C<sub>19</sub>H<sub>32</sub>O<sub>3</sub>SSi: C, 61.91; H, 8.75. Found: C, 61.90; H, 9.11.

**Ethyl (3*R*)-3-[(Dimethylhexylsilyloxy)-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  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 2975, 1725. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.05 (21/100 × 6H, s, Me<sub>2</sub>Si), 0.08, 0.09 (total 79/100 × 6H, each s, Me<sub>2</sub>Si), 0.80, 0.81 (total 21/100 × 6H, each s, Me<sub>2</sub>C<), 0.82, 0.83 (total 79/100 × 6H, each s, Me<sub>2</sub>C<), 0.85, 0.86 (total 21/100 × 6H, each d, *J* = 5.5 Hz, Me<sub>2</sub>CH), 0.870, 0.874 (total 79/100 × 6H, each d, *J* = 6.7 Hz, Me<sub>2</sub>CH), 1.12 (21/100 × 3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 1.16 (79/100 × 3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 1.25 (79/100 × 3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.26 (21/100 × 3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 2.62 (79/100 × 1H, ddd, *J* = 3.7, 6.7, 10.4 Hz, >CHCO<sub>2</sub>Et), 2.69 (21/100 × 1H, dt, *J* = 9.8, 4.9 Hz, >CHCO<sub>2</sub>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<sub>2</sub>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<sub>3</sub>), 4.01 (79/100 × 1H, quint, *J* = 6.1 Hz, >CHCH<sub>3</sub>), 4.119, 4.112 (total 79/100 × 2H, each q, *J* = 7.3 Hz, CH<sub>2</sub>CH<sub>3</sub>), 4.132, 4.144 (total 21/100 × 2H, each q, *J* = 7.3 Hz, CH<sub>2</sub>CH<sub>3</sub>), 7.16–7.37 (5H, m, Ph). Exact Mass Calcd for C<sub>21</sub>H<sub>36</sub>O<sub>3</sub>SSi - C<sub>6</sub>H<sub>13</sub>: 311.1137. Found: 311.1157.

**Ethyl (3*R*)-3-[(*tert*-Butyldiphenylsilyloxy)-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  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 2950, 1725. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.03 (12H, s, *tert*-Bu, CH<sub>3</sub>CH<), 1.21 (89/100 × 3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.22 (11/100 × 3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 2.75 (1H, ddd, *J* = 4.3, 6.1, 10.4 Hz, >CHCO<sub>2</sub>Et), 3.12 (89/100 × 1H, dd, *J* = 10.4, 13.4 Hz, CHHSPh), 3.20 (11/100 × 2H, m, CH<sub>2</sub>SPh), 3.24 (89/100 × 1H, dd, *J* = 4.3, 13.4 Hz, CHHSPh), 4.10 (3H, m, >CHCH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>), 7.24–7.66 (15H, m, Ph × 3). Exact Mass Calcd for C<sub>29</sub>H<sub>36</sub>O<sub>3</sub>SSi - *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<sub>4</sub> (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  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3625, 3575–3200. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.249 (89/100 × 3H, d, *J* = 6.8 Hz, CH<sub>3</sub>CH<), 1.303 (11/100 × 3H, d, *J* = 6.8 Hz, CH<sub>3</sub>CH<), 1.695 (11/100 × 1H, m, >CHCH<sub>2</sub>SPh), 1.825 (89/100 × 1H, m, >CHCH<sub>2</sub>SPh), 2.097 (1H, dd, *J* = 4.5, 5.2 Hz, HOCH<sub>2</sub>), 2.336 (11/100 × 1H, d, *J* = 5.0 Hz, HOCH<sub>2</sub>), 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<sub>11</sub>H<sub>16</sub>O<sub>2</sub>S: 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  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3020, 1150, 1080. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.195 (88/100 × 3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 1.213 (12/100 × 3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 1.388, 1.447 (total 12/100 × 6H, each s, Me<sub>2</sub>C<), 1.402, 1.454 (88/100 × 6H, each s, Me<sub>2</sub>C<), 1.426 (88/100 × 1H, m, >CHCH<sub>2</sub>SPh), 1.807 (12/100 × 1H, m,

$>CHCH_2SPh$ ), 2.637 (12/100  $\times$  1H, dd,  $J=9.2$ , 12.8 Hz,  $CHHSPh$ ), 3.024 (12/100  $\times$  1H, dd,  $J=3.7$ , 12.8 Hz,  $CHHSPh$ ), 3.200 (88/100  $\times$  2H, d,  $J=7.3$  Hz,  $CH_2SPh$ ), 3.683 (12/100  $\times$  1H, dd,  $J=10.5$ , 11.6 Hz,  $CHHO$ ), 3.808 (12/100  $\times$  1H, dq,  $J=9.8$ , 6.9 Hz,  $>CHCH_3$ ), 3.964 (88/100  $\times$  1H, dd,  $J=2.4$ , 11.9 Hz,  $CHHO$ ), 3.990 (12/100  $\times$  1H, dd,  $J=5.0$ , 11.6 Hz,  $CHHO$ ), 4.117 (88/100  $\times$  1H, dd,  $J=1.2$ , 11.9 Hz,  $CHHO$ ), 4.227 (88/100  $\times$  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  $\times$  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**).

**(3R)-3-[(*tert*-Butyldimethylsilyloxy)-*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<sub>2</sub>·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*-Butyldimethylsilyloxy)-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (*anti*-**12a**):  $[\alpha]_D^{22} -21.11^\circ$  ( $c=2.24$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3350, 1665. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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,  $OMe \times 2$ ), 4.105 (1H, quint,  $J=6.1$  Hz,  $>CHCH_3$ ), 4.273, 4.420 (total 2H, each dd,  $J=6.1$ , 14.0 Hz,  $NHCH_2Ar$ ), 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*)-[(*tert*-Butyldimethylsilyloxy)-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (*syn*-**12a**):  $[\alpha]_D^{22} +0.748^\circ$  ( $c=1.07$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3400, 1660. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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,  $OMe \times 2$ ), 4.21–4.27 (1H, m,  $>CHCH_3$ ), 4.243, 4.439 (total 2H, each dd,  $J=5.5$ , 14.0 Hz,  $NHCH_2Ar$ ), 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.

**(3R)-3-[(*tert*-Butyldimethylsilyloxy)-*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<sub>2</sub> (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*-Butyldimethylsilyloxy)-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (*anti*-**12b**):  $[\alpha]_D^{22} -19.80^\circ$  ( $c=0.970$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3010, 1660. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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,  $NHCH_2Ar$ ), 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*-Butyldimethylsilyloxy)-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (*syn*-**12b**):  $[\alpha]_D^{22} +14.44^\circ$  ( $c=2.106$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3010, 1660. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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,  $NHCH_2Ar$ ), 4.254 (1H, dq,  $J=3.7$ , 6.1 Hz,  $>CHCH_3$ ), 4.478 (1H, dd,  $J=6.1$ , 14.7 Hz,  $NHCH_2Ar$ ), 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.

**(3R)-3-[(*tert*-Butyldiphenylsilyloxy)-*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<sub>2</sub>·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*-Butyldiphenylsilyloxy)-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (*anti*-**12c**):  $[\alpha]_D^{25} -10.20^\circ$  ( $c=1.57$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3375. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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,  $OMe \times 2$ ), 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,  $NHCH_2Ar$ ), 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*-Butyldiphenylsilyloxy)-*N*-(2,4-dimethoxybenzyl)-2-(phenylthiomethyl)butanamide (*syn*-**12c**):  $[\alpha]_D^{26} +5.585^\circ$  ( $c=0.716$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3378. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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,  $OMe \times 2$ ), 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,  $NHCH_2Ar$ ), 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.

**(3R)-3-[(*tert*-Butyldiphenylsilyloxy)-*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<sub>2</sub> (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*-Butyldiphenylsilyloxy)-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (*anti*-**12d**):  $[\alpha]_D^{23} -13.32^\circ$  ( $c=2.82$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3358, 1666. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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,  $NHCH_2Ar$ ), 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*-Butyldiphenylsilyloxy)-*N*-(*p*-methoxybenzyl)-2-(phenylthiomethyl)butanamide (*syn*-**12d**):  $[\alpha]_D^{28} +8.891^\circ$  ( $c=1.500$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3350, 1650. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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,  $OMe \times 2$ ), 4.101 (1H, dq,  $J=3.5$ , 6.1 Hz,  $>CHCH_3$ ), 4.153 (1H, dd,  $J=4.9$ , 14.7 Hz,  $NHCH_2Ar$ ), 4.449 (1H, dd,  $J=5.8$ , 14.7 Hz,  $NHCH_2Ar$ ), 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  $\beta$ -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*-Butyldimethylsilyloxy)-*N*-(2,4-dimethoxybenzyl)-2-(phenylsulfanyl)methyl)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  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3460, 3400, 1660, 1620, 1595, 1040. <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 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  $\times$  1H, dd,  $J=3.0$ , 12.5 Hz,  $CHHS(O)Ph$ ), 2.688 (1/2  $\times$  1H, q,  $J=6.1$  Hz,  $>CHCO$ ), 2.847 (1/2  $\times$  1H, dd,  $J=6.1$ , 13.5 Hz,  $CHHS(O)Ph$ ), 3.013 (1/2  $\times$  1H, ddd,  $J=3.0$ , 5.0, 10.5 Hz,  $>CHCO$ ), 3.262 (1/2  $\times$  1H, dd,  $J=10.5$ , 12.5 Hz,  $CHHS(O)Ph$ ), 3.372 (1/2  $\times$  1H, dd,  $J=6.1$ , 13.5 Hz,  $CHHS(O)Ph$ ), 3.783, 3.785, 3.788, 3.807 (total 6H, each s,  $OMe \times 2$ ), 3.964 (1/2  $\times$  1H, quint,  $J=6.1$  Hz,  $>CHCH_3$ ), 4.109 (1/2  $\times$  1H, dq,  $J=5.0$ , 6.1 Hz,  $>CHCH_3$ ), 4.153, 4.339 (total 1/2  $\times$  2H, each dd,  $J=5.5$ , 14.0 Hz,  $NHCH_2Ar$ ), 4.312, 4.498 (total 1/2  $\times$  2H, each dd,  $J=5.5$ , 15.0 Hz,  $NHCH_2Ar$ ), 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.

**(2S,3R)-3-[(*tert*-Butyldimethylsilyloxy)-*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  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3355, 1655, 1027.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 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,  $CH_3CH_2$ ), 2.640 (1/2  $\times$  1H, dd,  $J=3.0$ , 12.8 Hz,  $CHHS(O)Ph$ ), 2.768 (1/2  $\times$  1H, dt,  $J=5.9$ , 6.1 Hz,  $>CHCO$ ), 2.853 (1/2  $\times$  1H, dd,  $J=6.1$ , 13.4 Hz,  $CHHS(O)Ph$ ), 3.058 (1/2  $\times$  1H, ddd,  $J=3.0$ , 4.9, 10.5 Hz,  $>CHCO$ ), 3.295 (1/2  $\times$  1H, dd,  $J=10.5$ , 12.8 Hz,  $CHHS(O)Ph$ ), 3.389 (1/2  $\times$  1H, dd,  $J=5.9$ , 13.4 Hz,  $CHHS(O)Ph$ ), 3.790, 3.796 (total 3H, each s, OMe), 3.990 (1/2  $\times$  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,  $NHCH_2Ar$ ), 4.162 (1/2  $\times$  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.

**(2S,3R)-3-[(*tert*-Butyldiphenylsilyloxy)-*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  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3450, 3390, 1660, 1039.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 0.913, 0.953 (total 3H, each d,  $J=6.0$  Hz,  $CH_3CH_2$ ), 0.976, 0.980 (total 9H, each s, *tert*-Bu), 2.553 (1/2  $\times$  1H, dd,  $J=1.2$ , 11.3 Hz,  $CHHS(O)Ph$ ), 2.689 (1/2  $\times$  1H, dd,  $J=6.1$ , 13.5 Hz,  $CHHS(O)Ph$ ), 2.855 (1/2  $\times$  1H, dt,  $J=6.1$ , 4.5 Hz,  $>CHCO$ ), 3.129 (1/2  $\times$  2H, m,  $>CHCO$ ),  $CHHS(O)Ph$ ), 3.350 (1/2  $\times$  1H, dd,  $J=6.1$ , 13.5 Hz,  $CHHS(O)Ph$ ), 3.720, 3.749, 3.780 (total 6H, each s, OMe  $\times$  2), 3.930, 4.093 (total 1H, each dq,  $J=4.5$ , 6.0 Hz,  $>CHCH_3$ ), 4.225, 4.392 (total 1/2  $\times$  2H, dd,  $J=5.1$ , 13.9 Hz,  $NHCH_2Ar$ ), 4.358, 4.538 (total 1/2  $\times$  2H, each dd,  $J=6.0$ , 13.9 Hz,  $NHCH_2Ar$ ), 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.

**(2S,3R)-3-[(*tert*-Butyldiphenylsilyloxy)-*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  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 3380, 1655, 1040.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 0.941, 0.999 (total 3H, each d,  $J=6.1$  Hz,  $CH_3CH_2$ ), 0.957, 0.959 (total 9H, each s, *tert*-Bu), 2.550 (1/2  $\times$  1H, d,  $J=9.8$  Hz,  $CHHS(O)Ph$ ), 2.724 (1/2  $\times$  1H, dd,  $J=6.1$ , 14.0 Hz,  $CHHS(O)Ph$ ), 2.919 (1/2  $\times$  1H, dt,  $J=4.5$ , 6.1 Hz,  $>CHCO$ ), 3.160 (1/2  $\times$  2H, m,  $>CHCO$ ),  $CHHS(O)Ph$ ), 3.366 (1/2  $\times$  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  $\times$  2H, dd,  $J=6.1$ , 14.6 Hz,  $NHCH_2Ar$ ), 4.355 (1/2  $\times$  2H, m,  $NHCH_2Ar$ ), 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  $\beta$ -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  $\beta$ -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  $\times$  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.

**(3S)-3-[(*R*)-1-[(*tert*-Butyldimethylsilyloxy)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.

**(3S,4R)-3-[(*R*)-1-[(*tert*-Butyldimethylsilyloxy)ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (*trans*-5a)]**  $[\alpha]_D^{25} - 36.09^\circ$  ( $c=1.05$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 1750, 1620, 1595.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : -0.074, 0.015 (total 6H, each s,  $Me_2Si$ ), 0.774 (9H, s, *tert*-Bu), 1.177 (3H, d,  $J=6.7$  Hz,  $CH_3CH_2$ ), 2.918 (1H, dd,  $J=2.4$ , 3.7 Hz,  $>CHCO$ ), 3.743, 3.795 (total 6H, each s, OMe  $\times$  2), 4.137 (1H, dq,  $J=3.7$ , 6.7 Hz,  $>CHCH_3$ ), 4.285, 4.499 (2H, AB-q,  $J=15.3$  Hz,  $>NCH_2Ar$ ), 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.

**(3S,4S)-3-[(*R*)-1-[(*tert*-Butyldimethylsilyloxy)ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (*cis*-5a)]**  $[\alpha]_D^{25} - 35.08^\circ$  ( $c=1.23$ ,

$CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 1745, 1615, 1590.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 0.012 (6H, s,  $Me_2Si$ ), 0.93 (9H, s, *tert*-Bu), 1.45 (3H, d,  $J=6.7$  Hz,  $CH_3CH_2$ ), 3.44 (1H, t,  $J=5.0$  Hz,  $>CHCO$ ), 3.59, 3.75 (total 6H, each s, OMe  $\times$  2), 4.11, 4.56 (2H, AB-q,  $J=15.0$  Hz,  $>NCH_2Ar$ ), 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.

**(3S)-3-[(*R*)-1-[(*tert*-Butyldimethylsilyloxy)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, 0.175 mmol), and  $ZnI_2$  (4.60 mg, 0.0143 mmol) in  $CH_3CN$  as a pale yellow oil.

**(3S,4R)-3-[(*R*)-1-[(*tert*-Butyldimethylsilyloxy)ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (*trans*-5b)]**  $[\alpha]_D^{25} - 23.13^\circ$  ( $c=1.58$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 1745, 1520.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : -0.0098, 0.0342 (total 6H, each s,  $Me_2Si$ ), 0.798 (9H, s, *tert*-Bu), 1.173 (3H, d,  $J=6.1$  Hz,  $CH_3CH_2$ ), 2.976 (1H, br s,  $>CHCO$ ), 3.792 (3H, s, OMe), 4.098, 4.628 (2H, AB-q,  $J=15.0$  Hz,  $>NCH_2Ar$ ), 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.

**(3S,4S)-3-[(*R*)-1-[(*tert*-Butyldimethylsilyloxy)ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (*cis*-5b)]**  $[\alpha]_D^{25} - 33.83^\circ$  ( $c=0.541$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 1745.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 0.105, 0.121 (total 6H, each s,  $Me_2Si$ ), 0.923 (9H, s, *tert*-Bu), 1.439 (3H, d,  $J=6.1$  Hz,  $CH_3CH_2$ ), 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,  $>NCH_2Ar$ ), 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.

**(3S)-3-[(*R*)-1-[(*tert*-Butyldiphenylsilyloxy)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.

**(3S,4R)-3-[(*R*)-1-[(*tert*-Butyldiphenylsilyloxy)ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (*trans*-5c)]**  $[\alpha]_D^{27} - 22.88^\circ$  ( $c=0.961$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 1740, 1620, 1590.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 0.929 (9H, s, *tert*-Bu), 1.001 (3H, d,  $J=6.1$  Hz,  $CH_3CH_2$ ), 2.949 (1H, dd,  $J=2.4$ , 5.3 Hz,  $>CHCO$ ), 3.682, 3.781 (total 6H, each s, OMe  $\times$  2), 4.262 (1H, dq,  $J=5.3$ , 6.1 Hz,  $>CHCH_3$ ), 4.266, 4.535 (2H, AB-q,  $J=15.2$  Hz,  $>NCH_2Ar$ ), 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.

**(3S,4S)-3-[(*R*)-1-[(*tert*-Butyldiphenylsilyloxy)ethyl]-1-(2,4-dimethoxybenzyl)-4-(phenylthio)azetidin-2-one (*cis*-5c)]**  $[\alpha]_D^{26} - 26.01^\circ$  ( $c=0.961$ ,  $CHCl_3$ ). IR  $\nu_{max}$  ( $CHCl_3$ )  $cm^{-1}$ : 1750, 1615, 1590.  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 1.068 (9H, s, *tert*-Bu), 1.304 (3H, d,  $J=6.7$  Hz,  $CH_3CH_2$ ), 3.476 (1H, dd,  $J=4.2$ , 5.1 Hz,  $>CHCO$ ), 3.595, 3.756 (total 6H, each s, OMe  $\times$  2), 4.147, 4.603 (2H, AB-q,  $J=15.1$  Hz,  $>NCH_2Ar$ ), 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.

**(3S)-3-[(*R*)-1-[(*tert*-Butyldiphenylsilyloxy)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.

**(3S,4R)-3-[(*R*)-1-[(*tert*-Butyldiphenylsilyloxy)ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (*trans*-5d)]**  $[\alpha]_D^{25} - 20.29^\circ$  ( $c=0.237$ ,  $CHCl_3$ ).  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 0.96 (9H, s, *tert*-Bu), 0.99 (3H, d,  $J=6.7$  Hz,  $CH_3CH_2$ ), 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,  $>NCH_2Ar$ ), 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.

**(3S,4S)-3-[(*R*)-1-[(*tert*-Butyldiphenylsilyloxy)ethyl]-1-(*p*-methoxybenzyl)-4-(phenylthio)azetidin-2-one (*cis*-5d)]**  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 1.07 (9H, s, *tert*-Bu), 1.30 (3H, d,  $J=6.7$  Hz,  $CH_3CH_2$ ), 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,  $>NCH_2Ar$ ), 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<sub>3</sub> (50 ml). The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (100 ml × 2). The combined organic extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, 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.

**(3S,4R)-3-[(R)-1-((tert-Butyldimethylsilyloxy)ethyl)-1-(2,4-dimethoxybenzyl)-4-(phenylsulfinyl)azetididin-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<sub>2</sub>Cl<sub>2</sub> as a pale yellow oil. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1765, 1615, 1590, 1050. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : -0.108, -0.100, -0.096, -0.008 (total 6H, each s, Me<sub>2</sub>Si), 0.001 (55/100 × 3H, d, *J* = 6.5 Hz, CH<sub>3</sub>CH<), 0.702, 0.879 (total 9H, each s, *tert*-Bu), 0.972 (45/100 × 3H, d, *J* = 6.5 Hz, CH<sub>3</sub>CH<), 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, >CHCH<sub>3</sub>), 4.142, 4.445 (45/100 × 2H, AB-q, *J* = 14.7 Hz, >NCH<sub>2</sub>Ar), 4.399 (55/100 × 1H, d, *J* = 1.8 Hz, >CHS(O)Ph), 4.512 (55/100 × 2H, d, *J* = 1.8 Hz, >NCH<sub>2</sub>Ar), 4.598 (45/100 × 1H, d, *J* = 1.8 Hz, >CHS(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<sub>26</sub>H<sub>37</sub>NO<sub>5</sub>SSi-*tert*-Bu: 446.1457. Found: 446.1458.

**(3S)-3-[(R)-1-((tert-Butyldimethylsilyloxy)ethyl)-1-(2,4-dimethoxybenzyl)-4-(phenylsulfinyl)azetididin-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<sub>2</sub>Cl<sub>2</sub> as a yellow oil. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1770, 1040. MS *m/z*: 378 (M<sup>+</sup> - S(O)Ph), 377 (M<sup>+</sup> - HOSPh). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) (signals of *cis-14a*)  $\delta$ : 0.1431, 0.1639, 0.1675, 0.1846 (total 20/100 × 6H, each s, Me<sub>2</sub>Si), 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<sub>3</sub>CH<), 2.7748, 4.2030 (10/100 × 2H, AB-q, *J* = 15.0 Hz, >NCH<sub>2</sub>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, >NCH<sub>2</sub>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, >CHS(O)Ph), 4.6 (10/100 × 1H, m, >CHCH<sub>3</sub>), 4.756 (10/100 × 1H, dq, *J* = 9.5, 6.1 Hz, >CHCH<sub>3</sub>), 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.)

**(3S,4R)-3-[(R)-1-((tert-Butyldimethylsilyloxy)ethyl)-1-(*p*-methoxybenzyl)-4-(phenylsulfinyl)azetididin-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<sub>2</sub>Cl<sub>2</sub> as a colorless oil. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1760, 1610, 1590, 1060. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : -0.049, -0.040, -0.008, 0.002 (total 6H, each s, Me<sub>2</sub>Si), 0.156 (55/100 × 3H, d, *J* = 6.7 Hz, CH<sub>3</sub>CH<), 0.7859 (9H + 45/100 × 3H, s, *tert*-Bu, CH<sub>3</sub>CH<), 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, >NCH<sub>2</sub>Ar), 4.135 (1H, m, >CHCH<sub>3</sub>), 4.338 (55/100 × 1H, d, *J* = 2.0 Hz, >CHS(O)Ph), 4.447, 4.614 (55/100 × 2H, AB-q, *J* = 15.0 Hz, >NCH<sub>2</sub>Ar), 4.533 (45/100 × 1H, d, *J* = 2.0 Hz, >CHS(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<sub>25</sub>H<sub>35</sub>NO<sub>4</sub>SSi-*tert*-Bu: 416.1350. Found: 416.1347.

**(3S,4R)-3-[(R)-1-((tert-Butyldiphenylsilyloxy)ethyl)-1-(2,4-dimethoxybenzyl)-4-(phenylsulfinyl)azetididin-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<sub>2</sub>Cl<sub>2</sub> as a colorless oil. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1770, 1050. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : -0.106 (45/100 × 3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 0.875, 0.964 (total 9H, each s, *tert*-Bu), 0.902 (55/100 × 3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 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, >NCH<sub>2</sub>Ar), 4.045 (45/100 × 1H, quint, *J* = 6.1 Hz, >CHCH<sub>3</sub>), 4.178 (55/100 × 1H, dq, *J* = 2.0, 6.1 Hz, >CHCH<sub>3</sub>), 4.520 (45/100 × 1H, d, *J* = 1.8 Hz, >CHS(O)Ph), 4.556 (55/100 × 1H, d, *J* = 1.8 Hz, >CHS(O)Ph), 4.596 (55/100 × 2H, d, *J* = 4.9 Hz, >NCH<sub>2</sub>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<sub>36</sub>H<sub>41</sub>NO<sub>5</sub>SSi-*tert*-Bu: 570.1767. Found: 570.1757.

**(3S,4R)-3-[(R)-1-((tert-Butyldiphenylsilyloxy)ethyl)-1-(*p*-methoxybenzyl)-4-(phenylsulfinyl)azetididin-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<sub>2</sub>Cl<sub>2</sub> as a colorless oil. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1765, 1050. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : -0.0586, 0.705 (total 3H, each d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 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, >NCH<sub>2</sub>Ar), 4.100 (41/100 × 1H, quint, *J* = 6.1 Hz, >CHCH<sub>3</sub>), 4.230 (59/100 × 1H, dq, *J* = 1.8, 6.1 Hz, >CHCH<sub>3</sub>), 4.478 (1H, br s, >CHS(O)Ph), 4.544, 4.651 (59/100 × 2H, AB-q, *J* = 15.3 Hz, >NCH<sub>2</sub>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<sub>35</sub>H<sub>39</sub>NO<sub>4</sub>SSi-*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-phenylsulfinylazetididinone (**14a—d**, 0.1 mmol) and ZnI<sub>2</sub> (0.01 mmol) in dry CH<sub>3</sub>CN (1 ml) at room temperature under nitrogen. The mixture was stirred at the same temperature for 3 h, then partitioned between CH<sub>2</sub>Cl<sub>2</sub> (30 ml) and saturated aqueous NaHCO<sub>3</sub> (10 ml). The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (30 ml × 3). The combined extract was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel with 30% hexane-AcOEt to give the ester.

**(3S,4R)-4-(Benzyloxycarbonylmethyl)-3-[(R)-1'-(tert-butyldimethylsilyloxy)ethyl]-1-(2,4-dimethoxybenzyl)azetididin-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<sub>2</sub> (1.40 mg, 0.0862 mmol) in CH<sub>3</sub>CN as a colorless oil.  $[\alpha]_D^{25}$  -3.675° (*c* = 0.816, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1740, 1615, 1590. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : -0.0244, 0.0232 (total 6H, each s, Me<sub>2</sub>Si), 0.792 (9H, s, *tert*-Bu), 1.104 (3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 2.494 (1H, dd, *J* = 7.0, 14.6 Hz, CHHCO<sub>2</sub>), 2.713 (1H, dd, *J* = 5.5, 14.6 Hz, CHHCO<sub>2</sub>), 2.879 (1H, dd, *J* = 1.8, 4.0 Hz, >CHCO), 3.767 (6H, s, OMe × 2), 3.958 (1H, m, >CHCH<sub>2</sub>CO<sub>2</sub>), 4.138 (1H, dq, *J* = 4.0, 6.1 Hz, >CHCH<sub>3</sub>), 4.197, 4.332 (2H, AB-q, *J* = 15.0 Hz, >NCH<sub>2</sub>Ar), 5.031 (2H, s, CO<sub>2</sub>CH<sub>2</sub>Ph), 6.40—7.36 (8H, m, ArH). Exact Mass Calcd for C<sub>29</sub>H<sub>41</sub>NO<sub>6</sub>SSi: 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<sub>2</sub> (2.90 mg, 0.00903 mmol) in CH<sub>3</sub>CN as a colorless oil.

**(3S,4R)-4-(Benzyloxycarbonylmethyl)-3-[(R)-1-((tert-butyldimethylsilyloxy)ethyl)-1-(*p*-methoxybenzyl)azetididin-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<sub>2</sub> (2.00 mg, 0.00691 mmol) in CH<sub>3</sub>CN as a colorless oil.  $[\alpha]_D^{26}$  -3.506° (*c* = 1.11, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1740, 1615. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.0223, 0.0516 (total 6H, each s, Me<sub>2</sub>Si), 0.8412 (9H, s, *tert*-Bu), 1.147 (3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 2.536 (2H, dd, *J* = 3.8, 6.7 Hz, CH<sub>2</sub>CO<sub>2</sub>), 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, >CHCH<sub>2</sub>CO<sub>2</sub>), 4.160 (1H, dq, *J* = 4.5, 6.1 Hz, >CHCH<sub>3</sub>), 4.248, 4.304 (2H, AB-q, *J* = 15.0 Hz, >NCH<sub>2</sub>Ar), 5.008 (2H, d, *J* = 2.6 Hz, CO<sub>2</sub>CH<sub>2</sub>Ph), 6.810, 7.156 (total 4H, each d, *J* = 8.5 Hz, ArH), 7.2—7.4 (5H, m, CH<sub>2</sub>Ph). Exact Mass Calcd for C<sub>28</sub>H<sub>39</sub>NO<sub>5</sub>SSi-*tert*-Bu: 440.1890. Found: 440.1887.

**(3S,4R)-4-(Benzyloxycarbonylmethyl)-3-[(R)-1-((tert-butyldiphenylsilyloxy)ethyl)-1-(2,4-dimethoxybenzyl)azetididin-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<sub>2</sub> (3.70 mg, 0.0116 mmol) in CH<sub>3</sub>CN as a colorless oil.  $[\alpha]_D^{30}$  -3.79° (*c* = 1.82, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1740, 1620, 1590. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.9445 (9H, s, *tert*-Bu), 0.9482 (3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 2.527, 2.716 (total 2H, each dd, *J* = 6.1, 15.3 Hz, CH<sub>2</sub>CO<sub>2</sub>), 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, >CHCH<sub>2</sub>CO<sub>2</sub>), 4.187 (1H, m, >CHCH<sub>3</sub>), 4.215, 4.371 (2H, AB-q, *J* = 15.3 Hz, >NCH<sub>2</sub>Ar), 5.012 (2H, s, CO<sub>2</sub>CH<sub>2</sub>Ph), 6.3—7.3 (18H, m, ArH). MS *m/z*: 651 (M<sup>+</sup>), 594 (M<sup>+</sup> - *tert*-Bu). Exact Mass Calcd for C<sub>39</sub>H<sub>45</sub>NO<sub>6</sub>SSi-*tert*-Bu: 594.2312. Found: 594.2319.

**(3S,4R)-4-(Benzyloxycarbonylmethyl)-3-[(R)-1-((tert-butyldiphenylsilyloxy)ethyl)-1-(*p*-methoxybenzyl)azetididin-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<sub>2</sub> (2.30 mg, 0.00841 mmol) in CH<sub>3</sub>CN as a pale yellow oil. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1740. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.97 (9H, s, *tert*-Bu), 0.99 (3H, d, *J* = 6.5 Hz, CH<sub>3</sub>CH<), 2.54 (2H, d, *J* = 6.0 Hz, CH<sub>2</sub>CO<sub>2</sub>), 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, >CHCH<sub>2</sub>CO<sub>2</sub>), 4.15 (1H, m, >CHCH<sub>3</sub>), 4.26 (2H, s, >NCH<sub>2</sub>Ar), 4.97 (2H, s, CO<sub>2</sub>CH<sub>2</sub>Ph), 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<sub>36</sub>H<sub>43</sub>NO<sub>5</sub>SSi-*tert*-Bu: 564.2206. Found: 564.2211.

**(3S,4R)-4-(Benzyloxycarbonylmethyl)-3-[(R)-1-((tert-butyldimethylsilyloxy)ethyl)azetididin-2-one (16)** A mixture of **15a** (15.3 mg, 0.0290 mmol), K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (78.3 mg, 0.290 mmol), and K<sub>2</sub>HPO<sub>4</sub> (25.2 mg, 0.145 mmol) in CH<sub>3</sub>CN/H<sub>2</sub>O (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<sub>3</sub> (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<sub>2</sub>SO<sub>4</sub> 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. [ $\alpha$ ]<sub>D</sub><sup>24</sup> + 14.46° (*c* = 0.558, CHCl<sub>3</sub>). mp 91–92°C (hexane). {lit.<sup>11</sup> [ $\alpha$ ]<sub>D</sub><sup>24</sup> + 17.4° (*c* = 1.75, CHCl<sub>3</sub>). mp 92–93°C (hexane)}. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3450, 1760, 1730. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.0659, 0.0696 (total 6H, each s, Me<sub>2</sub>Si), 0.869 (9H, s, *tert*-Bu), 1.193 (3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 2.612 (1H, dd, *J* = 9.8, 16.4 Hz, CHHCO<sub>2</sub>), 2.786 (1H, dd, *J* = 3.6, 16.4 Hz, CHHCO<sub>2</sub>), 2.808 (1H, dd, *J* = 2.0, 5.0 Hz, >CHCO), 3.990 (1H, ddd, *J* = 2.0, 3.6, 9.8 Hz, CHCH<sub>2</sub>CO<sub>2</sub>), 4.184 (1H, dq, *J* = 5.0, 6.1 Hz, >CHCH<sub>3</sub>), 5.147 (2H, s, CO<sub>2</sub>CH<sub>2</sub>Ph), 6.005 (1H, s, NH), 7.26–7.39 (5H, m, CH<sub>2</sub>Ph). These assignments are in good accord with those in the literature.<sup>11</sup>

**(2S,3R)-3-[(*tert*-Butyldimethylsilyloxy]-2-(phenylthiomethyl)butanamide (*anti*-17a) and (2R,3R)-3-[(*tert*-Butyldimethylsilyloxy]-2-(phenylthiomethyl)butanamide (*syn*-17a)** A 0.1 M solution of AlMe<sub>3</sub> in hexane (7.0 ml, 7.0 mmol) was added to a stirred suspension of NH<sub>4</sub>Cl (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<sub>3</sub>, and the whole was extracted with CH<sub>2</sub>Cl<sub>2</sub> (100 ml × 3). The combined organic layer was washed with water (50 ml), saturated aqueous NaHCO<sub>3</sub> (50 ml) and brine (50 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with CH<sub>2</sub>Cl<sub>2</sub> 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). [ $\alpha$ ]<sub>D</sub><sup>20</sup> + 10.4° (*c* = 0.82, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3500, 3350, 1680. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.06, 0.09 (total 6H, each s, Me<sub>2</sub>Si), 0.88 (9H, s, *tert*-Bu), 1.16 (3H, d, *J* = 6.0 Hz, CH<sub>3</sub>CH<), 2.56 (1H, dt, *J* = 6.0, 7.3 Hz, >CHCO), 2.96 (1H, dd, *J* = 7.3, 13.9 Hz, CHHSPH), 3.39 (1H, dd, *J* = 7.3, 13.9 Hz, CHHSPH), 4.19 (1H, quint, *J* = 6.0 Hz, >CHCH<sub>3</sub>), 5.38, 6.31 (total 2H, each brs, NH<sub>2</sub>), 7.16–7.38 (5H, m, SPh). Exact Mass Calcd for C<sub>17</sub>H<sub>29</sub>NO<sub>2</sub>SSi: 339.1685. Found: 339.1680. *Anal.* Calcd for C<sub>17</sub>H<sub>29</sub>NO<sub>2</sub>SSi: 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. [ $\alpha$ ]<sub>D</sub><sup>20</sup> - 4.4° (*c* = 0.39, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3500, 3350, 1680. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.14 (6H, s, Me<sub>2</sub>Si), 0.91 (9H, s, *tert*-Bu), 1.26 (3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 2.40 (1H, ddd, *J* = 3.8, 6.3, 8.3 Hz, >CHCO), 3.08 (1H, dd, *J* = 8.3, 13.3 Hz, CHHSPH), 3.26 (1H, dd, *J* = 6.3, 13.3 Hz, CHHSPH), 4.28 (1H, dq, *J* = 3.8, 6.1 Hz, >CHCH<sub>3</sub>), 5.38, 6.31 (total 2H, each brs, NH<sub>2</sub>), 7.16–7.38 (5H, m, SPh). MS *m/z*: 339 (M<sup>+</sup>), 282 (M<sup>+</sup> - *tert*-Bu). Exact Mass Calcd for C<sub>17</sub>H<sub>29</sub>NO<sub>2</sub>SSi - *tert*-Bu: 282.0992. Found: 282.0975.

**(2S,3R)-3-[(*tert*-Butyldiphenylsilyloxy]-2-(phenylthiomethyl)butanamide (*anti*-17b) and (2R,3R)-3-[(*tert*-Butyldiphenylsilyloxy]-2-(phenylthiomethyl)butanamide (*syn*-17b)** In a similar fashion, **9d** (1.30 g, 2.64 mmol) was treated with NH<sub>4</sub>Cl (705 mg, 13.2 mmol) and a 1.0 M solution of AlMe<sub>3</sub> 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). [ $\alpha$ ]<sub>D</sub><sup>22</sup> + 27.11° (*c* = 1.51, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3500, 3400, 3350, 1680. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.03 (3H, d, *J* = 6.1 Hz, CH<sub>3</sub>CH<), 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, CHHSPH), 3.31 (1H, dd, *J* = 7.3, 14.0 Hz, CHHSPH), 4.25 (1H, dq, *J* = 4.3, 6.1 Hz, >CHCH<sub>3</sub>), 5.46, 6.33 (total 2H, each brs, NH<sub>2</sub>), 7.15–7.34 (15H, m, ArH). Exact Mass Calcd for C<sub>27</sub>H<sub>33</sub>NO<sub>2</sub>SSi - *tert*-Bu: 406.1295. Found: 406.1288. *syn*-17b: mp 142–144°C (CH<sub>2</sub>Cl<sub>2</sub>/hexane). [ $\alpha$ ]<sub>D</sub><sup>22</sup> + 29.74° (*c* = 1.049, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3500, 3400, 3350, 1680. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.06 (9H, s, *tert*-Bu), 1.14 (3H, d, *J* = 6.7 Hz, CH<sub>3</sub>CH<), 2.33 (1H, dt, *J* = 3.1, 7.3 Hz, >CHCO), 3.22 (1H, d, *J* = 7.3 Hz, CHHSPH), 3.23 (1H, d, *J* = 7.3 Hz, CHHSPH), 4.15 (1H, dq, *J* = 3.1, 6.7 Hz, >CHCH<sub>3</sub>), 5.33, 5.83 (total 2H, each brs, NH<sub>2</sub>), 7.15–7.22 (15H, m, ArH). *Anal.* Calcd for C<sub>27</sub>H<sub>33</sub>NO<sub>2</sub>SSi: 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.

**(2S,3R)-3-Hydroxy-2-(phenylthiomethyl)butanamide (18)** i) BF<sub>3</sub>·OEt (0.78 ml, BF<sub>3</sub> = 47%) was added to a stirred solution of *anti*-17a (934 mg, 2.76 mmol) in dry CH<sub>3</sub>CN (18 ml) at 0°C under nitrogen. The mixture was stirred for 15 min under the same conditions, then partitioned between CH<sub>2</sub>Cl<sub>2</sub> and saturated aqueous NaHCO<sub>3</sub>. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (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<sub>2</sub>Cl<sub>2</sub>). [ $\alpha$ ]<sub>D</sub><sup>19</sup> - 109.4° (*c* = 0.38, MeOH). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3200–3550, 1675. <sup>1</sup>H-NMR

(CDCl<sub>3</sub> with CD<sub>3</sub>OD (5–10%))  $\delta$ : 1.17 (3H, d, *J* = 6.5 Hz, CH<sub>3</sub>CH<), 2.47 (1H, m, >CHCO), 2.72 (1H, br s, OH), 3.19 (2H, d, *J* = 7 Hz, CH<sub>2</sub>SPh), 4.02 (1H, m, >CHCH<sub>3</sub>), 5.96, 6.47 (total 2H, each br m, NH<sub>2</sub>), 7.09–7.40 (5H, m, SPh). Exact Mass Calcd for C<sub>11</sub>H<sub>15</sub>NO<sub>2</sub>S: 225.0823. Found: 225.0833. *Anal.* Calcd for C<sub>11</sub>H<sub>15</sub>NO<sub>2</sub>S: 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<sub>4</sub>NF·xH<sub>2</sub>O (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<sub>2</sub>Cl<sub>2</sub> and water. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (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.

**(2S,3R)-3-[(Methanesulfonyloxy]-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<sub>2</sub>Cl<sub>2</sub> (3 ml) at 0°C under nitrogen. The mixture was stirred for 10 min under the same conditions, then partitioned between CH<sub>2</sub>Cl<sub>2</sub> (50 ml) and water (30 ml). The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (50 ml × 2). The combined organic layer was washed with brine (50 ml), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel with 5% MeOH in CH<sub>2</sub>Cl<sub>2</sub> to give **19** (46.2 mg, 85%) as a colorless oil. [ $\alpha$ ]<sub>D</sub><sup>19</sup> + 2.8° (*c* = 0.69, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3520, 3400, 1690, 1355, 1330, 1175. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.42 (3H, d, *J* = 7 Hz, CH<sub>3</sub>CH<), 2.71–2.87 (1H, m, >CHCO), 3.02 (3H, s, MeSO<sub>2</sub>), 3.13–3.24 (2H, m, CH<sub>2</sub>SPh), 5.29 (1H, quint, *J* = 7 Hz, >CHCH<sub>3</sub>), 5.89 (2H, brs, NH<sub>2</sub>), 7.16–7.36 (5H, m, SPh). Exact Mass Calcd for C<sub>12</sub>H<sub>17</sub>NO<sub>4</sub>S<sub>2</sub>: 303.0596. Found: 303.0586.

**(2S)-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<sub>2</sub>Cl<sub>2</sub> (200 ml) and water (30 ml). The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (100 ml × 2). The combined organic layer was washed with brine (75 ml), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel with 2% MeOH in CH<sub>2</sub>Cl<sub>2</sub> to give **20** (443 mg, 96%) as colorless crystals, mp 78–79°C (CH<sub>2</sub>Cl<sub>2</sub>/hexane). [ $\alpha$ ]<sub>D</sub><sup>23</sup> - 61.8° (*c* = 0.21, CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3530, 3490, 3400, 1680. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.936 (3H, t, *J* = 7.2 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.63 (2H, m, CH<sub>2</sub>CH<sub>3</sub>), 2.29 (1H, m, >CHCO), 3.00 (1H, dd, *J* = 5.6, 13.0 Hz, CHHSPH), 3.21 (1H, dd, *J* = 8.6, 13.0 Hz, CHHSPH), 5.69, 6.07 (total 2H, each brs, NH<sub>2</sub>), 7.31 (5H, brs, SPh). *Anal.* Calcd for C<sub>11</sub>H<sub>15</sub>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.

**(2S)-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<sub>4</sub> (611 mg, 2.86 mmol). Colorless crystals, mp 161–170°C (CH<sub>2</sub>Cl<sub>2</sub>/hexane). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3475, 3420, 1680, 1035. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.904 (17/100 × 3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.018 (83/100 × 3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.849 (83/100 × 2H, quint, *J* = 7.3 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.860 (17/100 × 2H, quint, *J* = 7.3 Hz, CH<sub>2</sub>CH<sub>3</sub>), 2.736 (17/100 × 1H, dd, *J* = 2.9, 13.0 Hz, CHHS(O)Ph), 2.791 (1H, m, >CHCO), 2.857 (83/100 × 1H, dd, *J* = 7.5, 13.4 Hz, CHHS(O)Ph), 3.158 (83/100 × 1H, dd, *J* = 4.9, 13.4 Hz, CHHS(O)Ph), 3.176 (17/100 × 1H, dd, *J* = 2.5, 13.0 Hz, CHHS(O)Ph), 5.420, 6.044 (total 83/100 × 2H, each brs, NH<sub>2</sub>), 5.67, 6.43 (total 17/100 × 2H, each brs, NH<sub>2</sub>), 7.49–7.68 (5H, m, SPh). *Anal.* Calcd for C<sub>11</sub>H<sub>15</sub>NO<sub>2</sub>S: 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.

**(3S)-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<sub>2</sub> (6.70 mg, 0.0211 mmol). A pale yellow oil. <sup>1</sup>H-NMR showed *cis*:*trans* = 63:37. IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1745. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.165, 0.194, 0.225, 0.231 (total 6H, each s, Me<sub>2</sub>Si), 0.809 (37/100 × 3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 0.910, 0.921 (total 9H, each s, *tert*-Bu), 1.010 (63/100 × 3H, t, *J* = 7.3 Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.52–1.90 (2H, m, CH<sub>2</sub>CH<sub>3</sub>), 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, >CHSPH), 4.996 (63/100 × 1H, d, *J* = 4.9 Hz, >CHSPH), 7.16–7.40 (5H, m, SPh). Exact Mass Calcd for C<sub>17</sub>H<sub>27</sub>NOSSi: 321.1583. Found: 321.1583. *cis*-**22**: [ $\alpha$ ]<sub>D</sub><sup>20</sup> + 126.4° (*c* = 2.247, CHCl<sub>3</sub>). *trans*-**22**: [ $\alpha$ ]<sub>D</sub><sup>27</sup> - 96.03° (*c* = 0.924, CHCl<sub>3</sub>).

**(3S)-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  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1750, 1035, 1030. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.221, 0.260, 0.299, 0.310, 0.370, 0.381, 0.410, 0.418 (total 6H, each s, Me<sub>3</sub>Si), 0.437, 0.582, 0.839 (total 80/100  $\times$  3H, each t,  $J=7.5$  Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.033 (9H + 20/100  $\times$  3H, m, *tert*-Bu, CH<sub>3</sub>CH<sub>2</sub>), 1.21—1.41, 1.492, 1.904, 2.339 (total 2H, each m, CH<sub>2</sub>CH<sub>3</sub>), 2.911 (20/100  $\times$  1H, dt,  $J=2.5, 6.7$  Hz,  $\gt$ CHCO), 3.353, 3.493 (60/100  $\times$  1H, dt,  $J=11.0, 5.5$  Hz,  $\gt$ CHCO), 3.675 (20/100  $\times$  1H, m,  $\gt$ CHCO), 3.978 (20/100  $\times$  1H, d,  $J=2.0$  Hz,  $\gt$ CHS(O)Ph), 4.131 (20/100  $\times$  1H, d,  $J=2.5$  Hz,  $\gt$ CHS(O)Ph), 4.412, 4.624 (total 60/100  $\times$  1H, each d,  $J=5.5$  Hz,  $\gt$ 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<sub>17</sub>H<sub>27</sub>NO<sub>2</sub>SSi-*tert*-Bu: 280.0827. Found: 280.0828.

**(3R,4R)-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<sub>2</sub> (3.0 mg, 0.00938 mmol). A pale yellow oil.  $[\alpha]_D^{25} -36.4^\circ$  ( $c=0.481$ , CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1725. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.19, 0.23 (total 6H, each s, Me<sub>2</sub>Si), 0.95 (9H, s, *tert*-Bu), 0.96 (3H, t,  $J=7.3$  Hz, CH<sub>3</sub>CH<sub>2</sub>), 1.68 (2H, m, CH<sub>2</sub>CH<sub>3</sub>), 2.53 (1H, dd,  $J=9.8, 15.3$  Hz,  $\gt$ CHCH<sub>2</sub>HCO<sub>2</sub>), 2.87 (1H, dt,  $J=2.5, 7.3$  Hz,  $\gt$ CHCO), 2.88 (1H, dd,  $J=4.0, 15.3$  Hz,  $\gt$ CHCH<sub>2</sub>HCO<sub>2</sub>), 3.59 (1H, ddd,  $J=2.5, 4.0, 9.8$  Hz,  $\gt$ CHCH<sub>2</sub>CO<sub>2</sub>), 5.12 (2H, s, CH<sub>2</sub>Ph), 7.3—7.6 (5H, m, SPh). Exact Mass Calcd for C<sub>20</sub>H<sub>31</sub>NO<sub>2</sub>Si-*tert*-Bu: 304.1366. Found: 304.1358.

**(3R,4R)-4-(Benzyloxycarbonylmethyl)-3-ethylazetidin-2-one (25)** A solution of Bu<sub>4</sub>NF  $\cdot$  3H<sub>2</sub>O (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<sub>2</sub>Cl<sub>2</sub> (80 ml), washed with saturated aqueous NaHCO<sub>3</sub> (30 ml) and brine (20 ml), dried over MgSO<sub>4</sub>, 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.  $[\alpha]_D^{25} +33.7^\circ$  ( $c=1.11$ , CHCl<sub>3</sub>). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3425, 1755, 1730. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 0.99 (3H, t,  $J=7.1$  Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.72 (2H, m, -CH<sub>2</sub>CH<sub>3</sub>), 2.6—2.9 (total 3H, m, -CH<sub>2</sub>CO<sub>2</sub>,  $\gt$ CHCO), 3.64 (1H, ddd,  $J=2.1, 6.0, 8.6$  Hz, -CHCH<sub>2</sub>CO<sub>2</sub>), 5.13 (2H, s, -CH<sub>2</sub>Ph), 6.24 (1H, br, NH), 7.35 (5H, s, Ph). Exact MS Calcd for C<sub>14</sub>H<sub>17</sub>NO<sub>3</sub>-NHCO: 204.1151. Found: 204.1152.

**(3R,4R)-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<sub>2</sub>Cl<sub>2</sub>-C<sub>6</sub>H<sub>6</sub>),  $[\alpha]_D^{24} +13.65^\circ$  ( $c=0.300$ , EtOH). (lit.<sup>16</sup>) 113—115°C,  $[\alpha]_D^{24} +16^\circ$  ( $c=1$ , EtOH). IR  $\nu_{\max}$  (CHCl<sub>3</sub>) cm<sup>-1</sup>: 3400, 3100—3350, 1750, 1725. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 1.025 (3H, t,  $J=7.3$  Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.710, 1.817 (each 1H, each d, quint,  $J=7.3, 14.6$  Hz, -CH<sub>2</sub>CH<sub>3</sub>), 2.550 (1H, dd,  $J=9.8, 16.5$  Hz, -CHHCO<sub>2</sub>H), 2.778 (1H, dd,  $J=4.0, 16.5$  Hz, -CHHCO<sub>2</sub>H), 2.75—2.81 (1H, m,  $\gt$ CHCO), 3.638 (1H, m,  $\gt$ CHCH<sub>2</sub>CO<sub>2</sub>H), 7.080 (1H, br, s, NH). Exact MS Calcd for C<sub>7</sub>H<sub>11</sub>NO<sub>3</sub>: 157.0739. Found: 157.0747.

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