Supporting Information

Experimental Procedure for Compounds **7b**, **8b**, **9b**, **10b**, **13b**, **18**, **20**, and **1**.

Unless otherwise noted, all reactions were carried out in dry solvents under argon.

(2*R*,4*R*)-1-Benzyloxycarbonyl-2-(2-bromo-4-methoxyphenylmethyl)-2-methoxycarbonyl-4-(*tert*-butyldimethylsilyloxy)pyrrolidine (7b). To a stirred solution of **6** (5.75 g, 14.6 mmol) in THF (60 mL) was added dropwise a 1.0 M solution of LHMDS in THF (17.5 mL, 17.5 mmol) at -20 ˚C. After 2 h, a solution of 2-bromo-4-methoxybenzyl bromide (4.91 g, 17.5 mmol) in THF (15 mL) was added to the mixture at -20 ˚C, and then the mixture was stirred at room temperature for 2 h. The mixture was diluted with water and a saturated solution of NH_4Cl, and extracted with AcOEt. The organic phase was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel with hexane-AcOEt (4:1) to give a 4:1 mixture of **7b** and its diastereomer (7.86 g, 91%). IR ($CHCl_3$): 1740, 1698 cm^{-1}; Rotamers of **7b** and its diastereomer were observed by the ^1H NMR due to the benzyloxycarbonyl group; ^1H NMR (270 MHz, $CDCl_3$) δ -0.13-0.12 (6H, m), 0.75 (s), 0.76 (s), 0.79 (s, total 9H), 1.96-2.23 (1H, m), 2.42-2.67 (1H, m), 3.16-3.26 (1H x 4/5, m), 3.36-3.63 (4H, m), 3.50 (s), 3.74 (s), 3.76 (s), 3.77 (s, total 6H), 4.41-4.51 (1H x 1/5, m), 4.94-5.33 (2H, m), 6.57-7.44 (8H, m). Anal. Calcd for $C_{28}H_{38}BrNO_6Si$: C, 56.75; H, 6.46; N, 2.36. Found: C, 56.95; H, 6.59; N, 2.33.

(2*R*,4*R*)-1-Benzyloxycarbonyl-2-(2-bromo-4-methoxyphenylmethyl)-4-hydroxy-2-methoxycarbonylpyrrolidine (8b). To a stirred solution of **7b** (579 mg, 0.98 mmol) in THF (5 mL) was added dropwise a 1.0 M solution of tetrabutylammonium fluoride in THF (1.1 mL, 1.1 mmol) at room temperature. After 2 h, the mixture was diluted with water and extracted with AcOEt. The organic phase was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel with hexane-AcOEt (4:1)

to give a 4:1 mixture of **8b** and its diastereomers (451 mg, 97%). The mixture was further purified by recrystallization from hexane-Et_2O to afford **8b** (318 mg, 68% from **7b**) in diastereomerically pure form. mp 53-55 ˚C; $[\alpha]^{23}_D$ -154.6 (*c* 0.50, $CHCl_3$); IR ($CHCl_3$) 3021, 1744, 1698 cm^{-1}; Two rotamers (3:2) of **8b** were observed by the ^1H NMR due to the benzyloxycarbonyl group; ^1H NMR (270 MHz, $CDCl_3$) δ 2.10 (1H, br d, *J* = 14.5 Hz), 2.22 (1H x 3/5, dd, *J* = 14.5, 4.6 Hz), 2.27 (1H x 2/5, dd, *J* = 14.5, 5.3 Hz), 2.83 (1H x 3/5, dd, *J* = 11.9, 4.3 Hz), 2.92 (1 x 2/5, dd, *J* = 11.9, 4.3 Hz), 3.44-3.81 (6H, m), 3.54 (3H x 2/5, s), 3.76 (3H x 3/5, s), 3.77 (3H x 2/5, s), 3.87 (3H x 3/5, s), 5.11 (1H x 3/5, d, *J* = 12.5 Hz), 5.17 (1H x 2/5, d, *J* = 11.9 Hz), 5.26 (1H x 2/5, d, *J* = 11.9 Hz), 5.34 (1H x 3/5, d, *J* = 12.2 Hz), 6.58 (1H x 3/5, dd, *J* = 8.6, 2.6 Hz), 6.72-6.87 (1H+1H x 2/5, m), 7.07 (1H x 3/5, d, *J* = 2.6 Hz), 7.09 (1H x 2/5, d, J = 2.3 Hz), 7.20-7.50 (4H, m). Anal. Calcd for $C_{22}H_{24}BrNO_6$: C, 55.24; H, 5.06; N, 2.93. Found: C, 55.09; H, 5.17; N, 2.93.

(*R*)-1-Benzyloxycarbonyl-2-(2-bromo-4-methoxyphenylmethyl)-2-methoxycarbonyl-4-oxopyrrolidine (9b). To a stirred solution of **8b** (82.0 mg, 0.172 mmol) in CH_2Cl_2 (0.8 mL) was added PCC (100 mg, 0.344 mmol) and Florisil (200 mg) at room temperature. After 10 h, the mixture was diluted with Et_2O and filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with hexane-AcOEt (4:1) to give **9b** (97.4 mg, 97%) as a colorless oil. $[\alpha]^{23}_D$ -85.2 (*c* 1.12, $CHCl_3$); IR ($CHCl_3$) 1767, 1748, 1707 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.74 (1H, d, *J* = 18.5 Hz), 2.95 (1H, d, *J* = 18.5 Hz), 3.29-3.94 (4H, m), 3.57 (3H x 1/2, s), 3.80 (3H x 1/2, s), 3.76 (3H, s), 5.16 (1H, d, *J* = 12.2 Hz), 5.31 (1H, d, *J* = 12.2 Hz), 6.63 (1H, br d, *J* = 9.6 Hz), 6.82 (1H, br d, *J* = 6.8 Hz), 7.05 (1H, br s), 7.37-7.40 (5H, m). Anal. Calcd for $C_{22}H_{22}BrNO_6$: C, 55.48; H, 4.66; N, 2.94. Found: C, 55.23; H, 4.67; N, 2.89.

(*S*)-1-Benzyloxycarbonyl-2-(2-bromo-4-methoxyphenylmethyl)-2-methoxycarbonyl-4-(phenythiomethylene)pyrrolidine (10b). A suspension of anhydrous $CeCl_3$ (2.35 g, 9.55 mmol) in THF (27 mL) was stirred vigorously for 2 h at

room temperature, and then cooled to -78 ˚C. To the suspension was added a solution of $PhSCHLiP(O)Ph_2$ [prepared by treatment of a solution of $PhSCH_2P(O)Ph_2$ (2.66 mg, 8.19 mmol) in THF (15 mL) with a 1.6 M solution of BuLi in hexane (5.15 mL, 8.19 mmol) at -78 ˚C] at -78 ˚C for 20 min. After 30 min, a solution of **9b** (1.30 g, 2.73 mmol) in THF (15 mL) was added to the mixture at -78 ˚C, and then the mixture was allowed to warm to room temperature. After stirring at room temperature for 3 h, TMEDA (1.11 g, 9.55 mmol) was added to the mixture, and the mixture was stirred for 30 min. The mixture was diluted with a saturated solution of $NaHCO_3$ (80 mL), and the whole was extracted with $CHCl_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to give a crude adduct of **9b** with $PhSCH_2P(O)Ph_2$ as a pale yellow oil. The oil was dissolved in THF (50 mL). To the stirred solution was added NaH (60% dispersion, 800 mg, 20 mmol) at room temperature. After 3 h, the mixture was diluted with a saturated solution of NH_4Cl, and the whole was extracted with AcOEt. The organic phase was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford **10b** (1.27 g, 80%) as a mixture of geometrical isomers. IR ($CHCl_3$) 1738, 1701, 1605 cm^{-1}; Two rotamers (1:1) of **10b** were observed by the ^1H NMR due to the benzyloxycarbonyl group; ^1H NMR (270 MHz, $CDCl_3$) δ 2.79 (1H, d, *J* = 16.8 Hz), 3.16 (1H, dd, *J* = 16.8, 5.6 Hz), 3.44-4.29 (4H, m), 3.47 (3H x 1/2, s), 3.65 (3 x 1/2, s), 3.68 (3H x 1/2, s), 3.78 (3H x 1/2, s), 5.11 (1H x 1/2, d, *J* = 12.2 Hz), 5.14 (1H x 1/2, d, *J* = 12.5 Hz), 5.28 (1H x 1/2, d, *J* = 12.2 Hz), 5.11 (1H x 1/2, d, *J* = 12.5 Hz), 5.77 (1H, br d, *J* = 7.6 Hz), 6.60 (1H x 1/2, dd, *J* = 8.6, 2.6 Hz), 6.70 (1H x 1/2, dd, *J* = 8.6, 2.6 Hz), 6.76 (1H x 1/2, d, *J* = 8.6 Hz), 6.94 (1H x 1/2, d, *J* = 8.6 Hz), 7.07 (1H, d, *J* = 8.6 Hz), 6.97-7.42 (10H, m). Anal. Calcd for $C_{29}H_{28}BrNO_5S$: C, 59.80; H, 4.84; N, 2.40. Found: C, 60.10; H, 4.83; N, 2.20.

(1*S*,4*R*)-3-Benzyloxycalbonyl-8-methoxy-4-methoxycarbonyl-1-phenylthiomethyl-2,3,4,5-tetrahydro-1,4-methano-3-benzazepine (13b). To a solution of **10b** (1.30 g, 2.23 mmol) in boiling benzene (210 mL) was added dropwise a

mixture of Bu_3SnH (974 mg, 3.35 mmol) and AIBN (80 mg, 0.45 mmol) in benzene (40 mL) over 40 min, and the mixture was further heated at reflux for 3 h. After cooling, the mixture was concentrated under reduced pressure. The residue was dissolved in Et_2O (40 mL), and the solution was vigorously stirred with an 8% solution of KF overnight. The organic phase was separated, and the aqueous phase was further extracted with Et_2O. The organic phases were combined, washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with hexane-AcOEt (4:1) to give **13b** (855 mg, 76%) as a colorless oil. $[\alpha]^{25}_D$ -77.6 (*c* 0.60, $CHCl_3$); IR ($CHCl_3$) 1741, 1698 cm^{-1}; Two rotamers (1:1) of **13b** were observed by the ^1H NMR due to the benzyloxycarbonyl group; ^1H NMR (270 MHz, $CDCl_3$) δ 2.26 (1H, br d, *J* = 10.9 Hz), 2.41 (1H, m), 3.36-3.79 (6H, m), 3.44 (3H x 1/2, s), 3.77 (3H, s), 3.80 (3H x 1/2, s), 4.94 (1H x 1/2, d, *J* = 12.5 Hz), 4.96 (1H x 1/2, d, *J* = 12.5 Hz), 5.10 (1H x 1/2, d, *J* = 12.5 Hz), 5.20 (1H x 1/2, d, *J* = 12.5 Hz), 6.77 (1H x 1/2, dd, *J* = 8.2, 2.6 Hz), 6.79 (1H x 1/2, dd, *J* = 8.3, 2.6 Hz), 6.86 (1H, d, *J* = 2.3 Hz), 7.05 (1H x 1/2, d, *J* = 8.3 Hz), 7.11 (1H x 1/2, d, *J* = 8.6 Hz), 7.18-7.38 (10H, m). Anal. Calcd for $C_{29}H_{29}NO_5S$: C, 69.16; H, 5.80; N, 2.78. Found: C, 68.89; H, 5.93; N, 2.60.

(1*S*,4*R*)-3-Benzyloxycalbonyl-8-methoxy-1-phenylthiomethyl-2,3,4,5-tetrahydro-1,4-methano-3-benzazepine (18). A solution of **13b** (1.23 g, 2.44 mmol) in 5 N aqueous NaOH-MeOH (2:1, 15 mL) was heated at reflux for 2 h. The mixture was diluted with water (40 mL) and washed with Et_2O. The aqueous phase was acidified to pH 1-2 and extracted with $CHCl_3$. The organic phase was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to give crude carboxylic acid **16** (1.20 g, quant.) as a pale yellow oil. ^1H NMR (270 MHz, $CDCl_3$) δ 2.34 (1H, d, *J* = 11.2 Hz), 2.52 (1H, d, *J* = 11.2 Hz), 3.34-3.80 (6H, m), 3.77 (3H, s), 4.99 (1H, br d, *J* = 12.5 Hz), 5.12 (1H, dd, *J* = 12.2, 8.9 Hz), 6.76-6.88 (2H, m), 7.03 (1H x 1/2, d, *J* = 8.3 Hz), 7.11 (1H x 1/2, d, *J* = 8.6 Hz), 7.20-7.39 (10H, m). This compound was used immediately for the next step without further purification. To a stirred solution of the

crude acid **16** (1.13 g, 2.30 mmol) in benzene (30 mL) was added to a solution of 2-mercaptopyridine *N*-oxide (350 mg, 2.76 mmol), DMAP (421 mg, 3.45 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 660 mg, 3.45 mmol) in benzene (10 mL) at room temperature. After 30 min, to the mixture was added a solution of Bu_3SnH (2.00 g, 6.87 mmol) and AIBN (110 mg, 0.67 mmol) in benzene (150 mL), and then the mixture was heated at reflux for 3 h. After cooling, the mixture was concentrated under reduced pressure. The residue was dissolved in Et_2O (40 mL), and then the solution was vigorously stirred with an 8% solution of KF (30 mL) overnight. The organic phase was separated, and the aqueous phase was further extracted with Et_2O. The organic phases were combined, washed with brine, dried ($MgSO_4$) and concentrated under reduce pressure. The residue was purified by column chromatography on silica gel with hexane-AcOEt (4:1) to afford **18** (530 mg, 52%) as a colorless oil. $[\alpha]^{25}_D$ -95.6 (*c* 0.76, $CHCl_3$); IR ($CHCl_3$) 1693 cm^{-1}; Two rotamers (1:1) of **18** were observed by the ^1H NMR due to the benzyloxycarbonyl group; ^1H NMR (270 MHz, $CDCl_3$) δ 2.00-2.06 (2H, m), 2.89-2.96 (1H, m), 3.06 (1H x 1/2, d, *J* = 7.2 Hz), 3.20 (1H x 1/2, d, *J* = 6.8 Hz), 3.38-3.79 (4H, m), 3.76 (3H, s), 4.44 (1H x 1/2, dt, *J* = 5.9, 2.9 Hz), 4.51(1H x 1/2, dt, *J* = 5.9, 2.9 Hz), 4.95 (1H x 1/2, d, *J* = 12.2 Hz), 5.10 (1H x 1/2, d, *J* = 12.5 Hz), 5.12 (1H x 1/2, d, *J* = 12.2 Hz), 5.16 (1H x 1/2, d, *J* = 12.5 Hz), 6.73-6.78 (1H, m), 6.87 (1H, br s), 7.00 (1 x 1/2, d, *J* = 8.6 Hz), 7.06 (1H x 1/2, d, *J* = 8.3 Hz), 7.17-7.39 (10H, m). Anal. Calcd for $C_{27}H_{27}NO_3S$: C, 72.78; H, 6.11; N, 3.14. Found: C, 72.53; H, 6.28; N, 3.49.

***O*-Methyl-(-)-aphanorphine (20).** To a solution of **18** (32.0 mg, 0.072 mg) in MeOH (3 mL) was added W-2 Raney nickel (*ca* 50 mg), and then the mixture was heated at reflux for 6 h. After cooling, the mixture was filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on alumina with $CHCl_3$-MeOH (50:1) to give **20** (10.0 mg, 65%) as a colorless oil. $[\alpha]^{23}_D$ +9.39 (*c* 0.30, $CHCl_3$), {lit[1c] $[\alpha]^{29}_D$ +8.46 (*c* 0.35, $CHCl_3$), lit[1j] $[\alpha]^{21}_D$ +10.4 (*c* 1.24, $CHCl_3$)}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.47 (3H,

s), 1.84 (1H, d, *J* = 10.9 Hz), 2.00 (1H, dd, *J* = 9.6, 5.9 Hz), 2.46 (3H, s), 2.71 (1H, d, *J* = 8.8 Hz), 2.78-2.91 (3H, m), 3.38 (1H, m), 3.78 (3H, s), 6.68 (1H, dd, *J* = 8.3, 2.6 Hz), 6.78 (1H, d, *J* = 2.6 Hz), 7.02 (1H, d, *J* = 8.3 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 21.3, 34.9, 41.2, 41.6, 43.1, 55.3, 61.3, 70.8, 109.1, 111.2, 125.5, 130.2, 147.8, 157.9. These ^{1}H and ^{13}C NMR spectral data are identical with those reported.[1j]

(-)-Aphanorphine (1). According to the reported method,[1c,j] **20** was converted to **1**, mp 200-210 ˚C (lit[1c] mp 215-222 ˚C). $[\alpha]^{21}_{D}$ -23.6 (*c* 0.20, MeOH) {lit[1j] $[\alpha]^{23}_{D}$ -24.0 (*c* 0.33, MeOH)}; ^{1}H NMR (270 MHz, CD_3OD) δ 1.44 (3H, s), 1.86 (1H, d, *J* = 10.9 Hz), 2.02 (1H, dd, *J* = 10.9, 5.6 Hz), 2.48 (3H, s), 2.73 (1H, d, *J* = 9.2 Hz), 2.83 (1H, br d, *J* = 16.5 Hz), 2.87 (1H, d, *J* = 9.2 Hz), 3.03 (1H, d, *J* = 16.5 Hz), 3.42 (1H, quin, *J* = 2.6 Hz), 6.91 (1H, dd, *J* = 8.3, 2.3 Hz), 6.65 (1H, d, *J* = 2.3 Hz), 6.52 (1H, d, *J* = 8.3 Hz); ^{13}C NMR (67.8 MHz, CD_3OD) δ 21.6, 36.5, 42.1, 42.7, 44.2, 63.5, 72.6, 110.9, 114.5, 125.2, 131.2, 148.5, 156.5. These ^{1}H and ^{13}C NMR spectral data are identical with those kindly provided by Professor K. Ogasawara.