Supplemental materials for:

A Convergent and Enantioselective Synthesis of Amurensinine via Selective C-H and C-C Bond Insertion Reactions

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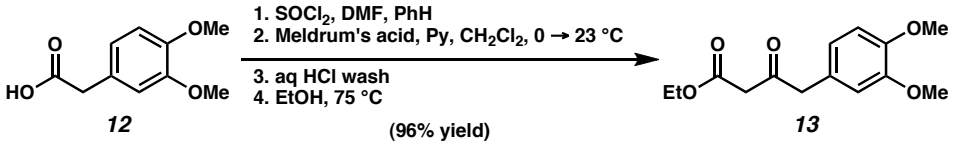
Table of Contents:

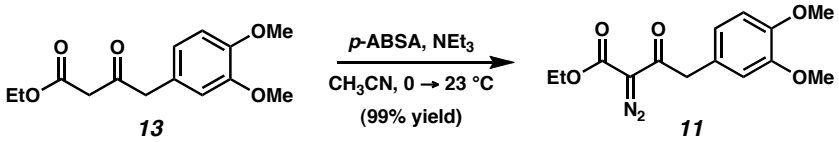
Materials and Methods. Unless stated otherwise, reactions were performed in flame-dried glassware sealed with rubber septa under a nitrogen atmosphere using dry, deoxygenated solvents. Commercially obtained reagents were used as received. Solvents were dried by passage through an activated alumina column under argon. Liquids and solutions were transferred via syringe. Reaction temperatures were controlled using an IKAmag temperature modulator. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates, (0.25 mm) and visualized using a combination of UV, anisaldehyde, ceric ammonium molybdate, and potassium permanganate staining. Preparative TLC was conducted with E. Merck silica gel 60 F254 pre-coated plates, (0.25 or 0.5 mm) and visualized using UV. ICN silica gel (particle size 0.032-0.063 mm) was used for flash column chromatography. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing a Chiralpak AD, Chiralcel OD-H, or Chiralcel OJ column (each is 4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd with visualization at 254 nm. ^{1}H NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz) or a Varian Inova 500 (at 500 MHz) and are reported relative to Me_4Si (δ 0.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR spectra were recorded on a Varian Mercury 300 (at 75 MHz) or Varian Inova 500 (at 125 MHz) and are reported relative to Me_4Si (δ 0.0). Data for ^{13}C NMR spectra are reported in terms of chemical shift. Optical rotations were measured with a Jasco P-1010 polarimeter at 589 nm. IR spectra were recorded on a Perkin Elmer Spectrum BXII spectrometer and are reported in terms of frequency of absorption (cm^{-1}). UV-Vis spectra were collected on an Agilent 8453 UV-Vis spectrometer and are reported in terms of

wavelength of absorption (nm). High resolution mass spectra were obtained from the California Institute of Technology Mass Spectral Facility.

Preparative Procedures.

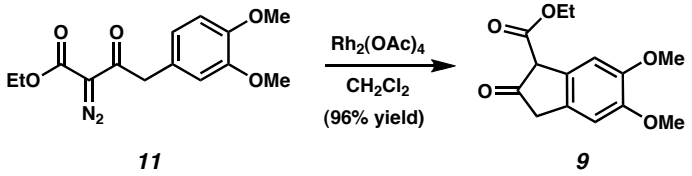


β-Ketoester 13. To a solution of (3,4-dimethoxyphenyl)acetic acid (**12**) (1.0 g, 5.1 mmol) in benzene (5 mL) was added thionyl chloride (741 μl, 10.2 mmol) and 4 drops of DMF. After stirring for 3 h, the reaction mixture was concentrated under reduced pressure. The resulting crude acid chloride was then dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C. To this solution was added pyridine (825 μL, 10.2 mmol) and Meldrum's acid (735 mg, 5.1 mmol). After stirring at 0 °C for 2 min, the mixture was stirred at room temperature for 8 h. The reaction was then washed with 10% aqueous HCl (10 mL) followed by H_2O (10 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was then dissolved in absolute EtOH (10 mL) and refluxed at 75 °C. After 11 h, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. Purification by flash chromatography (5:1→3:1→1:1 hexanes/EtOAc eluent gradient) provided β-ketoester **13** (1.31 g, 96% yield) as a clear oil. The characterization data matched the data reported in the literature.[1]



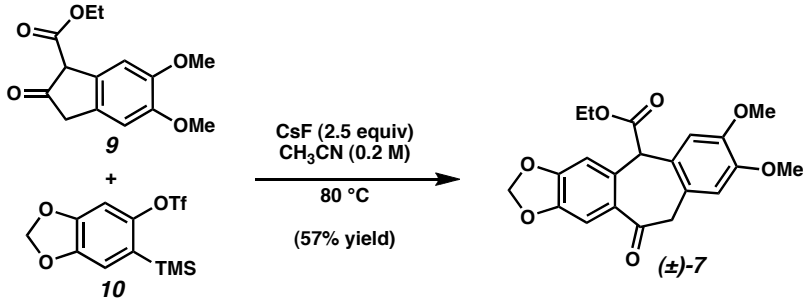
Diazoketoester 11. To a cooled solution (0 °C) of β-ketoester **13** (445 mg, 1.67 mmol) in acetonitrile (8 mL) was added *p*-ABSA (441 mg, 1.84 mmol) and NEt_3 (698 μL, 5.01 mmol). After stirring at 0 °C for 1 min, the mixture was stirred at room temperature for 90 min. Then, the reaction was washed with 10% aqueous NaOH (10 mL). The aqueous layer was then extracted with Et_2O (3 x 10 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (4:1 hexanes/EtOAc eluent) provided diazoketoester **11** (487 mg, 99% yield) as a clear oil: R_f 0.50 (1:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 7.00-6.94 (comp. m, 2H), 6.62 (d, J = 8.0 Hz, 1H), 4.12 (s, 2H), 3.89 (q, J = 7.1 Hz, 2H), 3.51 (s, 3H), 3.43 (s, 3H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, C_6D_6): δ 190.1, 161.4, 150.4, 149.7, 127.5, 122.7, 114.5, 112.7, 75.8, 61.6, 56.0, 55.9, 45.7, 14.5; IR (thin film/NaCl): 2938, 2836, 2136, 1714, 1650, 1515,

1263, 1029 cm^{-1}; HRMS-EI (*m/z*): $[M]^+$ calcd for $[C_{14}H_{16}N_2O_5]^+$, 292.1059; found, 292.1070.



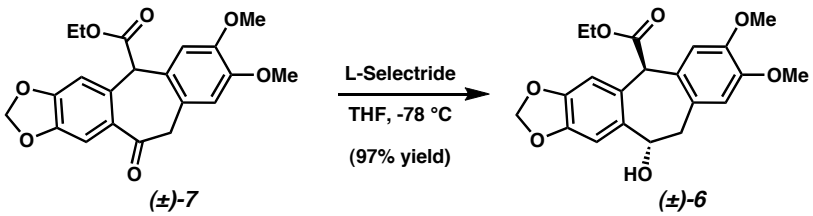
11 *9*

β-Ketoester 9. A flask equipped with an addition funnel and an N_2 inlet was charged with a catalytic amount of $Rh_2(OAc)_4$ (138 mg, 0.31 mmol) and CH_2Cl_2 (140 mL). A solution of diazoester **11** (9.12 g, 31.20 mmol) in CH_2Cl_2 (100 mL) was added dropwise over 90 min via an addition funnel. After stirring for 2.5 h at room temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash chromatography (7:3→1:1 hexanes/EtOAc eluent gradient) provided β-ketoester **9** (7.88 g, 96% yield) as a white solid: R_f 0.52 (1:1 hexanes/EtOAc); mp 117 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.85 (s, 1H), 7.23 (s, 1H), 6.92 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 3.52 (d, *J* = 0.8 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.1, 148.7, 146.3, 132.6, 125.1, 108.6, 105.2, 105.2, 105.0, 60.7, 56.6, 56.2, 37.8, 14.6; IR (thin film/NaCl): 2976, 2833, 1650, 1602, 1494, 1469, 1305 cm^{-1}; HRMS-FAB (*m/z*): $[M]^+$ calcd for $[C_{14}H_{16}O_5]^+$, 264.0998; found, 264.1003.

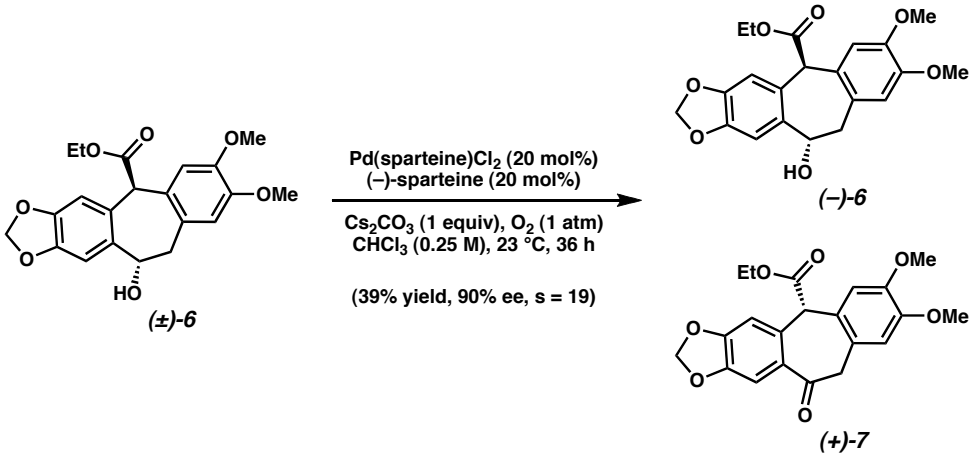


Ketoester (±)-7. To a solution of aryne precursor **10** (898 mg, 2.62 mmol) in dry acetonitrile (9 mL) was added β-ketoester **9** (415 mg, 1.57 mmol) and cesium fluoride (715 mg, 4.71 mmol). The reaction was quickly immersed in an 80 °C oil bath and allowed to reflux until **10** was consumed (2 h). The reaction mixture was then cooled to room temperature and washed with sat. brine (15 mL). The aqueous layer was back-extracted with Et_2O (3 x 15 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (1:1 hexanes/EtOAc eluent) provided ketoester (±)-**7** (348 mg, 57% yield) as a clear oil: R_f 0.23 (1:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 8.03 (s, 1H), 6.67 (s, 1H), 6.53 (s, 1H), 6.44 (s, 1H), 5.13 (d, *J* = 1.3 Hz, 1H), 5.10 (d, *J* = 1.3 Hz, 1H), 4.59 (d, *J* = 15.4 Hz, 1H), 4.54 (s, 1H), 3.90 (dq, *J* = 7.1, 2.0 Hz, 2H), 3.83 (d, *J* = 15.3 Hz, 1H), 3.41 (s, 3H), 3.24 (s, 3H), 0.84 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, C_6D_6): δ 192.4, 171.4, 151.7, 150.2, 149.1, 148.5, 137.1, 130.6, 130.5, 125.9, 115.6, 114.9, 111.4, 110.8, 102.1,

61.9, 59.7, 56.3, 55.9, 50.0, 14.4; IR (thin film/NaCl): 2908, 1727, 1663, 1616, 1518, 1506, 1485, 1254 cm^{-1}; HRMS-EI (*m/z*): $[M]^+$ calcd for $[C_{21}H_{20}O_7]^+$, 384.1209; found, 384.1212.

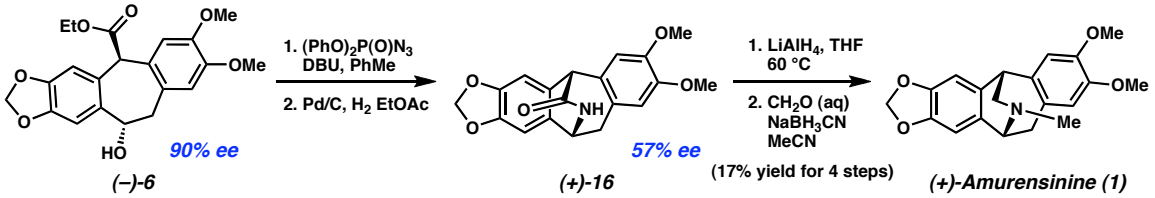


Hydroxyester (±)-6. To a solution of ketoester (±)-**7** (52.9 mg, 0.138 mmol) in THF (1.5 mL) at –78 °C was added dropwise a 1.0 M solution of L-Selectride in THF (200 µL, 0.206 mmol). The resulting solution was stirred for 25 min at –78 °C and then quenched with saturated aq NH_4Cl (5 mL). After warming to room temperature and stirring 25 min, the mixture was extracted with Et_2O (4 x 5 mL). The organics were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (1:1 hexanes/EtOAc eluent) provided hydroxyester (±)-**6** (51.4 mg, 97% yield) as a yellow solid: R_f 0.33 (1:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.99 (s, 1H), 6.77 (s, 1H), 6.72 (s, 1H), 6.69 (s, 1H), 5.94 (d, *J* = 1.5 Hz, 1H), 5.92 (d, *J* = 1.0 Hz, 1H), 5.02-4.96 (m, 1H), 4.59 (s, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.50 (dd, *J* = 15.1, 2.4 Hz, 1H), 2.93 (dd, *J* = 15.1, 6.8 Hz, 1H), 1.73 (d, *J* = 8.3 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.6, 148.4, 147.6, 147.6, 146.9, 135.2, 129.6, 128.0, 127.3, 114.9, 114.5, 111.3, 110.7, 101.4, 69.4, 61.8, 58.5, 56.2, 56.1, 39.6, 14.3; IR (thin film/NaCl): 3500, 2937, 1725, 1610, 1520, 1486, 1244 cm^{-1}; HRMS-EI (*m/z*): $[M]^+$ calcd for $[C_{21}H_{22}O_7]^+$, 386.1366; found, 386.1366.



Kinetic Resolution of Hydroxyester (±)-6: Hydroxyester (–)-6. To a 1 dram vial with stir bar was added oven-dried powdered 3Å molecular sieves (190 mg). After cooling, Pd(sparteine)Cl_2[2] (31.5 mg, 0.076 mmol) followed by $CHCl_3$ (750 µL, stabilized

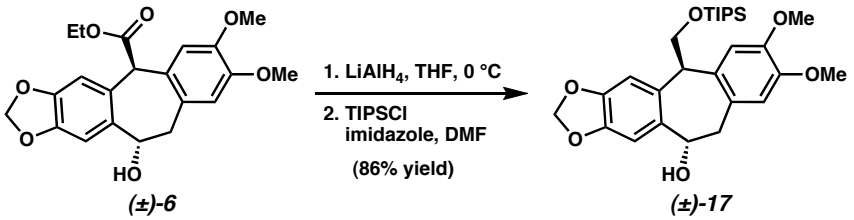
with amylenes) and (–)-sparteine (17.6 μL, 0.076 mmol) were added. The mixture was then cooled to –78 °C and alternately evacuated and backfilled with O_2 (3x). After allowing the mixture to warm to room temperature, powdered anhydrous Cs_2CO_3 (124.5 mg, 0.38 mmol) followed by a solution of hydroxyester (±)-**6** (147.7 mg, 0.38 mmol) in $CHCl_3$ (750 μL) were added, and the reaction was stirred vigorously under a balloon of O_2 for 36 h. The reaction mixture was then filtered through a short plug of silica gel (EtOAc eluent) and evaporated under reduced pressure. Purification by flash chromatography (3:1 hexanes/EtOAc eluent) afforded hydroxyester (–)-**6** (56.8 mg, 39% yield) and ketoester (+)-**7** (36.6 mg). Hydroxyester (–)-**6** was found to be 90.4% ee by chiral HPLC (AD column, 0.55 mL/min, 60% EtOH/hexanes, major peak 16.3 min, minor peak 26.7 min); $[\alpha]^{25}_D$ –64.3° (c 0.78, $CHCl_3$) (at 87.9% ee). Ketoester (+)-**7** was found to be 73.0% ee by chiral HPLC (AD column, 0.55 mL/min, 60% EtOH/hexanes, major peak 46.6 min, minor peak 20.5 min); $[\alpha]^{25}_D$ +19.9° (c 0.47, $CHCl_3$) (at 84.8% ee).



Lactam (+)-16. To a solution of hydroxyester (–)-**6** (9.7 mg, 0.025 mmol) in toluene (500 μL) at 0 °C was added $(PhO)_2P(O)N_3$ (27 μL, 0.126 mmol) and DBU (19 μL, 0.126 mmol). The resulting solution was stirred for 30 min at 0 °C and then stirred at room temperature for 12 h. The reaction was then quenched with H_2O (3 mL) and extracted with Et_2O (3 x 3 mL). The organics were combined and dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude azide was passed through a short pad of SiO_2 (EtOAc eluent) and concentrated under reduced pressure. To a solution of the azide in EtOAc (1.5 mL) was added Pd/C (10% by wt., 15 mg). The reaction flask was placed under a balloon of H_2 gas (1 atm) and stirred at room temperature for 9 h. The reaction mixture was then passed through a short pad of Celite (Et_2O eluent) and concentrated under reduced pressure. Lactam (+)-**16** was used in the next step without further purification: R_f 0.46 (9:1 $CHCl_3$/MeOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.75 (s, 1H), 6.74 (s, 1H), 6.72 (s, 1H), 6.55-6.52 (m, 1H), 6.49 (s, 1H), 5.94 (d, J = 1.5 Hz, 1H), 5.88 (d, J = 1.5 Hz, 1H), 4.58-4.54 (m, 1H), 4.21 (d, J = 2.0 Hz, 1H), 3.88 (s, 3H), 3.78 (s, 3H), 3.28 (dd, J = 16.8, 4.6 Hz, 1H), 3.07 (dd, J = 17.1, 2.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.4, 148.8, 147.6, 147.2, 146.7, 134.1, 130.0, 128.1, 125.2, 114.7, 112.1, 106.7, 105.6, 101.4, 56.7, 56.2, 56.1, 53.6, 36.9; IR (thin film/NaCl): 3221, 2916, 1680, 1517, 1485, 1465, 1246 cm^{-1}; HRMS-FAB (*m/z*): $[M+H]^+$ calcd for $[C_{19}H_{18}NO_5]^+$, 340.1185; found, 340.1181. Lactam (+)-**16** was found to be 57.0% ee by chiral HPLC (OD-H column, 1.0 mL/min, 15% EtOH/hexanes, major peak 29.0 min, minor peak 45.1 min).

(+)-Amurensinine (1). To a solution of crude lactam (+)-**16** in THF (1 mL) was added lithium aluminum hydride (30 mg, 0.0751 mmol). The resulting solution was stirred for 8 h at 60 °C. The reaction mixture was then cooled to 0 °C and sequentially

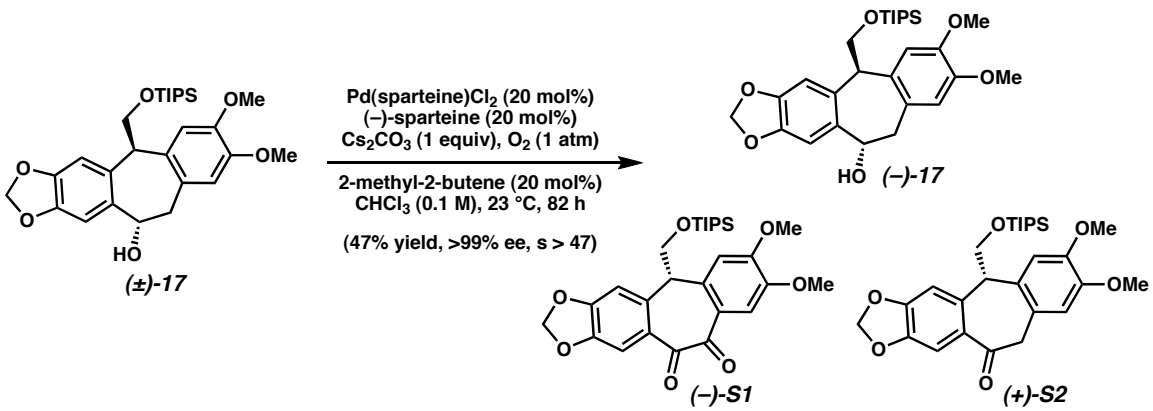
quenched with H_2O (30 μL), 15% aqueous NaOH (30 μL), and H_2O (90 μL). The slurry was stirred at room temperature for 25 min, passed through a short pad of Celite (Et_2O eluent), and concentrated under reduced pressure to afford the crude secondary amine. To a solution of the crude secondary amine in acetonitrile (1 mL) was added $NaBH_3CN$ (10 mg, 0.159) and aqueous formaldehyde (37 wt %, 50 μL). After stirring at room temperature for 2 h, the reaction mixture was washed with H_2O (2 mL). The aqueous layer was back-extracted with CH_2Cl_2 (3 x 3 mL). The organics were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by preparative TLC on silica gel (0.25 mm, 9:1 $CHCl_3$/MeOH eluent) provided (+)-amurensinine (**1**) (1.5 mg, 17% yield for 4 steps) as a colorless thin film: R_f 0.18 (9:1 $CHCl_3$/MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.72 (s, 1H), 6.71 (s, 1H), 6.62 (s, 1H), 6.52 (s, 1H), 5.91 (d, J = 1.4 Hz, 1H), 5.85 (d, J = 1.4 Hz, 1H), 3.86 (s, 3H), 3.84 (dd, J = 3.7, 3.7 Hz, 1H), 3.77 (s, 3H), 3.62 (dd, J = 4.5, 1.5 Hz, 1H), 3.53 (dd, J = 10.4, 1.6 Hz, 1H), 3.48 (dd, J = 17.0, 4.1 Hz, 1H), 2.90 (dd, J = 17.3, 3.5 Hz, 1H), 2.83 (dd, J = 10.6, 4.6 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.7, 146.6, 146.3, 145.9, 135.1, 134.5, 131.2, 126.5, 114.2, 111.1, 107.2, 106.1, 100.6, 62.5, 59.9, 56.0, 55.9, 46.0, 45.3, 38.2; IR (thin film/NaCl): 2916, 2848, 1607, 1517, 1482, 1249 cm^{-1}; HRMS-EI (m/z): $[M]^+$ calcd for $[C_{20}H_{21}NO_4]^+$, 339.1471; found, 339.1469; UV-Vis λ_{max} 294 nm, shoulders at 232 and 250 nm, λ_{min} at 263 nm; $[\alpha]^{25}_D$ +82.8° (*c* 0.035, CH_2Cl_2) [lit.[3] $[\alpha]^{20}_D$ –145.0° (*c* 1.0, CH_2Cl_2)].



(±)-6 *(±)-17*

(±)-Hydroxysilane (±)-17. To a solution of hydroxyester (±)-**6** (76.6 mg, 0.20 mmol) in THF (4 mL) was added lithium aluminum hydride (37.6 mg, 0.99 mmol) at 0 °C. After 30 min, the reaction was quenched at 0 °C by slow addition of EtOAc (5 mL) followed by 10% w/v aq sodium potassium tartrate (5 mL). After warming to room temperature and stirring vigorously for 1 h, the biphasic mixture was diluted with H_2O (10 mL) and extracted with EtOAc (4 x 20 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude diol, which was carried on to the next step without further purification. Diol: R_f 0.12 (2:3 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 7.10 (s, 1H), 6.69 (s, 1H), 6.56 (s, 1H), 6.49 (s, 1H), 5.36 (dd, J = 1.4, 0.5 Hz, 1H), 5.34 (dd, J = 1.4, 0.6 Hz, 1H), 4.82 (br d, J = 6.8 Hz, 1H), 3.86-3.78 (comp. m, 3H), 4.15 (s, 1H), 3.44 (s, 3H), 3.40 (s, 3H), 3.21 (dd, J = 15.0, 2.6 Hz, 1H), 2.83 (dd, J = 15.0, 7.9 Hz, 1H), 1.37 (br s, 1H), 1.03 (br s, 1H). To a solution of crude diol in DMF (4 mL) was added imidazole (40.5 mg, 0.60 mmol) then tri-isopropylchlorosilane (63.7 μL, 0.30 mmol). After stirring 12 h at room temperature, the solution was quenched by addition of H_2O (20 mL). The mixture was then extracted

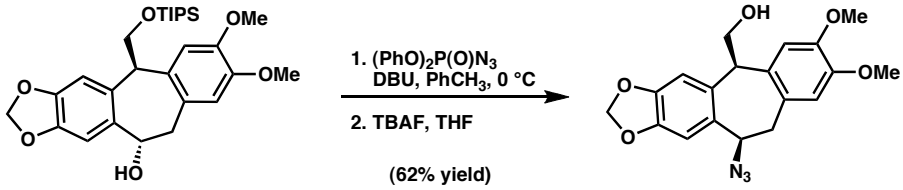
with EtOAc (4 x 30 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (2:3 hexanes/Et_2O eluent) provided hydroxysilane (±)-**17** (85.8 mg, 86% yield over 2 steps) as a white solid: R_f 0.28 (3:2 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 7.11 (s, 1H), 6.86 (s, 1H), 6.74 (s, 1H), 6.55 (s, 1H), 5.37 (d, J = 1.3 Hz, 1H), 5.34 (d, J = 1.3 Hz, 1H), 4.93 (ddd, J = 7.9, 7.9, 1.9 Hz, 1H), 4.18-4.15 (comp. m, 2H), 4.09 (dd, J = 15.5, 8.1 Hz, 1H), 3.53 (s, 3H), 3.41 (s, 3H), 3.41 (dd, J = 14.8, 2.2 Hz, 1H), 2.91 (dd, J = 14.9, 7.6 Hz, 1H), 1.36 (d, J = 8.4 Hz, 1H), 1.01 (comp. m, 21H); ^{13}C NMR (75 MHz, C_6D_6): δ 149.0, 148.5, 147.3, 147.1, 136.4, 132.0, 131.3, 116.6, 116.3, 112.2, 110.5, 101.1, 70.4, 68.2, 57.9, 55.9, 55.7, 41.5, 18.2, 12.3; IR (thin film/NaCl): 2941, 2865, 1520, 1487, 1240, 1098, 1041 cm^{-1}; HRMS-FAB (*m/z*): [M]$^+$ calcd for [$C_{28}H_{40}O_6Si$]$^+$, 500.2594; found, 500.2598.



Kinetic Resolution of Hydroxysilane (±)-17: Hydroxysilane (–)-17. To a 1 dram vial with stir bar was added oven-dried powdered 3Å molecular sieves (50 mg). After cooling, Pd(sparteine)Cl_2 (8.2 mg, 0.020 mmol) followed by $CHCl_3$ (500 μL, stabilized with amylenes) and (–)-sparteine (4.6 μL, 0.02 mmol) were added. The mixture was then cooled to –78 °C and alternately evacuated and backfilled with O_2 (3x). After allowing the mixture to warm to 23 °C, powdered anhydrous Cs_2CO_3 (32.6 mg, 0.10 mmol) and 2-methyl-2-butene (2.1 μL, 0.02 mmol) were added, followed by a solution of hydroxysilane (±)-**17** (50.1 mg, 0.10 mmol) in $CHCl_3$ (500 μL), and the reaction was stirred vigorously under a balloon of O_2 for 82 h. The reaction mixture was then filtered through a short plug of silica gel (EtOAc eluent) and evaporated under reduced pressure. Purification by preparative TLC (0.5 mm, 3:2 hexanes/EtOAc eluent) afforded hydroxysilane (–)-**17** (23.7 mg, 47% yield) and diketosilane (–)-**S1** (23.4 mg). Hydroxysilane (–)-**17** was found to be >99% ee by chiral HPLC (AD column, 1.0 mL/min, 5% EtOH/hexanes, major peak 13.0 min, minor peak 21.0 min); $[\alpha]^{25}_D$ –24.4° (c 0.86, C_6H_6). Reactions stopped earlier than 82 hours afforded another product in addition to hydroxysilane (–)-**17** and diketosilane (–)-**S1**. This compound was revealed to be ketosilane (+)-**S2**, which gradually oxidized to the diketone in the presence of O_2.

Diketosilane (–)-S1. R_f 0.35 (3:2 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 7.61 (s, 1H), 7.58 (s, 1H), 6.59 (s, 1H), 6.48 (s, 1H), 5.16 (s, 2H), 3.97 (d, J = 5.9 Hz, 2H), 3.79 (t, J = 5.7 Hz, 1H), 3.39 (s, 3H), 3.26 (s, 3H), 0.94 (comp. m, 21H); ^{13}C NMR (75 MHz, C_6D_6): δ 186.8, 185.8, 153.6, 151.6, 149.6, 147.9, 138.8, 136.8, 131.0, 114.5, 112.9, 111.5, 109.9, 101.9, 71.9, 58.9, 55.3, 18.1, 12.2; IR (thin film/NaCl): 2942, 2866, 1659, 1597, 1517, 1485, 1251 cm^{-1}; HRMS-FAB (*m/z*): $[M+H]^+$ calcd for $[C_{28}H_{37}O_7Si]^+$, 513.2309; found, 513.2313. Diketosilane (–)-**S1** was found to be 79.1% ee by chiral HPLC (AD column, 1.0 mL/min, 5% EtOH/hexanes, major peak 63.8 min, minor peak 24.7 min). The kinetic resolution therefore has a selectivity factor s > 47.[4] $[\alpha]^{25}_D$ –39.9° (c 1.21, C_6H_6) for 73.9% ee diketosilane (–)-**S1**.

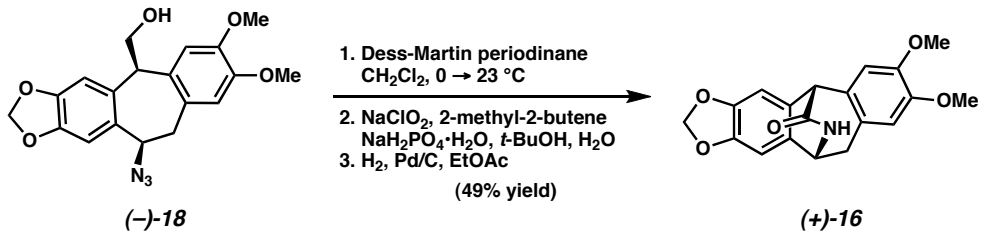
Ketosilane (+)-S2. R_f 0.50 (3:2 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 8.03 (s, 1H), 6.82 (s, 1H), 6.71 (s, 1H), 6.48 (s, 1H), 5.21 (d, J = 1.4 Hz, 1H), 5.17 (d, J = 1.2 Hz, 1H), 4.42 (d, J = 14.5 Hz, 1H), 4.37-4.26 (m, 2H), 4.24-4.13 (m, 1H), 3.83 (d, J = 14.9 Hz, 1H), 3.49 (s, 3H), 3.29 (s, 3H), 1.00 (comp. m, 21H); ^{13}C NMR (75 MHz, C_6D_6): δ 192.8, 151.3, 149.5, 148.7, 147.6, 139.9, 132.1, 130.8, 125.1, 115.2, 114.6, 110.9, 110.2, 101.7, 65.8, 56.0, 55.6, 50.3, 18.2, 12.2; IR (thin film/NaCl): 2941, 2865, 1665, 1516, 1484, 1102 cm^{-1}; HRMS-FAB (*m/z*): $[M]^+$ calcd for $[C_{28}H_{38}O_6Si]^+$, 498.2438; found, 498.2433. Ketosilane (+)-**S2** was found to be 76.8% ee by chiral HPLC (AD column, 1.0 mL/min, 5% EtOH/hexanes, major peak 20.6 min, minor peak 10.7 min); $[\alpha]^{25}_D$ +10.6° (c 0.65, C_6H_6).



(–)-17 *(–)-18*

Azidoalcohol (–)-18. To a solution of hydroxysilane (–)-**17** (100.1 mg, 0.20 mmol) in $PhCH_3$ (5 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 179 μL, 1.20 mmol) followed by diphenylphosphoryl azide (259 μL, 1.20 mmol) at 0 °C. After stirring 6 h at 0 °C, the reaction was quenched by addition of H_2O (25 mL). The mixture was then extracted with Et_2O (3 x 30 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude azidosilane was carried on to the next step without further purification. To a solution of the crude azidosilane in THF (2 mL) was added tetrabutylammonium fluoride (1 M in THF, 2.0 mL, 2.0 mmol). The reaction was warmed to 45 °C for 5 h. The solution was allowed to cool to room temperature and diluted with EtOAc (40 mL). The solution was washed with H_2O (3 x 20 mL) and sat. brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (7:3 hexanes/EtOAc eluent) followed by preparative TLC (0.5 mm, 1:1 hexanes/EtOAc eluent) afforded azidoalcohol (–)-**18** (45.9 mg, 62% yield over 2 steps) as a white foam:

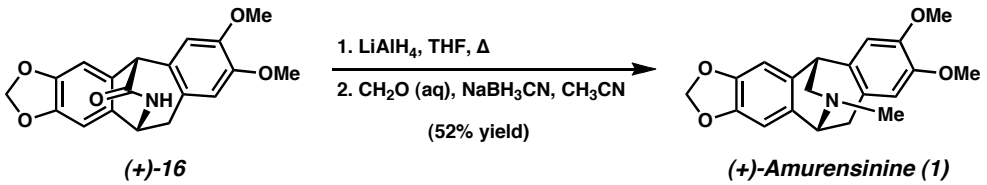
R_f 0.44 (2:3 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 7.03 (s, 1H), 6.67 (s, 1H), 6.54 (s, 1H), 6.40 (s, 1H), 5.31 (d, J = 1.4 Hz, 1H), 5.27 (d, J = 1.3 Hz, 1H), 4.27 (dd, J = 10.8, 4.6 Hz, 1H), 4.04-3.90 (comp. m, 2H), 3.86 (dd, J = 14.6, 7.3 Hz, 1H), 3.43 (s, 3H), 3.41 (s, 3H), 3.28 (dd, J = 14.7, 11.0 Hz, 1H), 2.87 (dd, J = 14.7, 4.7 Hz, 1H), 1.10 (br s, 1H); ^{13}C NMR (75 MHz, C_6D_6): δ 149.1, 148.8, 147.6, 147.3, 133.1, 132.5, 130.6, 115.1, 114.2, 110.5, 110.4, 101.3, 66.3, 62.8, 55.9, 55.9, 54.4, 38.2; IR (thin film/NaCl): 3492, 2935, 2099, 1517, 1487, 1236 cm^{-1}; HRMS-FAB (*m/z*): $[M]^+$ calcd for $[C_{19}H_{19}N_3O_5]^+$, 369.1325; found, 369.1328. Azidoalcohol (–)-**18** was found to be >99% ee by chiral HPLC (AD column, 1.0 mL/min, 30% EtOH/hexanes, major peak 17.0 min, minor peak 15.3 min); $[\alpha]^{28}_D$ –70.8° (c 0.91, CH_2Cl_2).



(–)-18 *(+)-16*

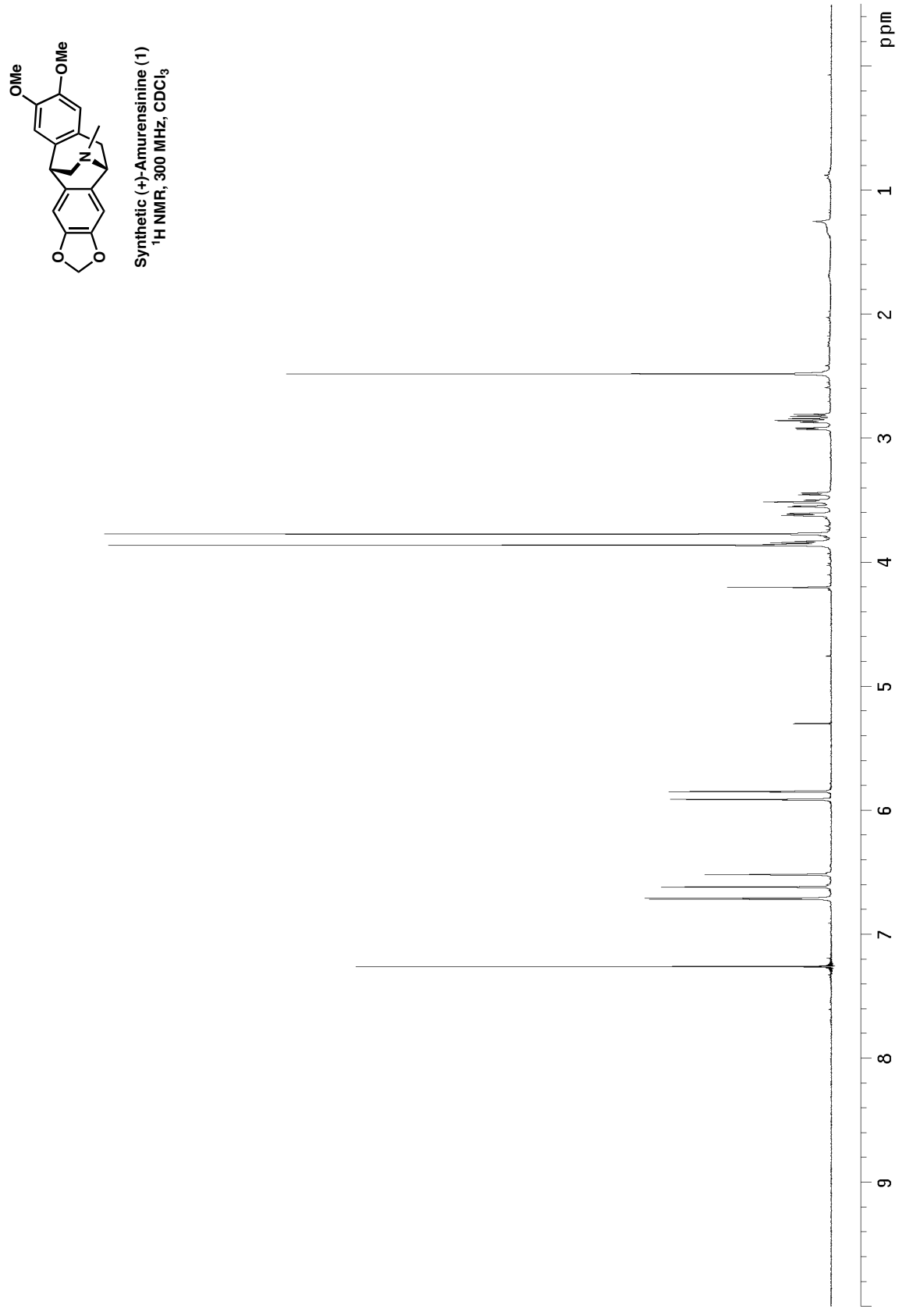
Lactam (+)-16. To a solution of azidoalcohol (–)-**18** (10.6 mg, 0.029 mmol) in CH_2Cl_2 (1 mL) was added Dess-Martin periodinane (24.3 mg, 0.057 mmol) at 0 °C. After 30 min, the mixture was diluted with Et_2O (3 mL) and filtered through a plug of Celite (Et_2O eluent). Concentration under reduced pressure afforded crude azidoaldehyde, which was used in the next step without further purification: R_f 0.77 (2:3 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6): δ 9.63 (s, 1H), 6.83 (s, 1H), 6.43 (s, 1H), 6.38 (s, 1H), 6.32 (s, 1H), 5.30 (d, J = 1.3 Hz, 1H), 5.23 (d, J = 1.3 Hz, 1H), 4.00 (dd, J = 10.6, 4.2 Hz, 1H), 3.84 (s, 1H), 3.42 (s, 3H), 3.40 (s, 3H), 3.12 (dd, J = 15.0, 10.7 Hz, 1H), 2.67 (dd, J = 15.0, 4.1 Hz, 1H). To a solution of crude azidoaldehyde in *tert*-butanol (1 mL) was added 2-methyl-2-butene (182 µL, 1.71 mmol) followed by a solution of sodium chlorite (technical grade [80%], 32.4 mg, 0.29 mmol) and sodium phosphate monobasic monohydrate (63.1 mg, 0.46 mmol) in water (1 mL). The biphasic mixture was stirred vigorously for 90 min. After diluting with sat. brine (4 mL), the mixture was extracted with EtOAc (5 x 4 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude azidoacid, which was used in the next step without purification: R_f 0.40 (9:1 $CHCl_3$/MeOH); ^{1}H NMR (300 MHz, C_6D_6): δ 6.89 (s, 1H), 6.53 (s, 1H), 6.51 (s, 1H), 6.35 (s, 1H), 5.26 (d, J = 1.4 Hz, 1H), 5.17 (d, J = 1.3 Hz, 1H), 4.32 (s, 1H), 4.07 (dd, J = 12.0, 5.2 Hz, 1H), 3.67 (dd, J = 14.4, 12.0, 1H), 3.40 (s, 3H), 3.38 (s, 3H), 2.78 (dd, J = 14.4, 5.1 Hz, 1H). To a

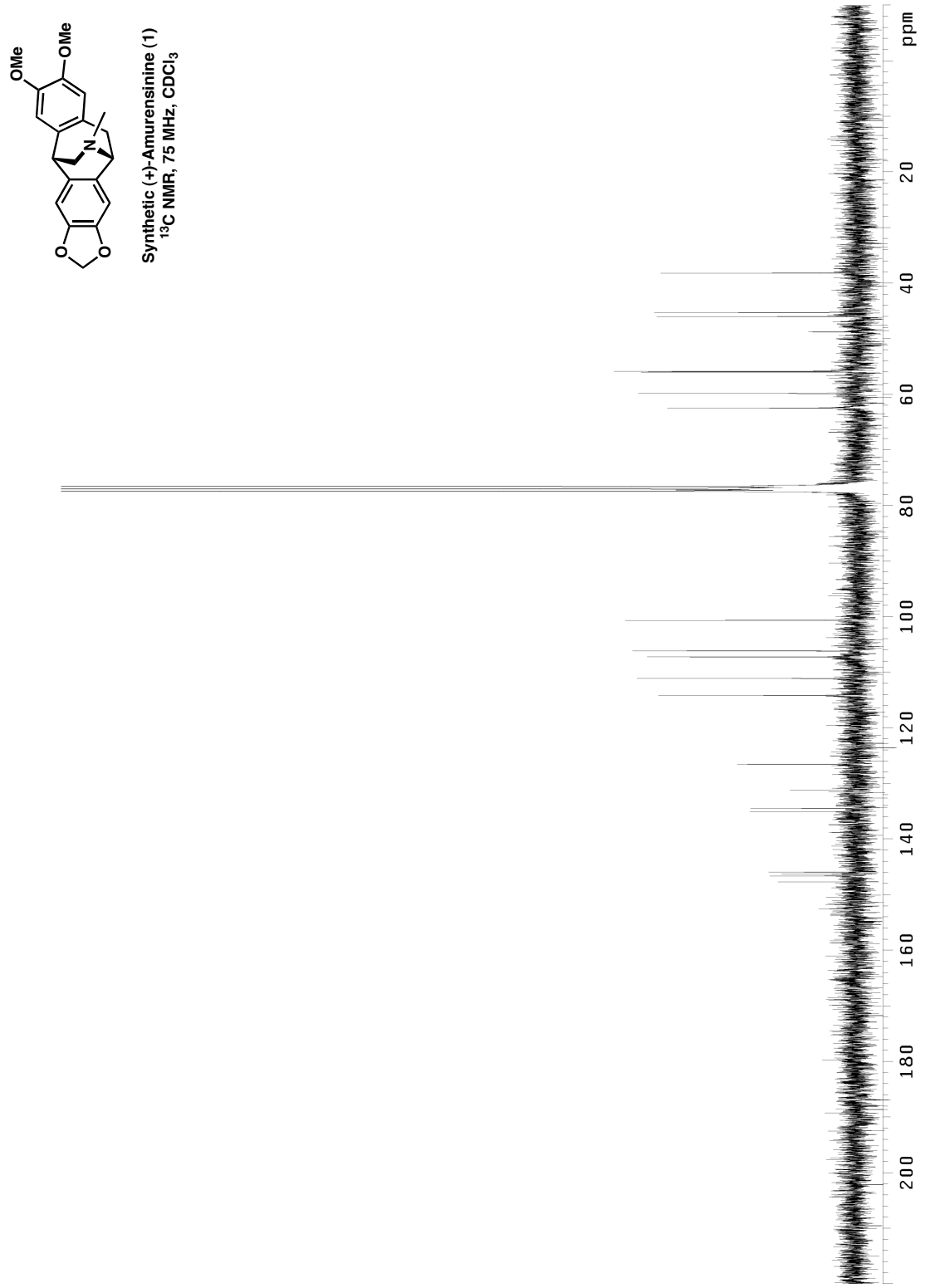
solution of crude azidoacid in EtOAc (1 mL) was added 10% Pd/C (30.4 mg, 0.029 mmol Pd). The suspension was stirred under a balloon of hydrogen for 12 h, after which it was filtered through a plug of Celite (MeOH eluent). Concentration under reduced pressure followed by purification by preparative TLC (0.25 mm, EtOAc eluent) afforded lactam (+)-**16** (4.8 mg, 49% yield over 3 steps) as a white solid. Lactam (+)-**16** was found to be >99% ee by chiral HPLC; $[\alpha]^{26}_{D}$ +3.0° (c 0.89, CH_2Cl_2).



(+)-16 *(+)-Amurensinine (1)*

(+)-Amurensinine (1). To a solution of lactam (+)-**16** (9.8 mg, 0.029 mmol) in THF (1 mL) was added lithium aluminum hydride (11.0 mg, 0.29 mmol) at 0 °C. The reaction was then heated to 65 °C for 4 h. The mixture was cooled to 0 °C and diluted with CH_2Cl_2 (1 mL). H_2O (100 μL), 10% w/v aq NaOH (100 μL), and H_2O (200 μL) were added sequentially dropwise. The biphasic mixture was warmed to room temperature and stirred vigorously for 1 h. The reaction was then filtered through a short plug of Celite (CH_2Cl_2 eluent) to remove suspended solids. After dilution with H_2O (2 mL) and 10% w/v aq NaOH (2 mL), the biphasic mixture was extracted with CH_2Cl_2 (5 x 5 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude secondary amine, which was carried on to the next step without further purification. To a solution of crude secondary amine in acetonitrile (1 mL) was added sodium cyanoborohydride (24.7 mg, 0.40 mmol) followed by aqueous formaldehyde (37 wt %, 110 μL, 1.48 mmol). After stirring for 5.5 h, the reaction was diluted with H_2O (2 mL) and extracted with CH_2Cl_2 (4 x 2 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by preparative TLC (0.25 mm, 19:1 $CHCl_3$/MeOH eluent) afforded (+)-amurensinine (**1**) (5.1 mg, 52% yield over 2 steps) as a colorless thin film. (+)-Amurensinine was found to be 99.0% ee by chiral HPLC (OJ column, 0.8 mL/min, 30% EtOH/hexanes, major peak 28.2 min, minor peak 20.5 min); $[\alpha]^{25}_{D}$ +125.8° (*c* 0.49, CH_2Cl_2).


OMe
OMe
N
O
O
Synthetic (+)-Amurensinine (1)
^{1}H NMR, 300 MHz, $CDCl_3$
ppm
1
2
3
4
5
6
7
8
9


OMe
OMe
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Synthetic (+)-Amurensinine (1)
^{13}C NMR, 75 MHz, $CDCl_3$
ppm
200
180
160
140
120
100
80
60
40
20

NMR Comparison of Synthetic (+)- and Literature[4] (–)-Amurensinine (1)

^{1}H NMR of Amurensinine, $CDCl_3$			
Synthetic (+), 300 MHz		**Literature (–), 250 MHz**	
Shift (ppm)	**Multiplicity/Coupling (Hz)**	**Shift (ppm)**	**Multiplicity/Coupling (Hz)**
6.72	s	6.71	s
6.71	s	6.70	s
6.62	s	6.61	s
6.52	s	6.51	s
5.91	d, *J* = 1.4 Hz	5.89	d, *J* = 1.2 Hz
5.85	d, *J* = 1.4 Hz	5.83	d, *J* = 1.2 Hz
3.86	s	3.85	s
3.84	dd, *J* = 3.7, 3.7 Hz	3.77-3.88	m
3.77	s	3.76	s
3.62	dd, *J* = 4.5, 1.5 Hz	3.61	d, *J* = 3.4 Hz
3.53	dd, *J* = 10.4, 1.6 Hz	3.50-3.54	m (2H)
3.48	dd, *J* = 17.0, 4.1 Hz		
2.90	dd, *J* = 17.3, 3.5 Hz	2.80-2.93	m (2H)
2.83	dd, *J* = 10.6, 4.6 Hz		
2.48	s	2.47	s

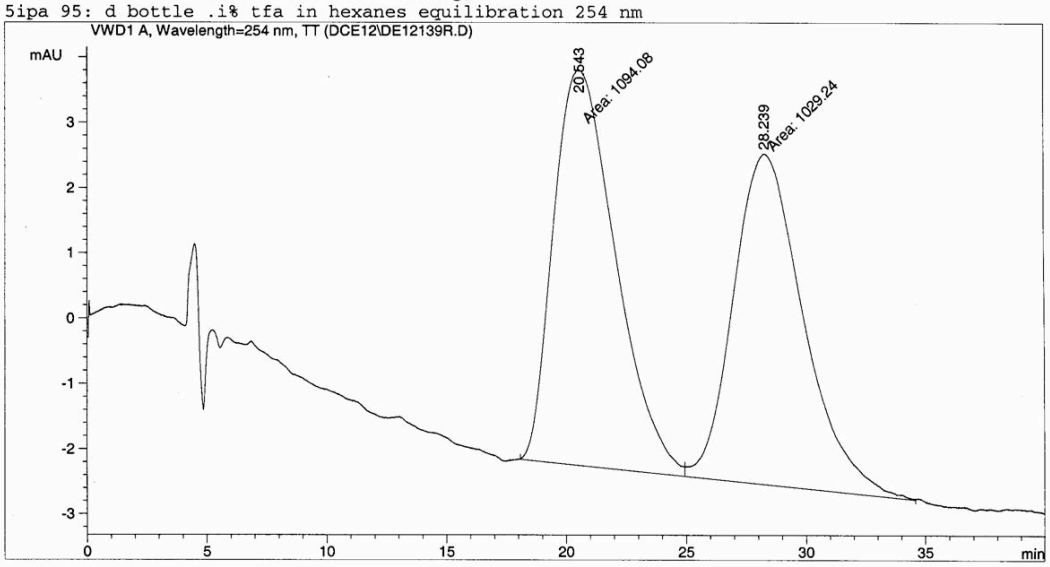
^{13}C NMR of Amurensinine, $CDCl_3$	
Synthetic (+), 75 MHz Shift (ppm)	**Literature (–), 62.8 MHz Shift (ppm)**
147.7	147.6
146.6	146.5
146.3	146.2
145.9	145.8
135.1	134.8
134.5	134.4
131.2	130.9
126.5	126.3
114.2	114.1
111.1	111.1
107.2	107.1
106.1	106.0
100.6	100.5
62.5	62.3
59.9	59.7
56.0	55.8
55.9	55.7
46.0	45.8
45.3	45.1
38.2	37.9

HPLC Trace for Synthetic (±)-Amurensinine (1)

Data File C:\HPCHEM\3\DATA\DCE12\DE12139R.D Sample Name: de12139r

Injection Date	: 7/12/2006 5:48:00 PM	Seq. Line	: 3
Sample Name	: de12139r	Location	: Vial 81
Acq. Operator	: dave	Inj	: 1
		Inj Volume	: 5 µl
Acq. Method	: C:\HPCHEM\3\METHODS\30-EOH40.M		
Last changed	: 9/20/2005 10:51:05 AM by dave		
Analysis Method	: C:\HPCHEM\3\METHODS\5IPA30DE.M		
Last changed	: 7/12/2006 6:52:51 PM by amh (modified after loading)		

5ipa 95: d bottle .i% tfa in hexanes equilibration 254 nm



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.543	MF	3.0059	1094.08337	6.06628	51.5269
2	28.239	FM	3.3819	1029.24048	5.07230	48.4731
Totals :				2123.32385	11.13858	

Results obtained with enhanced integrator!

*** End of Report ***

Instrument 3 7/13/2006 8:58:07 AM amh Page 1 of 1

HPLC Trace for Synthetic (+)-Amurensinine (1)

Data File C:\HPCHEM\3\DATA\DCE12\DE12273C.D Sample Name: de12273c

Injection Date	: 7/12/2006 6:29:00 PM	Seq. Line	: 4
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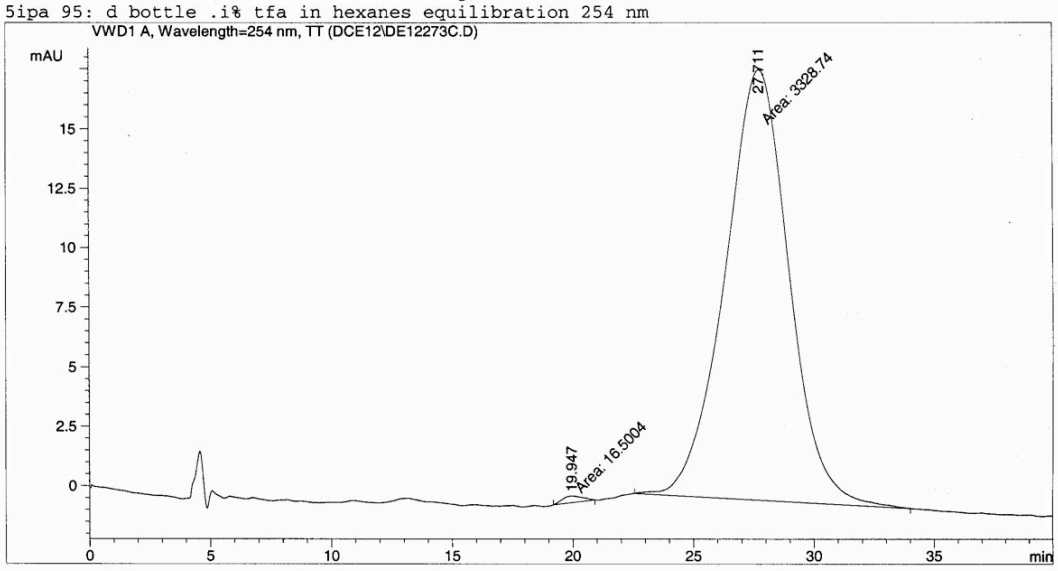
		Inj Volume	: 5 µl
Acq. Method	: C:\HPCHEM\3\METHODS\30-EOH40.M		
Last changed	: 9/20/2005 10:51:05 AM by dave		
Analysis Method	: C:\HPCHEM\3\METHODS\5IPA30DE.M		
Last changed	: 7/12/2006 6:52:51 PM by amh		
	(modified after loading)		

5ipa 95: d bottle .i% tfa in hexanes equilibration 254 nm



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.947	MM	0.9644	16.50043	2.85159e-1	0.4933
2	27.711	MM	3.0733	3328.74414	18.05211	99.5067
Totals :				3345.24457	18.33727	

Results obtained with enhanced integrator!

*** End of Report ***

Instrument 3 7/13/2006 11:34:10 AM amh Page 1 of 1

References

(1) Capozzi, G.; Roelens, S.; Talami, S. *J. Org. Chem.* **1993**, *58*, 7932-7936.

(2) Trend, R. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 4482-4483.

(3) Carrillo, L.; Badía, D.; Domínguez, E.; Vicario, J. L.; Tellitu, I. *J. Org. Chem.* **1997**, *62*, 6716-6721.

(4) The selectivity factor s was determined using the following equations:

$\frac{ee_{alc}}{ee_{diket}} = \frac{conv}{1-conv}$ and $s = \frac{\ln[(1-conv)(1-ee_{alc})]}{\ln[(1-conv)(1+ee_{alc})]}$, where ee_{alc} is the ee of (–)-**17**, ee_{diket} is the ee of (–)-**S1**, and *conv* is the total conversion of hydroxysilane **17** to diketone **S1**, see: Kagan, H. B.; Fiaud, J. C. In *Topics in Stereochemisry*; Eliel, E. L., Ed.; Wiley & Sons: New York, 1988; Vol. 18, pp 249-330.