

Synthesis of (-)-Dysiherbaine

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Epoxidation of allyl alcohol 7. *m*-CPBA (4.11 g, 0.019 mol) was added to **7** (2.7 g, 0.0193 mol) in 250 mL of dry CH₂Cl₂ at -20 °C. The reaction mixture was kept at -20 °C in the freezer for 1 week with occasional swirling. Solid NaHCO₃ and Na₂SO₃ were added to the mixture, which was stirred for 30 min. The mixture was then filtered through Celite and concentrated under reduced pressure. Flash chromatography of the residue on silica gel (4:1 hexanes/EtOAc) gave 2.2 g (73%) of **8**, 8% of recovered **7**, and 15% of the bis-epoxide.

Data for **8**: ¹H NMR 5.80 (ddt, 1, *J* = 17.2, 10.0, 6.8), 5.12 (dd, 1, *J* = 17.2, 1.2), 5.10 (dd, 1, *J* = 10.0, 1.2), 4.04 (dddd, 1, *J* = 10.0, 9.2, 6.0, 1.6), 3.75 (dd, 1, *J* = 6.8, 6.8), 3.66 (dd, 1, *J* = 11.2, 6.0), 3.42 (dd, 1, *J* = 4.0, 1.6), 3.26 (d, 1, *J* = 4.0), 3.09 (dd, 1, *J* = 11.2, 9.2), 2.30-2.44 (m, 2), 1.65 (d, 1, *J* = 10.0, OH); ¹³C NMR 133.3, 118.0, 72.6, 65.0, 64.3, 58.2, 53.8, 37.4; IR (neat) 3425, 3076, 2977, 2914, 2857, 1642, 1444, 1250, 1124, 1090, 1034; [α]_D -49.0° (c 0.75, CHCl₃); HRMS-DCI/CH₄ [M-H]⁺ calcd for C₈H₁₂O₃ 155.0708, found, 155.0701.

Nosylation of 8. NsCl (3.13 g, 0.014 mol), DMAP (1.6 g, 0.013 mol), and Et₃N (3.6 mL, 0.026 mol) were added to **8** (2.0 g, 0.013 mol) in 43 mL of dry CH₂Cl₂ at 0 °C. The resulting dark yellow solution was stirred for 30 min, washed with water, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was quickly filtered through a plug of silica gel using CH₂Cl₂ to afford 4.4 g (99%) of the nosylate: ¹H NMR 8.40 (d, 2, *J* = 8.8), 8.14 (d, 2, *J* = 8.8), 5.77 (ddt, 1, *J* = 16.8, 10.0, 6.4), 5.12 (dd, 1, *J* = 16.8, 1.2), 5.10 (dd, 1, *J* = 10.0, 1.2), 5.00 (ddd, 1, *J* = 10.0, 6.0, 2.0), 3.78 (dd, 1, *J* = 6.4, 6.4), 3.65 (dd, 1, *J* = 11.0, 6.0), 3.40 (dd, 1, *J* = 4.8, 2.0), 3.38 (dd, 1, *J* = 11.0, 10.0), 3.28 (d, 1, *J* = 4.8), 2.37 (dd, 2, *J* = 6.4, 6.4); ¹³C NMR 150.8, 142.2, 132.6, 129.1, 124.6, 118.5, 74.95, 74.91, 72.6, 61.0, 58.49, 58.45, 50.8, 37.4; IR (neat) 3100, 3008, 2918, 2868, 1643, 1611, 1543, 1407, 1371, 1331, 1317, 1182, 1092; [α]_D -51.9° (c 0.60, CHCl₃); HRMS-DCI/NH₃ [MNH₄]⁺ calcd for C₁₄H₁₅NO₇S 359.0913, found 359.0908.

Inversion of the Nosylate. CsOAc (12.5 g, 0.065 mol) and DMAP (160 mg, 1.3 mmol) were added to the nosylate (4.4 g, 0.013 mol) in 100 mL of dry toluene. The solution was refluxed for 8 h, cooled, filtered through Celite, and concentrated under reduced pressure. The resulting slurry was diluted with EtOAc, washed with water, brine, dried over Na₂SO₄, and concentrated to give 2.2 g (85%) of the inverted acetate: ¹H NMR 5.87 (ddt, 1, *J* = 17.2, 10.0, 6.8), 5.18 (dd, 1, *J* = 17.2, 1.2), 5.15 (dd, 1, *J* = 10.0, 1.2) 5.03 (br, 1, *W*_{1/2} = 6 Hz), 3.81 (dd, 1, *J* = 6.4, 6.4), 3.71 (dd, 1, *J* = 13.2, 1.2), 3.55 (dd, 1, *J* = 13.2, 2), 3.27 (br, 1, *W*_{1/2} = 8 Hz), 3.15 (d, 1, *J* = 4.0), 2.40-2.54 (m, 2), 2.32 (s, 3); ¹³C NMR 170.5, 133.1, 118.1, 73.3, 66.1, 63.8, 54.4, 49.5, 37.8, 21.1; IR (neat) 3007, 2929, 2923, 2850, 1735, 1642, 1433, 1372, 1234, 1124, 1039; HRMS-CH₄/CI [MH]⁺ calcd for C₁₀H₁₄O₄ 199.0970, found 199.0969.

Inverted Alcohol 9. K₂CO₃ (4.6 g, 0.033 mol) and NaHCO₃ (8.3 g, 0.099 mol) were added to the inverted acetate (2.2 g, 0.011 mol) in 100 mL of MeOH. The solution was stirred at room temperature for 1 h, and concentrated to remove 90% of the methanol under reduced pressure. The resulting slurry was diluted with water and extracted with EtOAc. The combined EtOAc portions were washed with brine, dried over Na₂SO₄, and concentrated to give 1.8 g (99%) of **9**: ¹H NMR 5.84 (ddt, 1, *J* = 17.2, 10.4, 7.2), 5.18 (dd, 1, *J* = 17.2, 1.6), 5.11 (dd, 1, *J* = 10.4, 1.6), 3.94 (br, 1, *W*_{1/2} = 12 Hz), 3.86 (br dd, 1, *J* = 6.4, 6.4), 3.59 (br s, 2), 3.27 (br, 1, *W*_{1/2} = 10 Hz), 3.11 (d, 1, *J* = 4.0), 2.44 (br dd, 2, *J* = 6.4, 7.2); ¹³C NMR 132.9, 118.5, 73.3, 66.1, 64.4, 54.4, 51.6, 37.9; IR (neat) 3417, 3076, 2977, 2925, 2867, 1641, 1443, 1250, 1125, 1090, 1035.

Carbamate 10. NaH (1.06 g, 0.26 mol) was added to **9** (1.8 g, 0.011 mol) in 150 mL of dry THF. The solution was stirred at room temperature for 5 min and methyl isocyanate (0.85 mL, 0.014 mol) was added and the mixture was refluxed for 2 h. The mixture was quenched by the dropwise addition of saturated NH₄Cl solution until two homogeneous phases formed. The solution was concentrated to dryness under reduced pressure. The resulting brown solid was dissolved in 100 mL of CH₂Cl₂ and cooled to 0 °C. MsCl (1.08 mL, 0.014 mol) and Et₃N (3.21 mL, 0.023 mol) were added to the CH₂Cl₂ solution. After 30 min, the solution was concentrated

under reduced pressure and the residue was purified by flash column chromatography (4:1 EtOAc/hexanes) to give 1.9 g (67%) of **10**: ^1H NMR 5.81 (ddt, 1, J = 17.2, 10.0, 6.8), 5.16-5.24 (m, 2), 4.72 (dd, 1, J = 3.6, 4.4), 4.63 (dd, 1, J = 9.2, 2.0), 4.13 (d, 1, J = 14.0), 4.08 (dd, 1, J = 9.2, 3.6), 3.77 (ddd, 1, J = 6.8, 6.8, 4.4), 3.71 (dd, 1, J = 14.0, 2.0), 3.08 (s, 3), 2.98 (s, 3), 2.38-2.46 (m, 2); ^{13}C NMR 157.7, 132.5, 119.1, 77.3, 74.7, 70.3, 65.8, 58.1, 39.2, 37.9, 30.3; IR (neat) 1750; HRMS-DCI/NH₃ [MH]⁺ calcd for C₁₁H₁₇NO₆S 292.0855, found 292.0847.

Dihydroxylation of **10.** A solution of **10** (1.0 g, 3.86 mmol) in 5 mL of acetone was added to NMO (443 mg, 3.78 mmol) in 1.4 mL of H₂O. OsO₄ (10 μ L, 2.5% OsO₄ in *t*-BuOH) was added and the resulting solution was stirred at rt for 2 d. Solid Na₂SO₃ was added until the solution turned brown. The solution was filtered through celite and concentrated under reduced pressure affording 1.1 g (99%) of crude diol as a approximately 1:1 mixture of diastereomers, which was used without further purification: ^1H NMR (acetone-*d*₆) 4.95 (dd, 0.5 \times 1, J = 4.0, 4.0), 4.91 (dd, 0.5 \times 1, 4.4, 3.6), 4.74 (m, 0.5 \times 1), 4.73 (m, 0.5 \times 1), 4.19-4.26 (m, 1), 4.02-4.10 (m, 1), 3.97-4.01 (m, 1), 3.90-3.78 (m, 3, 2 OH), 3.65-3.75 (m, 1), 3.52-3.40 (m, 2), 3.27 (s, 0.5 \times 3), 3.26 (s, 0.5 \times 3), 2.95 (s, 0.5 \times 3), 2.94 (s, 0.5 \times 3), 1.95 (ddd, 0.5 \times 1, J = 14, 4.8, 6.0), 1.65-1.80 (m, 1.5); ^{13}C NMR (acetone-*d*₆) 77.9, 77.1, 77.0, 76.6, 71.8, 71.6, 69.8, 69.3, 67.7, 66.7, 66.5, 66.4, 58.85, 58.81, 39.3, 39.1, 38.3, 38.2, 30.7 (2) (the carbamate carbonyl carbons were not observed); HRMS- DCI/NH₃ [MH]⁺ calcd for C₁₁H₁₉NO₈S 326.0909, found 326.0919.

Cyclization of the Diol. Crude diol (1.1 g, 3.78 mmol) in 50 mL of pyridine was refluxed for 4 h. The mixture was concentrated under reduced pressure to give crude bicyclic alcohol, which was used without further purification. A small amount of (10 mg) was purified using flash chromatography (10:1 EtOAc/MeOH) giving a 1:1 mixture of diastereomers: ^1H NMR (acetone-*d*₆) 4.32-3.92 (m, 5), 3.72-3.42 (m, 4), 3.84 (s, 0.5 \times 3), 3.83 (s, 0.5 \times 3), 2.29 (ddd, 0.5 \times 1, J = 5.2, 8.8, 12.8), 2.05 (ddd, 0.5 \times 1, J = 4.4, 8.4, 13), 2.02 (ddd, 0.5 \times 1, J = 1.2, 7.2, 13), 1.91 (ddd, 0.5 \times 1, J = 1.2, 4.8, 12.8); ^{13}C NMR (acetone-*d*₆) 79.0, 78.9, 77.3, 76.3, 75.0, 74.4, 69.9 (2), 65.3, 65.0, 66.0, 64.7, 55.4, 55.2, 36.3, 36.2, 30.5, 29.3 (the carbamate

carbonyl carbons were not observed); HRMS-20eV GC/MS $[M]^+$ calcd for $C_{10}H_{15}N_0_5$, 229.0950; found 229.0944.

Preparation of 11. Crude brown solid diol was taken up as a slurry in 20 mL of CH_2Cl_2 and Dess-Martin reagent (1.76 g, 4.15 mmol) was added at room temperature. After 45 min, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography (10:1, EtOAc/MeOH) to give 672 mg (78% from **10**) of **11** as a 2:1 mixture of diastereomers: 1H NMR (acetone- d_6) 9.64 (d, 0.34×1 , $J = 1.8$), 9.49 (s, 0.66×1), 4.45-4.07 (m, 6), 3.71 (m, 1) 2.91 (s, 0.34×3), 2.89 (s, 0.66×3), 2.48-2.42 (m, 0.5), 2.28-2.17 (m, 1.5); ^{13}C NMR (acetone- d_6) (205.2, 202.5), 159.9 (2), (81.73, 81.75), 76.2 (2), (75.6, 74.7), (70.1, 69.8), 65.0 (2), (55.2, 55.0), (39.0, 35.5) (two carbons obscured by acetone- d_6).

Preparation of 22. A solution of pyrrolidine (22.3 μ L, 0.267 mmol) and **11** (53 mg, 0.232 mmol) in 2 mL of dry CH_3CN and 2 mL of dry benzene was heated to 50 °C for 5 min. The solvent was removed by rotary evaporation and the residue was dissolved in 4 mL of dry CH_3CN . Allyl bromide (40 μ L, 0.464 mmol) was added to the solution and the temperature was slowly increased to 80 °C. The reaction was kept at 80 °C for 12 h and H_2O (0.05 mL) was added and the solution was stirred for an hour. The mixture was concentrated and the residue was purified through a plug of silica gel (10:1 EtOAc/MeOH) to provide 36 mg (58%) of **22** as a 3:1 inseparable diastereomeric mixture that was used without further purification.

Oxidation of 22. A solution of $NaClO_2$ (190 mg, 1.68 mmol) and NaH_2PO_4 (206 mg, 1.496 mmol) in 1.87 mL of H_2O was added to a solution of **22** (50 mg, 0.187 mmol) in 2 mL of acetone, 2 mL CH_3CN , and 4 mL of 2-methyl-2-butene at 0 °C. The solution was stirred at 0 °C for 4 h. A few drops of acetaldehyde were added to quench any remaining oxidant. The mixture was concentrated under reduced pressure, absorbed onto silica gel, and purified using flash column chromatography (10:0.05:0.01 EtOAc/MeOH/formic acid) to give (94% total yield) 10 mg of **24**, followed by 16 mg of a 2:1 mixture **23** and **24**, and 24 mg of **23**. The order of elution is opposite in 77:23 EtOAc/MeOH.

Data for **23**: ^1H NMR (CD₃OD) 5.79 (tdd, 1, J = 7.6, 10.4, 17.4), 5.10 (dd, 1, J = 2.4, 17.4), 5.08 (dd, 1, J = 2.4, 10.4), 4.36 (ddd, 1, J = 2.2, 2.2, 7.2), 4.11 (d, 1, J = 2.2, 14.0), 4.10 (dd, 1, J = 1.6, 5.2), 3.99 (dd, 1, J = 5.2, 7.2), 3.97 (dd, 1, J = 1.6, 3.6), 3.62 (dd, 1, J = 2.2, 14.0), 2.93 (s, 3), 2.55 (d, 1, J = 13.2), 2.54 (dd, 1, J = 7.6, 14.0), 2.43 (dd, 1, J = 7.6, 14.0), 2.22 (dd, 1, J = 3.6, 13.2); ^{13}C NMR (CD₃OD) 176.6, 161.6, 133.6, 119.1, 85.1, 76.9, 75.8, 71.5, 65.3, 56.0, 43.7, 43.4, 30.4, (the quaternary carbons were assigned from an HMBC experiment); $[\alpha]_D$ +38.4° (c 0.20, CH₃OH); HRMS- DCI/NH₃ [MH]⁺ calcd for C₁₃H₁₇NO₆ 284.1134, found 284.1146.

Data for **24**: ^1H NMR (CD₃OD) 5.79 (tdd, 1, J = 7.2, 10.4, 17.2), 5.04 (dd, 1, J = 2.6, 17.2), 5.00 (dd, 1, J = 2.6, 10.4), 4.36 (ddd, 1, J = 1.2, 2.0, 6.8), 4.16 (dd, 1, J = 1.2, 14.0), 4.11 (dd, 1, J = 2.0, 5.6), 4.03 (dd, 1, J = 5.6, 6.8), 4.00 (dd, 1, J = 4.8, 2.0), 3.65 (dd, 1, J = 2.0, 14.0), 2.97 (s, 3), 2.59 (d, 2, J = 6.4), 2.49 (dd, 1, J = 4.8, 14.6), 2.15 (d, 1, J = 14.6); ^{13}C NMR (CD₃OD) 176.5, 161.2, 143.6, 118.5, 84.5, 77.0, 75.6, 71.4, 65.3, 56.0, 44.3, 44.2, 30.4, (the quaternary carbons were assigned from an HMBC experiment); $[\alpha]_D$ -19.2° (c 0.345, CH₃OH).

Formation of the 2,4-Dimethoxybenxyl Amide. HOBr (12 mg, 0.089 mmol), EDC (11 mg, 0.059 mmol), and 2,4-dimethoxybenzylamine (22 μ L, 0.149 mmol) were added to **23** (8.4 mg, 0.029 mmol) in 5 mL of wet CH₃CN. The mixture was stirred at room temperature for 12 h. The mixture was concentrated under reduced pressure and purified using flash column chromatography (10:1 EtOAc/MeOH) to afford 11 mg (86%) of the amide: ^1H NMR 7.22 (d, 1, J = 9.2), 6.93 (br dd, 1, J = 6.9, 5.8, NH), 6.43-6.39 (m, 2), 5.71 (tdd, 1, J = 6.8, 16.8, 10.0), 5.10 (dd, 1, J = 2.0, 16.8), 5.07 (dd, 1, J = 2.0, 10.0), 4.42 (dd, 1, J = 6.9, 14.8), 4.33 (dd, 1, J = 5.6, 14.8), 4.22 (ddd, 1, J = 1.9, 1.9, 6.4), 4.05 (dd, 1, J = 1.9, 14.4), 4.03 (dd, 1, J = 1.4, 4.9), 3.85 (dd, 1, J = 1.4, 4.8), 3.82 (s, 3), 3.78 (s, 3) 3.73 (dd, 1, J = 4.9, 6.4), 3.51 (dd, 1, J = 1.9, 14.4), 2.94 (s, 3), 2.66 (d, 1, J = 14.0), 2.65 (dd, 1, J = 1.0, 7.0, 14.4), 2.42 (dd, 1, J = 8, 14.4), 2.28 (dd, 1, J = 4.8, 14.0); ^{13}C NMR 173.2, 159.9, 159.1, 158.4, 138.9, 132.5, 129.5, 119.3, 103.5, 98.1, 85.5, 75.1, 74.1, 68.8, 64.0, 55.3 (2), 54.7, 42.4 (2), 37.8, 29.9, (the quaternary carbons were assigned from an HMBC experiment); IR (neat) 3430, 2934, 1751, 16.54, 1508; $[\alpha]_D$ +14.1° (c 0.36, CHCl₃); HRMS- DCI/NH₃ [MH]⁺ calcd for C₂₂H₂₈N₂O₇ 433.1975, found 433.1962.

Formation of 25. A solution of 2.5% OsO₄ in *t*-BuOH (0.22 mL, 0.0178 mmol) and the amide (7 mg, 0.0162 mmol) in 1 mL of acetone and 20 μ L of H₂O was stirred for 16 h at room temperature. NaIO₄ (7 mg, 0.0324 mmol) was added and the solution was stirred for an additional 6 h. Solid Na₂SO₃ was added and the mixture was stirred for 30 min. The solvent was removed in vacuo and the residue was purified using flash column chromatography (10:1 EtOAc/MeOH) to afford 7 mg (99%) of **25**. ¹H NMR 9.63 (dd, 1, *J* = 1.2, 4.0), 7.21 (d, 1, *J* = 9.2), 7.11 (br dd, 1, NH), 6.42 (m, 2), 4.45 (dd, 1, *J* = 6.8, 14.8), 4.34 (dd, 1, *J* = 5.6, 14.8), 4.21 (m, 2), 4.03 (d, 1 *J* = 14.0), 3.90 (d, 1, *J* = 3.6), 3.83 (s, 3), 3.78 (s, 3), 3.78 (m, 1), 3.52 (dd, 1, *J* = 2.0, 14.0), 3.03 (dd, 1, *J* = 1.2, 16.0), 2.87 (s, 3), 2.75 (dd, 1, *J* = 4.0, 16.0), 2.66 (d, 1, *J* = 14.0), 2.33 (dd, 1, *J* = 3.6, 14.0); ¹³C NMR 199.3, 172.1, 160.2, 158.7, 158.5, 129.7, 118.8, 103.5, 98.2, 83.3, 74.9, 74.2, 68.7, 64.1, 55.35, 55.32, 54.4, 50.8, 43.7, 38.2, 29.8.

Lactamization of 25. K₂CO₃ (2 mg) was added to **25** (7 mg, 0.0162 mmol) in 2 mL of acetone. 20 μ L of H₂O was added to the mixture, which was stirred for 1 h. The mixture was concentrated, dissolved in CH₂Cl₂, and filtered through celite to give 7 mg (99%) of hydroxy lactams as a diastereomeric mixture that was carried on without purification: ¹H NMR 7.19 (d, 0.66 \times 1, *J* = 8.4), 7.12 (d, 0.34 \times 1, *J* = 8.0), 6.45 (dd, 0.66 \times 1, *J* = 2.4, 8.4), 6.35-6.40 (m, 1 + 0.34 \times 1), 4.96 (dd, 0.66 \times 1, *J* = 2.4, 6.0), 4.86 (br d, 0.34 \times 1, *J* = 4.8), 4.60-3.70 (m, 6), 3.76 (s, 0.66 \times 3), 3.72 (s, 0.34 \times 3), 3.70 (s, 0.34 \times 3), 3.69 (s, 0.66 \times 3), 2.84 (s, 0.34 \times 3), 2.81 (s, 0.66 \times 3), 2.59 (dd, 0.34 \times 1, *J* = 2.8, 14.2), 2.52 (dd, 0.66 \times 1, *J* = 3.2, 14.8), 2.34 (dd, 0.66 \times 1, *J* = 7.2, 14.8), 2.17 (dd, 0.66 \times 1, *J* = 6.4, 13.2), 2.10 (dd, 0.34 \times 1, *J* = 6.8, 14.2), 1.95 (br d, 0.34 \times 1, *J* = 14.0), 1.90 (dd, 0.34 \times 1, *J* = 5.6, 14.0), 1.78 (dd, 0.66 \times 1, *J* = 2.8, 13.2); ¹³C NMR (partial) (171.8, 171.3), (160.9, 160.7), (158.5, 158.0), 158.0, 132.6, 115.9, (105.5, 104.6), 99.0, 83.4, 79.4, 75.8, 73.1, 68.0, 55.9, 55.5, 54.9, 43.8, 42.2, 39.2, 38.8, 29.8.

Formation of nitriles 26a and 27a. TMSCN (11 μ L, 0.081 mmol) and ZnI₂ (cat.) were added to the lactam alcohols (7 mg, 0.0162 mmol) in 2 mL of dry CH₂Cl₂. The solution was stirred for 12 h at room temperature. Chelex 100 was added to the solution, which was stirred for an additional 30 min. This slurry was filtered through celite and concentrated under reduced

pressure to give 7.1 mg (99%) of a 1:1 mixture of nitriles. The diastereomers were separated by flash column chromatography (10:0.05 EtOAc/MeOH) affording 2 mg of **27a**, 3.4 mg of a mixture of **26a** and **27a**, which was rechromatographed, and 1.7 mg of **26a**.

Data for **26a**: ^1H NMR 7.21 (d, 1, J = 8.4), 6.47 (m, 2), 4.80 (d, 1, J = 14.6), 4.64 (ddd, 1, J = 5.6, 8.0, 8.4), 4.50 (m, 1), 4.37 (d, 1, J = 14.6), 4.21 (dd, 1, J = 8.0, 12.2), 4.20 (dd, 1, J = 1.0, 8.0), 4.15 (dd, 1, J = 4.4, 4.4), 3.94 (dd, 1, J = 4.4, 8.0), 3.87 (dd, 1, J = 5.6, 12.2), 3.83 (s, 3), 3.80 (s, 3), 2.98 (s, 3), 2.74 (br d, 1, J = 14.8), 2.42 (d, 1, J = 13.6), 2.24 (dd, 1, J = 7.2, 14.8), 2.07 (dd, 1, J = 8, 13.6); ^{13}C NMR 132.2, 117.3, 114.9, 104.6, 98.6, 82.8, 75.7, 73.2, 67.5, 62.0, 55.5 (2), 54.6, 44.6, 41.3, 41.2, 37.2, 29.7 (quaternary carbons not observed); $[\alpha]_D$ +21.1° (c 0.85, CHCl_3); HRMS- DCI/ NH_3 $[\text{MH}]^+$ calcd for $\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}_7$ 444.1771, found 444.1759. NOEs were observed between H_{3b} at δ 2.42 and H_7 at δ 4.15, and between H_{5a} at δ 2.71 and H_{10a} at δ 4.21 in a 2D NOESY experiment.

Data for **27a**: ^1H NMR 7.18 (d, 1, J = 8.4), 6.53 (d, 1, J = 8.0), 6.46 (s, 1), 4.99 (d, 1, J = 14.8), 4.67 (ddd, 1, 6.0, 6.4, 7.6), 4.53 (m, 1), 4.39 (dd, 1, J = 7.6, 12.0), 4.21 (d, 1, J = 14.8), 4.18 (dd, 1, J = 5.2, 8.0), 4.11 (dd, 1, J = 4.4, 4.4), 3.92 (dd, 1, J = 6.0, 12.0), 3.89 (dd, 1, J = 4.4, 6.4), 3.81 (s, 3), 3.80 (s, 3), 2.88 (s, 3), 2.74 (dd, 1, J = 2.4, 14.8), 2.48 (dd, 1, J = 7.6, 14.8), 2.45 (dd, 1, J = 8.0, 13.4), 2.22 (dd, 1, J = 5.2, 13.4); ^{13}C NMR 170.3, 161.3, 158.9, 158.3, 131.7, 117.1, 114.1, 104.6, 98.5, 82.5, 75.5, 73.5, 67.71, 61.8, 55.5, 55.4, 54.6, 44.3, 42.5, 40.9, 37.7, 29.5; $[\alpha]_D$ -25.68° (c 0.16, CHCl_3). NOEs were observed between H_{3a} at δ 2.45 and H_7 at δ 4.11 and H_6 at δ 4.53 in a 2D NOESY experiment.

Hydrolysis of **26a to Amide **26b**:** To a solution of **26a** (0.5 mg, 0.0011 mmol) in acetone (1 mL) was added K_2CO_3 (1 mg, 0.007 mmol) and 30% H_2O_2 (2 μL). The mixture was stirred overnight at RT and concentrated under reduced pressure to afford crude **26b**: ^1H NMR 7.18 (d, 1, J = 7.9), 6.43-6.41 (m, 2), 6.10 (br s, 1, NH), 5.33 (br s, 1, NH), 4.72 (d, 1, J = 14.2), 4.61 (ddd, 1, J = 7.2, 6.4, 6.4), 4.41 (m, 1), 4.34 (d, 1, J = 14.2), 4.31 (dd, 1, J = 7.2, 12.4), 4.07 (dd, 1, J = 4.4, 4.4), 3.92 (br d, 1, J = 9.2), 3.91 (dd, 1, J = 6.4, 12.4), 3.79 (dd, 1, J = 4.4, 6.4), 3.78 (s, 3), 3.77 (s, 3), 2.82 (s, 3), 2.80 (d, 1, J = 15.6), 2.32 (br d, 1, J = 14.0), 2.20 (dd, 1, J =

6.8, 15.6), 2.01 (dd, 1, J = 9.2, 14.0). Irradiation of H_{3a} at δ 2.01 in a 1D NOESY experiment showed NOEs to H_{3b} at δ 2.32 and H_2 at δ 3.92. Irradiation of H_{3b} at δ 2.32 in a 1D NOESY experiment showed NOEs to H_{3a} at δ 2.02, H_2 at δ 3.92, and H_7 at δ 4.06. Irradiation of H_2/H_{10b} at δ 3.91/3.92 in a 1D NOESY experiment showed NOEs to H_{3a} at δ 2.01 and H_{10a} at δ 4.31.

Hydrolysis of 27a to Amide 27b: To a solution of **27a** (0.5 mg, 0.0011 mmol) in acetone (1 mL) was added K_2CO_3 (1 mg, 0.007 mmol) and 30 % H_2O_2 (2 μ L). The mixture was stirred overnight at RT and concentrated under reduced pressure to afford crude **27b**: 1H NMR 7.11 (d, 1 J = 9.9), 6.52 (dd, 1, J = 2.4, 7.9), 6.40 (d, 1, J = 1.8), 5.65 (br s, 1, NH), 5.32 (br s, 1, NH), 4.95 (d, 1, J = 14.4), 4.65 (ddd, 1, J = 7.6, 7.6, 7.6), 4.48 (m, 1), 4.41 (dd, 1, J = 8.0, 12.6), 4.15 (d, 1, J = 14.4), 4.06 (dd, 1, J = 4.4, 4.4), 3.80-3.92 (m, 3), 3.79 (s, 3), 3.75 (s, 3), 2.88 (s, 3), 2.67 (dd, 1, J = 3.2, 15.0), 2.39 (dd, 1, J = 7.2, 15.0), 2.33 (dd, 1, J = 7.6, 13.4), 1.99 (dd, 1, J = 5.6, 13.4). Irradiation of H_{3b} at δ 2.20 in a 1D NOESY experiment showed NOEs to H_{3a} at δ 2.33 and H_2 at δ 3.82. Irradiation of H_{3a}/H_{5b} at δ 2.33/2.39 in a 1D NOESY experiment showed NOEs to H_{3b} at δ 2.20, H_2 at δ 3.82, and H_7 at δ 4.07. Irradiation of $H_2/H_8/H_{10b}$ at δ 3.82/3.87/3.87 in a 1D NOESY experiment showed NOEs to H_{3a} at δ 2.33, H_{10a} at δ 3.91, and H_9 at δ 4.34.

Hydrolysis of 26a. A solution of **26a** (1.7 mg, 0.0038 mmol) in 6 M HCl (2.5 mL) was heated at 120 °C for 4 days and concentrated under reduced pressure. The residue was washed with CH_2Cl_2 affording 1.2 mg of (-)-dysiherbaine (**1**) (99%): 1H NMR (D_2O , pH = 2) 4.32 (s, 1), 4.16 (s, 1), 3.88-3.85 (m, 2), 3.60-3.50 (m, 3), 2.73 (s, 3), 2.63 (dd, 1, J = 2.3, 15.0), 2.58 (d, 1, J = 14.0), 2.18 (dd, 1, J = 3.6, 14.0), 1.97 (dd, 1, J = 11.4, 15.0); ^{13}C NMR (D_2O , pH = 2) 180.4, 174.4, 89.4, 76.9, 75.9, 69.5, 63.0, 57.1, 53.6, 45.3, 39.6, 30.4, (the quaternary carbons were assigned from an HMBC experiment); $[\alpha]_D -5^\circ$ (c 0.06, H_2O).