Supporting Information:

Isolation, Structure Determination and Synthesis of Neodysiherbaine A, a New Excitatory Amino Acid from a Marine Sponge

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Experimental Procedure for the Isolation of Neodysiherbaine A (2).

Dysidea herbacea (e.g. 200g) collected in Yap State Micronesia in July 1998 was homogenized with the same amount of water. The homogenate was centrifuged (10000 rpm, 20 min). 2-Propanol (200 ml) was added to the supernatant and the mixture was evaporated to remove the alcohol. The resulting emulsion was centrifuged and the supernatant was lyophilized to give the aqueous extract (8.52 g). An aliquot of the extract (4.2 g) was separated by Sephadex LH 20 (Pharmacia, 5 x 63 cm). Bioactive fractions eluted between 600-670 mL were pooled and then further separated by BioGel P2 (BioRad, 5 x 63 cm). Fractions eluted between 470-530 mL were combined and then subjected to anion exchange chromatography on DE52 [Whatman, acetate form, 1.5 x 14 cm, solvents: H_2O (50 mL), acetic acid (0.05 N, 100 mL), linear gradient from acetic acid (0.05 N) to ammonium acetate (0.05 N), flow rate 1 mL/min]. Active fractions eluated between 270-320 min were combined to give fraction A (27 mg). ^{1}H NMR of this fraction was identical with that of shinorin, however, the authentic compound did not show epileptogenic activity in mice. Thus, fraction A was further separated by reversed phase HPLC (C18, Daisopak SP120, 1 x 30 cm, 0.2% acetic acid, 1 mL/min) to give pure neodysiherbaine A (**2**) (260 g, T_R = 29.5-32.5 min).

Experimental Procedures for the Synthesis of Neodysiherbaine A (2a) and Its C4 Epimer 20.

General Methods. All reactions sensitive to air or moisture were carried out under argon or nitrogen atmosphere in anhydrous, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Anhydrous acetonitrile (MeCN), dimethylformamide (DMF), and tetrahydrofuran (THF) were purchased from Kanto Chemical Co. Inc. Dichloromethane (CH_2Cl_2), 2,6-lutidine, and triethylamine were dried from calcium hydride, dimethylsulfoxide (DMSO) from calcium hydride under reduced pressure. All other reagents were used as supplied unless otherwise stated.

Analytical thin layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25-mm thickness). Column chromatography was performed using Kanto Chemical Co. Inc. silica gel 60N (spherical, neutral), and for flash column chromatography E. Merck silica gel 60 (230-400 mesh) was used.

NMR spectra were recorded on a JEOL A500, Bruker DRX-500, or JEOL Lambda 400 instrument. NMR chemical shift values are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) with reference to internal solvent [^{1}H NMR: $CHCl_3$ (7.24), C_6HD_5 (7.15), HOD (4.65 at 20 °C); ^{13}C NMR: $CDCl_3$ (77.0); C_6D_6 (128.0), CD_3OD (49.0)]. The following abbreviations were used to designate the multipilicities: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad. Coupling constants (*J*) are reported in hertz (Hz). IR spectra were recorded on a JASCO FT/IR-420 instrument. Low- and high-resolution mass spectra were recorded on a JEOL JMS-SX102L mass spectrometer under fast atom bombardment (FAB) conditions with *m*-

nitrobenzyl alcohol (NBA) as the matrix. Optical rotations were measured on a JASCO DIP-370 polarimeter.

The carbon numbering corresponding to that of neodysiherbaine was used.

Olefin 6. A solution of tri-*O*-acetyl-D-glucal (**5**) (3.00 g, 11.0 mmol) in CH_2Cl_2 (110 mL) was cooled to 0 °C and treated with triethylsilane (3.52 mL, 22.1 mmol) followed by $BF_3{\cdot}OEt_2$ (2.51 mL, 19.8 mmol). After 100 min, the reaction was quenched with saturated aqueous $NaHCO_3$ (50 mL). The mixture was extracted with $CHCl_3$ (300 mL), washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), dried (Na_2SO_4), filtered, and concentrated to give crude diacetate, which was used in the next reaction without further purification.

A solution of the above diacetate in methanol (110 mL) was treated with 1 N NaOMe (1 N in methanol, 11 mL, 11 mmol). After 15 min, the reaction was quenched with amberlyst-15, and the resin was filtered through a pad of Celite. The filtrate was concentrated to give crude diol, which was used in the next reaction without further purification.

To a solution of the above diol in CH_2Cl_2 (110 mL) were added benzaldehyde dimethylacetal (3.29 mL, 22.1 mmol) and camphorsulfonic acid (CSA) (510 mg, 2.20 mmol). After 30 min, the reaction was quenched with triethylamine (3 mL). The resultant mixture was concentrated, and the residue was purified by column chromatography on silica gel (0%→2%→5% ethyl acetate/hexane) to give olefin **6** (2.02 g, 84%) as a colorless solid: $[\alpha]_D^{22}$ = +27.2 (*c* 0.86, $CHCl_3$); IR (film) 2931, 2837, 1456, 1385, 1302, 1128, 1098, 998, 700, 643 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.62 (d, 2H, *J* = 7.1 Hz, ArH), 7.19-7.09 (m, 3H, ArH), 5.87 (d, 1H, *J* = 10.3 Hz, H-8), 5.36 (s, 1H, C*H*Ph), 5.20 (ddd, 1H, *J* = 10.3, 4.9, 2.4 Hz, H-9), 4.20 (dd, 1H, *J* = 10.2, 4.6 Hz, H-5), 4.00-3.97 (m, 1H, H-10), 3.87-3.78 (m, 2H, H-7, H-10), 3.57 (dd, 1H, *J* = 10.2, 10.2 Hz, H-5), 3.44 (ddd, 1H, *J* = 10.2, 8.2, 4.6 Hz, H-6); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 138.7, 128.9, 128.3, 127.7, 126.8, 126.6, 102.0, 75.6, 70.7, 69.7, 66.2; HRMS calcd for $C_{13}H_{14}O_3Na$ [$(M + Na)^+$] 241.0841, found 241.0824.

Diol 7. To a solution of olefin **6** (1.71 g, 7.84 mmol) in acetone-H_2O (4/1, v/v, 50 mL) were added NMO (2.76 g, 23.6 mmol) and OsO_4 (20.0 mg, 0.079 mmol). After 24 h, the reaction was quenched with 15% $Na_2S_2O_3$ (30 mL), and the resulting mixture was stirred for 30 min. The mixture was extracted with $CHCl_3$ (300 mL), dried (Na_2SO_4), filtered, and concentrated. Column chromatography on silica gel (50 → 80% ethyl acetate/hexane) gave diol **7** (1.56 g, 79%) along with its diastereomer (0.32 g, 16%) as colorless solids. **7**: $[\alpha]_D^{23}$ = -59.2 (*c* 0.52, $CHCl_3$); IR (film) 3257, 2960, 2852, 1133, 1095, 1040, 1000, 981, 854, 782, 749, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48-7.45 (m, 2H, ArH), 7.38-7.32 (m, 3H, ArH), 5.56 (s, 1H, C*H*Ph), 4.30 (dd, 1H, *J* = 10.4, 5.1 Hz, H-5), 4.10 (dd, 1H, *J* = 12.8, 1.7 Hz, H-10), 4.04 (d, 1H, *J* = 1.7 Hz, H-9), 3.92-3.87 (m, 2H, 7-H, H-8), 3.78 (dd, 1H, *J* = 10.4, 10.4 Hz, H-5), 3.65 (d, 1H, *J* = 12.8 Hz, H-10), 3.37-3.33 (m, 1H, H-6), 2.67 (brs, 1H, OH), 2.61 (brs, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.3, 129.3, 128.4, 126.2, 102.2, 79.2, 71.4, 71.4, 70.3, 69.3, 68.6; HRMS calcd for $C_{13}H_{16}O_5Na$ [$(M + Na)^+$] 275.0895, found 275.0902.

Primary Alcohol 8. A solution of diol **7** (1.21 g, 4.80 mmol) in DMF (25 mL) was cooled to 0 °C and treated with NaH (60% oil dispersion, 1.15 g, 28.8 mmol). The resulting mixture was allowed to warm to room temperature and stirred for 60 min. The mixture was treated with benzyl bromide (2.28 ml, 19.2 mmol). After 100 min, the reaction mixture was cooled to 0 °C, and the reaction was quenched with saturated aqueous NH_4Cl (20 mL). The mixture was extracted with ethyl acetate (200 mL), washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), dried (Na_2SO_4), filtered, and concentrated to give crude bisbenzyl ether.

A solution of the above bisbenzyl ether in methanol (50 mL) was treated with CSA

(220 mg, 0.95 mmol). After 20 h, the reaction was quenched with triethylamine (3 mL). Concentration and column chromatography on silica gel (30 → 80% ethyl acetate/hexane) afforded diol (1.63 g, 99%) as a colorless solid: $[\alpha]_D^{24}$ = -76.4 (*c* 1.78, $CHCl_3$); IR (film) 3391, 2913, 2867, 1496, 1454, 1351, 1105, 1063, 1027, 735, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.24 (m, 10H, ArH), 4.72(d, 1H, *J* = 12.4 Hz, C*H*$_2$Ph), 4.61(d, 1H, *J* = 12.4 Hz, C*H*$_2$Ph), 4.58(d, 1H, *J* = 11.8 Hz, C*H*$_2$Ph), 4.45(d, 1H, *J* = 11.8 Hz, C*H*$_2$Ph), 4.10 (d, 1H, *J* = 12.1 Hz, H-10), 3.99 (dd, 1H, *J* = 11.4, 9.4 Hz, H-7), 3.88 (d, 1H, *J* = 11.4 Hz, H-8), 3.76 (dd, 1H, *J* = 9.4, 5.4 Hz, H-5), 3.73 (s, 1H, H-9), 3.38 (dd, 1H, *J* = 9.4, 3.2 Hz, H-5), 3.33 (d, 1H, *J* = 12.7 Hz, H-10), 3.24 (ddd, 1H, *J* = 9.4, 5.4, 3.2 Hz, H-6), 3.01 (brs, 1H, OH), 2.63 (brs, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 137.9, 128.3, 128.3, 127.8, 127.8, 127.7, 127.6, 82.2, 80.2, 72.1, 71.2, 71.2, 67.6, 67.2, 63.0; HRMS calcd for $C_{20}H_{24}O_5Na$ $[(M + Na)^+]$ 367.1521, found 367.1524.

A solution of diol (8.91 g, 25.9 mmol) in CH_2Cl_2 (250 mL) was cooled to 0 °C and treated with 2,6-lutidine (15.1 mL, 130 mmol) followed by TBSOTf (17.8 mL, 77.5 mmol). After 5 h, the reaction was quenched with saturated aqueous NH_4Cl (100 mL). The mixture was extracted with ethyl acetate (1000 mL), washed with brine (200 mL), dried (Na_2SO_4), filtered, and concentrated to give crude bissilyl ether.

A solution of the above bissilyl ether was dissolved in methanol□CH_2Cl_2 (1/1, v/v, 250 mL) was cooled to 0 °C and treated with CSA (3.00 g, 12.9 mmol). After 1 h, the reaction was quenched with triethylamine (10 mL). Concentration and column chromatography on silica gel (10 → 30% ethyl acetate/hexane) afforded primary alcohol **8** (10.1 g, 85%) as a colorless oil: $[\alpha]_D^{24}$ = -23.8 (*c* 1.11, $CHCl_3$); IR (film) 3482, 2927, 2855, 1454, 1360, 1256, 1131, 1099, 1027, 837, 779, 734, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.24 (m, 10H, ArH), 4.67 (d, 1H, *J* = 12.4 Hz, C*H*$_2$Ph), 4.61 (d, 1H, *J* = 12.4 Hz, C*H*$_2$Ph), 4.57 (d, 1H, *J* = 11.9 Hz, C*H*$_2$Ph), 4.49 (d, 1H, *J* = 11.9 Hz, C*H*$_2$Ph), 4.04 (dd, 1H, *J* = 12.5, 2.3 Hz, H-10), 3.93 (dd, 1H, *J* = 9.2, 9.0 Hz, H-7), 3.84 (ddd, 1H, *J* = 10.4, 7.4, 2.8 Hz, H-5), 3.72 (dd, 1H, *J* = 3.2, 2.3 Hz, H-9), 3.70-3.66 (m, 1H, H-5), 3.34 (dd, 1H, *J* = 9.0, 3.2 Hz, H-8), 3.33 (d, 1H, *J* = 12.5 Hz, H-10), 3.20 (ddd, 1H, *J* = 9.2, 6.6, 2.8 Hz, H-6), 0.87 (s, 9H, Si*t*Bu), 0.07 (s, 3H, $SiCH_3$), 0.02 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 138.3, 128.3, 128.2, 127.7, 127.6, 127.6, 127.5, 82.9, 81.6, 72.6, 71.5, 71.3, 68.4, 67.3, 62.8, 25.9, 18.1, -3.8, -4.9; HRMS calcd for $C_{26}H_{38}O_5SiNa$ [(M + Na)$^+$] 481.2386, found 481.2387.

Terminal Olefin 9. A solution of alcohol **8** (7.04 g, 15.4 mmol) in CH_2Cl_2□DMSO (5/1, v/v, 180 mL) was cooled to 0 °C and treated with triethylamine (10.7 mL, 76.8 mmol) followed by SO_3·pyridine (7.35 g, 46.2 mmol). The resulting mixture was stirred at room temperature for 1 h. The mixture was extracted with ethyl acetate (1000 mL), washed with 1 N HCl (200 mL), saturated aqueous $NaHCO_3$ (200 mL), and brine (200 mL), dried (Na_2SO_4), filtered, and concentrated to give crude aldehyde.

A suspension of $Ph_3P^+CH_3Br^-$ (8.25 g, 23.1 mmo) in THF (150 mL) was cooled to 0 °C and treated with NaHMDS (1.0 M in THF, 20.0 mL, 20.0 mmol). After 30 min, a solution of the above aldehyde in THF (10, 5 mL) was added, and the resulting mixture was stirred at 0 °C for 20 min. The reaction was quenched with saturated aqueous NH_4Cl (100 mL). The mixture was extracted with ethyl acetate (1000 mL), washed with brine, dried (Na_2SO_4), filtered, and concentrated. Column chromatography on silica gel (10% ethyl acetate/hexane) gave olefin **9** (5.87 g, 83%) as a colorless oil: $[\alpha]^{25}_{D}$ = -29.0 (*c* 0.82, $CHCl_3$); IR (film) 2927,2855, 1496, 1454, 1348, 1253, 1132, 1107, 922, 837, 778, 733, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35-7.24 (m, 10H, ArH), 5.93 (ddd, 1H, *J* = 17.2, 10.5, 6.7 Hz, =CH), 5.35 (d, 1H, *J* = 17.2 Hz, =CH_2), 5.22 (d, 1H, *J* = 10.5 Hz, =CH_2), 4.71 (d, 1H, *J* = 12.5 Hz, CH_2Ph), 4.62 (d, 1H, *J* = 12.5 Hz, CH_2Ph), 4.57 (d, 1H, *J* = 12.0 Hz, CH_2Ph), 4.51 (d, 1H, *J* = 12.0 Hz, CH_2Ph), 4.04 (dd, 1H, *J* = 12.5, 2.4 Hz, H-10), 3.85 (dd, 1H, *J* = 8.8, 8.2 Hz, H-7), 3.70 (dd, 1H, *J* = 3.2, 2.4 Hz, H-9), 3.56 (dd, 1H, *J* = 8.8, 6.7 Hz, H-6), 3.34 (dd, 1H, *J* = 8.2, 3.2 Hz, H-8), 3.32 (d, 1H, *J* = 12.5 Hz, H-10), 0.84 (s, 9H, Si*t*Bu), 0.03 (s, 3H, $SiCH_3$), 0.02 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 138.4, 136.1, 128.3, 128.2, 127.8, 127.7, 127.5, 127.4, 118.2, 82.7, 82.7, 72.7, 71.7, 71.4, 71.4, 67.0, 26.0, 18.2, -3.8, -4.1; HRMS calcd for $C_{27}H_{38}O_5SiNa$ [(M + Na)$^+$] 477.2437, found 477.2454.

Alcohol 10. A solution of olefin **9** (5.19 g, 11.4 mmol) in THF (100 mL) was cooled to 0 °C and treated with 9-BBN (0.5 M in THF, 57.0 mL, 28.5 mmol). The resulting mixture was allowed to warm to room temperature and stirred for 2 h. The reaction mixture was cooled to 0 °C, and treated with saturated aqueous $NaHCO_3$ (50 mL) followed by 30% H_2O_2 (30 mL). The resultant mixture was stirred at room temperature for 90 min. The solution was diluted with ethyl acetate (1000 mL), washed with saturated aqueous $NaHCO_3$ (200 mL) and brine (200 mL), dried (Na_2SO_4), filtered, and concentrated. Column chromatography on silica gel (30% ethyl acetate/hexane) afforded alcohol **10** (5.12 g, 95%) as a colorless oil: $[\alpha]_D^{25}$ = -30.7 (*c* 0.49, $CHCl_3$); IR (film) 3448, 2927, 2856, 1496, 1472, 1454, 1360, 1255, 1132, 1096, 1062, 836, 778, 734, 697 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.37 (d, 2H, *J* = 7.6 Hz, ArH), 7.30 (d, 2H, *J* = 7.6 Hz, ArH), 7.21-7.03 (m, 6H, ArH), 4.44 (d, 1H, *J* = 12.3 Hz, C*H*$_2$Ph), 4.36 (d, 1H, *J* = 11.8 Hz, C*H*$_2$Ph), 4.26 (d, 1H, *J* = 12.3 Hz, C*H*$_2$Ph), 4.25 (d, 1H, *J* = 11.8 Hz, C*H*$_2$Ph), 4.04 (dd, 1H, *J* = 9.0, 8.9 Hz, H-7), 3.93-3.88 (m, 1H, H-4), 3.79-3.74 (m, 1H, H-4), 3.75 (dd, 1H, *J* = 12.6, 1.6 Hz, H-10), 3.29 (dd, 1H, *J* = 3.1, 1.6 Hz, H-9), 3.26 (ddd, 1H, *J* = 2.7, 4.0, 7.6 Hz, H-6), 3.06 (dd, 1H, *J* = 8.9, 3.1 Hz, H-8), 2.78 (d, 1H, *J* = 12.6 Hz, H-10), 2.17-2.14 (m, 1H, H-5), 1.85-1.79 (m, 1H, H-5), 0.95 (s, 9H, Si*t*Bu), 0.13 (s, 3H, $SiCH_3$), 0.04 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, C_6D_6) δ 139.1, 139.0, 128.5, 128.5, 128.3, 127.9, 127.8, 127.7, 83.0, 81.4, 72.9, 71.9, 71.2, 70.8, 66.7, 60.8, 34.8, 26.3, 18.5, -3.4, -4.5; HRMS calcd for $C_{27}H_{40}O_5SiNa$ [(M+Na)$^+$] 495.2543, found 495.2532.

Methyl Ketone 11. To a solution of alcohol **10** (5.47 g, 11.6 mmol) in CH_2Cl_2□DMSO (5/1, v/v, 150 mL) was added triethylamine (8.1 mL, 58.1 mmol). The solution was cooled to 0 °C and treated with SO_3·pyridine (5.5 g, 34.6 mmol). After 90 min, the reaction mixture was diluted with ethyl acetate (1000 mL), washed with 1 N HCl (200 mL), saturated aqueous $NaHCO_3$ (200 mL), and brine, dried (Na_2SO_4), filtered, and concentrated to give crude aldehyde.

A solution of the above aldehyde in THF (120 mL) was cooled to –78 °C and treated with MeMgBr (3.0 M in Et_2O, 11.6 mL, 34.8 mmol). The resultant mixture was stirred at –78 °C for 5 min and then at 0 °C for 30 min. The reaction was quenched with saturated aqueous NH_4Cl (100 mL). The mixture was extracted with ethyl acetate (1000 mL), washed with brine, dried (Na_2SO_4), filtered, and concentrated to give secondary alcohol.

A solution of the above alcohol in CH_2Cl_2 (120 mL) was treated with powdered 4Å molecular sieves (1.0 g), NMO (3.4 g, 29.0 mmol), and TPAP (210 mg, 0.60 mmol). After 3 h, the reaction mixture was filtered through a pad of silica gel and washed with ethyl acetate. Concentration and column chromatography on silica gel (15% ethyl acetate/hexane) afforded methyl ketone **11** (4.64 g, 83%) as a colorless crystal: $[\alpha]_D^{25}$ = -67.1 (*c* 0.11, $CHCl_3$); IR (film) 2927, 2856, 1717, 1454, 1358, 1248, 1135, 1107, 837, 778, 734, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34-7.22 (m, 10H, ArH), 4.67 (d, 1H, *J* = 12.5 Hz, C*H*$_2$Ph), 4.58 (d, 1H, *J* = 12.5 Hz, C*H*$_2$Ph), 4.56 (d, 1H, *J* = 11.9 Hz, C*H*$_2$Ph), 4.46 (d, 1H, *J* = 11.9 Hz, C*H*$_2$Ph), 3.95 (dd, 1H, *J* = 12.6, 2.4 Hz, H-10), 3.79 (dd, 1H, *J* = 8.8, 8.8 Hz, H-7), 3.71 (ddd, 1H, *J* = 3.1, 2.4, 0.6 Hz, H-9), 3.60 (ddd, 1H, *J* = 9.9, 8.8, 2.4 Hz, H-6), 3.33 (dd, 1H, *J* = 8.8, 3.1 Hz, H-8), 3.29 (dd, 1H, *J* = 12.6, 0.6 Hz, H-10), 2.80 (dd, 1H, *J* = 15.8, 2.4 Hz, H-5), 2.64 (dd, 1H, *J* = 15.8, 9.9 Hz, H-5), 2.16 (s, 3H, CH_3), 0.83 (s, 9H, Si*t*Bu), 0.06 (s, 3H, $SiCH_3$), 0.02 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 138.2, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 82.5, 78.0, 72.6, 71.4, 71.2, 71.2, 67.1, 46.1, 30.9, 26.0, 18.1, -3.7, -4.6; HRMS calcd for $C_{28}H_{40}O_5SiNa$ [$(M + Na)^+$] 507.2543, found 507.2552.

Enol Triflate 4. To a –78 °C solution of KHMDS (0.5 M in toluene, 22.5 mL, 11.3 mmol) in THF (150 mL) was added dropwise a solution of methyl ketone **11** (3.03 g, 6.26 mmol) in THF (30, 10 mL). After 30 min, a solution of $PhNTf_2$ (5.59 g, 15.6 mmol) in THF (30 mL) was added dropwise. The resultant mixture was stirred at –78 °C for 20 min and then at 0 °C for 20 min. The reaction was quenched with saturated aqueous NH_4Cl (100 mL). The mixture was extracted with ethyl acetate (500 mL), washed with brine (100 mL), dried (Na_2SO_4), filtered, and concentrated to give crude enol triflate **4** as a pale yellow oil, which was immediately used in the next coupling reaction without further purification.

Cross-Coupled Product 12. To a suspension of zinc (E. Merk, 10.3 g, 156 mmol) in THF (20 mL) was added 1,2-dibromoethane (2.5 mL, 29 mmol). The resultant mixture was heated to reflux and then cooled to room temperature, and this process was repeated four times. TMSCl (2.5 mL, 20 mmol) was added and the mixture was vigorously stirred at room temperature for 30 min. A solution of *N*-*t*-butoxycarbonyl-β-iodoalanine methyl ester (8.24 g, 25.0 mmol) in THF□DMA (1/1, v/v, 450 mL) was added, and the resulting solution was stirred at 35 °C for 1 h. $PdCl_2(PPh_3)_2$ (440 mg, 0.627 mmol) and a solution of the crude **4** in THF□DMA (1/1, v/v) (150, 30 mL) were sequentially added over 30 min. The resultant mixture was stirred at 60 °C for 2 h. The mixture was filtered through a pad of Celite and washed with ethyl acetate. The filtrate and washings were treated with saturated aqueous $NaHCO_3$ (200 mL). The mixture was extracted with ethyl acetate (2000 mL), washed with 1 N HCl (300 mL), H_20 (300 mL), and saturated aqueous $NaHCO_3$ (300 mL), and brine (300 mL), dried (Na_2SO_4), filtered, and concentrated. Column chromatography on silica gel (15% ethyl acetate/hexane) afforded cross-coupled product **12** (2.17 g, 52%) as a pale yellow oil: $[\alpha]_D^{25}$ = -23.3 (*c* 0.90, $CHCl_3$); IR (film) 3359, 2928, 2856, 1748, 1497, 1454, 1365, 1249, 1168, 1106, 1027, 836, 778, 734, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.23 (m, 10H, ArH), 5.04 (d, 1H, *J* = 7.0 Hz, NH), 4.96 (s, 1H, $=CH_2$), 4.88 (s, 1H, $=CH_2$), 4.68 (d, 1H, *J* = 12.5 Hz, CH_2Ph), 4.58 (d, 1H, *J* = 12.5 Hz, CH_2Ph), 4.55 (d, 1H, *J* = 12.0 Hz, CH_2Ph), 4.46 (d, 1H, *J* = 12.0 Hz, CH_2Ph), 4.40-4.30 (m, 1H, H-2), 4.02 (d, 1H, *J* = 12.6 Hz, H-10), 3.77 (dd, 1H, *J* = 8.7, 8.7 Hz, H-7), 3.72 (s, 1H, H-9), 3.70 (s, 3H, CO_2CH_3), 3.32-3.21 (m, 2H, 8-H, H-6), 3.24 (d, 1H, *J* = 12.6 Hz, H-10), 2.65 (d, 1H, *J* = 14.6 Hz, H-5), 2.56-2.38 (m, 2H, H_2-3), 2.12 (dd, 1H, *J* = 14.6, 10.4 Hz, H-5), 1.41 (s, 9H, *t*BuCO), 0.86 (s, 9H, Si*t*Bu), 0.07 (s, 3H, $SiCH_3$), 0.04 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 142.2, 138.4, 138.3, 128.2, 128.2, 127.7, 127.6, 127.5, 127.4, 115.0, 82.6, 72.4, 71.8, 71.2, 71.1, 66.8, 52.2, 52.0, 38.8, 38.3, 34.7, 28.3, 26.0, 18.6, -3.7, -4.5; HRMS calcd for $C_{37}H_{55}NO_8SiNa$ $[(M + Na)^+]$ 692.3595, found 692.3621.

Alcohol 13. A solution of **12** (2.00 g, 2.99 mmol) in THF (30 mL) was treated with TBAF (1.0 M in THF, 7.5 mL, 7.5 mmol), and the resultant mixture was stirred at room temperature for 5 h. Concentration and column chromatography on silica gel (40% ethyl acetate/hexane) gave alcohol **13** (1.37 g, 83%) as a colorless oil: $[\alpha]_D^{25}$ = -64.7 (*c* 1.08, $CHCl_3$); IR (film) 3430, 3348, 2929, 2865, 1745, 1712, 1497, 1454, 1365, 1248, 1164, 1105, 1066, 1027, 737, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.24 (m, 10H, ArH), 5.11 (d, 1H, *J* = 7.9 Hz, NH), 5.00 (s, 1H, $=CH_2$), 4.89 (s, 1H, $=CH_2$), 4.73 (d, 1H, *J* = 12.5 Hz, CH_2Ph), 4.60 (d, 1H, *J* = 11.8 Hz, CH_2Ph), 4.56 (d, 1H, *J* = 12.5 Hz, CH_2Ph), 4.44-4.38 (m, 1H, H-2), 4.40 (d, 1H, *J* = 11.8 Hz, CH_2Ph), 4.09 (d, 1H, *J* = 12.7 Hz, H-10), 3.77 (dd, 1H, *J* = 9.8, 9.2 Hz, H-7), 3.74 (d, 1H, *J* = 3.2 Hz, H-9), 3.68 (s, 3H, CO_2CH_3), 3.33 (dd, 1H, *J* = 9.2, 3.2 Hz, H-8), 3.27 (d, 1H, *J* = 12.7 Hz, H-10), 3.26-3.21 (m, 1H, H-6), 2.62 (d, 1H, *J* = 15.0 Hz, H-5), 2.57-2.35 (m, 2H, H_2-3), 2.25 (dd, 1H, *J* = 15.0, 8.0 Hz, H-5), 1.40 (s, 9H, *t*BuCO); ^{13}C NMR (125 MHz, $CDCl_3$)

δ 173.1, 141.5, 138.1, 137.8, 128.5, 128.3, 127.9, 127.8, 127.7, 127.6, 116.1, 115.9, 82.3, 71.9, 71.1, 70.1, 69.6, 66.9, 52.2, 52.1, 38.9, 38.0, 37.5, 28.3; HRMS calcd for $C_{31}H_{41}NO_8Na$ $[(M + Na)^+]$ 578.2730, found 578.2717.

Alcohol 14. A solution of alcohol **13** (794.1 mg, 1.43 mmol) in CH_2Cl_2 (15 mL) was treated with solid $NaHCO_3$ (1.20 g, 14.3 mmol) followed by Dess-Martin periodinane (1.83 g, 4.31 mmol). After 10 h, the reaction mixture was diluted with ethyl acetate (200 mL), washed with aqueous $Na_2S_2O_3$ (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (50 mL), dried (Na_2SO_4), filtered, and concentrated to give crude ketone.

A solution of the above ketone in methanol□THF (1/1, v/v, 15 mL) was cooled to –78 °C and treated with $NaBH_4$ (270 mg, 7.14 mmol). The resultant mixture was stirred at –78 °C for 5 min, and then gradually warmed to 0 °C. After 10 min, the reaction was quenched with saturated aqueous NH_4Cl (10 mL). The mixture was extracted with ethyl acetate (150 mL), washed with brine (50 mL), dried (Na_2SO_4), filtered, and concentrated. Column chromatography on silica gel (30% ethyl acetate/hexane) afforded alcohol **14** (665.7 mg, 84%) as a colorless oil: $[\alpha]_D^{26}$ = -37.1 (*c* 0.32, $CHCl_3$); IR (film) 3496, 3343, 2920, 2859, 1744, 1711, 1497, 1453, 1365, 1250, 1166, 1105, 1056, 738, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.24 (m, 10H, ArH), 5.08 (d, 1H, *J* = 7.4 Hz, NH), 4.98 (s, 1H, $=CH_2$), 4.90 (s, 1H, $=CH_2$), 4.76 (d, 1H, *J* = 12.1 Hz, CH_2Ph), 4.74 (d, 1H, *J* = 12.7 Hz, CH_2Ph), 4.71 (d, 1H, *J* = 12.7 Hz, CH_2Ph), 4.56 (d, 1H, *J* = 12.1 Hz, CH_2Ph), 4.41-4.35 (m, 1H, H-2), 4.11 (d, 1H, *J* = 12.7 Hz, H-10), 3.83 (dd, 1H, *J* = 8.9, 2.8 Hz, H-7), 3.77 (s, 1H, H-9), 3.69 (s, 3H, CO_2CH_3), 3.42 (dd, 1H, *J* = 5.7, 2.8 Hz, H-8), 3.30 (d, 1H, *J* = 12.7 Hz, H-10), 3.31-3.28 (m, 1H, H-6), 2.58-2.51 (m, 2H, H-3, H-5), 2.44-2.31 (m, 2H, H-3, H-5), 1.40 (s, 9H, *t*BuCO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 141.2, 138.0, 137.6, 128.4, 128.4, 128.0, 127.8, 127.7, 127.6, 116.2, 115.9, 76.5, 74.4, 72.5, 69.4, 69.2, 68.3, 52.4, 52.1, 39.1, 37.5, 31.6, 28.3; HRMS calcd for $C_{31}H_{41}NO_8Na$ $[(M + Na)^+]$ 578.2730, found 578.2708.

Epoxide 15. To a solution of alcohol **14** (26.9 mg, 0.0485 mmol) in CH_2Cl_2 (1.5 mL)-pH 7 phosphate buffer (0.5 mL) was added *m*CPBA (70% content, 36 mg, 0.15 mmol), and the resultant mixture was stirred at room temperature for 3 h. The mixture was diluted with $CHCl_3$ (20 mL), washed with 15% $Na_2S_2O_3$ (5 mL), saturated aqueous $NaHCO_3$ (5 mL), and brine, dried (Na_2SO_4), filtered, and concentrated. Column chromatography on silica gel (40% ethyl acetate/hexane) gave epoxide **15** (24.4 mg, 88%) as an inseparable mixture of diastereomers; HRMS calcd for $C_{31}H_{41}NO_9Na$ $[(M + Na)^+]$ 594.2679, found 594.2698.

Hydroxy Acid 17. A solution of epoxide **15** (88.1 mg, 0.154 mmol) in CH_2Cl_2 (5 mL) was treated with CSA (7.1 mg, 0.031 mmol). After 30 min, the reaction was quenched with triethylamine (0.1 mL), and the resultant mixture was concentrated.

The crude product was dissolved in THF (5 mL) and treated with 1 N aqueous NaOH (1 mL). After 30 min, the solvent was evaporated and the residue was purified by column chromatography on silica gel (10% methanol/$CHCl_3$ containing 1% Et_3N) to give hydroxy acid **17** (39.5 mg, 46%) as an approximately 2:1 mixture of diastereomers; HRMS calcd for $C_{13}H_{14}O_3$ $[(M + Na)^+]$ 580.2523, found 580.2518 .

Protected Neodysiherbaine A (18) and its C4 epimer 19. A solution of the above hydroxy acid in CH_3CN (2 mL) was treated with 4Å molecular sieves (30 mg), NMO (33 mg, 0.28 mmol), and TPAP□9.7 mg, 0.028 mmol□. After 46 h, the reaction mixture was concentrated to give a residue, which was dissolved in methanol (2 mL) and treated with trimethylsilyldiazomethane (2.0 M in hexane, 0.28 mL, 0.56 mmol). After 18 h, the reaction mixture was concentrated and the residue was purified by column chromatography on silica gel (70% ethyl acetate/hexane) to give protected neodysiherbaine A **18** (14.2 mg, 43%) and its C4-epimer **19** (8.0 mg, 24%) as colorless oils, respectively. **18**: $[\alpha]_D^{26}$ = -56.0 (*c* 0.073, $CHCl_3$); IR (film) 3363, 2916, 2848, 1742, 1711, 1497, 1454, 1366, 1165, 1127 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39-7.24 (m, 10H, ArH), 5.43 (d, 1H, *J* = 6.8 Hz, NH), 4.72 (d, 1H, *J* = 12.5 Hz, CH_2Ph), 4.68 (s, 2H, CH_2Ph), 4.66 (d, 1H, *J* = 12.5 Hz, CH_2Ph), 4.35-4.30 (m, 1H, H-2), 4.07 (s, 1H, H-7), 4.03-3.99 (m, 1H, H-6), 4.01 (d, 1H, *J* = 12.4 Hz, H-10), 3.69 (s, 3H, CO_2CH_3), 3.60 (dd, 1H, *J* = 3.6, 3.6 Hz, H-8), 3.55 (s, 1H, H-9), 3.42 (s, 3H, CO_2CH_3), 3.24 (d, 1H, *J* = 12.5 Hz, H-10), 2.81 (dd, 1H, *J* = 13.6, 2.3 Hz, H-5), 2.36 (dd, 1H, *J* = 14.5, 4.2 Hz, H-3), 2.21 (dd, 1H, *J* = 14.5, 7.2 Hz, H-3), 2.05 (dd, 1H, *J* = 13.6, 4.7 Hz, H-5), 1.40 (s, 9H, *t*BuCO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 172.5, 155.3, 138.8, 138.3, 128.3, 128.2, 127.7, 127.6, 127.5, 127.4, 84.8, 79.8, 77.3, 74.7, 71.7, 71.4, 70.8, 65.2, 52.4, 52.1, 50.9, 40.7, 40.4, 28.3; HRMS: calcd for $C_{32}H_{41}NO_{10}Na$ $[(M + Na)^+]$ 622.2628, found 622.2607. NOEs were observed between H_2-3 and H-5β, and between H-5β and H-6 in a 2D NOESY experiment.

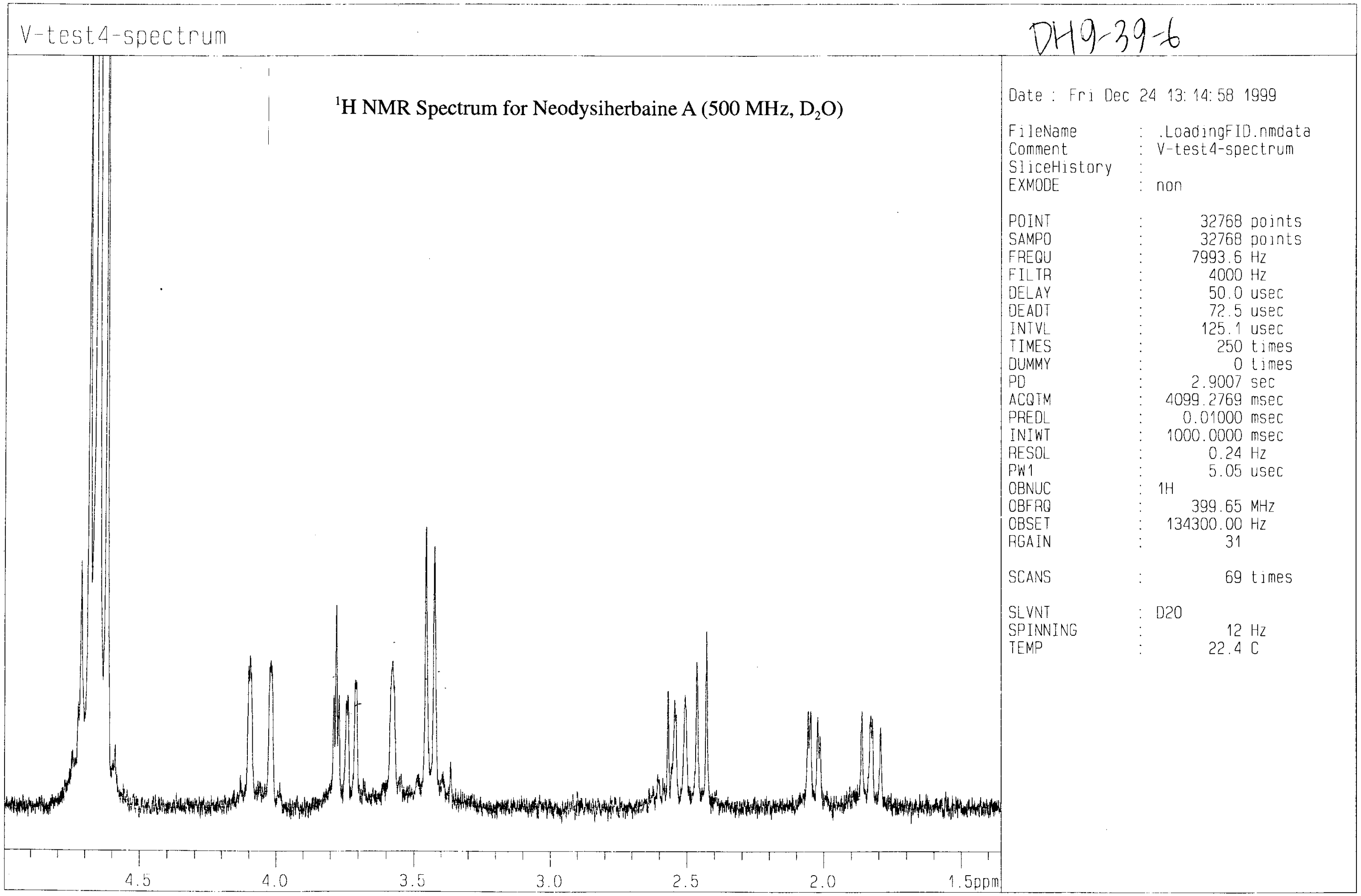
19: $[\alpha]_D^{24}$ = -4.6 (*c* 0.16, $CHCl_3$); IR (film) 3360, 2951, 2893, 1743, 1709, 1507, 1454, 1365, 1249, 1163, 1104, 736, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.24 (m, 10H, ArH), 6.95 (d, 1H, *J* = 3.7 Hz, NH), 4.88 (d, 1H, *J* = 13.2 Hz, CH_2Ph), 4.78 (d, 1H, *J* = 13.2 Hz, CH_2Ph), 4.67 (d, 1H, *J* = 12.6 Hz, CH_2Ph), 4.52 (d, 1H, *J* = 12.6 Hz, CH_2Ph), 4.30 (s, 1H, H-9), 4.20-4.16 (m, 1H, H-2), 3.95-3.93 (m, 1H, H-6), 3.89 (d, 1H, *J* = 12.9 Hz, H-10), 3.76 (s, 3H, CO_2CH_3), 3.69 (s, 3H, CO_2CH_3), 3.59 (d, 1H, *J* = 3.6 Hz, H-7), 3.46 (dd, 1H, *J* = 3.6, 3.6 Hz, H-8), 3.10 (d, 1H, *J* = 12.9 Hz, H-10), 2.61 (dd, 1H, *J* = 14.3, 11.9 Hz, H-3), 2.36 (d, 1H, *J* = 14.3 Hz, H-3), 2.31 (dd, 1H, *J* = 14.1, 4.7 Hz, H-5), 2.17 (d, 1H, *J* = 14.1 Hz, H-5), 1.36 (s, 9H, *t*BuCO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 173.4, 156.6, 138.2, 138.0, 128.8, 128.7, 128.4, 128.3, 127.7, 127.7, 79.3, 77.6, 76.1, 73.5, 71.1, 70.0, 69.4, 66.3, 52.9, 52.5, 52.0, 44.3, 38.2, 28.5; HRMS calcd for $C_{32}H_{41}NO_{10}Na$ $[(M + Na)^+]$ 622.2628, found 622.2635.

Diol 20. A solution of protected neodysiherbaine A **18** (21.6 mg, 0.0361 mmol) in methanol (2 mL) was treated with 10% Pd/C (5 mg), and stirred under hydrogen for 24 h. The reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated. Column chromatography on silica gel (ethyl acetate) afforded diol **20** (11.6 mg, 77%); $[\alpha]_D^{21}$ = 42.9 (*c* 0.59, $CHCl_3$); IR (film) 3434, 2955, 2846, 1742, 1713, 1507, 1438, 1367, 1279, 1219, 1165, 1111, 1178, 732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.32 (d, 1H, *J* = 6.3 Hz, NH), 4.73 (d, 1H, *J* = 12.3 Hz, OH), 4.32 (ddd, 1H, *J* = 6.3, 5.4, 3.6 Hz, H-2), 4.01 (s, 1H, H-7), 3.95 (dd, 1H, *J* = 12.6, 2.1 Hz, H-10), 3.93 (s, 1H, H-6), 3.79 (s, 3H, CO_2CH_3), 3.76 (s, 3H, CO_2CH_3), 3.65 (d, 1H, *J* = 12.3 Hz, H-9), 3.62 (s, 1H, H-8), 3.39 (d, 1H, *J* = 12.6 Hz, H-10), 2.99 (brs, 1H, OH), 2.78 (dd, 1H, *J* = 14.5, 5.4 Hz, H-3), 2.51 (d, 1H, *J* = 14.1 Hz, H-5), 2.24 (dd, 1H, *J* = 14.5, 3.6 Hz, H-3), 2.11 (dd, 1H, *J* = 14.1, 3.6 Hz, H-5), 1.41 (s, 9H, *t*BuCO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 172.2, 155.1, 83.3, 81.0, 80.0, 76.7, 70.2, 67.7, 67.3, 53.0, 52.8, 51.1, 46.2, 40.4, 28.3; HRMS: calcd for $C_{18}H_{29}NO_{10}Na$ [$(M + Na)^+$] 442.1689, found 442.1687.

Neodysiherbaine A (2a). A solution of diol **20** (6.5 mg, 0.016 mmol) in 6 N aqueous HCl (3 mL) was heated at 60 °C for 15 h. The reaction mixture was lyophilized to give neodysiherbaine A (**2a**) as the hydrochloride salt (5.0 mg, 99 %): CD (H_2O) λ_{ext} 204 nm, $\Delta\varepsilon$ 1.7; ^1H NMR (400 MHz, D_2O) δ 4.07 (brs, 1H, H-7), 3.99 (brs, 1H, H-6), 3.76 (t, 1H, *J* = 3.7 Hz, H-8), 3.71 (dd, 1H, *J* = 12.6, 2.5 Hz, H-10a), 3.55 (brs, 1H, H-9), 3.42 (brd, 1H, *J* = 12.7 Hz, H-2), 3.42 (brd, 1H, *J* = 12.7 Hz, H-10b), 2.50 (dd, 1H, *J* = 14.9, 1.5 Hz, H-3a), 2.42 (d, 1H, *J* = 14.2 Hz, H-5a), 2.01 (dd, 1H, *J* = 14.0, 3.4 Hz, H-5b), 1.81 (dd, 1H, *J* = 15.1, 12.1 Hz, H-3b); ^{13}C NMR (100 MHz, D_2O with CD_3OD 50 μL) δ 180.9 (C-11), 174.5 (C-1), 88.2 (C-4), 81.1 (C-7), 77.4 (C-6), 70.3 (C-8), 68.5 (C-10), 67.9 (C-9), 54.4 (C-2), 45.3 (C-5), 39.9 (C-3); HRMS calcd for $C_{11}H_{18}NO_8$ [$(M+H)^+$] 292.1032, found 292.1053.

4-Epineodysiherbaine A. A solution of protected 4-epineodysiherbaine A (**19**) (3.2 mg, 0.0053 mmol) in methanol (1 mL) was treated with 10% Pd/C (2 mg), and stirred under hydrogen for 24 h. The reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated. Column chromatography on silica gel (ethyl acetate) afforded diol (1.9 mg, 85%); $[\alpha]_D^{24}$ = -21.6 (*c* 0.10, $CHCl_3$); IR (film) 3361, 2917, 2850, 1734, 1507, 1367, 1280, 1164, 1115, 1024 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.43 (d, 1H, *J* = 7.2 Hz, NH), 4.48-4.43 (m, 1H, H-2), 4.16 (s, 1H, H-7), 4.01 (dd, 1H, *J* = 12.6, 1.7 Hz, H-10), 3.96 (d, 1H, *J* = 4.9 Hz, H-6), 3.75 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 3.74-3.69 (m, 2H, H-8, H-9), 3.43 (d, 1H, *J* = 12.6 Hz, H-10), 2.92 (d, 1H, *J* = 9.5 Hz, OH), 2.85 (d, 1H, *J* = 9.3 Hz, OH), 2.64-2.58 (m, 1H, H-3), 2.42-2.38 (m, 1H, H-3), 2.39 (dd, 1H, *J* = 14.5, 4.9 Hz, H-5), 2.20 (d, 1H, *J* = 14.5, 4.9 Hz, H-5), 1.42 (s, 9H, *t*BuCO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 97.8, 81.1, 75.9, 69.7, 67.6, 67.6, 52.8, 52.6, 50.8, 44.6, 40.5, 28.3; HRMS calcd for $C_{18}H_{29}NO_{10}Na$ [(M+Na)$^+$] 442.1689, found 442.1703.

A solution of the above diol (1.7 mg, 0.0041 mmol) in 6 N aqueous HCl (2 mL) was heated at 60 °C for 15 h. The reaction mixture was lyophilized to give 4-epineodysiherbaine A as the hydrochloride salt (1.4 mg, 99 %): ^1H NMR (400 MHz, D_2O) δ 4.14 (brt, 1H, *J* = 4.4 Hz, H-6), 4.14 (brt, 1H, *J* = 4.4 Hz, H-7), 3.92 (brt, 1H, *J* = 3.7 Hz, H-8), 3.87 (dd, 1H, *J* = 11.9, 2.2 Hz, H-10a), 3.85 (brs, 1H, H-9), 3.74 (d, 1H, *J* = 11.0 Hz, H-2), 3.53 (d, 1H, *J* = 12.2 Hz, H-10b), 2.67 (d, 1H, *J* = 15.6 Hz, H-3a), 2.47 (dd, 1H, *J* = 14.7, 4.2 Hz, H-5b), 2.27 (dd, 1H, *J* = 15.1, 11.0 Hz, H-3b), 2.14 (d, 1H, *J* = 14.9 Hz, H-5a); ^{13}C NMR (100 MHz, D_2O with CD_3OD 50 μL) δ 179.2 (C-11), 174.1 (C-1), 86.5 (C-4), 81.5 (C-7), 78.6 (C-6), 70.3 (C-8), 67.6 (C-10), 67.4 (C-9), 53.0 (C-2), 44.0 (C-5), 39.9 (C-3); HRMS calcd for $C_{11}H_{18}NO_8$ [(M+H)$^+$] 292.1032, found 292.1060.



V-test4-spectrum

DH9-39-6

^{1}H NMR Spectrum for Neodysiherbaine A (500 MHz, D_2O)

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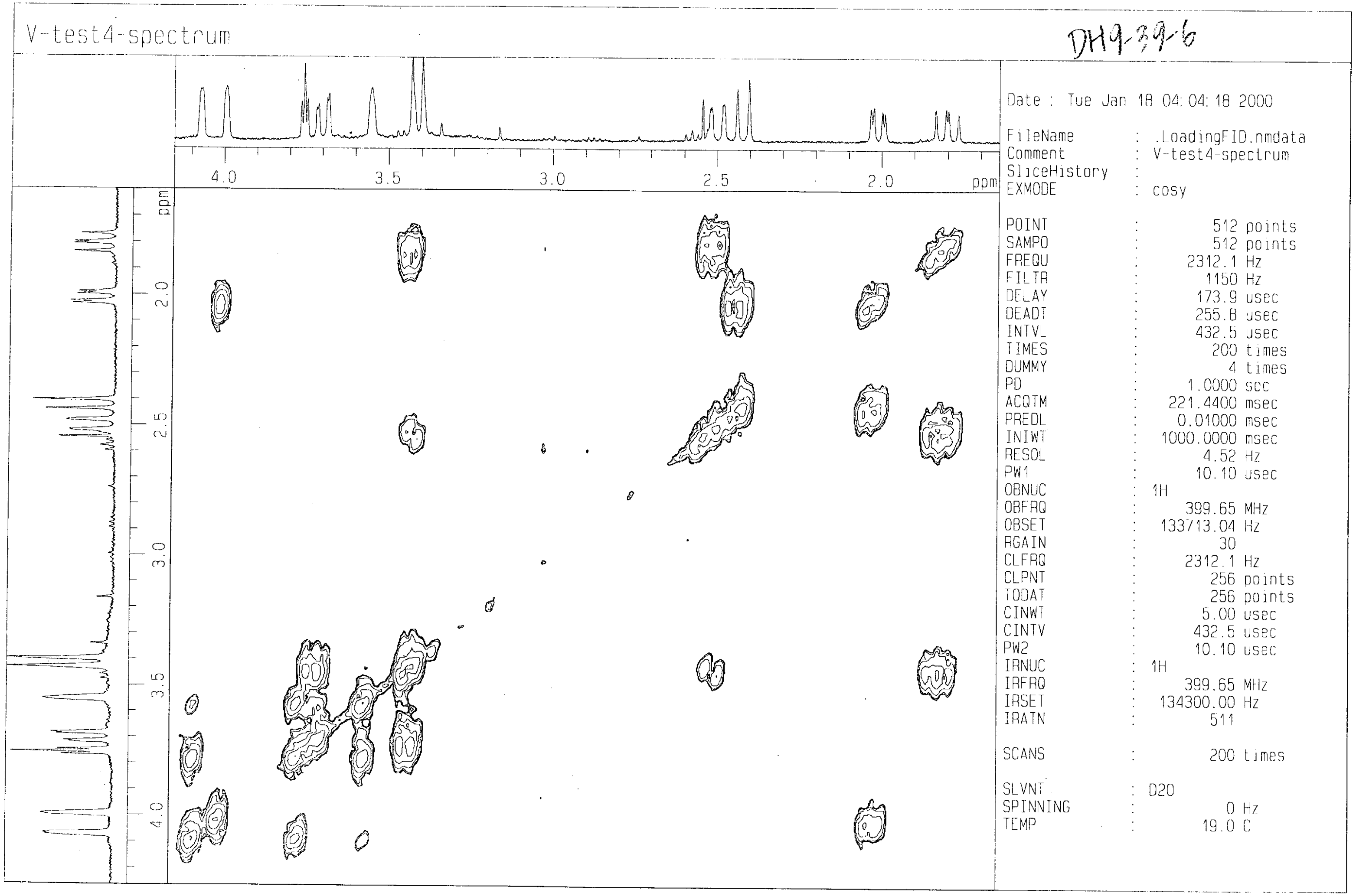
FILTR           :          4000 Hz
DELAY           :          50.0 usec
DEADT           :          72.5 usec
INTVL           :         125.1 usec
TIMES           :           250 times
DUMMY           :             0 times
PD              :        2.9007 sec
ACQTM           :     4099.2769 msec
PREDL           :       0.01000 msec
INIWT           :     1000.0000 msec
RESOL           :          0.24 Hz
PW1             :          5.05 usec
OBNUC           : 1H
OBFRQ           :        399.65 MHz
OBSET           :     134300.00 Hz
RGAIN           :            31

SCANS           :            69 times

SLVNT           : D2O
SPINNING        :            12 Hz
TEMP            :          22.4 C
```

COSY Spectrum for Neodysiherbaine A (500 MHz, D_2O)



DH9-39-6

```
Date :  Tue Jan 18 04:04:18 2000

FileName        : .LoadingFID.nmdata
Comment         : V-test4-spectrum
SliceHistory    :
EXMODE          : cosy

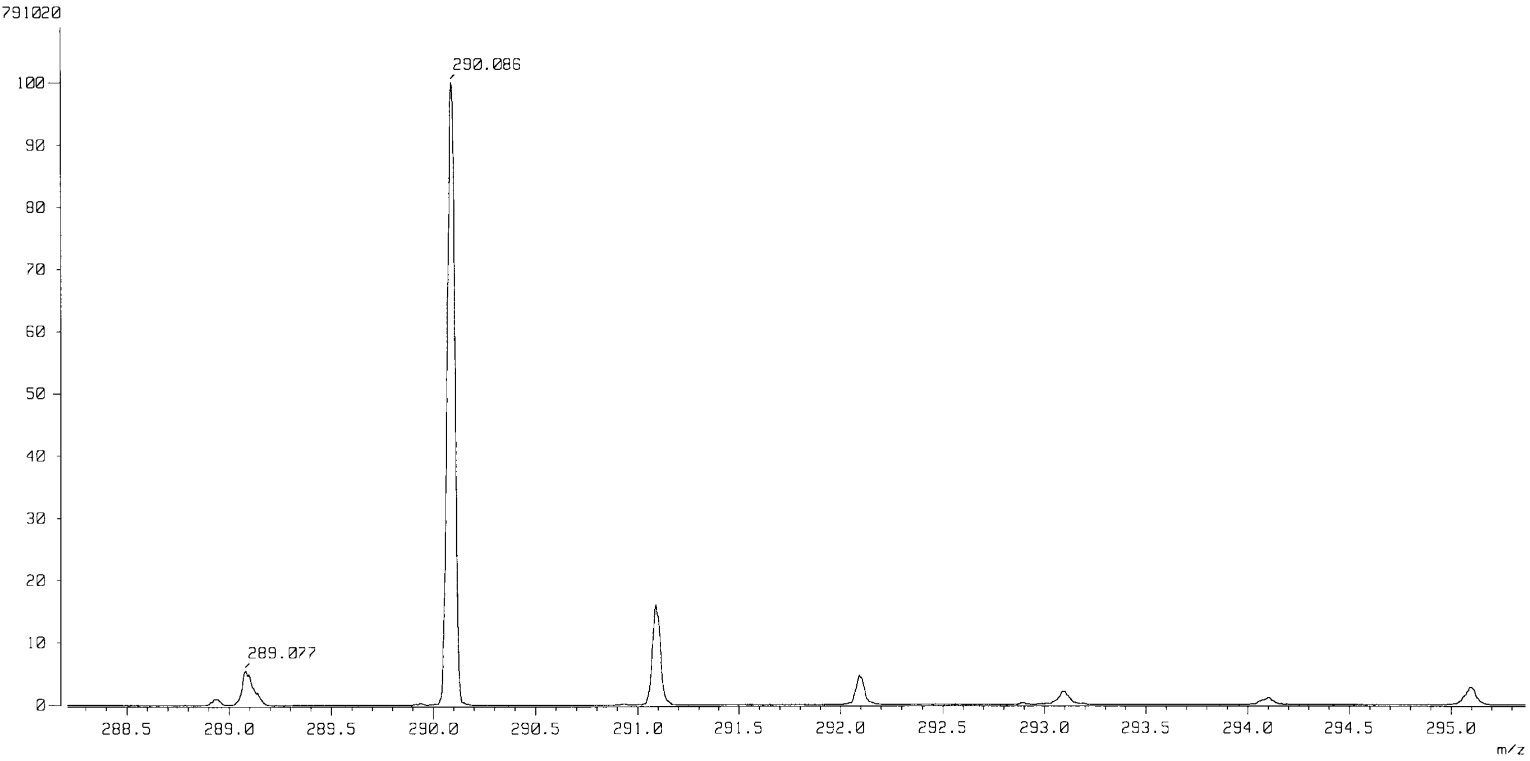
POINT           :        512 points
SAMPO           :        512 points
FREQU           :     2312.1 Hz
FILTR           :       1150 Hz
DELAY           :      173.9 usec
DEADT           :      255.8 usec
INTVL           :      432.5 usec
TIMES           :        200 times
DUMMY           :          4 times
PD              :     1.0000 sec
ACQTM           :   221.4400 msec
PREDL           :    0.01000 msec
INIWT           :  1000.0000 msec
RESOL           :       4.52 Hz
PW1             :      10.10 usec
OBNUC           : 1H
OBFRQ           :     399.65 MHz
OBSET           :  133713.04 Hz
RGAIN           :         30
CLFRQ           :     2312.1 Hz
CLPNT           :        256 points
TODAT           :        256 points
CINWT           :       5.00 usec
CINTV           :      432.5 usec
PW2             :      10.10 usec
IRNUC           : 1H
IRFRQ           :     399.65 MHz
IRSET           :  134300.00 Hz
IRATN           :        511

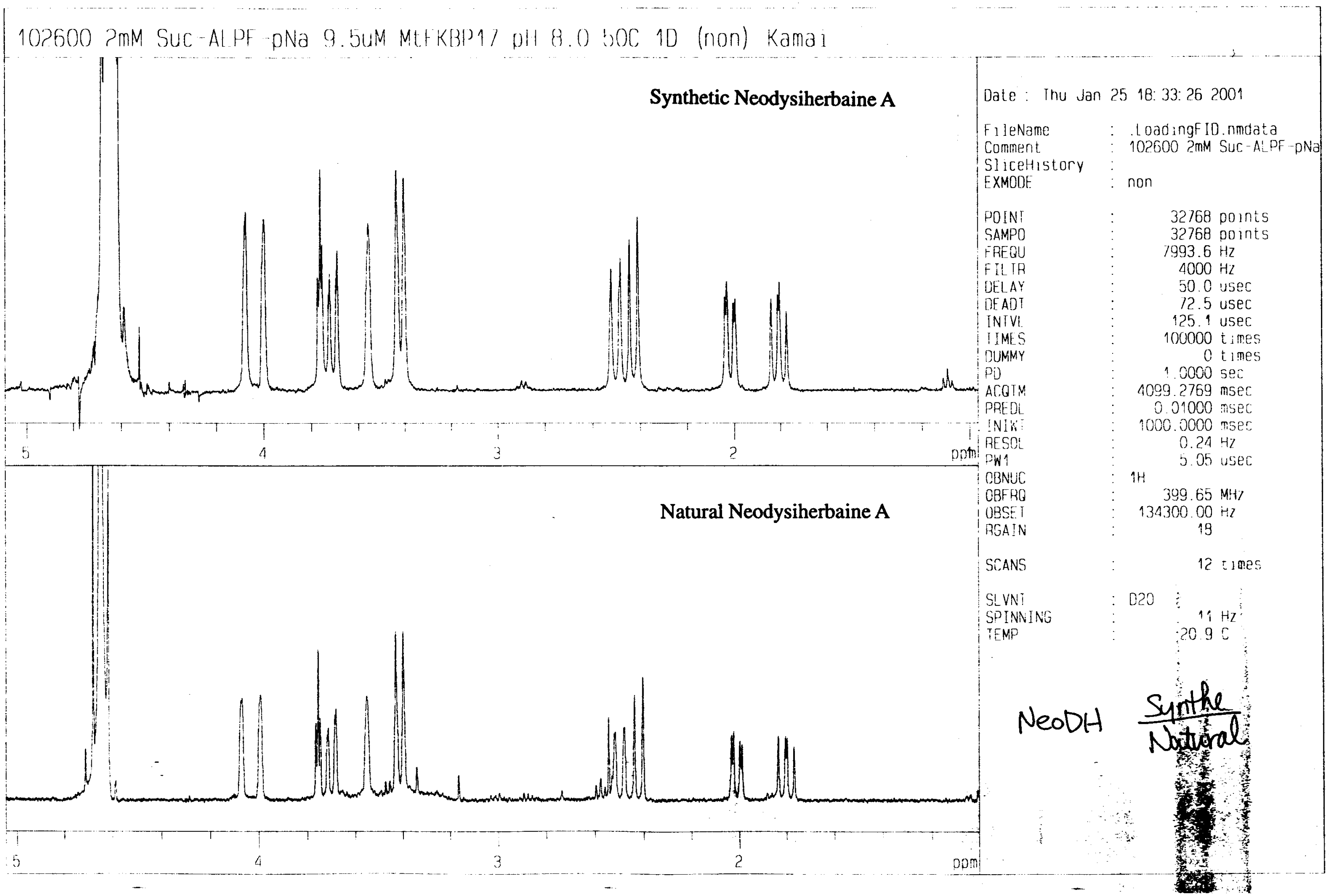
SCANS           :        200 times

SLVNT           : D2O
SPINNING        :          0 Hz
TEMP            :       19.0 C
```

Negative Ion FABMS for Neodysiherbaine A

```
[ Mass Spectrum ]
Data  : NeoDH-NegFab-HIRES           Date : 15-Feb-2000 16:01
Sample: -
Note : -
Inlet : Direct                       Ion Mode : FAB-
Spectrum Type : Normal Ion [EF-Linear]
RT : 19.60 min         Scan# : 99
BP : m/z 290.0865      Int.   : 1558.35
Output m/z range : 288.2081 to 295.3672       Cut Level : 0.00 %
```





102600 2mM Suc-ALPF-pNa 9.5uM MtFKBP17 pH 8.0 50C 1D (non) Kamai

Synthetic Neodysiherbaine A

Natural Neodysiherbaine A

```
Date :  Thu Jan 25 18:33:26 2001

FileName       :  .LoadingFID.nmdata
Comment        :  102600 2mM Suc-ALPF-pNa
SliceHistory   :
EXMODE         :  non

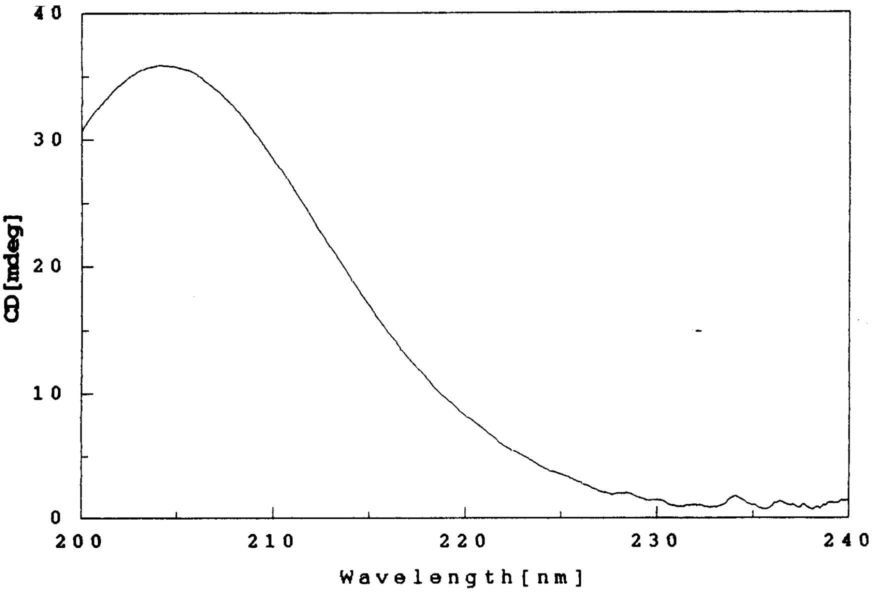
POINT          :        32768 points
SAMPO          :        32768 points
FREQU          :       7993.6 Hz
FILTR          :         4000 Hz
DELAY          :         50.0 usec
DEADT          :         72.5 usec
INTVL          :        125.1 usec
TIMES          :       100000 times
DUMMY          :            0 times
PD             :       1.0000 sec
ACQTM          :    4099.2769 msec
PREDL          :      0.01000 msec
INIWT          :    1000.0000 msec
RESOL          :         0.24 Hz
PW1            :         5.05 usec
OBNUC          :  1H
OBFRQ          :       399.65 MHz
OBSET          :    134300.00 Hz
RGAIN          :           18

SCANS          :           12 times

SLVNT          :  D20
SPINNING       :           11 Hz
TEMP           :         20.9 C
```

NeoDH Synthe / Natural

Natural Neodysiherbaine A



Synthetic Neodysiherbaine A