Stereocontrolled Synthesis of 8,11-Dideoxytetrodotoxin, Unnatural Analog of Puffer Fish Toxin

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1. Proof of the configuration of C-9 OH group of **13**^a

^aReagents and conditions: (a) TMS-C₄H₉-Li, THF, -78°C; (b) K₂CO₃, MeOH, rt.

2. Characterization data

General: Melting point were recorded on a Yanaco MP-S3 melting point apparatus and not corrected. Optical rotation were measured on a JASCO DIP-370 digital polarimeter. Infrared spectra were recorded on a JASCO FT/IR-8300 spectrophotometer and are reported in wave number (cm⁻¹). Proton nuclear magnetic resonance (¹H NMR) spectra were recorded on a Bruker ARX-600 (600 MHz), a JEOL A-600 (600 MHz), a Bruker ARX-400 (400 MHz) or a Varian Gemini-2000 (300 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane (δ = 0.00 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, br = broadened, m = multiplet), coupling constant and assignment. Carbon nuclear magnetic resonance (¹³C NMR) spectra were recorded on a Bruker ARX-600 (150 MHz), a JEOL A-600 (150 MHz), a

Bruker ARX-400 (100 MHz) or a Varian Gemini-2000 (75 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane using the solvent resonance as internal standard (CDCl_3 : $\delta = 77.0$ ppm). High resolution mass spectra (HRMS) were recorded on a JEOL JMS-700 spectrometer and reported in m/z . Elemental analyses were performed by Analytical Laboratory at Graduate School of Bioagricultural Sciences, Nagoya University.

Cyclic iminoether 8. $[\alpha]_{\text{D}}^{26} +164^\circ$ (c 1.14, CHCl_3). IR (KBr) ν_{max} 2987, 1668, 1236, 1075, 790 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 1.34 (3H, s, CH_3 of acetonide), 1.36 (3H, s, CH_3 of acetonide), 1.86 (1H, dd, $J = 13.5, 2.5$ Hz, CH_AH_B), 1.90 (3H, t, $J = 1.5$ Hz, $\text{CH}=\text{C}-\text{CH}_3$), 1.93 (1H, dd, $J = 13.5, 3$ Hz, CH_AH_B), 2.80 (1H, m, $-\text{CH}-$), 3.52 (1H, dd, $J = 9, 7.5$ Hz, $\text{O}-\text{CH}-\text{CH}_A\text{H}_B-\text{O}$), 3.87 (1H, dd, $J = 7.5, 5.5$ Hz, $\text{O}-\text{CH}-\text{CH}_A\text{H}_B-\text{O}$), 4.11 (1H, dt, $J = 9, 5.5$ Hz, $\text{CH}=\text{CMe}-\text{CH}-\text{O}$), 4.74 (1H, t, $J = 3$ Hz, $\text{O}-\text{CH}-\text{C}-\text{CH}_3$), 5.21 (1H, dd, $J = 10.5, 1$ Hz, $\text{CH}=\text{CH}_A\text{H}_B$), 5.30 (1H, dd, $J = 17, 1$ Hz, $\text{CH}=\text{CH}_A\text{H}_B$), 5.68 (1H, m, $\text{CH}=\text{CCH}_3$), 6.22 (1H, dd, $J = 17, 10.5$ Hz, $\text{CH}=\text{CH}_2$). ^{13}C NMR (CDCl_3 , 75 MHz) δ 21.2, 25.8, 26.3, 28.5, 47.9, 55.8, 66.1, 73.4, 74.9, 92.7, 108.2, 114.0, 124.8, 133.3, 141.0, 151.9. Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{Cl}_3\text{NO}_3$: C, 50.48; H, 5.30; N, 3.68. Found: C, 50.47; H, 5.35; N, 3.75.

Allylic alcohol 9. $[\alpha]_{\text{D}}^{26} +90.8^\circ$ (c 1.08, CHCl_3). IR (KBr) ν_{max} 3482, 3353, 2982, 1728, 1527, 1063, 854 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 1.34 (3H, s, CH_3 of acetonide), 1.43 (3H, s, CH_3 of acetonide), 1.82 (3H, m, $\text{CH}=\text{C}-\text{CH}_3$), 1.84 (1H, dd, $J = 13, 9.5$ Hz, $\text{CH}_{\text{ax}}\text{H}_{\text{eq}}$), 2.72 (1H, dq, $J = 10, 2.5$ Hz, $-\text{CH}-$), 3.44 (1H, dd, $J = 13, 6$ Hz, $\text{CH}_{\text{ax}}\text{H}_{\text{eq}}$), 3.69 (1H, t, $J = 8$ Hz, $\text{O}-\text{CH}-\text{CH}_A\text{H}_B-\text{O}$), 4.01 (1H, ddd, $J = 10, 8, 6$ Hz, $\text{O}-\text{CH}-\text{CH}_2-\text{O}$), 4.20 (1H, dd, $J = 8, 6$ Hz, $\text{O}-\text{CH}-\text{CH}_A\text{H}_B-\text{O}$), 4.27 (1H, m, $\text{CH}-\text{OH}$), 4.90 (1H, m, $\text{CH}=\text{CMe}$), 5.32 (1H, d, $J = 11$ Hz, $\text{CH}=\text{CH}_A\text{H}_B$), 5.34 (1H, d, $J = 17.5$ Hz, $\text{CH}=\text{CH}_A\text{H}_B$), 5.88 (1H, dd, $J = 17.5, 11$ Hz, $\text{CH}=\text{CH}_2$), 8.57 (1H, br s, NH). ^{13}C NMR (CDCl_3 , 75 MHz) δ 19.2, 25.7, 26.6, 39.8, 48.3, 62.0, 68.0, 68.8, 76.1, 93.7, 109.9, 116.5, 119.4, 133.1, 139.5, 160.6. Anal. Calcd for $\text{C}_{16}\text{H}_{22}\text{Cl}_3\text{NO}_4$: C, 48.20; H, 5.56; N, 3.51. Found: C, 48.34; H, 5.74; N, 3.62.

β -Epoxide 10. Mp 158-159 $^\circ\text{C}$. (as prism from ether-hexane). $[\alpha]_{\text{D}}^{26} +34.4^\circ$ (c 1.01, CHCl_3). IR (KBr) ν_{max} 3562, 3309, 1716, 1529, 1075, 824 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 1.35 (3H, s, CH_3 of acetonide), 1.45 (3H, s, CH_3 of acetonide), 1.47 (3H, s, CH_3), 1.50 (1H, dd, $J = 13, 11$ Hz, $\text{CH}_{\text{ax}}\text{H}_{\text{eq}}$), 1.51 (1H, d, $J = 10$ Hz, OH), 2.19 (1H, d, $J = 11$ Hz, $-\text{CH}-$), 2.53 (1H, s, epoxidic), 3.36 (1H, dd, $J = 13, 6$ Hz, $\text{CH}_{\text{ax}}\text{H}_{\text{eq}}$), 3.87 (1H, t, $J = 8$ Hz, $\text{O}-\text{CH}-\text{CH}_A\text{H}_B-\text{O}$), 4.07 (1H, ddd, $J = 11, 10, 6$ Hz, $\text{CH}-\text{OH}$), 4.18 (1H, ddd, $J = 11, 8, 6$ Hz, $\text{O}-\text{CH}-\text{CH}_2-\text{O}$), 4.33 (1H, dd, $J = 8, 6$ Hz, $\text{O}-\text{CH}-\text{CH}_A\text{H}_B-\text{O}$), 5.34 (1H, d, $J = 17$ Hz, $\text{CH}=\text{CH}_A\text{H}_B$), 5.41 (1H, d, $J = 11$ Hz, $\text{CH}=\text{CH}_A\text{H}_B$), 5.70 (1H, dd, $J = 17, 11$ Hz, $\text{CH}=\text{CH}_2$), 8.38 (1H, br s, NH). ^{13}C NMR (CDCl_3 , 75 MHz) δ 19.0, 25.5, 26.6, 36.0, 48.9, 59.6, 60.6, 61.5, 68.2, 68.9, 74.9, 93.6, 110.4, 117.9, 132.1, 160.5. Anal. Calcd for $\text{C}_{16}\text{H}_{22}\text{Cl}_3\text{NO}_5$: C, 46.34; H, 5.35; N, 3.38. Found: C, 46.35; H, 5.40; N, 3.42.

α -Alcohol 11. Mp 132-134 °C. (as tiny needles from ether-hexane). $[\alpha]_D^{26} +2.3^\circ$ (*c* 0.94, CHCl₃). IR (KBr) $\nu_{\max}$ 3494, 3291, 1713, 1521, 1059, 844 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 1.35 (3H, s, CH₃), 1.45 (6H, s, CH₃ x 2), 1.98 (1H, dd, *J* = 15, 5.5 Hz, CH_AH_B), 2.16 (1H, d, *J* = 4.5 Hz, OH), 2.16 (1H, d, *J* = 10.5 Hz, -CH-), 2.52 (1H, s, epoxidic), 3.11 (1H, dd, *J* = 15, 2.5 Hz, CH_AH_B), 3.86 (1H, t, *J* = 8 Hz, O-CH-CH_AH_B-O), 4.23 (1H, ddd, *J* = 10.5, 8, 6 Hz, O-CH-CH₂-O), 4.26 (1H, m, CH-OH), 4.32 (1H, dd, *J* = 8, 6 Hz, O-CH-CH_AH_B-O), 5.23 (1H, d, *J* = 17 Hz, CH=CH_AH_B), 5.32 (1H, d, *J* = 10.5 Hz, CH=CH_AH_B), 6.26 (1H, dd, *J* = 17, 10.5 Hz, CH=CH₂), 8.43 (1H, br s, NH). ¹³C NMR (CDCl₃, 75 MHz) δ 18.9, 25.5, 26.6, 36.5, 49.3, 59.0, 59.1, 59.6, 66.9, 68.5, 75.1, 93.6, 110.2, 115.3, 134.7, 160.7. Anal. Calcd for C₁₆H₂₂Cl₃NO₅: C, 46.34; H, 5.35; N, 3.38. Found: C, 46.34; H, 5.43; N, 3.41.

Aldehyde 12. IR (KBr) $\nu_{\max}$ 3372, 1713, 1506, 1254, 846 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 0.15 (9H, s, TMS), 1.32 (3H, s, CH₃), 1.36 (3H, s, CH₃), 1.40 (3H, s, CH₃), 1.82 (1H, dd, *J* = 14, 3 Hz, CH_AH_B), 2.89 (1H, s, epoxidic), 2.95 (1H, dd, *J* = 14, 3.5 Hz, CH_AH_B), 3.22 (1H, d, *J* = 7 Hz, -CH-), 3.72 (1H, t, *J* = 8 Hz, O-CH-CH_AH_B-O), 4.16 (1H, dd, *J* = 8, 6 Hz, O-CH-CH_AH_B-O), 4.21 (1H, br t, *J* = 3 Hz, CH-OTMS), 4.27 (1H, ddd, *J* = 8, 7, 6 Hz, O-CH-CH₂-O), 8.22 (1H, br s, NH), 9.86 (1H, s, -CHO). ¹³C NMR (CDCl₃, 75 MHz) δ 0.2, 19.1, 25.3, 25.8, 36.9, 41.3, 60.0, 60.7, 63.0, 68.2, 68.4, 75.2, 92.8, 110.2, 160.6, 197.3.

Diacetate 14. $[\alpha]_D^{23} -22.8^\circ$ (*c* 0.89, CHCl₃). IR (KBr) $\nu_{\max}$ 3304, 1750, 1272, 857 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 1.31 (3H, s, CH₃), 1.42 (3H, s, CH₃), 1.46 (3H, s, CH₃), 2.09, (3H, s, Ac), 2.14 (3H, s, Ac), 2.22 (1H, dd, *J* = 10.5, 2 Hz, -CH-), 2.35 (1H, dd, *J* = 15.5, 5 Hz, CH_AH_B), 2.63 (1H, d, *J* = 2 Hz, C+CH), 2.71 (1H, d, *J* = 2 Hz, epoxidic), 2.78 (1H, dd, *J* = 15.5, 5.5 Hz, CH_AH_B), 3.84 (1H, t, *J* = 8 Hz, O-CH-CH_AH_B-O), 4.38 (1H, dd, *J* = 8, 6 Hz, O-CH-CH_AH_B-O), 4.75 (1H, ddd, *J* = 10.5, 8, 6 Hz, O-CH-CH₂-O), 5.23 (1H, br t, *J* = 5.5 Hz, CH₂-CH-OAc), 5.96 (1H, d, *J* = 2 Hz, HC+C-CH-OAc), 8.24 (1H, br s, NH). ¹³C NMR (CDCl₃, 75 MHz) δ 17.6, 20.7, 20.8, 25.8, 26.6, 32.8, 48.8, 58.3, 59.5, 60.7, 64.3, 68.1, 69.0, 74.9, 77.2, 78.9, 93.0, 110.4, 161.0, 168.4, 169.8. Anal. Calcd for C₂₁H₂₆Cl₃NO₈: C, 47.88; H, 4.97; N, 2.66. Found: C, 47.75; H, 4.87; N, 2.49.

Lactone 15. Mp 242-243 °C. (as prism from ether-hexane). $[\alpha]_D^{23} -62.4^\circ$ (*c* 1.01, CHCl₃). IR (KBr) $\nu_{\max}$ 3488, 3308, 1758, 1221, 854 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 1.42 (6H, s, CH₃ x 2), 1.48 (3H, s, CH₃), 2.10 (3H, s, Ac), 2.11 (3H, s, Ac), 2.36 (1H, dd, *J* = 15, 4 Hz, CH_AH_B), 2.74 (1H, br d, *J* = 10 Hz, -CH-), 3.33 (1H, dd, *J* = 15, 2.5 Hz, CH_AH_B), 3.68 (1H, t, *J* = 8 Hz, O-CH-CH_AH_B-O), 3.95 (1H, t, *J* = 1 Hz, CO-O-CH-), 4.32 (1H, dd, *J* = 8, 5.5 Hz, O-CH-CH_AH_B-O), 4.65 (1H, ddd, *J* = 10, 8, 5.5 Hz, O-CH-CH₂-O), 5.11 (1H, m, CH₂-CH-OAc), 6.20 (1H, d, *J* = 1 Hz, CO-CH-OAc), 8.93 (1H, br s, NH). ¹³C NMR (CDCl₃, 100 MHz) δ 20.6, 20.8, 23.2, 25.9, 26.6, 34.7, 40.0, 56.7, 68.4, 69.1, 69.8,

72.0, 74.3, 81.7, 92.7, 110.8, 161.1, 165.7, 167.4, 169.1. Anal. Calcd for $C_{20}H_{26}Cl_3NO_{10}$: C, 43.93; H, 4.79; N, 2.56. Found: C, 43.94; H, 4.69; N, 2.54.

Acetal 16a. $[\alpha]_D^{24} +22.1^\circ$ (c 0.82, $CHCl_3$). IR (KBr) ν_{max} 3469, 3364, 1752, 1238, 824 cm^{-1} . 1H NMR (300 MHz, $CDCl_3$) δ 1.39 (3H, s, CH_3), 2.07 (3H, s, Ac), 2.45 (1H, br s, OH), 2.59 (1H, dd, $J = 16, 5$ Hz, CH_AH_B), 2.85 (1H, dd, $J = 16, 4$ Hz, CH_AH_B), 3.14 (1H, dd, $J = 2.5, 1.5$ Hz, -CH-), 3.48 (3H, s, OMe), 4.34 (1H, dd, $J = 2.5, 1$ Hz, CO-O-CH-), 4.87 (1H, d, $J = 1.5$ Hz, CH-OOC-), 4.97 (1H, ddd, $J = 5, 4, 1$ Hz, CH_2 -CH-OAc), 5.23 (1H, s, CH-OMe), 7.97 (1H, br s, NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.8, 22.8, 29.0, 44.7, 55.9, 58.8, 71.0, 72.3, 80.4, 80.7, 92.4, 105.8, 161.3, 165.5, 170.4. HRMS (FAB) for $C_{15}H_{19}Cl_3NO_8$ (M+H), calcd 446.0176, found 446.0147.

Acetal 16b. 1H NMR (300 MHz, $CDCl_3$) δ 1.34 (3H, s, CH_3), 2.06 (1H, dd, $J = 15.5, 6.5$ Hz, CH_AH_B), 2.09 (3H, s, Ac), 2.76 (1H, dd, $J = 15.5, 6$ Hz, CH_AH_B), 3.03 (1H, br s, OH), 3.55 (3H, s, OMe), 3.67 (1H, br dt, $J = 4, 2$ Hz, -CH-), 4.43 (1H, d, $J = 1.5$ Hz, CH-COO-), 4.61 (1H, d, $J = 2$ Hz, CO-O-CH-), 5.18 (1H, br t, $J = 6$ Hz, CH_2 -CH-OAc), 5.31 (1H, d, $J = 4$ Hz, CH-OMe) 6.78 (1H, br s, NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.9, 22.1, 29.5, 40.1, 57.6, 61.5, 71.6, 75.0, 79.0, 79.9, 92.0, 104.9, 161.4, 165.6, 171.4. HRMS (FAB) for $C_{15}H_{19}Cl_3NO_8$ (M+H), calcd 446.0176, found 446.0186.

Silylether 21. Mp 182-183.5 $^\circ C$ (as tiny needles from ether-hexane). $[\alpha]_D^{23} -3.0^\circ$ (c 0.31, $CHCl_3$). IR (KBr) ν_{max} 3480, 1719, 1250, 842 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 0.18 (6H, s, $Si(CH_3)_2 \times 2$), 0.91 (9H, s, Si-*t*Bu), 1.62 (3H, s, CH_3), 2.63 (1H, dd, $J = 13.5, 2$ Hz, CH_AH_B), 2.80 (1H, dd, $J = 3.5, 1.5$ Hz, -CH-), 3.06 (1H, dd, $J = 13.5, 4$ Hz, CH_AH_B), 3.43 (3H, s, OMe), 3.83 (1H, dd, $J = 3.5, 2$ Hz, -CH-CH-O-C-OSi), 3.88 (1H, dt, $J = 4, 2$ Hz, -CH₂-CH-O-C-OSi), 4.33 (1H, d, $J = 1.5$ Hz, CH-C-OSi), 5.09 (1H, s, CH-OMe), 7.81 (1H, br s, NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ -3.2, -3.1, 17.8, 25.4, 25.7, 26.6, 46.1, 55.4, 58.9, 65.2, 76.0, 76.2, 82.3, 93.0, 106.5, 109.0, 160.9. HRMS (FAB) for $C_{19}H_{31}Cl_3NO_7Si$ (M+H), calcd 518.0935, found 518.0911.

***N,N'*-Bis(*tert*-butoxycarbonyl)guanidine 22.** $[\alpha]_D^{23} +31^\circ$ (c 0.22, $CHCl_3$). IR (KBr) ν_{max} 3269, 1729, 1644, 1617, 1351, 1132 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 0.19 (6H, s, $Si(CH_3)_2 \times 2$), 0.91 (9H, s, Si-*t*Bu), 1.44 (9H, s, Boc), 1.48 (9H, s, Boc), 1.55 (3H, s, CH_3), 2.30 (1H, dd, $J = 14, 3.5$ Hz, CH_AH_B), 3.34 (3H, s, OMe), 3.37 (1H, dd, $J = 14, 2$ Hz, CH_AH_B), 3.41 (1H, dd, $J = 3.5, 1.5$ Hz, -CH-), 3.83 (1H, dd, $J = 3.5, 2$ Hz, CH-CH-O-C-OSi), 3.86 (1H, m, CH_2 -CH-O-C-OSi), 4.11 (1H, d, $J = 1.5$ Hz, CH-C-OSi), 5.05 (1H, s, CH-OMe), 8.67 (1H, br s, NH), 11.26 (1H, br s, NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ -3.3, -3.1, 17.9, 23.6, 25.8, 28.0, 28.2, 29.1, 44.3, 55.2, 56.8, 65.5, 76.3, 76.5, 78.8, 83.0, 83.6, 107.0, 109.1, 152.7, 155.0, 162.5. HRMS (FAB) for $C_{28}H_{50}N_3O_{10}Si$ (M+H), calcd 616.3265, found 616.3237.

8,11-dideoxytetrodotoxin (3). $[\alpha]_{\text{D}}^{26} +1.5^\circ$ (*c* 0.065, 0.05N AcOH). ^1H NMR (600 MHz, 4% $\text{CD}_3\text{COOD}/\text{D}_2\text{O}$) (hemilactal form) δ 1.62 (3H, s, Me-11), 2.17 (1H, dd, $J = 13, 4$ Hz, H-8 α), 2.34 (1H, d, $J = 13$ Hz, H-8 β), 2.45 (1H, d, $J = 9.5$ Hz, H-4a), 3.61 (1H, s, H-9), 4.03 (1H, br s, H-7), 4.10 (1H, br s, H-5), 5.46 (1H, d, $J = 9.5$ Hz, H-4). (lactone form) δ 1.48 (3H, s, Me-11), 2.37 (1H, dd, $J = 14, 4$ Hz, H-8 α), 2.42 (1H, dd, $J = 9.5, 2.5$ Hz, H-4a), 2.50 (1H, br d, $J = 14$ Hz, H-8 β), 3.90 (1H, br s, H-5), 4.27 (1H, s, H-9), 4.42 (1H, br s, H-7), 5.49 (1H, d, $J = 9.5$ Hz, H-4). ^{13}C NMR (CDCl_3 , 150 MHz) (hemilactal form) δ 25.6, 36.7, 41.5, 55.6, 68.1, 73.5, 75.3, 78.1, 79.2, 110.9, 156.4. (lactone form) δ 24.7, 34.7, 46.9, 56.1, 72.5, 73.5, 75.3, 78.4, 82.6, 155.8, 176.6. HRMS (FAB) for $\text{C}_{11}\text{H}_{18}\text{N}_3\text{O}_6$ (M+H), calcd 288.1196, found 288.1198.

4,9-anhydro-8,11-dideoxytetrodotoxin (20). $[\alpha]_{\text{D}}^{26} +14^\circ$ (*c* 0.090, 0.05N AcOH). ^1H NMR (600 MHz, 4% $\text{CD}_3\text{COOD}/\text{D}_2\text{O}$) δ 1.56 (3H, s, Me-11), 2.27 (1H, dd, $J = 13, 4$ Hz, H-8 α), 2.58 (1H, d, $J = 13, 1.5$ Hz, H-8 β), 2.87 (1H, d, $J = 3$ Hz, H-4a), 4.09 (1H, dt, $J = 4, 2$ Hz, H-7), 4.15 (1H, dd, $J = 3, 2$ Hz, H-5), 4.33 (1H, s, H-9), 5.42 (1H, s, H-4). ^{13}C NMR (CDCl_3 , 150 MHz) δ 25.9, 29.5, 42.7, 58.7, 67.7, 77.0, 78.7, 85.2, 89.3, 110.5, 157.4. HRMS (FAB) for $\text{C}_{11}\text{H}_{16}\text{N}_3\text{O}_5$ (M+H), calcd 270.1090, found 270.1068.

3. NMR spectra of 8,11-dideoxytetrodotoxin (3) and 4,9-anhydro-8,11-dideoxytetrodotoxin (19)

Table 1. ^1H NMR and ^{13}C NMR Spectra of 8,11-dideoxytetrodotoxin (3)

<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> hemilactal </div> <div style="text-align: center;"> $\rightleftharpoons$ </div> <div style="text-align: center;"> lactone </div> </div>				
hemilactal			lactone	
No.	^1H (δ) (multi.) J (Hz)	^{13}C (δ)	^1H (δ) (multi.) J (Hz)	^{13}C (δ)
2		156.4		155.8
4	5.46 (d, 9.5)	73.5	5.49 (d, 9.5)	75.3
4a	2.45 (d, 9.5)	41.5	2.42 (dd, 9.5, 2.5)	46.9
5	4.10 (br s)	78.1	3.90 (br s)	72.5
6		68.1		73.5
7	4.03 (br s)	79.2	4.42 (br s)	82.6
8 α	2.17 (dd, 13, 4)	36.7	2.37 (dd, 14, 4)	34.7
8 β	2.34 (d, 13)		2.50 (br d, 14)	
8a		55.6		56.1
9	3.61 (s)	75.3	4.27 (s)	78.4
10		110.9		176.6
11	1.62 (s)	25.6	1.48 (s)	24.7

(1) All spectra were taken in 4% $\text{CD}_3\text{COOD}/\text{D}_2\text{O}$. (2) ^1H NMR 600 MHz and ^{13}C NMR 150 MHz. (3) The signal due to CHD_2COOD at 2.06 ppm was used as reference for ^1H NMR, and that due to $^{13}\text{CD}_3\text{COOD}$ at 22.4 ppm was used for ^{13}C NMR.

Table 2. ^1H NMR and ^{13}C NMR spectra of 4,9-anhydro-8,11-dideoxytetrodotoxin (20)

No.	^1H (δ) (multi.) J (Hz)	^{13}C (δ)
2		157.4
4	5.42 (s)	85.2
4a	2.87 (d, 3)	42.7
5	4.15 (dd, 3, 2)	77.0
6		67.7
7	4.09 (dt, 4, 2)	78.7
8 α	2.27 (dd, 13, 4)	29.5
8 β	2.58 (dd, 13, 1.5)	
8a		58.7
9	4.33 (s)	89.3
10		110.5
11	1.56 (s)	25.9

(1) All spectra were taken in 4% $\text{CD}_3\text{COOD}/\text{D}_2\text{O}$.

(2) ^1H NMR 600 MHz and ^{13}C NMR 150 MHz.

(3) The signal due to CHD_2COOD at 2.06 ppm was used as reference for ^1H NMR, and that due to $^{13}\text{CD}_3\text{COOD}$ at 22.4 ppm was used for ^{13}C NMR.

NAME urabe
EXPNO 8
PROCNO 10

F2 - Acquisition Parameters

Date_ 1020308
Time 9.41
INSTRUM AMX2600
PROBHD 5 mm Dual 19
PULPROG zg0
TD 32768
SOLVENT CDCL3
NS 512
DS 2
SWH 5434.783 Hz
FIDRES 0.165856 Hz
AQ 3.0147059 sec
RG 4096
DM 92.000 usec
DE 115.00 usec
TE 300.0 K
HL1 2 dB
D1 1.00000000 sec
P0 4.10 usec
DE 115.00 usec
SF01 600.1401405 MHz
NUCLEUS 1H

F2 - Processing parameters

SI 16384
SF 600.1378951 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 32.00 cm
F1P 7.000 ppm
F1 4200.96 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.21875 ppm/cm
HZCM 131.28015 Hz/cm

8,11-didoxytetrodotoxin (3)

NAME urabe
EXPNO 24
PROCNO 1

F2 - Acquisition Parameters

Date_ 1020330
Time 18.04
INSTRUM AMX2600
PROBHD 5 mm Dual 1H
PULPROG zgpg30
TD 65536
SOLVENT water
NS 30000
DS 2
SWH 33333.332 Hz
FIDRES 0.508626 Hz
AQ 0.9830900 sec
RG 32768
DM 15.000 usec
DE 18.75 usec
TE 300.0 K
D11 0.0300000 sec
CPDPRG waltz16
P31 100.00 usec
S2 25 dB
HL1 90 dB
D1 1.0000000 sec
P0 5.00 usec
DE 18.75 usec
SF01 150.9190259 MHz
NUCLEUS 13C

F2 - Processing parameters

SI 65536
SF 150.9044050 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 32.00 cm
F1P 200.000 ppm
F1 30180.88 Hz
F2P -10.000 ppm
F2 -1509.04 Hz
PPMCM 6.56250 ppm/cm
HZCM 990.31006 Hz/cm

NAME urabe
EXPNO 10
PROCNO 10

F2 - Acquisition Parameters

Date_ 1020309
Time 14.34
INSTRUM AMX2600
PROBHD 5 mm Dual 1H
PULPROG zg0
TD 32768
SOLVENT CDCL3
NS 1024
DS 2
SWH 8474.576 Hz
FIDRES 0.258624 Hz
AQ 1.9335620 sec
RG 4096
DM 59.000 usec
DE 84.29 usec
TE 300.0 K
HL1 2 dB
D1 1.00000000 sec
P0 4.10 usec
DE 84.29 usec
SF01 600.1416400 MHz
NUCLEUS 1H

F2 - Processing parameters

SI 16384
SF 600.1378925 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 32.00 cm
F1P 7.000 ppm
F1 4200.95 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.21875 ppm/cm
HZCM 131.28015 Hz/cm

NAME urabe
EXPNO 11
PROCNO 1

F2 - Acquisition Parameters

Date_ 1020309
Time 15.52
INSTRUM AMX2600
PROBHD 5 mm Dual 1H
PULPROG zgpg30
TD 65536
SOLVENT water
NS 30000
DS 2
SWH 33333.332 Hz
FIDRES 0.508626 Hz
AQ 0.9830900 sec
RG 32768
DM 15.000 usec
DE 18.75 usec
TE 300.0 K
D11 0.0300000 sec
CPDPRG waltz16
P31 100.00 usec
S2 25 dB
HL1 90 dB
D1 1.00000000 sec
P0 5.00 usec
DE 18.75 usec
SF01 150.9182719 MHz
NUCLEUS 13C

F2 - Processing parameters

SI 65536
SF 150.9044048 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 32.00 cm
F1P 200.000 ppm
F1 30180.88 Hz
F2P -10.000 ppm
F2 -1509.04 Hz
PPMCM 6.56250 ppm/cm
HZCM 990.31006 Hz/cm

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