Supporting Information

Efficient Synthesis of the Azaspirocyclic Core Structure of Halichlorine and Pinnaic Acid by Intramolecular Acylnitroso Ene Reaction

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Methyl 4-(5-Oxo-1-cyclopenten-1-yl)butanoate (7). IR (neat) 1738, 1698 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.83 (quint, $J = 7.58$ Hz, 2 H), 2.20 (td, $J = 7.80, 1.47$ Hz, 2 H), 2.33 (t, $J = 7.46$ Hz, 2 H), 2.39–2.41 (m, 2 H), 2.55–2.59 (m, 2 H), 3.68 (s, 3 H), 7.35 (ddt, $J = 2.62, 2.58, 1.31$ Hz, 1 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 22.98, 24.21, 26.39, 33.57, 34.52, 51.53, 145.41, 157.90, 173.72, 209.70; EIMS m/z (rel intensity) 182 (M^+ , 9), 151 (11), 123 (86), 91 (100); HRMS (EI) calcd for $\text{C}_{10}\text{H}_{14}\text{O}_3$ (M^+) 182.0943, found 182.0946.

Methyl 4-[(5*R)-5-(Methoxymethoxy)-1-cyclopenten-1-yl]butanoate (8).** IR (neat) 1739 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.74–1.91 (m, 3 H), 2.09–2.22 (m, 4 H), 2.32 (td, $J = 7.51, 1.44$ Hz, 2 H), 2.36–2.44 (m, 1H), 3.37 (s, 3 H), 3.65 (s, 3 H), 4.54–4.56 (m 1 H), 4.63 and 4.71 (ABq, $J = 6.75$ Hz, 2 H), 5.60 (s, 1 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 22.89, 27.66, 30.02, 30.97, 33.80, 51.46, 55.42, 83.84, 95.79, 128.62, 143.38, 174.02; EIMS m/z (rel intensity) 228 (M^+ , 3), 227 (2), 197 (5), 183 (37), 167 (85), 151 (51), 135 (34), 106 (25), 93 (54), 79 (35), 67 (14), 55 (19), 45 (100); Anal. Calcd for $\text{C}_{12}\text{H}_{20}\text{O}_4$: C, 63.14; H, 8.83. Found: C, 62.78; H, 8.69.

***N*-Hydroxy-4-[(5*R**)-5-(methoxymethoxy)-1-cyclopenten-1-yl]butanamide (9).** IR (neat) 3281, 1612 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.70–1.90 (m, 3 H), 2.05–2.25 (m, 7 H), 2.36–2.43 (m, 1 H), 3.38 (s, 3 H), 4.55–4.58 (m, 1 H), 4.65 and 4.71 (ABq, $J = 6.73$ Hz, 2 H), 5.60 (s, 1 H), 8.78–9.43 (br s, 1 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 23.37, 27.36, 30.04, 30.91, 32.44, 55.53, 84.15, 95.79, 129.10, 142.94, 171.61; EIMS m/z (rel intensity) 211 ($\text{M}^+ - \text{H}_2\text{O}$, 59), 198 (77), 197 (100), 193 (29), 182 (13), 166 (39), 151 (33), 137 (63), 135 (96).

(4*R,5*R**)-6-Hydroxy-4-(methoxymethoxy)-6-azaspiro[4.5]dec-1-ene-7-one (11).** mp 101.5–103.5 $^\circ\text{C}$ (evacuated sealed tube); IR (KBr) 3076, 1623 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.67–1.76 (m, 2 H), 1.99–2.09 (m, 1 H), 2.28–2.35 (m, 2 H), 2.49 (td, $J = 6.29, 1.44$ Hz, 2 H), 2.77 (dddd, $J = 16.19, 7.65, 1.52, 1.49$ Hz, 1 H), 3.36 (s, 3 H), 4.65 and 4.67 (ABq, $J = 6.54$ Hz, 2 H), 4.79 (t, $J = 7.36$ Hz, 1 H), 5.66 (ddd, $J = 6.18, 2.36, 1.53$ Hz, 1 H), 5.85 (ddd, $J = 6.16, 3.09, 1.99$ Hz, 1H), 8.49 (s, 1 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 17.71, 29.08, 30.71, 36.55, 55.64, 74.61, 79.25, 96.56, 130.46, 133.94, 165.17; EIMS m/z (rel intensity) 227 (M^+ , 17), 210 (7), 196 (4), 182 (100), 166 (12), 150 (4), 138 (15), 137 (18); Anal. Calcd for $\text{C}_{11}\text{H}_{17}\text{NO}_4$: C, 58.14; H, 7.54; N, 6.16. Found: C, 57.82; H, 7.45; N, 6.12.

(4*R,5*R**)-6-(Benzyloxy)-4-(methoxymethoxy)-6-azaspiro[4.5]dec-1-ene-7-one (12).** IR (neat) 1668 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.66–1.78 (m, 2 H), 1.95–2.05 (m, 1 H), 2.25–2.31 (m, 2 H), 2.51 (t, $J = 6.63$ Hz, 2 H), 2.74 (dddd, $J = 16.27, 7.44, 2.84, 1.67$ Hz, 1 H), 3.35 (s, 3 H), 4.64 and 4.66 (ABq, $J = 6.62$ Hz, 2 H), 4.69 (dd, $J = 7.36, 6.33$ Hz, 1 H), 4.80 and 5.06 (ABq, $J = 9.32$ Hz, 2 H), 5.64 (dt, $J = 6.17, 1.92$ Hz), 5.83 (ddd, $J = 6.14, 2.77, 2.22$ Hz, 1 H), 7.26–7.34 (m, 3 H), 7.40–7.42 (m, 2 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 18.11, 29.93, 33.87, 37.15, 55.72, 77.39, 77.73, 79.69, 96.46, 128.35 (2 carbons), 128.46, 129.26 (2 carbons), 130.70, 134.09, 135.44, 168.71; EIMS m/z (rel intensity) 824 ($\text{M}^+ + 1$, 62), 272 (89), 256 (25), 210 (40), 148 (63), 138 (36), 91 (100); Anal. Calcd for $\text{C}_{18}\text{H}_{23}\text{NO}_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 68.03; H, 7.31; N, 4.40.

(4*R,5*R**,7*S**)-6-(Benzyloxy)-7-ethynyl-4-(methoxymethoxy)-6-azaspiro[4.5]dec-1-ene and (4*R**,5*R**,7*R**)-6-(Benzyloxy)-7-ethynyl-4-(methoxymethoxy)-6-azaspiro[4.5]dec-1-ene (13).** IR (neat) 3288 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.36–1.47 and 1.51–1.72 (br m and br m, total 3 H), 1.76–2.18 (br m, 3 H), 2.20–2.28 and 2.29 (br m and d, *J* = 2.06 Hz, total 1 H), 2.29–2.39 and 2.58–2.82 (br m and br m, total 2 H), 3.30–3.40 and 3.85 (m and d, *J* = 12.00 Hz, total 1 H), 3.40 and 3.42 (s and s, total 3 H), 4.52 and 4.62 (dd, *J* = 7.09, 5.09 Hz and t, *J* = 6.88 Hz, total 1 H), 4.67 and 4.68 (d, *J* = 5.79 Hz and d, *J* = 6.58 Hz, total 1 H), 4.73 and 4.76 (d, *J* = 6.36 Hz and d, *J* = 6.55 Hz, total 1 H), 4.88 and 4.97 (br s and dd, *J* = 43.7, 9.75 Hz, total 2 H), 5.48 and 5.73–5.90 (t, *J* = 7.44 Hz and m, total 2 H), 7.22–7.42 (m, 5 H); EIMS *m/z* (rel intensity) 327 (M⁺, 9), 282 (100), 262 (9), 236 (77), 220 (61), 205 (10), 176 (10); HRMS (EI) calcd for C₂₀H₂₅NO₃ (M⁺) 327.1834, found 327.1838.

(4*R,5*R**,7*S**)-2-[6-(Benzyloxy)-4-(methoxymethoxy)-6-azaspiro[4.5]dec-1-ene-7-yl]ethanol and (4*R**,5*R**,7*R**)-2-[6-(Benzyloxy)-4-(methoxymethoxy)-6-azaspiro[4.5]dec-1-ene-7-yl]ethanol (14).** IR (neat) 3424 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.48–2.17 (br m, 9 H), 2.35 (br d, *J* = 16.82 Hz, 1 H), 2.78 (br d, *J* = 14.67 Hz), 3.03 and 3.11–3.17 (br s and m, total 1 H), 3.39 (br s, 3 H), 3.67–4.03 (m, 2 H), 4.67 (br s, 4 H), 4.89 and 4.96 (br s and d, *J* = 10.86 Hz, total 1 H), 5.62 and 5.90 (br s and br s, total 1 H), 5.79 and 6.14 (br s and br s, total 1 H), 7.17–7.39 (m, 5 H); EIMS *m/z* (rel intensity) 347 (M⁺, 3), 302 (23), 286 (3), 256 (100), 240 (5), 224 (9), 194 (19), 91 (75); HRMS (EI) calcd for C₂₀H₂₉NO₄ (M⁺) 347.2097, found 347.2125.

(1*R,5*R**,7*S**)-6-(Benzyloxy)-7-(2-[[*tert*-butyl(dimethyl)silyl]oxy]ethyl)-6-azaspiro[4.5]dec-3-ene-1-ol and (1*R**,5*R**,7*R**)-6-(Benzyloxy)-7-(2-[[*tert*-butyl(dimethyl)silyl]oxy]ethyl)-6-azaspiro[4.5]dec-3-ene-1-ol (15).** IR (neat) 3489 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.045 and 0.055 (s and s, total 6 H), 0.89 and 0.90 (s and s, total 9 H), 1.05–2.43 (br m, 10 H), 2.69 and 2.90 (br s and br d, *J* = 15.4 Hz, total 1 H), 3.06 and 3.18 (br s and br s, total 1

H), 3.67–3.75 and 3.80 (m and br s, total 2 H), 4.56 and 4.73 (br s and br s, total 1 H), 4.61 and 4.80–4.86 (d, $J = 9.43$ Hz and m, total 2 H), 5.63 and 5.82 (br s and br s, total 2 H), 7.18–7.41 (m, 5 H); EIMS m/z (rel intensity) 417 (M^+ , 3), 402 (3), 360 (2), 340 (4), 326 (100), 310 (32), 308 (6), 292 (3); HRMS (EI) calcd for $C_{24}H_{39}NO_3Si$ 417.2699, found 417.2683.

(5*R,7*S**)-6-(Benzyloxy)-7-(2-([*tert*-butyl(dimethyl)silyl]oxy)ethyl)-6-azaspiro[4.5]**

dec-3-ene-1-one (16). IR (neat) 1743 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.043 (s, 6 H), 0.89 (s, 9 H), 1.15–1.31 (br m, 2 H), 1.54–1.64 (m, 2 H), 1.75 (td, $J = 13.39, 4.01$ Hz, 1 H), 1.82–1.92 (br m, 2 H), 2.16 (dtd, $J = 13.21, 6.60, 3.60$ Hz, 1 H), 2.78 and 2.85 (ABX, $J = 22.7, 2.00$ Hz, 2 H), 3.64 (ddt, $J = 11.48, 8.26, 3.30$ Hz, 1 H), 3.71 (t, $J = 7.14$ Hz, 2 H), 4.62 and 4.76 (ABq, $J = 9.99$ Hz, 2 H), 6.07 (br d, $J = 7.04$ Hz, 1 H), 6.20 (dt, $J = 7.06, 2.20$ Hz, 1 H), 7.20–7.31 (m, 5 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ –5.22, –5.21, 18.27, 18.33, 26.00 (3 carbons), 31.22, 32.79, 36.92, 43.33, 58.26, 60.88, 72.14, 77.98, 127.80, 128.25 (2 carbons), 128.30 (2 carbons), 128.65, 136.76, 138.17, 217.13; EIMS m/z (rel intensity) 416 ($M^+ + 1$, 10), 388 (28), 387 (100), 370 (16), 304 (24), 296 (19).

(5*R,7*R**)-6-(Benzyloxy)-7-(2-([*tert*-butyl(dimethyl)silyl]oxy)ethyl)-6-azaspiro[4.5]**

dec-3-ene-1-one (17). IR (neat) 1743 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.03 (s, 6 H), 0.88 (s, 9 H), 1.36–1.54 (m, 3 H), 1.61–1.75 (m, 2 H), 1.86–1.95 (m, 2 H), 2.19–2.29 (m, 1 H), 2.87 (s, 2 H), 3.01–3.08 (m, 1 H), 3.69–3.76 (m, 2 H), 4.56 and 4.70 (ABq, $J = 10.25$ Hz, 2 H), 6.32 (dt, $J = 7.44, 2.21$ Hz, 1 H), 6.56 (br dt, $J = 7.45, 2.02$ Hz, 1 H), 7.17–7.30 (m, 5 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ –5.27, 5.20, 18.30, 20.18, 25.96 (3 carbons), 31.23, 34.34, 36.16, 41.44, 60.44, 60.51, 75.67, 77.86, 127.84, 128.34 (2 carbons), 128.42 (2 carbons), 129.96, 131.58, 136.69, 216.18; EIMS m/z (rel intensity) 416 ($M^+ + 1$, 18), 388 (30), 387 (100), 296 (19).

(1*R,5*S**)-6-(Benzyloxy)-1-(methoxymethoxy)-6-azaspiro[4.5]decan-7-one (19).**

IR (neat) 1667 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.48–1.76 (m, 6 H), 1.84–1.93 (m, 1 H), 2.02–2.11 (m, 2 H), 2.17–2.24 (m, 1 H), 2.47 (dd, $J = 8.11, 5.13$ Hz, 2 H), 3.35 (s, 3 H), 4.40 (t,

$J = 8.49$ Hz, 1 H), 4.65 and 4.66 (ABq, $J = 6.60$ Hz, 2 H), 5.00 and 5.06 (ABq, $J = 9.61$ Hz, 2 H), 7.29–7.38 (m, 3 H), 7.44–7.47 (m, 2 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 17.31, 17.87, 27.96, 28.83, 31.24, 33.84, 55.56, 72.78, 76.73, 77.19, 78.52, 96.12, 128.39 (2 carbons), 128.95 (2 carbons), 135.55, 169.61; EIMS m/z (rel intensity) 320 ($\text{M}^+ + 1$, 100), 288 (86), 274 (37), 258 (53), 242 (14), 212 (11), 197 (30), 151 (78), 90 (74); Anal. Calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_4$: C, 67.39; H, 7.89; N, 4.39. Found: C, 67.49; H, 7.81; N, 4.42.

(1*R,5*R**,7*R**)-6-(Benzyloxy)-7-ethynyl-1-(methoxymethoxy)-6-**

azaspiro[4.5]decane (21). IR (neat) 3288 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.32–1.59 (br m, 7 H), 1.77–1.83 (br m, 2 H), 1.92–2.17 (br m, 3 H), 2.27 (d, $J = 2.13$ Hz, 1 H), 3.41 (s, 3 H), 3.57 (br d, $J = 11.47$ Hz, 1 H), 4.35 (s, 1 H), 4.61–5.01 (m, 2 H), 4.81 (A part of ABq, $J = 9.86$ Hz, 1 H), 5.33 (B part of ABq, $J = 9.59$ Hz, 1 H), 7.27–7.36 (m, 3 H), 7.40–7.42 (m, 2 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 19.04, 19.55, 24.30, 29.49, 29.74, 33.40, 55.44, 55.58, 70.36, 72.86, 77.37, 80.11, 85.23, 96.09, 127.78, 128.30 (2 carbons), 128.57 (2 carbons), 137.33; EIMS m/z (rel intensity) 329 (M^+ , 29), 298 (13), 284 (20), 268 (13), 238 (100), 222 (11), 176 (6), 91 (46); HRMS (EI) calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_3$ (M^+) 329.1991, found 329.2000; Anal. Calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_3$: C, 72.92; H, 8.26; N, 4.25. Found: C, 72.58; H, 8.43; N, 4.08.

(5*R,7*R**)-6-(Benzyloxy)-7-(2-([*tert*-butyl(dimethyl)silyl]oxy)ethyl)-6-azaspiro[4.5]**

decane-1-one (22). IR (neat) 1743 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.041 (s, 6 H), 0.88 (s, 9 H), 1.33–1.72 (m, 5 H), 1.76–1.90 (m, 1 H), 1.92–2.05 (m, 2 H), 2.10–2.38 (m, 3 H), 2.47 (br dd, $J = 19.73$, 12.08 Hz, 1 H), 2.77–2.86 (br m, 1 H), 3.66–3.77 (m, 2 H), 4.63 and 4.69 (ABq, $J = 10.17$ Hz, 2 H), 7.21–7.32 (m, 5 H); ^{13}C NMR (100.6 MHz, CDCl_3) δ -5.26, -5.19, 18.30, 18.53, 19.69, 24.82, 25.96 (3 carbons), 30.82, 31.76, 36.06, 37.95, 60.38, 60.51, 73.68, 77.43, 127.82, 128.33 (2 carbons), 128.56 (2 carbons), 136.95, 219.29; EIMS m/z (rel intensity) 418 ($\text{M}^+ + 1$, 17), 389 (96), 326 (7), 298 (100), 270 (9), 231 (13), 198 (28), 166 (13), 97 (5), 91 (27); Anal. Calcd for $\text{C}_{24}\text{H}_{37}\text{NO}_3\text{Si}$: C, 69.02; H, 9.41; N, 3.35. Found: C, 68.89; H, 9.36; N, 3.35.